Mechanochemical Endovenous Occlusion of Varicose Veins Using the ClariVein® Device

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ABSTRACT

Introduction: In the last decade, minimally invasive endothermal ablation techniques have replaced surgery for the treatment of superficial venous insufficiency to reduce postoperative complications and recovery time and to improve quality of life. To avoid the risks of nerve damage and need for tumescent anesthesia to improve patient comfort, an alternative heatless technique has been introduced recently.

Methods: Endovenous mechanochemical occlusion using the ClariVein® catheter (Vascular Insights LLC, Quincy, MA) is a new technique combining mechanical injury to the venous endothelium coupled with simultaneous catheter-guided infusion of a liquid sclerosant. This produces irreversible damage to the endothelium resulting in fibrosis of the vein.

Results: The technique is related to a low complication rate and a success rate of 96% at two years and sustained quality of life improvement. This closure rate is comparable to endothermal techniques, but significantly less postoperative pain and earlier return to normal activities and work has been reported with endovenous mechanochemical occlusion.

Conclusion: Mechanochemical occlusion using ClariVein® has proven to be safe and effective and has several advantages compared to endothermal techniques. The possibility of retrograde ablation of distal SSV insufficiency in C6 ulceration is considered a significant advantage. Randomized comparative studies with long-term follow up will continue to define the definite place of mechanochemical occlusion.

INTRODUCTION

Varicose veins of the lower extremity are a common medical problem with an overall prevalence of 20% to 60%.[1,2] Varicosis is the result of venous hypertension due to reflux of blood through incompetent valves or venous obstruction.

Symptoms can vary and range from less serious conditions, such as aching, fatigue, heaviness, cramps, itching, and restless legs, to more serious clinical symptomatology including edema, lipodermatosclerosis, and ulceration.[3] From the two main superficial venous systems, the great (GSV) and small (SSV) saphenous veins and their tributaries, the GSV is most commonly affected.[2-4]

Traditionally, the standard treatment of GSV varices consists of saphenofemoral ligation and stripping of the GSV to the knee. Visible truncal and non-saphenous varices in the calf as well as varicose GSV branches in the thigh could additionally be treated with phlebectomies through stab avulsions or sclerotherapy. Recurrence rates up to 28% have been reported when saphenofemoral ligation was performed and these rates double when saphenofemoral ligation was not performed.[4,5,6] Complication rates up to 20% are reported, including wound hematoma, wound infections, lymphatic leaks, common femoral vein and artery injuries, and neurological complications.[4]

In recent years, minimally invasive endovenous ablation techniques were developed as alternatives to standard surgery to reduce postoperative complications, increase the speed of recovery, and improve quality of life (QOL).[3,7] Both endovenous laser therapy (EVLT) and radio frequency ablation (RFA) proved to be as effective as standard surgery reporting occlusion rates over 90%. Also, a lower rate of complications—such as wound infection, hematoma, pain, and a faster return to work—was noted.[4,7-10]

With effectiveness of these newer treatment options proven, more emphasis is placed on secondary outcome measures, such as intra- and postoperative pain, number of complications, quality of life, and time interval to return to normal activities. New techniques are developed to overcome the main pitfalls of the endothermal ablation techniques which include (1) need for tumescent anesthesia; (2) risk of thermal injury to skin, nerves, muscle, and blood vessels; (3) need for capital expenditure secondary to maintenance of a complex energy source; and (4) post-procedural pain/phlebitis.

Endovenous mechanochemical occlusion using the ClariVein® catheter is a new technique, which involves mechanical injury to the venous endothelium combined with simultaneous catheter-guided infusion of a liquid sclerosant. The liquid sclerosant then produces irreversible damage to the cellular membranes of the endothelium, resulting in fibrosis of the vein. No heat is generated and, therefore, tumescent is not required.[11-14] In this chapter, the ClariVein® device, the technique used with its assets and liabilities, and also a review of the literature is presented.

THE CLARIVEIN® DEVICE AND TECHNIQUE

In May 2008, the ClariVein® infusion catheter gained clearance from the US Food and Drug Administration (FDA) for the indication of infusion of physician-specified agents in the peripheral vasculature. ClariVein® obtained the CE mark in April 2010, with a specific indication for endovascular occlusion of incompetent veins with superficial venous reflux.

