Mechanochemical Ablation of Superficial Veins

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Clinical Pearls

1. Mechanochemical ablation reduces procedural pain during superficial vein ablation.
2. The risk of nerve injury is low and treatment of the distal saphenous vein at the ankle is feasible.
3. The efficacy is comparable to thermal vein ablation methods up to 1 year in most studies.

Introduction

The Society of Vascular Surgery/American Venous Forum and the National Institute of Health and Clinical Excellence (NICE) guidelines recommend the use of endothermal ablation (ETA) in the form of endovenous laser ablation (EVLA) and radiofrequency ablation (RFA) as the first line treatment (grade 1B evidence) for truncal venous reflux in varicose veins since 2011 and 2013, respectively [1, 2]. Endovenous thermal ablation of saphenous vein reduces the rate of postoperative complications, increases the speed of recovery resulting in faster return to work, and improves the quality of life compared to surgical ligation and stripping [3]. However, ETA requires tumescent anesthesia around the targeted vein to buffer the heat and prevent damage to the surrounding structures [4, 5].

The need for tumescent anesthesia has a few disadvantages as it prolongs the procedural time and adds to patient discomfort and constitutes the most painful part of an ablation procedure. There is also a risk of endothermal heat-induced thrombosis with thermal ablation techniques since there is no control on forward dissipation of energy [4, 6, 7]. Recent novel techniques have thus been devised to minimize these negative aspects of endothermal ablation, while incorporating its clinical benefits.

Endovenous mechanochemical ablation (MOCA) using ClariVein® (Vascular Insights, LLC, Quincy, MA) which is discussed in this chapter is a new evolving technique, which induces vein closure by a combination of mechanical injury of venous endothelium with simultaneous chemical injury using a physician-guided infusion of liquid sclerosing agent. The procedure does not involve the use of thermal energy and, therefore, does not require tumescent anesthesia.

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Mechanism of Action

MOCA produces inflammation of the vein wall and subsequent thrombosis by combining mechanical injury with chemical irritation. In a recent study, Boersma et al. conducted a prospective experimental trial using dairy animals to test the working mechanism of MOCA and provide histological analysis of its effect on targeted vein wall. The experiment revealed that the mechanical action inflicted by the device causes damage to the endothelium without signs of any histological injury to other layers of the vessel wall. The liquid sclerosant then produces irreversible damage to the cellular membrane of the endothelium resulting in fibrosis of the vein. The study thus confirmed the hypothesis that MOCA yields venous occlusion by a combination of mechanical injury of the endothelium layer and vasoconstriction, which further increases the permeability of the sclerosant and increases area of exposure into the deeper layers of the vessel wall [8]. In another recent ex vivo "vein section" study conducted by Whiteley et al., it was suggested that there was deeper penetration of the sclerosant as a result of disruption of tunica intima along with profound damage to tunica media [9].

ClariVein® Device and Technique

The ClariVein® infusion catheter (Vascular Insights, LLC, Quincy, MA) received clearance from the US Food and Drug Administration (FDA) in May 2008 for the indication of infusion of physician-specified agents (sclerosants) in the peripheral vasculature. ClariVein® device itself obtained the CE mark for the specific indication of venous occlusion of incompetent superficial veins to treat venous reflux in lower extremities in April 2010. In addition to its use in patients who do not particularly tolerate tumescent anesthesia, we have used MOCA in our practice to treat recurrent venous reflux in the distal saphenous vein. The saphenous nerve is close to the vein in that area of the leg, and there is an increased risk of nerve injury and numbness after thermal ablation. MOCA allows access at the ankle and ablation of the distal vein. In these cases, the saphenous vein is occluded at the knee and the risk of dissipation of the sclerosant to the deep veins is minimal. In fact, the sclerosant tends to dissipate to the superficial varicosities connected to the saphenous vein and can potentially increase the efficiency of the treatment by sclerosis of venous tributaries.

Device

The ClariVein® device consists of two main components: an infusion catheter with a rotating dispersion wire extending within its lumen and a motor unit/handle. The infusion catheter is a disposable plastic device which consists of a main lumen supporting the wire and a side port connection leading to the main lumen. The side port system is used as a connection to attach the syringe to flush saline as well inject sclerosant. The distal end of the ablation is angled at about 2 cm from the tip and has a small metal ball attached to the end (Fig. 10.1). This metallic ball at the tip has been designed to enhance ultrasound catheter guidance to accurately place the tip of the catheter at the targeted location and prevent vein wall perforation.

