Mechanochemical ablation as an alternative to venous ulcer healing compared with thermal ablation

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ABSTRACT

Objective: We aimed to compare mechanochemical ablation (MOCA) and thermal ablation (radiofrequency ablation and endovenous laser therapy) for venous ulcer healing in patients with clinical class 6 chronic venous insufficiency.

Methods: Electronic medical records were reviewed of patients with venous ulcers who underwent truncal or perforator ablation between February 2012 and November 2015. These records contained history of venous disease and ulcer history, procedures, complications, follow-up, method of wound care, and current status of the ulcer. The patients were grouped according to the method of ablation for comparison.

Results: In 66 patients, 82 venous segments were treated, 29 with thermal methods and 53 with MOCA; 16% of patients had prior venous intervention. Before ablation, three patients in the thermal group had a history of deep venous thrombosis compared with seven in the MOCA group. On average, patients treated with MOCA were older (thermal ablation, 57.2 years; MOCA, 67.9 years; $P = .0003$). Ulcer duration before intervention ranged from 9.2 months for thermal ablation to 11.2 months for MOCA ($P =$ NS). In total, 74% of patients treated with MOCA healed their ulcers compared with 35% of those treated with thermal ablation ($P = .01$). A healed ulcer was defined as elimination of ulcer depth and superficial skin coverage. The mean time to heal was 4.4 months in the thermal ablation group compared with 2.3 months with MOCA ($P = .01$). The mean length of follow-up was 12.8 months after thermal ablation and 7.9 months after MOCA ($P = .02$). Both age ($P = .03$) and treatment modality ($P = .03$) independently had an impact on ulcer healing on multiple logistic regression analysis. All but two patients were treated with an Unna boot after venous ablation. Complications included readmission of two patients with nonaccess-related infections, one nonocclusive deep venous thrombosis, and one late death unrelated to the procedure second to pneumonia in the setting of advanced colon cancer. There were three recurrent ulcers at 1 week, 2 months, and 7 months after MOCA that rehealed with Unna boot therapy and continued compression.

Conclusions: MOCA is safe and effective in treating chronic venous ulcers and appears to provide comparable results to methods that rely on thermal ablation. Younger age and use of MOCA favored wound healing. MOCA was an independent predictor of ulcer healing. Randomized studies are necessary to further support our findings. (J Vasc Surg: Venous and Lym Dis 2019;7:699-705.)

Keywords: Ulcer; Venous ablation; Venous insufficiency

More than 24 million Americans suffer from chronic venous disease ranging in severity from small spider veins that cause cosmetic concerns to chronic venous ulcers that impair quality of life. To standardize the reporting and treatment of the manifestations of chronic venous disorders, a comprehensive classification system was developed.[1]

More than 500,000 Americans have the most severe form of chronic venous disease, venous ulceration. These patients require extensive and repeated therapy, leading to an annual U.S. payer burden of $14.9 billion for venous leg ulcers.[2] To maintain healing, patients must comply with long-term use of venous compression stockings that are both expensive and uncomfortable. When patients are noncompliant, the ulcers recur and additional interventions are required. Risk factors include age, sex, heredity, and obesity.[3] Essential to venous ulceration is venous hypertension, which leads to a cascade of cellular events magnified by genetic factors.[4]

Healing of venous ulcerations begins with conservative management, the pillars of which are compression therapy, leg elevation, and bandage dressings, notably in the absence of underlying arterial disease. Those who fail to respond to conservative treatment advance to therapy for the underlying venous disease, such as obstruction or insufficiency. Subfascial endoscopic perforator surgery is an open surgical option,[5] whereas less invasive

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Author conflict of interest: none.

Presented as a poster at the 2016 Vascular Annual Meeting of the Society for Vascular Surgery, National Harbor, Md, June 8-11, 2016.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2213-333X

