Ultrasound-guided foam sclerotherapy of the saphenous trunks is associated with a low 5-year recurrence rate and improved quality of life in patients with chronic venous disease: A multicenter study

Fabrizio Mariani, MD,[a,b] Ludovico Carbone, MD,[c] Giampaolo Sozio, MD,[b,c] Rosaria Massaroni, MD,[a] Eleonora Andreucci, MD,[c] Valerio Bianchi, MD,[d] *and* Matteo Bucalossi, MD,[d] *Siena, Italy; Bruxelles, Belgium; and Firenze, Italy*

ABSTRACT

Objective: The study attempts to test whether ultrasound-guided foam sclerotherapy (UGFS) is a durable treatment for incompetent great saphenous vein (GSV) and incompetent small saphenous vein (SSV) in primary chronic venous disease (CVD), Clinical-Etiology-Anatomy-Pathophysiology (CEAP) clinical grade 2 to 4 disease. Secondary end points are to evaluate its safety in terms of complications, to compare patients' quality of life before and after the treatment, and to identify risk factors that may predict recurrence of CVD after UGFS.

Methods: Multicenter retrospective cohort study on 346 patients. The sclerosing agent was sodium tetradecyl sulfate (STS) in foam. The foam was prepared with the double-syringe technique (liquid-to-gas $CO_2O_{2\ 30:70}$ ratio of 1:4). The sclerosing agent concentrations were 1% for saphenous trunk diameter 4 to 7 mm, 3% for saphenous trunk of >7 mm. Sodium tetradecyl sulfate was injected directly into the GSV/SSV, achieving a total maximum volume of 10 mL per session. A median of two sessions was performed (range, 1-5).

Results: In this cohort, 205 patients were categorized as CEAP C2 (59.2%), and 141 (40.8%) had worse CVD (CEAP ≥3). The median follow-up was 60 months (range, 6-60 months). At the end of follow-up, 296 patients (85.5%) had no truncal reflux, with a 5-year disease-free time (between last procedure and evidence of recurrent disease) of 77.7 ± 2.16%. GSV and SSV showed similar 5-year recurrence-free time rates (69.9% vs 76.8%; P = ns), whereas patients with a diameter of the saphenous trunk of ≤8 mm had lower recurrence than those with >8 mm (91.3% vs 46%; $P < .0001$). Ninety patients (26%) showed CVD recurrence, occurring at a median of 48 months. A further UGFS treatment was needed in 50 symptomatic patients (14.4%), resulting in an 80% success rate. At univariate analysis, large diameter of the saphenous trunk ($P < .0001$), male sex ($P = .030$) and greater number of treatment sessions ($P = .009$) were identified as significant prognostic factors for recurrence. Immediate complications occurred in 3.7% of patients: seven headache and six visual disturbances. Endovenous foam-induced thrombosis was detected in six patients (2.8%) 1 week after treatment. Cutaneous hyperpigmentation appeared in 37 patients (10.7%). Post-treatment revised Venous Clinical Severity Score and Chronic Venous Disease Quality of Life Questionnaire 14 scores were significantly lower than before treatment ($P < .001$).

Conclusions: UGFS of the GSV/SSV is effective, safe in the long term and well-accepted by patients. UGFS is a viable option to surgery and endovenous thermal or nonthermal ablation in the treatment of saphenous trunk incompetence (CEAP clinical grade 2-4). (J Vasc Surg Venous Lymphat Disord 2025;13:102212.)

Keywords: Ultrasound-guided foam sclerotherapy; Saphenous trunks incompetence; Recurrence rate; Complications; Quality of life

Varicose veins, often associated with chronic venous disease (CVD), affect 10.4% to 39.0% of the population.[1] The high prevalence of the disease, the frequent occurrence of painful swelling of the lower limbs, the impairment of daily activities, and the increasing costs to health care systems have raised the need to identify modifiable risk factors and permanent treatments.[2,3]

Compared with conservative treatments, invasive procedures are long lasting, even when compression therapy is the mainstay of treatment. Conventional treatments of incompetent great saphenous vein (GVS) and small saphenous vein (SSV) are the surgical high ligation and stripping with local phlebectomy. However, minimally invasive techniques have been shown to be