The catheter is currently available in two sizes: 45 and 65 cm length, with a white mark indicating 5 cm of the distal end. The catheter, along with the wire, is connected to a battery-motorized handle on the proximal end, which controls wire rotation. The motor has four speeds ranging from 2000 to 3500 rpm. The maximum speed is most often used as the default (Fig. 10.2). The rotating wire works by activating the coagulation pathway by instigating mechanical injury to the endothelium. Secondly, it induces vasospasm which reduces the vein diameter and increases the action of sclerosant by increasing the penetration. The rotating wire thus ensures an even distribution of the sclerosant at the vessel wall (Fig. 10.3).

The whole device can be introduced via ultrasound guidance through a micro-introducer (4–5 Fr) at the puncture site [4, 10]. Once the two units, namely, the catheter and the motor handle,

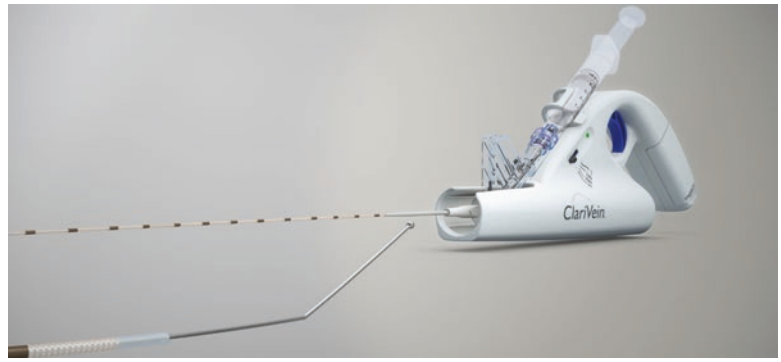

Fig. 10.1 ClariVein® infusion catheter showing the rotating tip at the end (courtesy of Vascular Insights LLC, Quincy, MA)

Fig. 10.2 ClariVein® device showing the motorized handle unit attached with a syringe holder to facilitate physician-controlled infusion of the liquid sclerosant (courtesy of Vascular Insights LLC, Quincy, MA)

have been connected, it cannot be disassembled or reused. The device is designed for single use only, easy to handle, and disposable after use.

Technique

The patient is horizontally positioned in reverse Trendelenburg based on the location of the targeted vein, and the area is prepped and draped in a sterile manner (Fig. 10.4A). Local anesthesia is infiltrated at the site of the puncture. Under ultrasound guidance, the introducer wire and catheter sheath are inserted into the vein. For treatment of below-the-knee saphenous vein reflux, access can be obtained close to the ankle (Fig. 10.4B). The ClariVein catheter is then inserted through the lumen such that the tip of the wire is placed just below the saphenofemoral junction (SFJ).

The ClariVein® catheter is then connected to the motorized handle unit, and the distal end of the dispersion wire is unsheathed to expose the dispersion tip which is then positioned 1 cm distal to the SFJ or 1 cm proximal from the "fascia" as the small saphenous vein (SSV) angles toward the saphenopopliteal junction [11]. In the case illustrated, the catheter is advanced as close as possible proximally to the segment that was ablated prior (Fig. 10.5). Since the position of the catheter is steerable only with the cartridge wing at distal end, it is important to position the catheter tip at the desired position before attaching it to the motorized handle [12].

Once the location of the catheter is confirmed by ultrasound, the catheter is attached to the handle and the 2-cm-long angled tip is exposed. A 5 mL syringe filled with 1.5% sotradecol is then connected to the handle for delivery of the