This single-use, disposable ClariVein® infusion catheter contains a rotating dispersion wire (Fig. 1) that extends through its lumen. At the distal end of the wire, there is an angled tip that protrudes 2cm with a small metal ball attached to the far end (Fig. 2). The purpose of the rotating wire is fourfold: (1) promoting the coagulation activation by minimal mechanical damage to the endothelium; (2) inducing a vasospasm which reduces the diameter of the vein; (3) increasing the action of sclerosant by an increase in surface; and (4) ensuring an even distribution of the sclerosant at the endothelium (Figs. 3a and b). The catheter, together with the stainless steel wire, is connected to an interface cartridge unit for connection to the nine-volt DC battery motorized handle unit on the proximal end, which controls wire rotation (Fig. 4). The handle unit also provides a grip and syringe holder to facilitate physician-controlled infusion. The whole device can be introduced via ultrasound guidance (Fig. 5) through a micro introducer (4-Fr or 5 Fr) at the puncture site, or via an 18-G or larger intravenous access. As such,

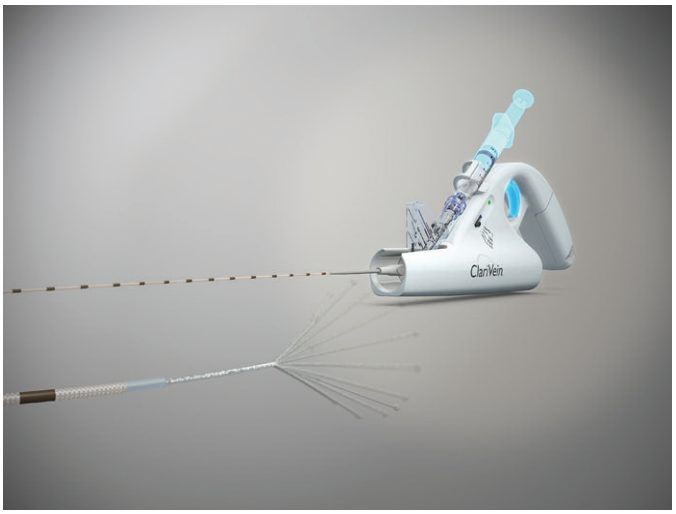

Figure 1. The ClariVein® catheter showing the rotating tip at the end (courtesy of Vascular Insights LLC, Quincy, MA).

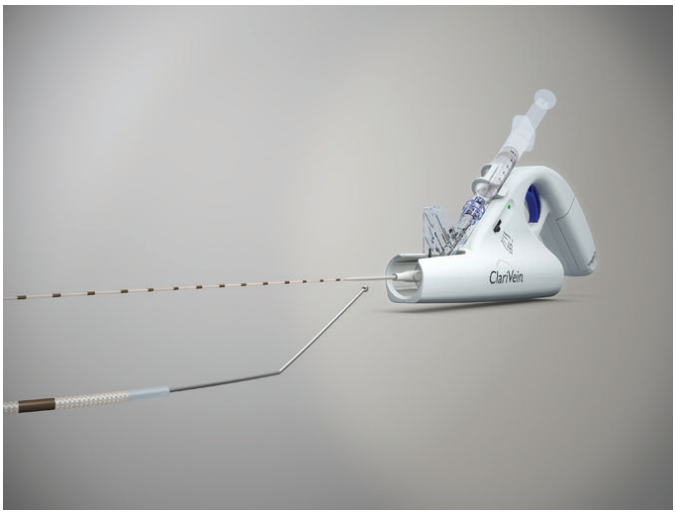

Figure 2. The ClariVein® infusion catheter (courtesy of Vascular Insights LLC, Quincy, MA).