From the Angiomedica Vein Clinic, UEMS European Training Centre in Phlebology, Siena[a]; the European Union of Medical Specialists (UEMS), Multidisciplinary Joint Committee in Phlebology, European Board of Phlebology, Bruxelles[b]; the Surgical Department Usl Toscana SudEst, Multidisciplinary Day Surgery, Alta Val d'Elsa Hospital, UEMS European Training Centre in Phlebology, Siena[c]; and the Surgical Department, Valdisieve Hospital, Florence.[d]

Correspondence: Giampaolo Sozio, MD, Surgical Department Usl Toscana Sud-Est, Zona Alta Val D'Elsa, Località Campostaggia 8, Poggibonsi, 53036 Siena, Italy (e-mail: giampaolo.sozio@uslsudest.toscana.it).

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.2025.102212

at least as effective as open surgery, leading to an expansion of indications for this type of treatment in many countries.[4,5]

Both ultrasound-guided foam sclerotherapy (UGFS) and other thermal endovenous procedures have been described to improve symptoms and related quality of life (QoL) with high levels of patient satisfaction and lower morbidities. In the short term, outcomes from UGFS, radiofrequency, and endovenous laser ablation (EVLA) seem to be quite similar,[6,7] although UGFS is likely to be more cost effective.[8] Nonetheless, most published studies on UGFS have heterogeneous cohorts and describe questionable treatment methods. Consequently, there is very low to low certainty evidence that UGFS is an effective long-term treatment for saphenous trunk.[9,10] To date, last European Society for Vascular Surgery guidelines recommended UGFS for the treatment of tributary varicose veins and incompetent GSV/SSV with a diameter of <6 mm.[11]

This study aimed to evaluate the long-term efficacy of UGFS of GSV and SSV. Secondary end points were to assess safety in terms of complications, even in larger diameter varicose trunks, and to compare patients' QoL before and after treatment.

ARTICLE HIGHLIGHTS

- **Type of Research:** Multicenter retrospective cohort study
- **Key Findings:** Ultrasound-guided foam sclerotherapy in 346 patients with primary chronic venous disease resulted in a 5-year disease-free rate of 77.7 ± 2.16%, with most recurrences in patients with a saphenous trunk diameter of >8 mm (91.3% vs 46%). In post-treatment surveys, patients reported improved quality of life ($P < .001$).
- **Take Home Message:** Ultrasound-guided foam sclerotherapy is an effective, long-term, safe, and well-accepted procedure for saphenous trunks incompetence.

METHODS

We performed a multicenter retrospective cohort study on 346 patients.

Patient selection. All patients undergoing only UGFS for GSV/SSV incompetence between January 2018 and December 2023 were identified retrospectively from three regional referral centers (Campostaggia Hospital, Poggibonsi, Siena, Italy; Angiomedica Vein Clinic, Colle Val d'Elsa, Siena, Italy; and Valdisieve Hospital, San Francesco, Firenze, Italy).

The inclusion criteria were primary CVD, unilateral GSV or SSV axial reflux in a symptomatic patient confirmed by duplex ultrasound examination, Clinical-Etiology-Anatomy-Pathophysiology (CEAP) clinical classification C2 to C4 and age 20 to 85 years.

A complete duplex ultrasound scan of the deep and superficial venous system of the lower limb was performed with the patient in the supine position. Duplex ultrasound examination for venous reflux was performed with the patient in an upright position with the knee of the leg being examined slightly flexed at the GSV at the saphenofemoral junction (SFJ) and at the thigh, and at the SSV at the saphenopopliteal junction (SPJ) and at the calf.[12] Reflux had to be provoked by a Valsalva maneuver and manual compression of the thigh or calf. Incompetence was defined as a reflux of >0.5 seconds. The diameter of the saphenous trunk was measured in the upright position in a vein segment without focal dilatation (at 15 cm from the SFJ and at 3 cm below the SPJ). Other useful ultrasound information included accurate venous mapping, showing the course of the reflux, the length of the refluxing trunk, local saphenous dilatations and/or aneurysms, and the course and diameters of the main tributaries and communicating veins.[13]