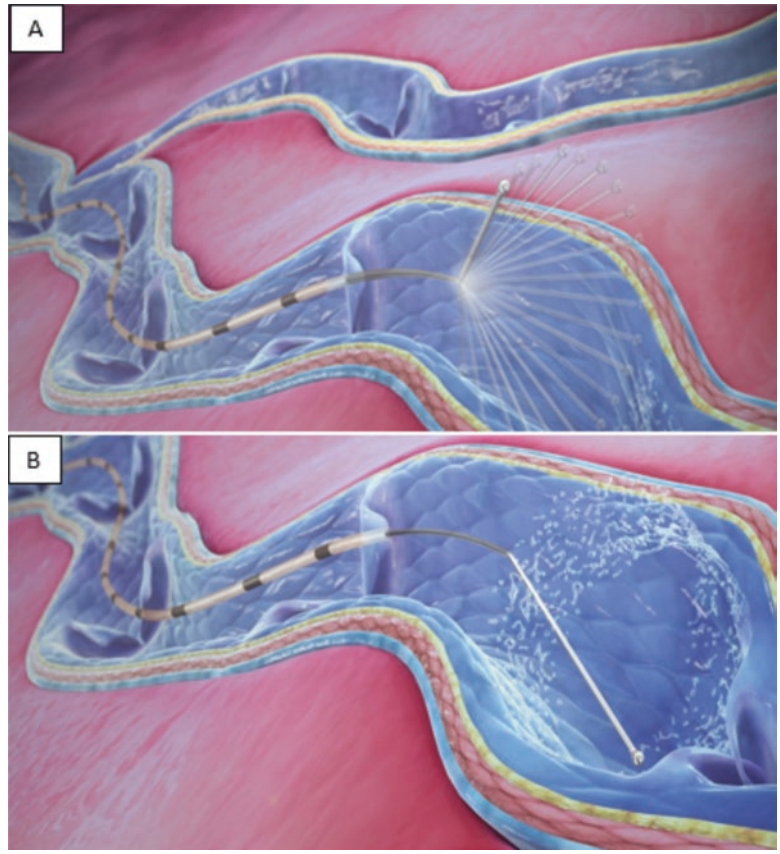

Fig. 10.3 ClariVein® device catheter with activation of the rotation mechanism of the dispersion tip (**A**). Even distribution of the sclerosant at the endothelium (**B**) (courtesy of Vascular Insights LLC, Quincy, MA)

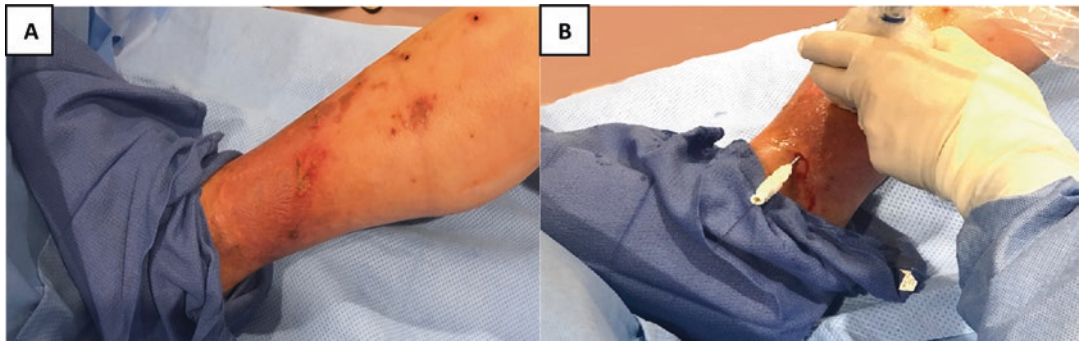

Fig. 10.4 (**A**) Pre-procedure: leg prepped below knee, positioned and draped. (**B**) After injecting local anesthesia, introducer wire and catheter sheath are introduced at the ankle under ultrasound guidance to treat GSV below knee reflux

sclerosing agent. This step comprises full assembly of the device.

The access sheath is usually removed prior to initiation of treatment to ensure a smooth, continuous, uninterrupted pullback (Fig. 10.6). The first 2–3 cm is treated only with mechanical ablation to induce vasospasm and avoids propagation of the sclerosing agent into the deep venous system. Next, the activated catheter with rotating tip is gradually withdrawn at a speed of approximately 6–7 s per cm, while the sclerosant (polidocanol/sodium tetradecyl sulfate) is injected at a rate of 0.2 mL per cm approximately. Ultrasound compression of the vein is not routinely