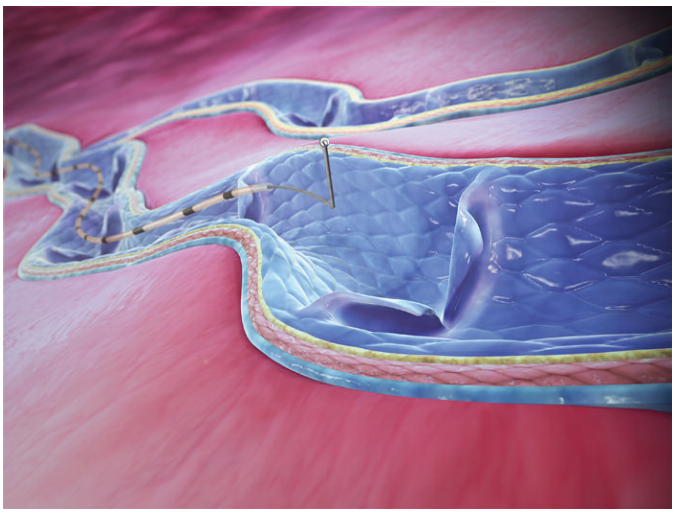

Figure 3a. After insertion, the ClariVein® catheter is unsheathed to expose the dispersion tip (courtesy of Vascular Insights LLC, Quincy, MA).

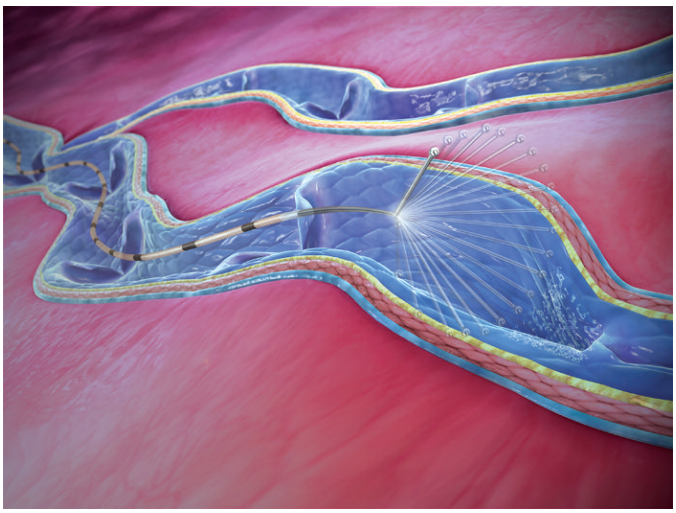

Figure 3b. By activation of the rotation mechanism, the tip evenly distributes the sclerosant at the endothelium (courtesy of Vascular Insights LLC, Quincy, MA).

the technique is minimally invasive, and the materials are single-use and fully disposable. One important advantage of the ClariVein® system is the catheters' steerability. This can be accomplished due to the angled tip (while sheathed) (Fig. 6) that can be directed when the proximal cartridge is rotated/torqued transferring the motion to the catheter's distal tip. Moderately tortuous vein segments can be traversed, in contradistinction to catheters used for thermal ablation where these maneuvers are more difficult.

To perform a mechanochemical occlusion with the ClariVein® device, local anesthesia is used only at the insertion site. Subsequently, and under ultrasound guidance, the introducer wire and catheter sheath are inserted into the vein percutaneously. Then, the ClariVein® catheter is inserted and the tip of the stainless steel wire is placed below the saphenofemoral junction (Fig. 7). By connecting the motorized handle unit, the distal end of the dispersion wire is unsheathed to expose the dispersion tip, which is then positioned approximately 2cm distal to the saphenofemoral junction (SFJ) or, just below the orifice of the epigastric vein, as verified by ultrasound. The patient is treated in a horizontal position. The wire is then activated for two to three seconds to induce vasospasm. Next, the activated catheter with rotating tip is slowly withdrawn at a speed of approximately seven seconds per centimeter, while the sclerosant is continuously injected (Fig. 8). Both Polidocanol and Sotradecol can be used, depending on the availability in the region and the preference of the operator. It appears to be useful to apply a higher concentration of Polidocanol, being less powerful than Sotradecol, near the SFJ. Currently, we use 2ml 3% Polidocanol for the first 10 to 15cm and 1.5% Polidocanol for the remainder of the GSV. Obviously, there are different strategies with varying dosages, but the one mentioned here proved to be very effective in our practice. The maximum amount of liquid sclerosant is specified on the drug insert and, in some cases, determined according to the patients' weight. After treatment, the deep venous system is studied with ultrasound. While the patient is still in the horizontal position, liberal calf massages and patient-induced dorsiflexion is performed. Patients are then advised to walk immediately after completion of the procedure and are discharged with class two compression stockings (30–40mm Hg) for 24 hours continuously and then during the day for two weeks.[11-14]

