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Treatment of superficial venous insufficiency in a large patient cohort with retrograde administration of ultrasound-guided polidocanol endovenous microfoam versus endovenous laser ablation

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ABSTRACT

Objective: To evaluate outcomes among symptomatic patients with superficial chronic venous insufficiency treated with retrograde ultrasound-guided polidocanol endovenous microfoam 1% (PEM) or endovenous laser ablation (EVLA).

Methods: This study is a retrospective chart review from a single vein center between October 2013 and June 2019. Procedures were performed on 1070 patients with Clinical, Etiologic, Anatomic, and Pathophysiologic class 2 to 6 disease and symptomatic superficial venous reflux of the great saphenous vein or anterior accessory saphenous vein.

Results: PEM was used for 550 procedures and patients were followed for 43 ± 13 months; EVLA was used for 520 procedures and patients were followed for 57 ± 18 months. After complete treatment, the elimination of reflux was documented in 93.5% (514/550) and 92.8% (482/520) of the PEM and EVLA procedures, respectively. During the follow-up period, 18% of patients treated with EVLA returned for additional treatment to address residual symptoms in the affected leg. In C6 patients treated with PEM, 69% of ulcers (11/16) healed in less than 1 month, compared with 5% of patients (1/21) treated with EVLA. In C4 patients with lesions, resolution of spontaneous bleeding was 100% in both groups. There were no neurological or cardiac adverse events in the PEM group. Minor complications included asymptomatic deep vein thrombosis (0.5%), one common femoral vein thrombus extension, and superficial venous thrombosis (4%) in the PEM group and asymptomatic deep vein thrombosis (0.8%) and two endovenous heat-induced thromboses in the EVLA group.

Conclusions: PEM is comparable in safety and efficacy with EVLA for the treatment of saphenous reflux and associated symptoms. PEM was an effective intervention for most patients with C6 disease. Closure rates in both groups were maintained 36 months after treatment. (J Vasc Surg Venous Lymphat Disord 2022;10:999-1006.)

Keywords: Venous disease; Ablation; CEAP; Reflux

Chronic venous insufficiency is an underestimated public health problem that impacts approximately 25% of women and 15% of men over the age of 15 years.[1] Symptoms associated with lower limb venous insufficiency significantly impact a patient's quality of life.

In patients with advanced Clinical, Etiologic, Anatomic, and Pathophysiologic (CEAP) 6 disease, venous skin ulcers further exacerbate the problem. Medicare and commercial insurance programs in the United States estimate that the annual cost to manage a patient with venous leg ulcer is $18,986 and $13,653, respectively.[2] This amount represents an annual burden of $15 billion annually for payors in the United States.[2]

In the past decade, several minimally invasive techniques have resulted in greater patient access to treatment, including those with advanced disease. Nonthermal, nontumescent technologies present several advantages over their thermal, catheter-based predecessors. Although ultrasound-guided sclerotherapy using physician-compounded foam (PCF), created from mixtures of polidocanol or sodium tetradecyl sulfate and room air or CO_2, was generally used to treat smaller varicosities below the knee, it was not until recently that a Food and Drug Administration (FDA)-approved foam treatment afforded surgeons the opportunity to address venous insufficiency above and below

From the Deak Vein NJ Clinic.

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the knee in veins up to 25.9 mm.[3-7] The implementation of polidocanol endovenous microfoam (PEM) as a primary modality has slowly increased over the past few years. However, there has been some hesitancy among providers owing to concerns with safety and efficacy because of previous experiences with non-FDA-approved PCF.[8-10]

PEM was designed to treat above- and below-knee saphenous vein segments, tortuous veins, veins that had been treated previously, and smaller varicosities.[11,12] In addition to its efficacy in multiple vein segments, PEM was also designed to eliminate safety issues associated with PCF, such as neurological and thrombotic adverse events.[8,10] This goal is accomplished with a proprietary canister that produces a low-nitrogen foam with optimized physical characteristics compared with PCF.[11,12] The lower nitrogen content is intended to eliminate the chances of adverse neurological events. Further, a consistent formula for each procedure allows surgeons to deliver an appropriate volume of foam to the incompetent vein, potentially decreasing the chances of developing a deep vein thrombosis (DVT).