https://doi.org/10.1016/j.jvsv.2019.05.005

alternatives also exist to treat superficial venous insufficiency, such as endovenous laser therapy (EVLT), radiofrequency ablation (RFA), and mechanochemical ablation (MOCA). These therapies are helpful adjuncts to compression and wound care and have been favored as of late as they are less invasive, have shorter recovery times, and are less expensive. With respect to efficacy, the Effect of Surgery and Compression on Healing and Recurrence (ESCHAR) study showed that open surgery results in longer periods of closure relative to compression and various types of bandaging alone.[6] RFA and EVLT offer similar long-term outcomes but at less cost and disruption of daily activity.[7-10] MOCA has been shown in a case series of six patients to heal lower extremity ulcers (average, 4.1 cm^2) in 28 ± 11 days compared with 5 months by traditional compressive nonoperative methods.[11] The proximity of the veins involved in skin ulcer formation to the overlying skin as seen in Fig 1 makes MOCA an attractive option to avoid the risk of thermal burns below the knee. The putative advantage of MOCA over thermal techniques such as RFA and EVLT is the lack of energy production and resultant avoidance of nerve injury due to the relation of the lower extremity veins to their respective nerves[12] and the ability of MOCA to treat multiple branches in a single procedure. The aim of our study was to compare thermal and nonthermal endovenous closure (MOCA) and to determine whether there is a difference in venous ulcer healing and time to heal.

METHODS

This study was performed at the Mount Sinai Hospital and Icahn School of Medicine at Mount Sinai, an urban tertiary care hospital and medical school located in New York City. Only deidentified information was recorded in the study database by investigators. Patients were given unique identifiers, or subject IDs, that were assigned to their deidentified health information.

The investigators were educated on Health Insurance Portability and Accountability Act regulations and understood that every effort must be made to protect patients' privacy. The study included an approved waiver of informed consent because it involved no more than minimal risk to participants. Participants were not contacted or approached about the study, and their rights and welfare were not affected. The Institutional Review Board approved the study in April 2017, and approval was continued into 2018.

We conducted a retrospective review of all patients treated specifically for venous ulcers. Records of patients with level C6 venous disease who underwent truncal or perforator ablation between February 2012 and November 2015 were extracted from our electronic medical record. Patients had been assigned treatment according to the physician's preference.

Variables of interest included the history of venous disease with specific focus on venous ulcers, interventions, number and location of the treated vessels, postprocedure complications, methods of postprocedure ulcer care, and current status of the ulcer. Wound dimensions were not recorded in the study. For all patients, nonoperative management had been trialed for 3 months previously. Patients with venous ulcers who had significant reflux on venous duplex ultrasound imaging were included. The primary outcome was time to heal. The patients were stratified on the basis of treatment type (thermal ablation vs MOCA). The unit of analysis was the patient or vein segment as appropriate. Univariate testing was performed on preoperative variables, and the significant variables were subsequently run in a Cox proportional hazards regression to predict time to ulcer healing. Kaplan-Meier curves were created to demonstrate the differing ulcer healing rates between MOCA and thermal ablation cohorts. All data were analyzed using Stata/MP 13.1 software (StataCorp LP, College Station, Tex).

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center retrospective cohort study
- **Key Findings:** Of 53 patients treated with mechanochemical ablation (MOCA), 74% healed their ulcers compared with 35% of 29 treated with thermal ablation ($P = .01$), with a mean time to heal of 2.27 months vs 4.43 months ($P = .01$), respectively. Age and treatment modality ($P = .03$) affected ulcer healing on multiple logistic regression analysis, whereas MOCA was an independent factor.
- **Take Home Message:** MOCA is safe and effective for treating venous ulcers and can be considered an alternative modality to thermal ablation techniques.

RESULTS

Of all patients treated for venous ulcers, 66 patients underwent 82 venous procedures involving 105 venous segments that qualified for inclusion in the analysis. All patients had undergone at least 3 months of compression, if tolerated. The lower extremity venous segments of interest to the study included the great saphenous vein (GSV), small saphenous vein, accessory saphenous vein, Giacomini vein, and perforator veins (often in combination with GSV segments as described by Tadros et al[5]). Twenty-nine patients were treated with thermal methods (18 EVLT and 11 RFA); 53 were treated with MOCA. EVLT patients also had concurrent sclerotherapy using sodium tetradecyl sulfate below the knee for lesions at high risk of thermal injury. All patients underwent weekly Unna boot therapy with the exception of two patients in the MOCA group, one electing to receive a noncompressive dressing because of pain and the other a multilayered compression with Profore (Smith & Nephew, Memphis, Tenn).