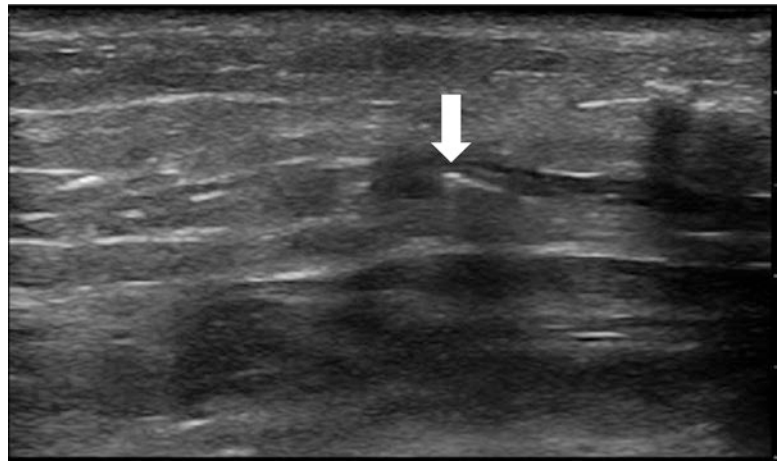

Fig. 10.5 Figure showing position of tip of ClariVein catheter (*arrow*) in the tissue, confirmed with ultrasound guidance

Fig. 10.6 The ClariVein catheter device with rotating wire is then pulled back at 7 s per cm speed while injecting sclerosant

used during treatment but is suggested for veins larger than 10 mm in diameter to enhance contact of the rotating tip with the wall of the vein. A white mark on the catheter indicates the last 5 cm of the catheter. An additional 2 cm of therapy can then be performed. The tip of the wire is re-sheathed and the catheter is withdrawn with pressure on the access site.

Immediately after procedure, an ultrasound should be performed to assess for patency of deep veins of the treated leg and examine the proximal ablation edge position, especially near the junction. The treated vein may still be compressible initially, but that does not indicate failure of treatment. Eventual thrombosis occurs subsequently with inflammation and continuous action of the sclerosing agent (Fig. 10.7).

There is a variation in the use of sclerosing agents (polidocanol/sotradecol) in terms of concentration and dosage. Some experts suggest that a higher concentration of polidocanol should be used near the junction, as it appears to be weaker than sotradecol [4]. In most cases the amount of sclerosant is calculated based on the patient's weight, and the maximum amount should not exceed the amount mentioned on the drug insert. According to Tang et al. the maximum recommended treatment dose of sotradecol for one procedure should not exceed 10 mL of 3% strength (equivalent to 15 mL of 2% sotradecol) [13]. Currently, some surgeons also suggest the dose of sclerosant used should be 2 mL, 3% polidocanol for the first 10–15 cm, and 1.5% polidocanol for the remainder of the great saphenous vein (GSV) [4, 14, 15]. There is however no standard recommendation regarding choice of sclerosant, concentration, or dosage to date.

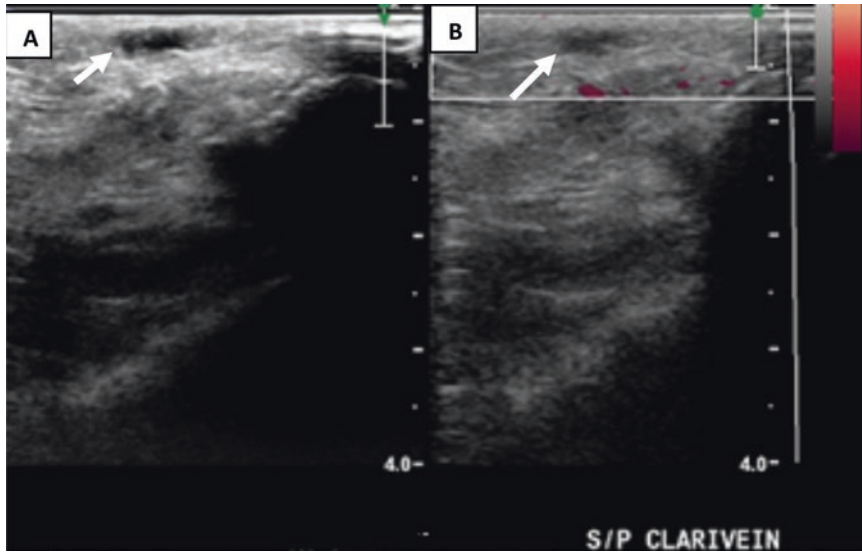

Fig. 10.7 Post-procedural venous occlusion seen after mechanochemical ablation showing ultrasound images of a treated vein without compression (**A**) and after ultrasound compression (**B**)