To date, several pivotal clinical trials have been published regarding PEM, its safety profile, and its impact on improving patient symptoms and appearance.[4-7,13,14] However, in these studies, the closure rate was not included as an outcome measure. As a result, it was difficult to compare the published efficacy outcomes of PEM with traditional measures of venous occlusion. Further, long-term studies regarding patient recurrence several months to years after treatment were not available. For this reason, we published a previous single-center study of patients treated with PEM in our practice. In that study, we reported closure rates of 94.4% in 236 patients and followed the patients for approximately 1 year.[14] Since that publication, the use of PEM in our practice has grown. Therefore, to assess the true impact of incorporating this treatment modality into our clinical care pathway, our goal with this retrospective chart review was to evaluate PEM in a larger cohort of patients for a longer period of follow-up (36 months) to compare the safety and efficacy of PEM with that of endovenous laser ablation (EVLA).

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center retrospective cohort study
- **Key Findings:** In 1070 patients with Clinical, Etiologic, Anatomic, and Pathophysiologic class 2 to 6 disease with symptomatic superficial venous reflux of the great saphenous vein or an anterior accessory saphenous vein treatment with polidocanol endovenous microfoam 1% (PEM) or endovenous laser ablation (EVLA) resulted in elimination of reflux in 93.5% (514/550) and 92.8% (482/520) of the PEM- and EVLA-treated patients, respectively. Results were maintained through 3 years of follow-up.
- **Take Home Message:** PEM is comparable in safety and efficacy with EVLA for the treatment of saphenous reflux and associated symptoms. The closure rates in both groups were maintained at 36 months after treatment.

METHODS

This retrospective chart review was performed using data collected from a single vein center using an electronic database. All patients provided written informed consent to be treated with either PEM or EVLA. The Saint Peters University Institutional Review Board guidelines determined the study to be exempt because it was a retrospective chart review of deidentified data. The data were collected and analyzed by the investigator who provided medical care to all participants. Routine data collected for all patients included demographics, use of adjunctive therapies, clinical and procedural details, and any postoperative complications. The venous valvular reflux was measured in each patient in the greater saphenous vein at the saphenofemoral junction, proximal thigh, mid-thigh, distal thigh, knee, proximal calf, mid-calf, and distal calf. The reflux was also measured in the short saphenous vein at the saphenopopliteal junction, proximal calf, mid-calf, and distal calf.

Patients were offered treatment with PEM or EVLA if they were CEAP class 2 to 6, were symptomatic, had superficial axial reflux of the great saphenous vein (GSV) or anterior accessory saphenous vein classified as retrograde flow in the saphenous vein of more than 0.5 seconds when standing, a vein diameter of more than 2 mm, and failure to have improvement in symptoms after 3 months of compression therapy (20-30 mm Hg stockings). Patients were treated with PEM if their insurance plan authorized the treatment.

Patients with treatment failure, documented as the vein not meeting criteria for closure, were treated with various methods, including phlebectomy, in the weeks and months after their initial PEM and EVLA treatment. If a patient had a failed EVLA, either ambulatory phlebectomy or PEM was used to treat the open vein. The exception would be that if a patient had treatment with PEM and had residual patent veins below the knee with significant symptoms and more than 0.50 seconds of reflux. Those patients received a second PEM treatment with polidocanol. If a patient had a failed EVLA then either ambulatory phlebectomy or PEM was used to treat the open failed vein.

Patients were followed postoperatively to collect data regarding the presence or absence of symptoms, duplex ultrasound assessments, and observation of spontaneous bleeding in C4 patients, and wound healing in C6 patients. Because this was a retrospective study, follow-up

visits were not scheduled at precise intervals. However, all patients included in the data review returned for postoperative assessment at least three times. The first visit took place between 5 and 10 days after treatment, the second between 8 and 12 weeks after treatment, and then patients returned annually to assess for recurrence of symptoms or reflux.

At each follow-up visit, patients underwent a physical examination and duplex ultrasound examination. Patients were also assessed for DVT using ultrasound examination, thrombophlebitis, skin discoloration, and phlebitis. Common femoral vein thrombus extension (CFVTE) in the PEM group is comparable to endovenous heat-induced thrombus (EHIT), but because it is a result of chemical injury to the vessel, versus heat, it is referred to as CFVTE. Examinations were performed from the common femoral vein to the tibial veins, with the saphenofemoral stump included for assessment. Examinations were performed in the standing position using a 5-MHz linear probe (Tearson15L4). Venous valve competence was assessed in the superficial, perforator, and deep veins by manual calf compression-release maneuver according to a standardized protocol.[15] Within the common femoral vein and the proximal GSV, reflux was also tested by Valsalva manoeuvres.[16] Venous reflux in the deep venous system was graded semiquantitatively using the Doppler flow information with respect to its maximum reflux velocity (0 = none, 1 = mild, 2 = moderate, and 3 = severe reflux).[17,18] Maximum reflux velocities between 10–20 cm/s were considered to be of grade 1.