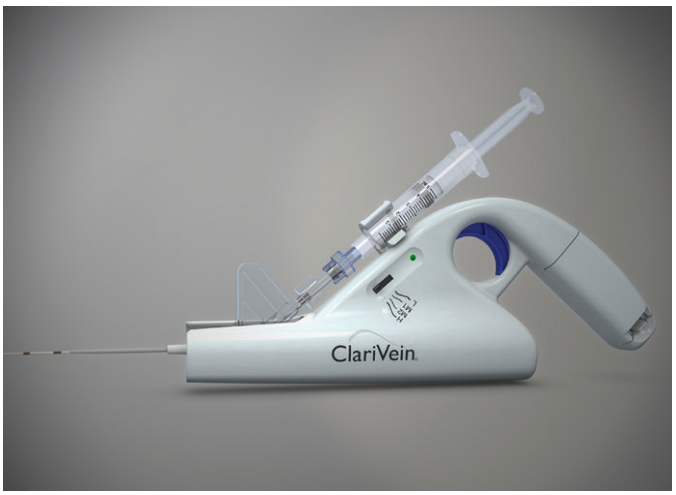

Figure 4 The motorized handle unit of the ClariVein® system, containing a grip and syringe holder to facilitate physician-controlled infusion of the liquid sclerosant (courtesy of Vascular Insights LLC, Quincy, MA).

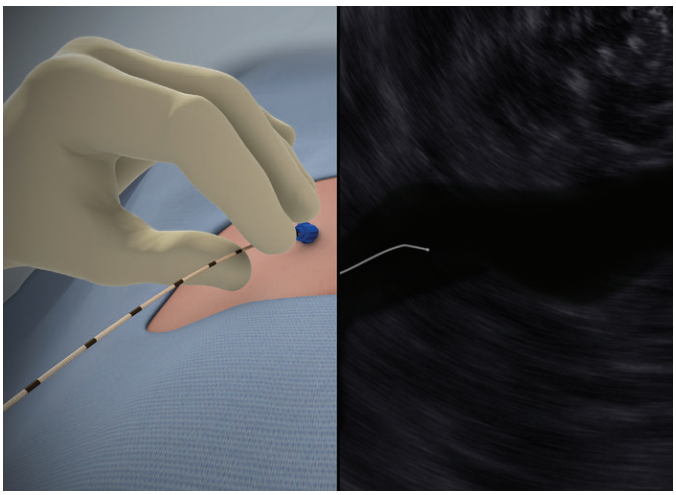

Figure 5. After insertion under local anesthesia, the ClariVein® catheter is placed near the saphenofemoral junction under ultrasound guidance (courtesy of Vascular Insights LLC, Quincy, MA).

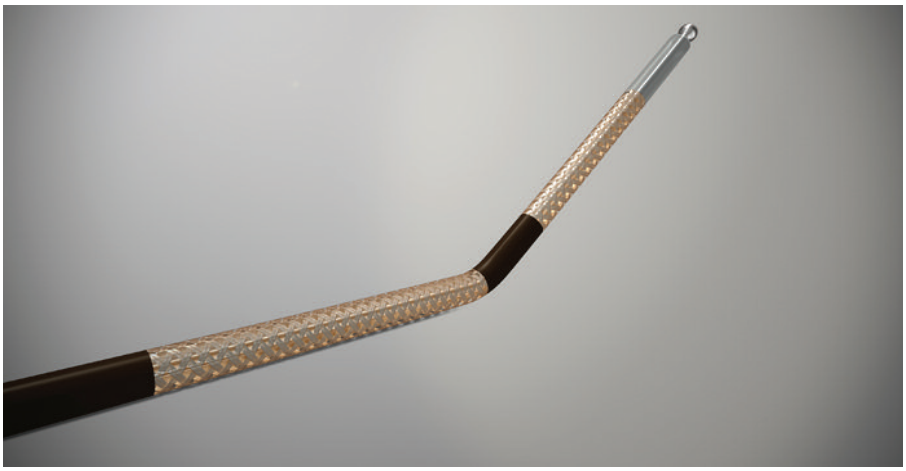

Figure 6. The bent tip of the ClariVein® catheter promotes its steerability (courtesy of Vascular Insights LLC, Quincy, MA).