Post-procedural Care

- Patients can be discharged with class II thigh-high compression stockings (20–30 mm Hg) use for 48 h continuously and then during daytime for at least 2 weeks.
- Follow-up ultrasound and clinical visit should be scheduled within 1–2 weeks after procedure.
- The patients should be advised to walk immediately post-procedure for at least 10 min.
- Some studies also recommend to advice walking for at least 10 min every hour on the day of the procedure [12].

Clinical Outcomes

Ultrasound-guided foam sclerotherapy was one of the first nonthermal techniques developed but has not proved to be as effective as endovenous laser ablation (EVLA) and radiofrequency ablation (RFA) techniques, with a 5-year success rate of 74% [16]. Furthermore, it usually requires multiple treatment sessions and is associated with a small but well-documented risk of stroke using foam sclerotherapy [17, 18].

The first human study demonstrating clinical safety and efficacy of MOCA was conducted by Elias et al. in 2012 (Table 10.1). The study included 30 incompetent GSVs in 29 patients treated for primary venous insufficiency. The primary closure rate was reported as 96.7%, with no major adverse complications [19]. Although this was the first human study conducted, it was not the first one published as in 2011; van Eekeren et al. reported their experience on clinical efficacy of MOCA. In this study, 30 GSVs in 25 patients with venous insufficiency were treated in two centers. The immediate postoperative technical success rate was 100%. After a follow-up of 6 weeks, 26 (87%) remained occluded, three veins showed partial recanalization, and one vein completely recanalized. Patient satisfaction was reported at 8.5 on a 10-point scale, and the median VCSS decreased significantly from 3 to 1 [10].

The first prospective multicenter study on efficacy of MOCA in patients with chronic venous insufficiency was described by Bishawi et al. The study included 126 patients who were noted to be significantly older and with higher BMI compared to previous studies using endothermal techniques but reported high successful closure rates in the great saphenous vein at 1 week, 3

Table 10.1 Clinical safety and efficacy studies conducted for mechanochemical ablation

Author	Year	Study sample (*n*)	Vein type	Sclerosant used	Clinical efficacy (%)	Complication rate (%)	Follow-up
van Eekeren et al. [10]	2011	25	GSV	Polidocanol (1.5%)	87	Ecchymosis (30) Phlebitis (13)	6 weeks
Elias et al. [19]	2012	29	GSV	Sotradecol (1.5%)	96.7	Ecchymosis (10)	6 months
Boersma et al. [15]	2012	50	SSV	Polidocanol proximal (2%) Distal (1.5%)	94	Ecchymosis (12) Induration (12) Phlebitis (14)	1 year
Bishawi et al. [20] (multicenter study)	2014	126	GSV	Sotradecol Polidocanol (center based)	94%	Hematoma (1) Ecchymosis (9) Phlebitis (10)	6 months
van Eekeren et al. [21]	2014	106	GSV	Polidocanol Proximal (2%) Distal (1%)	93	Phlebitis (3) Hematoma (9) Induration (12) Pigmentation (5)	1 year
Deijen et al. [14]	2016	449	GSV SSV	Polidocanol proximal (2%) Distal (1.5%)	92% 84%	Phlebitis (2) Nerve injury (0.2) Hematoma (0.2) DVT/PE (0.6)	12 weeks
Kim et al. [22]	2017	126	GSV	Sotradecol Polidocanol (1.5%)	92%	Phlebitis (10) Ecchymosis (9) Hematoma (0.7)	2 years
Tang et al. [13]	2017	300	GSV SSV	Sotradecol (2%)	97% 100%	Phlebitis (4)	8 weeks

months, and 6 months (100%, 98%, and 94%), respectively. Also, there was a significant improvement in the venous clinical severity score (VCSS) post-procedure [20]. The following year, van Eekeren et al. published 1-year results for MOCA of GSV insufficiency in 106 patients. The initial technical success rate was 99% on duplex imaging immediately after treatment. Post-procedural pain scores were reported with mean pain during the first 14 days after treatment at 7.5 mm (0–100 visual analog scale). The time to return to daily life activities was noted as 1 day. At 1-year follow-up, the clinical success rate was 93% and 88.2% of the GSV remained occluded. Twelve patients were reported to have recanalization, of which eight were partial. The venous clinical severity score (VCSS) decreased significantly from 4.0 to 1.0 at 1 year [21].