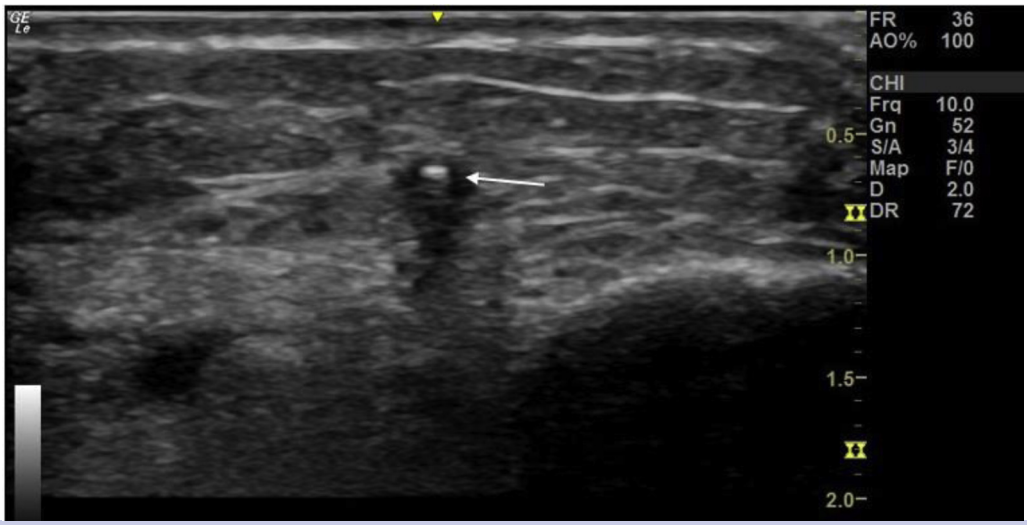

Fig 1. Procedural ultrasound demonstrating proximity of treated vein to skin (the *arrow* indicates intravenous catheter with depth measurements in centimeters along right border of image).

Table I characterizes the pretreatment population. On average, MOCA patients were significantly older than those having thermal treatment (67.9 ± 11.6 years vs 57.2 ± 13.5 years; $P < .001$) and had a statistically insignificant higher incidence of prior deep venous thrombosis (13.2% vs 10.3%; $P = .70$). Ulcer duration was 11.2 ± 14.4 months in the MOCA group compared with 9.2 ± 14.0 months in the thermal group. Prior interventions or treatments were less frequent in the MOCA group, although this was not statistically significant (17.2% vs 20.8%; $P = .70$). Of the 12 patients with prior intervention, 8 had a prior venous ablation in the MOCA cohort and 4 in the thermal group. For the MOCA group, the eight patients all had prior attempted thermal closure. For the thermal group, two patients had undergone sclerotherapy treatment.

Table II demonstrates that treatment focused on a wider variety of vein segments in the MOCA group, especially in the smaller segments, such as the small saphenous vein (21.3% vs 10%) and perforator veins (17.3% vs 2.6%). MOCA patients had more segments treated (1.4 per patient vs 1 per patient in the thermal group) and more multiple vessel procedures (63% vs 16%). Multiple segments included each type of segment (eg, GSV, perforator). If multiple perforator veins were treated, they were considered individually.

Table III summarizes the outcomes in the population stratified by treatment group. At the time of the final follow-up (46 months), 32 of 41 patients (78.05%) in the MOCA group were healed compared with 10 of 25 (40%) in the thermal group. The mean time to heal was 2.27 ± 2.33 months with MOCA and 4.43 ± 5.92 months in the thermal group ($P = .074$), as seen in Fig 2. Complications included readmission of two patients with nonaccess-related infections, one nonocclusive deep venous thrombosis, and one late death unrelated to the procedure second to pneumonia in the setting of advanced colon cancer. The median time to heal was 2 months for the thermal group and 1.5 months for the MOCA group. Multivariate analysis using a Cox proportional hazards regression with the variables that were significant on univariate testing was

Table I. Patients' pretreatment characteristics

	MOCA	Thermal ablation	*P* value
No. of patients	41	25	N/A
Age, years	67.9 ± 11.6	57.2 ± 13.5	.0003
Ulcer duration, months	11.2 ± 14.4 (1-68)	9.2 ± 13.9 (1-36)	.5414
Prior DVT	13.2%	10.3%	.7049
Prior procedures	17.2%	20.8%	.7011

DVT, Deep venous thrombosis; *MOCA*, mechanochemical ablation; *N/A*, not applicable.

Table II. Mechanochemical ablation (*MOCA*) patients had a greater variety of vessels "treated" compared with thermal ablation patients

	MOCA, %	Thermal ablation, %	*P* value
GSV	56	83	.701
SSV	21.3	10	.042
ASV	4	4	.657
Giacomini	1.3	0	.457
Perforator	17.3	2.6	.0483
Multiple segments	63	16	.0010

ASV, Accessory saphenous vein; *GSV*, great saphenous vein; *SSV*, small saphenous vein.