Exclusion criteria were incompetent saphenous trunk with hypoplastic segments (usually at the thigh), prior treatment for CVD, allergy to the sclerosant, acute deep vein thrombosis (DVT) and/or pulmonary embolism, acute superficial venous thrombosis, local infection in the area of sclerotherapy or severe generalized infection, prolonged immobility and bed rest, known right-to-left shunting through a patent foramen ovale, pregnancy, severe peripheral arterial occlusive disease, strong predisposition to allergies, moderate to severe risk of venous thromboembolism, neurological disorders, migraine and visual disturbances after previous foam sclerotherapy, lymphoedema, BMI of >40 kg/m^2, severe general illness, and malignancy.

Anticoagulants, warfarin/direct thrombin inhibitors, low-molecular-weight heparins, fondaparinux, and antiplatelet agents (aspirin, clopidogrel) were not discontinued.

This study was conducted in accordance with the tenets of the Declaration of Helsinki. Patient confidentiality and data protection were ensured throughout the study by anonymizing patient information and using secure electronic databases. All patients provided written informed consent before participating in the study and the institutional review board approved the collection of data (UGFS ver. 1, USL Toscana sudest). Publication consent is not required, because no photographs or images that contain identifiable individual characteristics or vascular images were used. The results of this study were reported according to the STROBE statement for cohort studies.[14]

Peri-UGFS treatment care. All cases were performed by vascular surgeons or angiologists with same technique. To be credentialed for study entry and minimize bias,

the performing physicians has to have experience in both open and minimally invasive techniques. All vascular specialists were not blinded when formulating the hypothesis.

Patients in CEAP clinical classes 3 to 4 were treated with compression therapy (bandages and elastic stockings) to reduce edema before starting UGFS.

The sclerosing agent was sodium tetradecyl sulfate (STS [Fibrovein]) in foam. The foam was prepared with the double-syringe method (liquid-to-gas CO_2O_2 $^{30:70}$ ratio 1:4). The automated Varixio foam preparation system has replaced the physician compounded foam in the last 2 years of our study. The sclerosing agent concentrations were 1% for a saphenous trunk diameter of 4 to 7 mm and 3% for saphenous trunk of >7 mm.

Started injections (5 mL Terumo syringe, 21G needle) were proximal with the patient in the lying position. Usually, the first injection of 4 mL of foam was given between 5 and 10 cm from the SFJ or SPJ, and the second at mid-thigh/mid-calf in the first session. The thigh (GSV) or calf (SSV) injections are given near to the outlets of the major tributaries and/or the incompetent perforating veins. Foam was injected rapidly over a few seconds, with a maximum foam dose of 4 mL per injection and 10 mL per session. Foam progression is carefully monitored with duplex ultrasound imaging. The total amount of foam used depends on the size of the veins and the degree of vein spasm when the foam is injected. Typically, 4 mL of foam will treat approximately 10 to 15 cm of saphenous trunk with an average diameter of ≤8 mm. However, we recommend injecting enough foam so that the vein is in spasm and full of foam as observed by duplex ultrasound examination. Normally, we have injected fresh foam every 15 to 20 cm along the saphenous trunk, although there is no evidence to support that specific distance. The foam fills the vein and spreads first proximally and then distally from the injection point for approximately 10 to 15 cm. The foam loses its structural stability and is usually disrupted at the outlet of the superficial epigastric vein at the SFJ. The foam is usually disrupted and deactivated near the popliteal vein at the SPJ, or near the gastrocnemius trunk if the SSV flows into it. If hyperechogenic firm foam was detected in axial veins below the fascia, the injection is stopped and the patient asked to dorsiflex and plantarflex his or her ankle. A minimum of 1 to 2 minutes between each injection shall be counted to minimize the amount of foam used, although this is a non-evidenced-based time. No ultrasound-guided compression was performed. Because the GSV was competent below the knee in 239 legs (90.9%), we treated the GSV at the thigh first and the tributaries were treated afterward.