In 2013, Boersma et al. published the first report on safety and efficacy of mechanochemical ablation of small saphenous vein (SSV) insufficiency. The study included 50 consecutive patients treated with MOCA and assessed at 6 weeks and 1 year. The initial technical success rate was 100% and 94% remained occluded at 1 year. VCSS decreased significantly from 3.0 (IQR 1-3) to 1.0 (IQR 1-2) at 1 year. No major complications were noted, especially no nerve injury [15]. A recent prospective study by Tang et al. not only recommend the use of ClariVein for ablation for both great and small saphenous varicose veins (100% at 1 week and 94% at 8 weeks post-procedure) but also noted successful procedures when performed on multiple veins in the same leg or bilaterally [13]. Furthermore, MOCA has proved to be a great technique for treatment of SSV incompetence with 1-year follow-up showing 94% anatomic success rate and no major complications especially because of close proximity to sural or saphenous nerve in the distal calf [13, 15].

Another advantage of MOCA is that the procedure has proved to be painless and can be completed more rapidly compared to ETA. It can also be combined with phlebectomies during the same procedure under local anesthetic [13].

Table 10.2 Randomized clinical trials performed for mechanochemical ablation of superficial veins

Author	Year	Sample size (*n*)	Vein type	Study objective	Results	Follow-up
van Eekeren et al. [2]	2013	68	GSV	MOCA vs. RFA postoperative pain scores, early QoL	4.8 ± 9.7 mm vs. 18.6 ± 17 mm ($P < 0.001$)	14 days 6 weeks
Vun et al. [24]	2015	64 MOCA 50 RFA 40 EVLA	GSV SSV	MOCA vs. RFA/ EVLA success, medial pain scores	91% (MOCA) 93% (RFA/ EVLA) 1 vs. 5 vs. 6 ($P < 0.001$)	10 months
Bootun et al. [23]	2016	60 MOCA 59 RFA	GSV SSV	MOCA vs. RFA Mean pain scores	92% (BOTH) 13.4 ± 16 mm vs. 24.4 ± 18 mm ($P < 0.001$)	1 month
Lam et al. (dose-finding) [25]	2016	87	GSV	Polidocanol: 1% foam vs. 2% liquid vs. 3% liquid closure rate	1%: 56.5% 2%: 100% 3%: 96.4% ($P < 0.001$)	6 weeks (interim results)
Leung et al. (LAMA) [26, 27]	2016	140	GSV SSV	MOCA vs. EVLA with concomitant phlebectomies. Intra-/post-procedural pain, efficacy, cost-effectiveness	Preliminary results: MOCA 92% vs. EVLA 94%; less procedural pain with MOCA, no difference in QOL or return to work (median 7 vs. 6 days)	6 weeks 6 months (preliminary results)
Ramon et al. (MARADONA) [21]	2014	460	GSV	MOCA vs. RFA success, post-procedural pain	Ongoing trial	1 year
Boersma et al. (MESSI) [28]	2014	160	SSV	MOCA vs. RFA success, post-procedural pain	Ongoing trial	1 year
Lane et al. [29]	2016	170	GSV	MOCA vs. RFA Postoperative pain scores	VAS:15 mm vs. 34 mm ($P = 0.003$) Numeric:3 mm vs. 4 mm ($P = 0.002$)	6 months

QoL quality of life, *VAS* visual analog scale

The first randomized trial comparing MOCA and RFA was conducted by van Eekeren in 2013 in 68 patients with GSV insufficiency to compare the differences in postoperative pain and early quality of life after both procedures. Patients treated with MOCA reported significantly less postoperative pain in the first 14 days (4.8 ± 9.7 mm) compared to RFA (18.6 ± 17 mm, $P < 0.001$). The lower postoperative pain was associated with early return to daily life activities (1.2 ± 1.8 days vs. 2.4 ± 2.8 days, $P = 0.02$). At follow-up of 6 weeks, patients in both groups had an improved change in health status and quality of life [2]. In addition to similar results regarding postoperative pain scores and quality of life, Bootun et al. in 2016 noted an equivalent clinical success rate of 92% in both the groups (MOCA vs. RFA) [23] (Table 10.2).