Table III. Postprocedural outcomes

	MOCA	Thermal ablation	*P* value
Healed	73.6%	34.5%	.0006
Time to heal, months	2.27 (0.5-13)	4.43 (0.05-20)	.074
Length of follow-up, months	7.9 (0.5-20)	12.8 (0-46)	.0220
Postprocedural DVT	1.89%	3.45%	.6612
Recurrence	5.63%	0%	.192
Complications	4.89%	12%	.0598

DVT, Deep venous thrombosis; *MOCA*, mechanochemical ablation.

then performed. The two variables included were age and method of treatment. This analysis showed that MOCA was associated with statistically significantly higher rates of healing (odds ratio, 4.65; 95% confidence interval, 2.12-10.2; $P < .001$), whereas age was no longer significant ($P = .153$).

The average follow-up period was shorter in the MOCA group (7.93 ± 5.85 months), whereas thermal patients were observed for 12.8 months ($P = .022$). All patients were seen in the office postoperatively monthly, if possible. No patients were lost to follow-up. The complication rate was 4.89% in the MOCA group and 12% in the thermal group. Of the 25 patients treated with thermal ablation, there were no recurrences at mean follow-up of 12.8 months. In the MOCA arm, two patients developed ulcer recurrence and one patient developed pain resulting from inflammation at the site of a previously healed ulcer. All three of the patients were re-treated with MOCA and ultimately healed. The recurrences, after re-treatment with MOCA, were considered healed.

DISCUSSION

There have been no randomized clinical trials as yet to determine whether chronic venous ulcers heal more frequently and rapidly when patients are treated with MOCA relative to EVLT or RFA, but evidence of its efficacy is emerging from prospective and retrospective studies.[13,14] In our experience, treatment modality independently affected ulcer healing on multiple logistic regression analysis.

This finding is even more impressive when the patients are compared using variables that are associated with healing. Patients treated with MOCA suffered longer compared with thermally treated patients. Advancing age is a risk for nonhealing, yet the MOCA patients were >10 years older on average than those in the thermal group. They also had a potentially higher incidence of prior deep venous thrombosis, which delays healing.

EVLT and RFA employ thermal energy to damage the venous endothelium and to occlude insufficient veins. Because they rely on thermal energy, they require tumescent anesthesia. There is a risk of thermal skin burns and intraoperative pain.[7] There is also a risk of damage to the saphenous nerve near the GSV[15] (Fig 3). Below-knee GSV

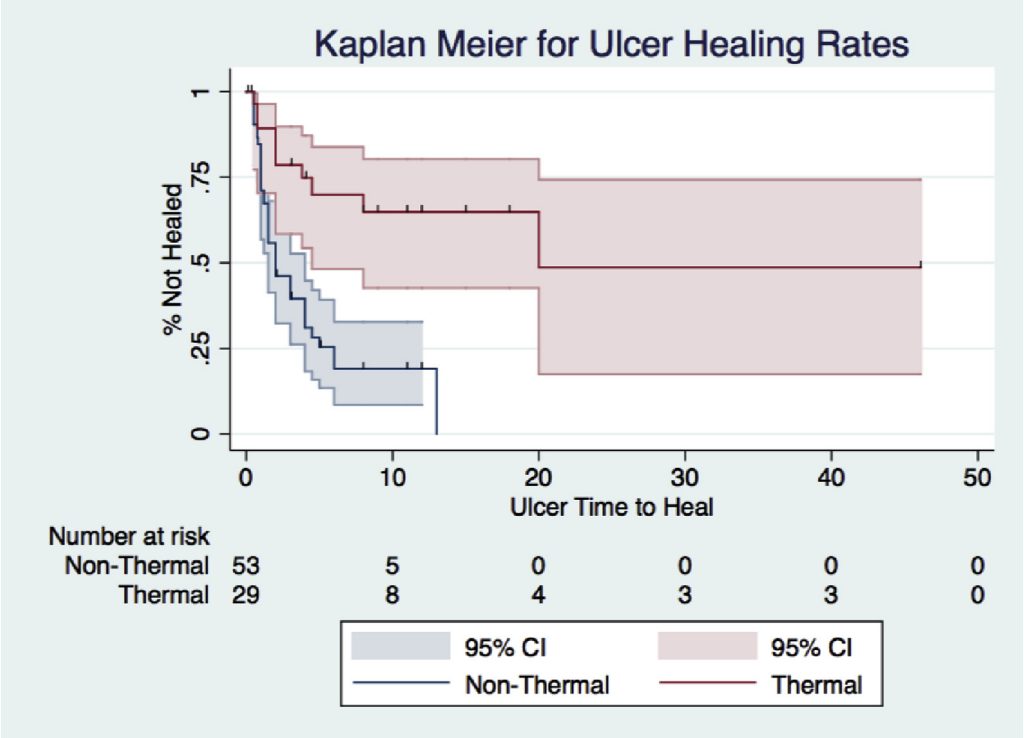

Fig 2. Kaplan-Meier curves for time to heal of thermal and nonthermal cohorts. *CI*, Confidence interval.