Grade 2 corresponded with maximum reflux velocities ranging between 20 and 30 cm/s whereas grade 3 reflux was present at maximum reflux velocities of more than 30 cm/s and/or reflux velocities exceeding the antegrade manually provoked reflux velocities. Reflux in perforators with diameters of less than 3 mm, was considered to be insignificant. Otherwise, grades 2 and 3 reflux in the perforator veins was considered to be pathological. Deep venous insufficiency was recorded in all patients, but its presence or absence at the saphenofemoral junction or in the common femoral vein did not alter treatment.

During follow-up visits, treated veins were also evaluated along the entire length of treatment to document occlusion and/or pathological reflux. Veins were determined to be closed if there is occlusion along the entire length of the treated segment with no distinct segments of patency that were more than 5 cm long. Patients with residual varicosities or veins that are not completely occluded after the initial treatment were treated with a second treatment in the PEM group or with ambulatory phlebectomy or PEM in the EVLA group.

Data records excluded from the study included those from patients seeking treatment for cosmetic reasons, patients who did not return for follow-up visits, patients with previous DVT or superficial venous thrombosis, patients with deep vein obstruction, and patients with peripheral arterial disease (would not be able to comply with the compression protocol after treatment).

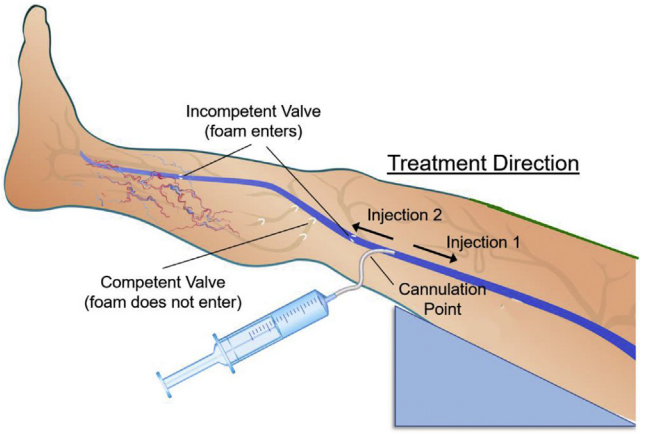

Fig 1. Retrograde administration of ultrasound-guided polidocanol endovenous microfoam (PEM). Proper positioning of patient, foam wedge, and access points for treatment. The leg is positioned at a 45° angle for several minutes before treatment.

We previously reported our technique for administering PEM 1% (Varithena; BTG International Ltd, London, UK).[14] Briefly, before administration all patients undergo a duplex ultrasound study to map perforators and identify the veins to be treated. In the patients treated with PEM, the skin at the venous access site is anesthetized with a local anesthetic. The incompetent GSV is then accessed with a 5F micropuncture needle distal to the mid-thigh perforator 10 cm above the knee fold. The lower extremity is then elevated on a foam wedge at an angle of 45° to decrease the amount of blood in the varicose veins (Fig 1). The appropriate volume of PEM is injected at a rate of 0.5 (accessory veins) to 1.0 ml/s (GSV) using ultrasound guidance. Using manual compression, the vein junction is compressed once the PEM is 3 to 5 cm caudal to the saphenofemoral junction. Venospasm is confirmed using ultrasound examination. After spasm of the GSV is noted in the treated vein, an additional 4 to 5 mL injections of PEM are delivered through the same vascular catheter. The GSV is then compressed manually in the midthigh to allow the PEM to flow retrograde into the calf. This approach, along with compression of the incompetent pathologic (grades 2 and 3) perforating vein, decreases the volume of PEM entering the calf perforators. The injected veins are observed for 3 to 5 minutes to confirm spasm. To minimize the risk of deep vein thrombi, the patient is asked to dorsiflex the foot for 30 seconds to activate the calf muscle pump and help to close the patent perforators.

Once PEM is administered and venospasm confirmed, the limb is elevated at 45° for 10 to 15 minutes with short stretch bandages wrapped over the course of the treated veins from the foot to several inches below the groin. Bandages are secured with 20 to 30 mm Hg stockings.