Compression therapy was provided by eccentric compression with pads and post-operative stocking after treatment for 7 days.[15] After first week, the stocking was worn during the day and removed at night until the end of treatment. Low-molecular-weight heparin (40-60 mg enoxaparin) was given in patients with limited mobility, with larger varicose veins (diameter of >8 mm), confirmed prior CEAP class 3 to 4 disease and/or with previous deep or superficial vein thrombosis and known inherited or acquired untreated thrombophilia. Patients were instructed to maintain daily habits and exercise.

Up to five sessions were performed to complete the first treatment. Patients had duplex ultrasound evidence of complete ablation at the end of the treatment. Patients attended the outpatient clinic at 1, 3, 6, and 12 months and then annually. A full physical examination and lower extremity duplex ultrasound examination were performed routinely at each follow-up visit.

As described by the National Institute for Health and Care Excellence, complete ablation refers to complete occlusion of the incompetent GSV and SSV along the entire length of the vein; recanalization refers to the presence of venous flow with or without reflux in a previously occluded vein.[16] The presence of symptomatic residual or recurrent saphenous trunks reflux after the end of UGFS treatment was considered a treatment failure. Patients with residual, recurrent, or new truncal symptomatic reflux are offered further UGFS treatment.

Measures. Demographic information, such as age and sex, along with basal characteristics (including duplex ultrasound mapping, anatomy and length/diameter of the saphenous trunk, QoL and venous disease severity), UGFS procedure data (including concentrations and injected volumes of sclerosing agent, preparation of the foam, injection technique, sites of the injection points, duplex ultrasound checks during and after the foam injections, compression therapy), postprocedure adverse sequelae, and complications were recorded. Adverse sequelae are hyperpigmentations, temporary swelling, teleangectatic matting, pain, localized urticaria, and stress-related symptoms, such as vasovagal reflex. Immediate complications are systemic allergic reactions, intraarterial injections, headaches, nausea, vomiting, paresthesias, and transient visual disturbance (defined as transient visual phenomena related to the onset of a migraine headache attack without visual aura lasting 5-60 minutes), and delayed complications are DVT, superficial vein thrombosis, endovenous foam-induced thrombosis, or skin necrosis.

CVD was classified using the CEAP classification system and its 2020 revision.[17] CEAP classification was determined by direct physical inspection and color duplex investigation of the lower extremities by providers at each site (C0, no visible or palpable signs of venous disease; C1, telangiectasias or reticular veins; C2, varicose veins; C3, edema; C4, skin and subcutaneous tissue changes; C5, healed venous ulcer; and C6, active venous ulcer).

QoL was assessed with the scoring tools: the revised Venous Clinical Severity Score (r-VCSS),[18] and the short Chronic Venous Disease Quality of Life Questionnaire (CIVIQ-14),[19] at baseline before treatment and in the post-treatment period. The r-VCSS included 10 features of venous disease and was scored on a severity scale of 0 to 3. These included skin changes (extended to include pigmentation), inflammation and induration, ulcers (including number, size, and duration), and a category for compression, with higher scores indicating better compliance. Total score ranges from 0 to 30. In the abbreviated CIVIQ-14 questionnaire, symptoms experienced in the 4 weeks before screening were rated on a Likert scale from 1 to 5 (1 [no pain/not bothered at all] to 5 [severe pain/impossible to do anything]). The 14 questions used in the abbreviated CIVIQ were categorized as follows: pain (3 questions), physical functioning (5 questions), and social activities (6 questions). Three scores were calculated: a score per item (range, 1-5), a score per dimension (range, 0-100), and a global score (range, 0-100). The score for each dimension was obtained by adding the scores for each individual item, and the global index was obtained by summing the scores for the 14 items. Absolute scores were converted to an index. Patient satisfaction was defined as a CIVIQ 14 score of <35.

Statistical analysis. Owing to the descriptive nature of this study, sample size calculations were not performed, and the cohort size was determined by the selected criteria.

Categorical variables were reported as numbers and percentages. Continuous variables were reported as mean and standard deviation or median and range, depending on the normal distribution of the data.