CLINICAL SAFETY STUDIES

In 2012, Elias and Raines published the final results of the first human study demonstrating safety and efficacy of mechanochemical endovenous occlusion. In this study, 30 GSVs in 29 patients with primary GSV insufficiency were treated with 1.5% liquid sodium tetradecyl sulphate (Sotradecol©, Bioniche Pharma Group, Geneva, Switzerland). All patients reached a six-month follow-up and no adverse events were noted during that time. The primary closure rate was 96.7%.[15] Although this study was the first human study conducted, it was not the first one published. In 2011, van Eekeren et al. report that endovenous mechanochemical occlusion is deemed feasible and safe in the treatment of GSV incompetence. In this pilot study, 30 limbs in 25 patients with GSV incompetence were treated with endovenous mechanochemical occlusion using a 1.5% Polidocanol solution (Aetoxisclerol™; Kreussler Pharma, Wiesbaden, Germany) in two centers. Directly after the operation, the occlusion rate was 100%. After six weeks, 26 (87%) of 30 veins were completely occluded, three veins showed partial and one vein total recanalization. There were no major adverse events. Minor complications consisted of local ecchymosis at the puncture site and superficial phlebitis; all were resolved within one week. Patient satisfaction was high.[11]

CLINICAL COHORT STUDIES

With safety and efficacy proven, the first series of mechanochemical occlusion using ClariVein® for GSV insufficiency appeared. In 2013, Bishawi et al. report results of endovenous mechanochemical occlusion using ClariVein® in GSV insufficiency in a prospective multicenter study, which included 126 patients. Closure rates were 100% at one week, 98% at three months and 94% at six months. Post-procedure complications included hematoma (1%), ecchymosis (9%), and thrombophlebitis (10%). No major complications were encountered. There was significant improvement in VCSS for all time intervals. The authors conclude that endovenous mechanochemical occlusion is an

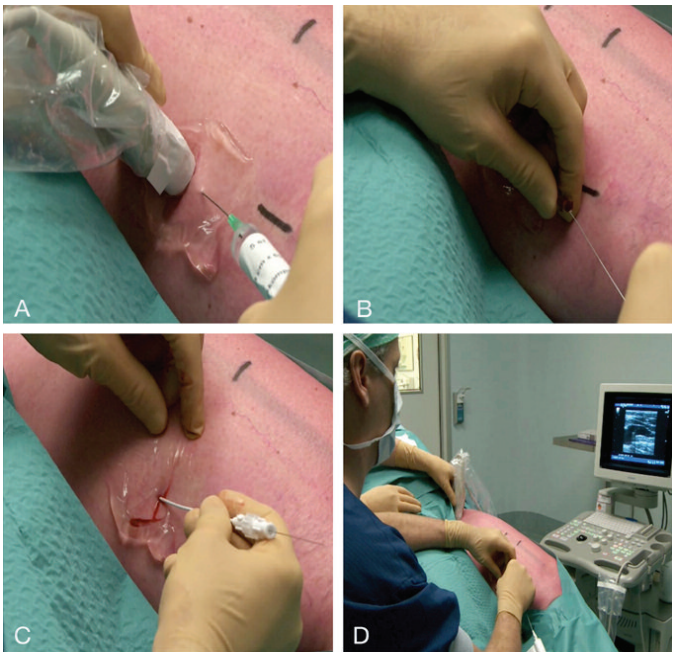

Figure 7. After the introduction of local anesthesia (A), the vein is punctured and subsequently the guidewire (B) and sheath (C) are introduced. Then the ClariVein® catheter is introduced under ultrasound guidance (D).