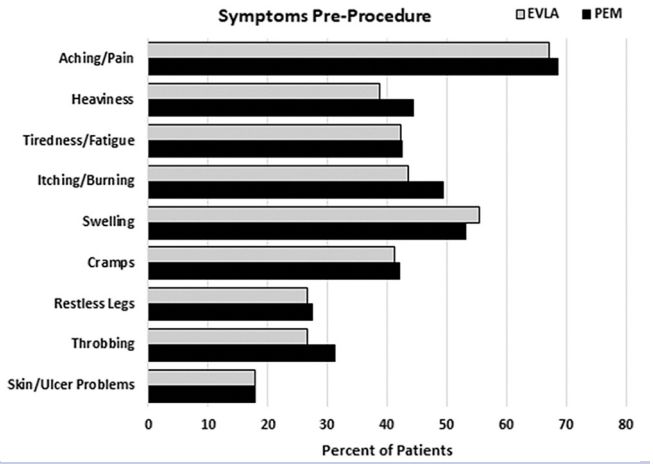

Fig 2. Symptoms before the procedure. Percent of patients reporting on individual symptoms. Patients were queried as to the symptoms that resulted in them seeking treatment. Note that most patients reported more than one symptom at baseline.

Patients are then asked to ambulate in the office for 10 minutes under observation and instructed to walk for a few minutes every waking hour after treatment. Patients remove the short stretch bandages after 24 hours and wear compression stockings for 2 weeks after treatment.

Follow-up visits took place within 5 to 7 days after treatment. Duplex ultrasound examinations were used to locate patent veins, areas of residual reflux, and deep vein thrombi. Owing to the extensive nature of chronic venous disease in many patients, and the recommendation of the FDA that no more than 15 mL of PEM be used per treatment, some patients treated with PEM required a second injection of PEM to close areas of patent veins. The second treatment of PEM was administered during follow-up visits. Patients with healed C6 ulcers were examined on two separate visits at least 2 weeks apart.

For EVLA, we use a sterile 0.035" optical integrity wire laser fiber and a total vein percutaneous introducer (5F $\times$ 45 cm). Similar to PEM treatment, the patient is placed horizontal, but the leg is not elevated before or during treatment. Tumescent anesthesia is infiltrated around the entire length of the target vein under ultrasound guidance. The treatment sheath is introduced, and the tip is positioned 2 to 3 cm below the saphenofemoral junction under ultrasound guidance. EVLA treatment is delivered using the VenaCure 1470-nm laser system (Angiodynamics, Waterlooville, UK) set at a continuous power delivery of 10 W. The EVLA patients were treated with 78.6 $\pm$ 19.5 joules/cm of GSV.

Descriptive statistics were used to analyze the patient demographics and symptoms before and after treatment. Changes in the CEAP class and wound status (healed vs unhealed) were compared with baseline values. Closure rate was compared using a two-tailed *t* test with significance set at a *P* value of less than .05.

RESULTS

In total, 1070 patients were treated for axial vein reflux. Of them, 550 were treated with PEM and 520 were treated with EVLA. The symptoms reported most frequently from both groups included pain, swelling, itching/burning, cramps, and feelings of tiredness/fatigue in the legs. Patient characteristics were similar. Complete data are provided in Fig 2. The PEM patients were observed for 43 $\pm$ 13 months and the EVLA patients were observed for 57 $\pm$ 18 months. In the PEM and EVLA groups, 65.6% (361/550) and 70% (364/520) of the patients were women, respectively ($P > .05$; Table I). Patients were of similar age, with a mean age for the PEM group of 55.4 $\pm$ 11.5 years, and 62.3 $\pm$ 12.0 years for the EVLA group ($P > .05$). CEAP class distribution in the PEM and EVLA groups was calculated. In the PEM and EVLA groups, 42% (231/550) and 46% (239/520) of patients were CEAP 2. Fifty-eight (319/550) and 54% (281/520) of patients fell into the C3 to C6 classification in the PEM and EVLA groups, respectively (Fig 3).

In the PEM group, mean vein diameter was 7.9 $\pm$ 2.8 mm. Vein diameter was similar in the EVLA group with the mean vein diameter measuring 7.9 $\pm$ 2.3 mm ($P > .05$). Reflux in the treated veins measured 2.48 $\pm$ 1.34 seconds in the PEM group and 2.20 $\pm$ 1.39 seconds in the EVLA groups, respectively ($P > .05$; Table I). The length of vein treated was longer in the PEM group, with a mean vein length across patients approximating 32.7 $\pm$ 4.1 cm. Vein length in the EVLA group was 19.8 $\pm$ 4.6 cm ($P < .05$). Most patients had moderate or severe deep venous reflux in the common femoral vein 75% (413/550) in the PEM group and 65% (343/520) in the EVLA group (Table II). Of the patients treated with EVLA, a closure rate of 92.3% (480/520) was achieved after one treatment.

Of the patients treated with PEM, 17.1% (94/550) required a second procedure to treat residual patent veins below the knee that were symptomatic and had venous valvular reflux of more than 0.50 seconds. This approach achieved a closure rate of 93.5% (514/550) in the PEM group after the second treatment. No patients in the PEM group or the EVLA group received concomitant phlebectomy.