Recurrence-free time was defined as the months between the first procedure and evidence of recurrent disease, and disease-free time was defined as the number of months between the last procedure and evidence of recurrent disease. Both were plotted using the Kaplan-Meier estimator. Odds ratios (ORs) and 95% confidence intervals (CI) for risk factors associated with recurrence disease were estimated using Cox regression.

The r-VCSS and CIVIQ-14 were compared using Wilcoxon matched-pairs signed rank test.

Statistical analysis was performed using the SPSS 20.0 software package (SPSS Inc., Chicago, IL).

RESULTS

A total of 346 patients met inclusion/exclusion criteria: 85.5% were female (n = 296), median age was 62 years (range, 23-83 years). The median follow-up was 60 months (range, 6-60 months).

Before treatment. Clinical characteristics have been reported in Table I. Most patients presented with involvement of the GSV (n = 263 [76%]). More than one-half of the patients presented symptoms (n = 240 [70%]), such as edema, heaviness and/or pain, and median CIVIQ-14 was 45 (range, 18-70). At physical examination 205 patients were categorized as CEAP C2 (59.2%), 124 (35.8%) as CEAP C3, and 17 (5.0%) as CEAP C4.

UGFS. Procedure data are reported in Table II. At each session, a median of 6 mL of foam was injected directly into the saphenous trunk. Foam was equally prepared by mixing 1% or 3% STS. A median of two treatment sessions was performed (range, 1-5).

Immediate complications occurred in 3.7% of patients: headache seven cases and transient visual disturbance in six patients. These complications resolved spontaneously within an hour of onset. Among delayed complications, endovenous foam-induced thrombosis (American Venous Forum ARTE classification[20]: 5 cases in class 1, 1 case in class 2) was described in six patients (2.8%) 1 week after UGFS. No superficial vein thrombosis superficial vein thrombosis and/or DVT was detected during treatments. Cutaneous hyperpigmentation appeared in 37 patients (10.7%) and in 21 patients the transient pigmentation faded within 24 months.

Follow-up. After treatment characteristics have been reported in Table III. The median follow-up time was 60 months (range, 6-60 months).

On lower limb venous Duplex ultrasound examination, evidence of reflux was described in 125 cases (36.1%) occurring in a median time of 48 months. Notably, marked recurrence was reported in 90 (26%) patients, whereas 35 patients had asymptomatic reflux. Fig 1, *A*, shows recurrence-free rate of the entire population. A total of 50 symptomatic patients (14.4%) underwent a further UGFS treatment, resulting in an 80% success rate (40 cases). At the end of follow-up, 296 patients (85.5%) had no (261 cases) or asymptomatic (35 cases) truncal reflux, with a five5year disease-free time rate of 77.7 ± 2.16% (Fig 1, *B*).

Patients with marked reflux in the GSV or SSV showed similar 5-year recurrence-free time rates (69.9% vs 76.8%; P = ns; OR, 1.395; 95% CI, 0.85-2.28) (Fig 2, *A*), whereas significantly differences in terms of patients' satisfaction were found (Table IV). When categorized by the saphenous trunk diameter, 5-year reflux-free time was longer in patients with a preoperative diameter of ≤8 mm than >8 mm (91.3% vs 46%; $P < .0001$; OR, 0.115; 95% CI, 0.05-0.23) (Fig 2, *B*).

Baseline prognostic factors. Table V shows the predictive factors for the recurrence of clinical reflux disease. A greater number of treatment sessions was associated with a higher recurrence rate, especially for patients who received four or more sessions ($P < .0001$).

QoL. Almost all patients (n = 329 [95.1%]) reported being satisfied with the procedure (CIVIQ-14 score of <35).