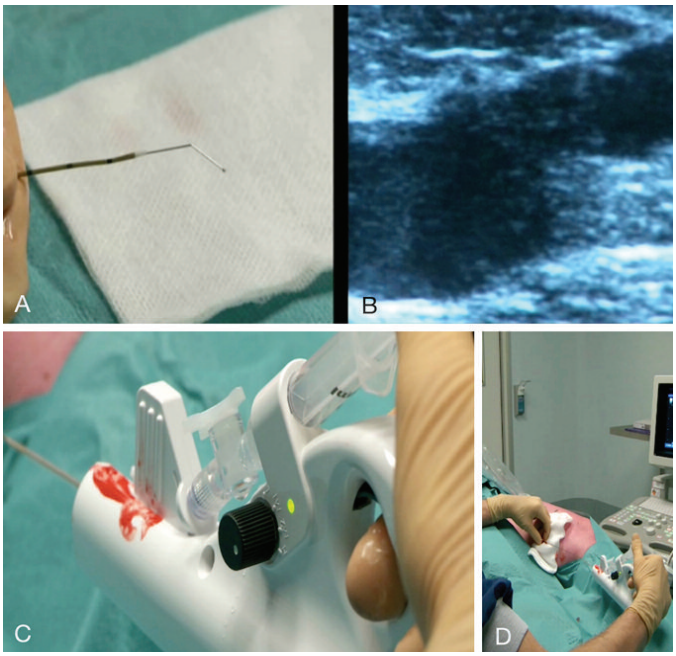

Figure 8. The unsheathed bent tip (A) is positioned approximately 2cm distal to the saphenofemoral junction (SFJ), or just below the orifice of the epigastric vein, as verified by ultrasound (B). Then the wire is activated by the motorized handle (C), after which the catheter with rotating tip is slowly withdrawn at a speed of approximately seven seconds per centimeter, while the sclerosant is continuously injected (D).

almost pain-free procedure with high occlusion rates and significant clinical improvement in the short term.[16]

In the following year, van Eekeren et al. published one-year results of endovenous mechanochemical occlusion using ClariVein®. In this study, 106 patients were treated for primary GSV insufficiency by the ClariVein device and Polidocanol. They were evaluated at six weeks, six months, and one year after the procedure. The initial technical success was 99% directly after treatment. The mean post-procedural pain during the first 14 days after treatment was 7.5mm per day on a 0 to 100mm visual analog scale. The time to return to normal activities and work was one day. No major complications were recorded. At one-year follow-up, the clinical success was 93%. The Venous Clinical Severity Score decreased significantly from 4.0 to 1.0 at one year. At one year, 88.2% of the treated GSVs remained occluded as measured by duplex ultrasonography. Twelve patients had a recanalization, of which eight were partial. Disease-specific quality of life and the RAND 36-Item Health Survey scores improved significantly at one-year follow-up. The conclusion was that mechanochemical occlusion is a safe and effective technique in the treatment of GSV insufficiency. The technique is related to low post-procedural pain scores, low complication rate, improved quality of life, and rapid resumption of normal activities and work.[17]

In 2013, Boersma et al. published the first results of endovenous mechanochemical occlusion using ClariVein® for SSV insufficiency in a prospective cohort study.[13] They treated 50 patients for primary SSV insufficiency using 2% Polidocanol for the first 10 to 15cm and 1.5% Polidocanol for the remainder. The initial success rate and the success rate after six weeks was 100%. At one year follow-up, the anatomical success rate was 94%. The venous clinical severity score (VCSS), which includes nine hallmarks of venous disease, each scored on a severity scale from zero to three,[18] decreased significantly from three to one. Also the mean procedural VAS, a visual analog pain score ranging from 0 for no experienced pain to 10 for maximum pain[19] was 2 and no major complications were observed.