Of the 550 patients in the PEM group, 20.3% (112/550) had a previous failed thermal ablation of the vein treated in this study. In the EVLA group, 17.7% (88/520) had a previous thermal ablation that failed (vein was no longer closed) and resulted in a recurrence of symptoms. There was no difference in the method of treatment of patients treated with PEM for the first time, or if they had a previous failed treatment with EVLA or surgery.

The closure rate was 82.7% of patients (455/550) treated with PEM after one treatment. The average PEM volume used to treat the saphenous vein was 9.9 $\pm$ 2.6 mL with the initial treatment. The second treatment of PEM

Table I. Closure results with polidocanol endovenous microfoam 1% (*PEM*) and endovenous laser ablation (*EVLA*)

	PEM (n = 550)	EVLA (n = 520)
Gender, % women	65.6	70
Age, years	55.4 ± 11.5	62.3 ± 12.0
Vein diameter, mm	7.9 ± 2.8	7.9 ± 2.3
Length of treated vein, cm	32.7 ± 4.1	19.8 ± 4.6
Reflux, seconds	2.48 ± 1.34	2.20 ± 1.39
Treatment	9.9 ± 2.6 mL	78.6 ± 19.5 joules/cm
Initial closure rate	82.9	92.8
Closure rate after seconds treatment	93.5	–

Values are percent or mean ± standard deviation.

took place during the first or second follow-up visit. The average volume of PEM used at the second treatment was 8 ± 1.2 mL. Follow-up assessments for closure using duplex ultrasound examination took place at 1 week, 3 months, 6 months, and up to 5 years after treatment. Few patients (5/550) required more than two treatments with PEM owing to recurrent symptoms in the years after the initial treatment. At the completion of treatment in the PEM group, the closure rate was 93.5% (514/550). Similarly, in the EVLA group, the closure rate was 92.8% (482/520) ($P > .05$). Of the patients treated with EVLA, 18% (94/520) required follow-up treatments for residual or recurrent symptoms. Fifty-four patients required ambulatory phlebectomy and 34 patients were treated with PEM. No patients were treated with a second EVLA procedure.

Ulcer closure. C6 patients comprised 3% (16/550) and 4% (21/520) of the patients in the PEM and EVLA groups, respectively. In C6 patients treated with PEM and EVLA, 69% (11/16) and 5% (1/21) of ulcers healed in less than 1 month (Supplementary Tables I and II, online only). Of the 16 patients with C6 ulcers treated with PEM, 93% (15/16) had successful closure of their GSV and 69% of these patients (11/16) healed their ulcer within 30 days of treatment. Of the 21 patients with C6 ulcers treated with EVLA, 100% (21/21) had successful closure of their GSV and 5% (1/21) of these patients healed their ulcer within 30 days of treatment. Recurrence was documented in two PEM patients during the follow-up period. The wound that healed in the first 30 days in the patient treated with EVLA recurred during the follow-up period. Resolution of spontaneous bleeding lesions in C4 patients was 100% in both groups.

There were no neurologic or cardiac adverse events in the PEM group. Minor treatment complications in the PEM group included asymptomatic DVT (0.4%), one CFVTE, and superficial venous thrombosis (4%). Superficial venous thrombosis in this context refers to inflammation and thrombosis of the veins, resulting in pain and swelling at the surface of the skin. The patients with asymptomatic DVT were treated with anticoagulation. The EVLA group had asymptomatic DVT (0.8%) and two EHIT. All EHITs were type II.

In all patients with DVT, thrombus resolved within 30 days of treatment, with no long-term evidence of deep reflux or obstruction found on duplex ultrasound examination. Patients with superficial venous thrombosis were monitored and encouraged to use heat, nonsteroidal anti-inflammatory drugs, and compression stockings to alleviate discomfort. All cases resolved within 30 days.

DISCUSSION

The goal of this retrospective chart review was to compare the safety, efficacy, and long-term outcomes of PEM and EVLA in our practice to determine if the outcomes were similar. With many patients presenting for treatment with failed prior treatments and/or advanced stage venous disease, there has long been a desire to incorporate a nonthermal, nontumescent modality into the clinical treatment pathway. Before the FDA approval