Fig 3. Patient 1 underwent left great saphenous vein (GSV) and small saphenous vein treatment with mechanochemical ablation (MOCA) on November 14, 2015. By March 12, 2016, the ulcer had healed.

thermal ablation had a paresthesia rate of 4%, although self-limited.[16] MOCA relies on a nonthermal combination of mechanical and chemical irritation to achieve ablation. The literature suggests that MOCA may be preferable to thermal techniques as no heat is generated and it does not require tumescent anesthesia, thereby making it less painful. This also lessens the risk of nerve damage during the procedure in the vein segments near nerve fibers.[17] Foam sclerotherapy can be performed with ultrasound as a standalone treatment as well but has a poor primary success rate at 50% 3 years later.[18] This often is due to the inability of the technique to handle treatment of long venous segments effectively.

Fig 4. Patient 2 showing two ulcers, 3.1 × 2.5 cm and 3.0 × 4.2 cm, resulting in significant reduction 2 weeks after great saphenous vein (GSV) ablation with mechanochemical ablation (MOCA) and full healing at 4 weeks (not pictured).

The lower risk of nerve damage or skin burns associated with MOCA may have led physicians to be more aggressive in their treatment of multiple segments and smaller vessels, especially perforators. Figs 3 and 4 show preprocedure and postprocedure images of patients who healed. There is a dramatic difference visible in a short time. There were three patients who had recurrence compared with none in the thermal group. This finding may be acceptable, given the low side effect profile of the MOCA technique. In addition, as with any new technology, there may be an associated learning curve. Although it has been shown that thermal ablation of the saphenous vein without previous nonoperative treatment may heal ulcers faster, the same has not been investigated for MOCA.[19] The goal of any future study involving MOCA will be to determine whether it is truly superior to other methods in healing rates and time, given that open venous ulcers carry significant morbidity.

Limitations. Whereas we believe there are important conclusions to be drawn from our study, there are limitations as well. This was a retrospective single-center review of a relatively small sample size rather than a prospective randomized controlled trial. Furthermore, patients who received MOCA had a greater number of vein segments treated compared with the thermal ablation group, which could explain some differences in healing. Notably, the follow-up period for the two groups was not the same, which has the potential to affect the statistical analysis. Prior interventions and indications for each patient were not recorded in the data collection phase. The presence or absence of deep reflux was not examined. Moreover, our primary outcome, time to heal, depends on assessment of wound healing, which is not a completely objective measure. Because ulcer dimensions were not uniformly collected, they were not included in the study, and thus it is not possible to state that ulcer treatment with MOCA was superior to treatment with thermal techniques. Because this was a single-center study, physician selection of patients to undergo thermal ablation vs MOCA could potentially have been biased.

CONCLUSIONS

MOCA is a safe and effective method for treating chronic venous ulcers and appears to provide comparable results to techniques relying on thermal ablation.

MOCA avoids the potential pitfalls of thermal ablation (thermal energy, nerve injury, skin burns) but has the ability to treat multiple venous branches and to decrease venous hypertension. Younger age and use of MOCA favored wound healing. Both time to heal and overall healing rate were better in patients treated with MOCA, although this was not based on objective ulcer healing, so a superiority claim cannot be made between the two techniques. Whereas there is not large-scale literature regarding the newer treatments of the underlying pathologic process for ulcers, there are encouraging case series and registered trials.[11,20] The best large-scale randomized trial for venous ulcers, the ESCHAR study, is a model but examined only open venous surgery and did not have a representative sample as patients may have had to wait a considerable time before being brought into the operating room. Randomized endovenous studies are necessary to further support these findings.

AUTHOR CONTRIBUTIONS

Conception and design: SK, RT
Analysis and interpretation: SK, SS, PF, WT, AV, MM
Data collection: CP
Writing the article: SK, SS, CP
Critical revision of the article: PF, WT, AV, MM, RT
Final approval of the article: SK, SS, CP, PF, WT, AV, MM, RT
Statistical analysis: SS, CP
Obtained funding: Not applicable
Overall responsibility: SK

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Submitted May 2, 2018; accepted May 1, 2019.