CLINICAL TRIALS

After publication of the first series of mechanochemical occlusion of GSV and SSV insufficiency using ClariVein®, the first trials were performed to compare ClariVein® with endothermal ablation. To assess the postoperative pain and quality of life after endovenous mechanochemical occlusion compared to RFA, van Eekeren et al. treated 68 patients with unilateral GSV incompetence with either endovenous mechanochemical occlusion or RFA in a prospective observational study. They conclude that patients treated with endovenous mechanochemical occlusion report significantly less postoperative pain during the first two weeks after treatment and return to normal activities and work earlier than patients treated with RFA. At six weeks, patients in both groups perceived an improved change in health status and an improved disease-specific quality of life.[20]

To compare intra-procedural patient experiences of pain and return to function for treatment of GSV or SSV incompetence with RFA or endovenous mechanochemical occlusion, Bootun et al. performed a randomized controlled trial in 2014. In total, 119 patients attending for treatment of primary varicose veins were randomized to receive mechanochemical occlusion (ClariVein®) or RFA (Covidien ClosureFast™ Venefit™, Dublin, Ireland). Baseline characteristics were similar. Maximum pain score was significantly lower in the mechanochemical occlusion group (19.3mm versus 34.5mm) and the average pain score was also significantly lower in the mechanochemical ablation group (13.4mm versus 24.4mm). Sixty-six percent attended follow-up at one month, and the complete or proximal occlusion rates were 92% for both groups. At one month, the clinical and quality of life scores for both groups had similar improvements.[21]

Vun et al. assessed the efficacy of endovenous mechanochemical ablation in GSV and SSV incompetence compared to EVLT and RFA. In total, 64 patients were treated with ClariVein® using 1.5% sodium tetradecyl sulphate. Of these 64 patients, nine were lost during follow-up. Within a 10 month follow-up, a technical success rate of 91% was achieved for ClariVein® and 93% for RFA and EVLT. Comparison with 50 RFA and 40 EVLT showed procedure times were significantly less for ClariVein® than for either RFA or EVLT. Median pain scores were significantly lower for ClariVein® than RFA and EVLT. No major complications or deep vein thrombosis were reported.[22]

NEW CLINICAL APPLICATIONS

In 2014, a few reports of successful retrograde mechanochemical occlusion in patients with venous ulcers appeared. Moore et al. presented a case report, in which a 73-year old man with a non-healing venous ulcer on the left leg—despite previous successful endovenous treatment of his left GSV—was treated by retrograde mechanochemical occlusion using ClariVein®. This retrograde technique ensured that the cannulation site was distant from the site of ulceration, which may reduce the risk of infection, with the added benefit that no additional skin punctures were required for tumescent anesthesia. Furthermore, the risk of thermal injury was avoided by using endovenous mechanochemical occlusion. At the three month follow-up, the ulcer had significantly improved.[23]

Sullivan et al. also presented the use of retrograde mechanochemical endovenous occlusion for ablating the remaining below-knee great saphenous vein in six patients with venous stasis ulcers persisting after above-knee great saphenous vein ablation. No complications, especially nerve injury, were encountered. These patients had an average of 28±11 days healing time, compared with a mean of five months in traditional method as described in literature.[24]

EXPERIMENTAL STUDIES

To explore the working mechanism of ClariVein®, several experimental studies were performed. In 2012, Kendler et al. first described the histological changes in vein walls after ClariVein® treatment. They obtained five GSV specimens with crossectomy. The veins were treated ex vivo with ClariVein® without sclerotherapy. Treated specimen were compared histologically

and immunohistochemically with plain specimen. As postulated in earlier studies, the mechanical part of the ClariVein® catheter caused a subtle incomplete destruction of endothelium with no observed changes to the media or adventitia in contrast to EVLT or RFA in which transmural damage of the vein wall may be seen. Reduced expression of factor VIII in the treated veins may be caused by the release of preformed factor VIII granules as a result of mechanical irritation.[25]

In 2014, van Eekeren et al. published a case report evaluating histological changes in a vein one year after treatment with endovenous mechanochemical occlusion. A 59-year-old patient was treated with ClariVein® for bilateral GSV incompetence using 2% Polidocanol for the proximal segment and 1.5% for the remainder of both veins. The patient's medical history showed a high ligation of the saphenofemoral junction in 2001. After one-year follow-up, edema of the right leg was caused by recurrent SFJ insufficiency and the patient was treated with a recrossectomy. An insufficient anterolateral vein was ligated and the proximal part of the completely obliterated GSV was excised and sent for histological investigation. This vein was compared to a normal untreated GSV from another patient. Microscopic evaluation of the mechanochemical-treated vein showed a circumferential disappearance of the endothelial layer and fibrosis of the vein. The media was considerably damaged, with changes in collagen structure, supporting the therapeutic effect of endovenous mechanochemical ablation.[26]