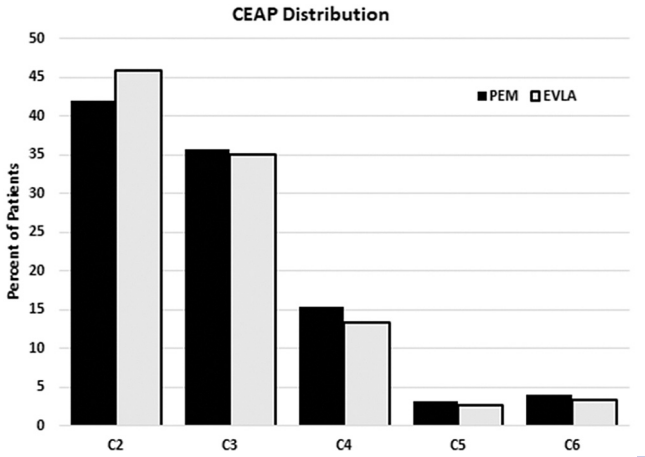

Fig 3. Clinical, Etiologic, Anatomic, and Pathophysiologic (*CEAP*) distribution of polidocanol endovenous microfoam (*PEM*) 1% and endovenous laser ablation (*EVLA*) patients. CEAP distribution. There were 22 patients with C6 ulcers or C4 bleeding ulcers treated with PEM and 23 patients with C6 ulcers or C4 bleeding ulcers treated with EVLA.

Table II. Deep venous reflux polidocanol endovenous microfoam 1% (*PEM*) and endovenous laser ablation (*EVLA*)

	PEM (n = 550)			EVLA (n = 520)		
	Mild	Moderate	Severe	Mild	Moderate	Severe
Common femoral vein	9	367	46	43	210	134
Femoral vein	–	69	10	9	87	24
Deep femoral vein	–	13			10	4
Popliteal vein	4	59	12	5	39	20
Posterior vein	–	–	–	–	–	3
Peroneal vein	–	–	–	–	–	1

of PEM in 2014, patients who were not candidates for thermal ablation, those with tortuous veins, or those with venous insufficiency below the knee were treated with PCF.

However, PCF was limited in its clinical efficacy and overall safety profile.[19,20] PEM was developed to eliminate the physical properties of PCF that led to neurological and cardiac adverse events including inconsistent bubble size and nitrogen bubbles that lead to gas embolism.[8,11,20-24]

In our practice, the main treatment has been EVLA. However, in most patients, there is a requirement to introduce a second treatment modality to reach smaller veins, tortuous veins, or areas of the leg that present with venous ulceration. Although we previously published our experiences with PEM in a large cohort of patients, there were still questions related to the efficacy of PEM versus EVLA, particularly regarding the durability of treatment. Here, we report similar closure rates (93.5% in the PEM group and 92.8% in the EVLA group) in both groups with no significant differences in recurrence at the 36-month time point after treatment. An important point is that the closure rate of 93.5% in the PEM group was achieved with two treatments in some patients to close the below-knee GSV and its tributaries. This outcome is similar to results obtained with EVLA. Although the initial closure rate with EVLA is very high (>90%), almost 20% of patients subsequently require ambulatory phlebectomy or PEM for residual symptoms during the follow-up period. This was the case with 88 of the 520 patients in this study.

Only a small number of C6 patients were included in this review. We report on outcomes at 1 month after a single treatment with EVLA or PEM to demonstrate the improvement in ulcer healing after treatment with PEM. The large discrepancy between the ulcer healing rates between the PEM and EVLA group is because the PEM can be delivered to the areas beneath the ulcer bed at the site of venous hypertension. To promote skin healing, it is necessary to abolish the venous valvular reflux at or near the site of the venous ulcer. The Linton procedure attempted to do this by interrupting the perforators near the ulcer bed.[25]

Although ulcer healing is observed without the use of venous ablation, modalities such as Unna boots have high levels of recurrence owing to the continued vascular incompetence compromising skin integrity. Although this study is not powered appropriately to draw conclusions about wound healing, there was a consistent and noticeable improvement in C4 and C6 patients at 1 month after treatment with PEM. A larger multicenter trial is needed to define the long-term durability of this treatment on ulcer healing and recurrence rates.

A concern with the use of PEM in axial veins is the potential for the foam to migrate into the deep system through a perforator, resulting in a DVT or pulmonary embolism. Pulmonary embolism was not reported in the phase III clinical trials, but DVT rates were higher than with other ablative methods.[4-6] Patients should dorsiflex the foot to activate the calf muscle pump. We documented four patients with DVT in the PEM group (0.5%). All patients were asymptomatic with nonocclusive DVTs that resolved within 30 to 90 days after treatment.