The LAMA trial (endovenous laser ablation versus mechanochemical ablation with ClariVein) has been designed to compare the outcomes of both procedures at 1 year as well as intraprocedural

pain (n = 140 patients). Secondary outcomes for the trial include post-procedural pain, analgesic use, patient satisfaction and quality of life, and complications along with a cost-effective analysis following EVLA and MOCA [26]. The results of the trial were recently presented and showed decrease intraprocedural pain with MOCA compared to EVLA during truncal ablation. However, the overall post-procedural pain was not different since most patients underwent phlebectomy during the same procedure. The technical success rate was also comparable between MOCA (92%) and EVLA (94%). There was no difference in overall quality of life and return to work [27].

The MARADONA trial (mechanochemical endovenous ablation versus radiofrequency ablation in the treatment of primary GSV incompetence) has been designed to compare the anatomical and clinical success rate of MOCA compared to RFA at 1 year (n = 460 patients) [21]. Patients will then be followed up for 5 years to determine long-term data. The results of this study are expected in 2020. Another similar randomized clinical trial has been designed (MESSI trial) to look at anatomical and clinical success rates of MOCA and RFA for the SSV (n = 160 patients in total) [28].

Complications

Minor complications after mechanochemical ablation include mild hyperpigmentation, ecchymosis, local hematoma, and phlebitis. Transient phlebitis is the most common minor complication noted in patients treated with MOCA (4–14%) [14] (Table 10.1). The incidence of phlebitis is however lower compared to ETA techniques using radiofrequency ablation or foam/liquid sclerotherapy [17, 30]. This low incidence of superficial phlebitis with MOCA may be because of no heat being generated to occlude the vein with ClariVein compared to other alternative techniques. However, the risk of phlebitis should be explained to patients prior to procedure. Patients need to be advised to use compression/NSAIDs to treat if symptoms of phlebitis are noticed.

During venous ablation of SSV, there lies an additional risk of nerve injury due to the anatomic proximity of the sural nerve in the distal calf. A recent meta-analysis by Hirsch et al. compared the risk of nerve injury after the different known techniques for treatment of varicose veins. They concluded that the use of nonthermal endovenous techniques such as MOCA has proved to be better alternatives than ETA to avoid nerve injuries [31]. A study by Pan et al. compared open technique to endovenous and concluded that it had twice the risk of nerve injury/paresthesia compared to thermal ablation using EVLA (11.27% vs. 6.73%). Previous studies have shown transient nerve injury between 1.3 and 11% for EVLA [17, 32–34]. Dermody et al. have shown that RFA has a lower risk of nerve injury compared to EVLA (3.8 vs. 5.5%). The incidence of nerve injury with MOCA is rare and has been reported in only one study (0.2%) to date [14].

Deijen et al. have published the study with largest patient population to date (n = 449) and is the only study to have reported an incidence of deep vein thrombosis (one patient) and pulmonary emboli (two patients) [14]. There has been otherwise no case of venous thromboembolism, deep vein thrombus, or skin necrosis reported with MOCA [35, 36].

A rare complication of retrograde inversion stripping of the small saphenous vein was reported in a recent case study in 2015, where during an elective procedure, the tip of the ClariVein® catheter wire got caught into a small calcified tributary and on gradual withdrawal leading to stripping of the vein along with the device. This case illustrated the possibility of rare adverse events occurring during an elective routine procedure; however in this case, the patient suffered no recurrence or nerve injury [37].

Conclusion

The ClariVein system is the first venous ablation technique to employ a hybrid (dual energy) technique—mechanical and chemical, combined in a catheter-based device. It decreases procedural pain and discomfort related to tumescence. Most

studies have demonstrated good clinical efficacy at 1 year. Currently, there is no clear consensus on what strength and dosage of sclerosant is ideal for MOCA. This technology continues to evolve and there is an ongoing randomized clinical trial "dose-finding study" to determine the ideal sclerosant dosage to use [25, 38].

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