Recently, Tal et al. treated 12 lateral saphenous veins of 11 male goats. Five were treated with ClariVein® using 1.5% sodium tetradecyl sulfate (STS), one vein was treated with ClariVein® using 0.9% saline. The remaining six received injection sclerotherapy with 5ml of 1.5% STS or 0.9% saline. Subsequent histological examination showed complete occlusion of the vein in all subjects treated with ClariVein® and STS, whereas complete patency was noted in all other treatment modalities, suggesting that the combination of mechanical and chemical therapy is essential in the working mechanism of ClariVein®.[27]

DISCUSSION

With five-year success rates that are comparable with open surgery, 80% for RFA, 95% for EVLT, and 76% for surgical stripping, endothermal ablation techniques—including EVLT and RF—have become the first line of treatment for superficial venous reflux. Even though these endothermal techniques show excellent results, they require tumescent anesthesia to buffer the heat and prevent damage to the surrounding tissues, which prolongs the procedural time and adds to patient discomfort during treatment. Moreover, nerve damage and prolonged pain are known, but rare, complications and skin burns were reported in early endovenous laser ablation experience.[11,28]

To avoid these risks and improve patient comfort, non-thermal non-tumescent ablation techniques were developed. Ultrasound-guided foam sclerotherapy was one of the first non-thermal techniques developed, but proved to be not as effective as EVLT and RFA, with a five-year success rate of 74%. There is also a rare but well-documented risk of stroke.[28] A newly reported technique is the VenaSeal™ Sapheon Closure System (Morrisville, SC) which comprises the endovenous delivery of cyanoacrylate tissue adhesive to the vein causing fibrosis. Short-term results are encouraging and, although peri-operative discomfort seems to be minimal, thrombophlebitis has been reported in up to 15% of patients, hindering postoperative recovery. Long-term results have to be awaited.[29]

The other non-thermal non-tumescent ablation technique is mechanochemical occlusion using the ClariVein® system as described in this article. The combination of mechanical endothelial damage using a rotating wire combined with the infusion of a liquid sclerosant is essential to the working mechanism of this technique.[27] Local anesthesia is used at the insertion site only, no tumescence is required, and the patient only feels a slight vibration of the rotating wire. With over 40,000 ClariVein® devices used globally to date, reported complications are minimal; deep vein thrombosis occurs in < 0.5% of cases, and no nerve or skin injury has been reported because the technology is non-thermal. ClariVein® can be used for both GSV and SSV insufficiency, as there is no potential risk of nerve damage. Several peer-reviewed journal articles have been published on a global basis by different authors with very consistently positive results. Retrograde access in the lower leg is an advantage when distal ulceration is present, avoiding introduction at the level of damaged skin. Follow-up of patients at less than two years reveals a 96% occlusion rate and sustained quality of life improvement.[28] When compared to RFA, the success rates are comparable, but significantly less postoperative pain and earlier return to normal activities and work is reported with endovenous mechanochemical ablation.[20,21] Results of two randomized controlled trials currently running in The Netherlands, the MARADONA[14] and MESSI[30] trials, comparing endovenous mechanochemical ablation with RFA in the treatment of GSV and SSV insufficiency, respectively, have to be awaited.

CONCLUSION

Mechanochemical occlusion using ClariVein® is a non-thermal, non-tumescent ablation technique for both GSV and SSV insufficiency. It has proven to be safe and effective, eliminating the need for tumescent anesthesia and nerve damage, and significantly less postoperative pain and earlier return to normal activities and work were reported when compared to RFA. The possibility of retrograde ablation of distal SSV insufficiency in C6 ulceration is considered an advantage. **STI**

AUTHORS' DISCLOSURES

Dr. Reijnen is a consultant for Vascular Insights, Dr. de Vries is a consultant for Angiocare, and Dr. Zeebregts is a consultant for Vascutek.

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