Before approval of the CPT code for PEM, there was a clear financial benefit to using EVLA as a primary treatment modality.[26] With CPT code reimbursement on par with thermal ablation modalities, and improving coverage across most major insurance plans, most patients are candidates for PEM and there is little financial difference between the two.[27,28]

This study does have limitations that should be noted. Primarily, it was a retrospective chart review. Consequently, the outcome measures were limited to those collected in routine examinations and follow-up visits that occurred at variable time points after treatment. Patients included in the study were those who continued to return to the office for follow-up visits, so we do not have data on patients who did not return for treatment. We cannot conclude whether those patients did not return because their symptoms resolved or if they sought treatment elsewhere. Also, subjective measures of patient symptoms are self-reported and binary (present, not present). It was not possible to perform a quantitative analysis on symptom severity or degree of resolution. Instead, we present data on the overall percentage of patients reporting specific symptoms pre first treatment

and for patients requesting treatment for persistent or recurrent symptoms.

The lack of an outcome validation tool sch as the Aberdeen varicose vein questionnaire or the Venous Clinical Severity Score is a major weakness in this study. We relied on the patients' complaints of pain, aching, heaviness, swelling, tingling, itching, and skin problems and the presence of venous valvular reflux of greater than 0.5 seconds as criteria for treating patients who presented for treatment and who returned for persistent or recurrent symptoms during the follow-up period. It would have been helpful to validate the treatment outcomes in these patients. Finally, the patients in this cohort had various anatomical presentations of venous disease that required more than one treatment or adjunctive treatment to resolve symptoms or reflux in accessory veins. Our data are focused on the primary treatment used to treat the axial veins (PEM or EVLA). Although clinical trials often prohibit adjunctive treatments during observational periods to eliminate confounding variables, these data truly represent real-world scenarios in which the goal is to treat patients for venous insufficiency and associated symptoms.

CONCLUSIONS

This retrospective chart review supports the efficacy of PEM as a versatile and primary treatment modality in C2 to C6 patients, with comparable results to EVLA treatment. Closure rates in both groups were greater than 92%, with durability through at least 3 years after treatment. Overall, the outcomes reported in this article provide sufficient evidence to support the use of PEM as a single agent to treat saphenous reflux and varicosities in clinical practice. Patients reported a reduction in symptoms, the complication rate was low, and there were no neurological or cardiac adverse events reported. PEM is a practical and durable treatment option for C2 to C6 patients with superficial venous reflux.

AUTHOR CONTRIBUTIONS

Conception and design: SD
Analysis and interpretation: SD
Data collection: SD
Writing the article: SD
Critical revision of the article: SD
Final approval of the article: SD
Statistical analysis: SD
Obtained funding: SD
Overall responsibility: SD

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Supplementary Table I (online only). Patients treated for ulcer or bleeding with polidocanol endovenous microfoam 1% (*PEM*)

No.	Age, years	Sex	Ulcer size, cm^2	C4/C6	Vein treated	Vein size, mm	Reflux, seconds	Previous treatment	PEM used, mL	Vein length, cm	Ulcer outcome	Subsequent treatment	Recurrence
1	95	F	3	C6	L GSV, Acc	6.4	0.84	L+S L GSV 136 Unna Boots	5	20	Healed 31 days		
2	65	M	1.5	C6	R GSV	10.6	1.59		8	35	Healed 20 days		
3	59	M	4.3	C6	R GSV	7.4	0.5		10	30	Not healed		
4	46	M	2.5	C6	R GSV	12	1.19		10	35	Healed 21 days		
5	39	F	2	C6	R GSV BK	10.3	1.4		14		Healed 12 days	2 Unna Boots PEM	210 days
6	38	M	1.5	C6	R GSV	15.1	3.47		15	35	Healed 20 days		
7	65	F	3	C6	R GSV	6.2	1.03	5 Unna Boots	9	30	Healed 27 days		
8	66	M	2.5	C6	R GSV	6.9	1.26	Phlebectomy, 3 Unna Boots	9	35	Healed 14 days		
9	49	M	6	C6	L GSV	8.1	1.07	11 Unna Boots	13	35	Not Healed		
10	49	M	0.5	C6	L GSV	4.6	1.37	PCF, 25 Unna Boots	11	20	Not Healed		
11	66	F	3	C6	R GSV	8.0	1.46		10	35	Healed 21 days		
12	53	F	6	C6	R GSV	10.5	3.54	4 Unna Boots	15	35	Not healed		
13	51	M	2	C6	R GSV	9.1	4.42		14	35	Not healed		
14	52	M	5	C6	L GSV	10.9	2.69	9 Unna Boots	13	35	Healed 7 days	1 Unna Boot	44 Days
15	60	M	1.5	C6	L GSV	10.5	2.79	3 Unna Boots	1,9	35	Healed 16 days		
16	59	M	1.5	C6	R GSV	3.3	2.36	40 Unna Boots	14	35	Not Healed		
17	72	F	Bleeding	C4	R GSV	5.6	0.5	ECS	9	35	GSV closed No bleeding		
18	57	M	Bleeding	C4	L GSV	10.6	2.83		9	40	GSV closed No bleeding		
19	39	M	Bleeding	C4	R GSV	6.4	2.03	RFA, EVLA	13	22	GSV closed No bleeding		
20	39	F	Bleeding	C4	R GSV	7.4	1.0		9	28	GSV closed No bleeding		
21	56	F	Bleeding	C4	L GSV	9.9	2.44	PCF	10	35	GSV closed No bleeding		
22	48	M	Bleeding	C4	R GSV	11.9	1.82		14	35	GSV closed No bleeding		

Acc, Accessory; *BK*, below knee; *ECS*, elastic compression stocking; *EVLA*, endovenous laser ablation; *GSV*, great saphenous vein; *F*, female; *L*, left; *M*, male; *PCF*, physician-compounded foam; *R*, right; *RFA*, radiofrequency ablation.

Supplementary Table II (online only). Patients treated for ulcer or bleeding with endovenous laser ablation (*EVLA*)

No.	Age, years	Sex	Ulcer size, cm^2	C4/C6	Vein treated	Vein size, mm	Reflux, seconds	Previous treatment	Joules	Vein length, cm	Ulcer outcome	Subsequent Treatment	Recurrence
1	58	F	2	C6	L GSV	7.7	0.5	2 Unna Boots	1537	18	Not healed		
2	60	M	2.5	C6	L GSV	4.5	0.87	EVLA, L+S phlebectomy 3 Unna boots	2026	26	Not healed		
3	60	M	3	C6	R GSV	7.7	1.5	ECS 4 Unna Boots	2510	29	Not healed	1 Unna Boots	
4	58	F	4	C6	R GSV	11.7	0.50	2 Unna Boots	1516	18	Not healed	1 Unna Boots	
5	77	M	1.5	C6	R GSV	8.8	N/A	10 Unna Boots	1908	23	Not healed	1 Unna Boots	
6	77	M	1.5	C6	R GSV	8.8	N/A	EVLA 14 Unna Boots	1889	23	Not healed	2 Unna Boots	
7	77	M	2.5	C6	L GSV	8.8	N/A	14 Unna Boots	1326	18	Not healed	18 Unna Boots	
8	79	M	2.5	C6	L GSV	8.8	N/A	EVLA 75 Unna Boots	1674	22	Not healed		
9	83	M	7	C6	L GSV	14.8	1.65	57 Unna Boots	1705	21	Not healed	47 Unna Boots	
10	44	F	8	C6	L GSV	10.5	3.89	27 Unna Boots	1463	18	Not healed	3 Unna Boots	
11	46	F	8	C6	L GSV	10.5	3.89	EVLA 29 Unna Boots	1463	18	Not healed		
12	60	M	3	C6	L GSV	7.4	3.67	15 Unna Boots	1781	22	Healed 139 days	2 Unna boots	149 days
13	66	M	5	C6	R GSV	7.9	3.42	22 Unna Boots	2005	25	Not healed	17 Unna Boots	
14	54	M	2	C6	L GSV	8.0	1.9	9 Unna Boots	2355	32	Not healed	5 Unna Boots	
15	64	F	1	C6	R GSV	7.4	1.82	2 Unna Boots	1696	22	Healed 13 days		
16	44	M	5	C6	L GSV	10.8	2.22	22 Unna Boots	1587	20	Not healed	30 Unna Boots	
17	71	F	3	C6	R GSV	8.1	0.8	L+S 68 Unna Boots	848.8	15	Not healed	69 Unna Boots	
18	60	M	2	C6	R GSV	6.7	3.0	156 Unna Boots	1527	19	Not healed	40 Unna Boots	
19	83	F	2	C6	R GSV	8.0	2.63	42 Unna Boots	1544	20	Not healed	27 Unna Boots	
20	74	M	4	C6	L GSV	7.2	2.5	134 Unna Boots Circade	1801	22	Not healed	3 Unna Boots	
21	74	M	4	C6	R GSV	7.4	0.8	134 Unna Boots, Circade	1296	16	Not healed	3 Unna Boots	
22	72	F	Bleeding	C4	R GSV	9.9	3.9	L+S, EVLA	863.2	12	GSV closed No bleeding		
23	54	M	Bleeding	C4	R GSV	10	1.02		869.3	12	GSV closed No bleeding		

ECS, elastic compression stockings; *GSV*, great saphenous vein; *F*, female; *L*, left; *L+S*, ligation and stripping; *M*, male; *R*, right.