Table I. Before treatment characteristics

Characteristics	No. (n = 346)	Percentage
Male/female	50/293	14.5/85.5
Age, years	60.5 ± 13.2	
Basal CEAP		
2	205	59.2
3	124	35.8
4	17	5
GSV/SSV	263/83	76/23
Right/left	213/133	61.6/38.4
Diameter, mm	7.1 ± 1.3	
Basal symptoms		
Edema	131	37.9
Heaviness	106	30.6
Pain	76	22
Basal r-VCSS	5.4 ± 2.3[a]	
Basal CIVIQ-14	45 (38-54)[a]	

CEAP, Clinical-Etiology-Anatomy-Pathophysiology classification system; *CVD*, chronic venous disease; *GSV*, great saphenous veins; *SSV*, small saphenous veins; *r-VCSS*, revised Venous Clinical Severity Score; *CIVIQ-14*, short Chronic Venous Disease Quality of Life Questionnaire. Values are mean ± standard deviation, number (%), or median (interquartile range).
[a]Data available for 213 patients.

Fig 3 compared before treatment and after treatment r-VCSS score (Fig 3, *A*) and CIVIQ-14 score (Fig 3, *B*). Patients with higher scores are equally distributed among the centers (92.9%, 96.2%, and 95.6% in each group).

After treatment symptoms were registered in 3.8% of patients and no case of edema, heaviness, or pain were reported, although 109 patients (31.5%) required prolonged use of thigh compression stockings (Table III).

DISCUSSION

UGFS treatment shows a high level of variability, with no validated techniques currently available. Published case studies are generally unspecific; there is a tendency to group sclerotherapy of varicose veins with different anatomical and clinical characteristics, such as saphenous veins, tributary veins, and the anterior accessory saphenous vein or others.[21] The current main goal is to select the optimal treatment, tailored to the severity of the CVD, to ensure long-lasting results while providing the most cost-effective and least invasive outcome.[22] We focused on patients with a symptomatic CVD of the GSV or SSV using a standardized technique that relies heavily on accurate venous mapping, measurement of vein diameter, and assessment of flow rates (trunks, tributaries and perforating veins). C5 and C6 patients were excluded from our retrospective analysis to ensure a homogeneous study cohort and to provide precise data on the efficacy of UGFS in a well-defined patient population that commonly undergoes the technique. It was mandatory that major symptomatic refluxes were treated first, and that nonrefluxing venous tracts were preserved to ensure optimal superficial venous outflow. Our method allowed the use of low doses (4 mL per injection and 10 mL per session), concentrations (1% for saphenous trunk diameter of 4-7 cm, 3% for trunk diameter of >7 cm) of foam sclerosing agents, and the selectivity of the treatment.

Table II. Ultrasound-guided foam sclerotherapy (UGFS) characteristics

Characteristics	No. (n = 346)	Percentage
Sodium tetradecyl sulphate 1%/3% (first session)	176/170	50.9/49.1
Injected foam (first session), volume (range)	6 (4-8)	
Total sessions		
1	49	14.2
2	153	44.2
3	113	32.7
4	23	6.6
5	8	2.3
Stockings	250	72.2

Values are number (%) or mean ± standard deviation.

Table III. Follow-up data

Characteristics	No. (n = 346)	Percentage
Saphenous reflux (after first treatment)	125	36.1
Retreatment	50	14.4
Saphenous trunk (at the end of follow-up)[a]		
Total occlusion	245	70.9
Partial recanalization without symptoms	51	14.6
Partial recanalization with symptoms	3	1
Complete recanalization with symptoms	47	13.5
After treatment CEAP		
1	126	59.1[b]
2	77	36.2[b]
3	6	2.8[b]
4	4	1.9[b]
r-VCSS	1.84 ± 1.7[b]	
CIVIQ-14	16 (14-22)[b]	

CEAP, Clinical-Etiology-Anatomy-Pathophysiology classification system; *CVD*, chronic venous disease; *GSV*, great saphenous veins; *SSV*, small saphenous veins; *r-VCSS*, revised Venous Clinical Severity Score; *CIVIQ-14*, short Chronic Venous Disease Quality of Life Questionnaire. Values are mean ± standard deviation, number (%), or median (interquartile range).
[a]"Total" when occlusion of the saphenous trunk without reflux was achieved after last treatment, otherwise "partial recanalization"; in "complete recanalization" reflux was symptomatic.
[b]Data available for 213 patients.

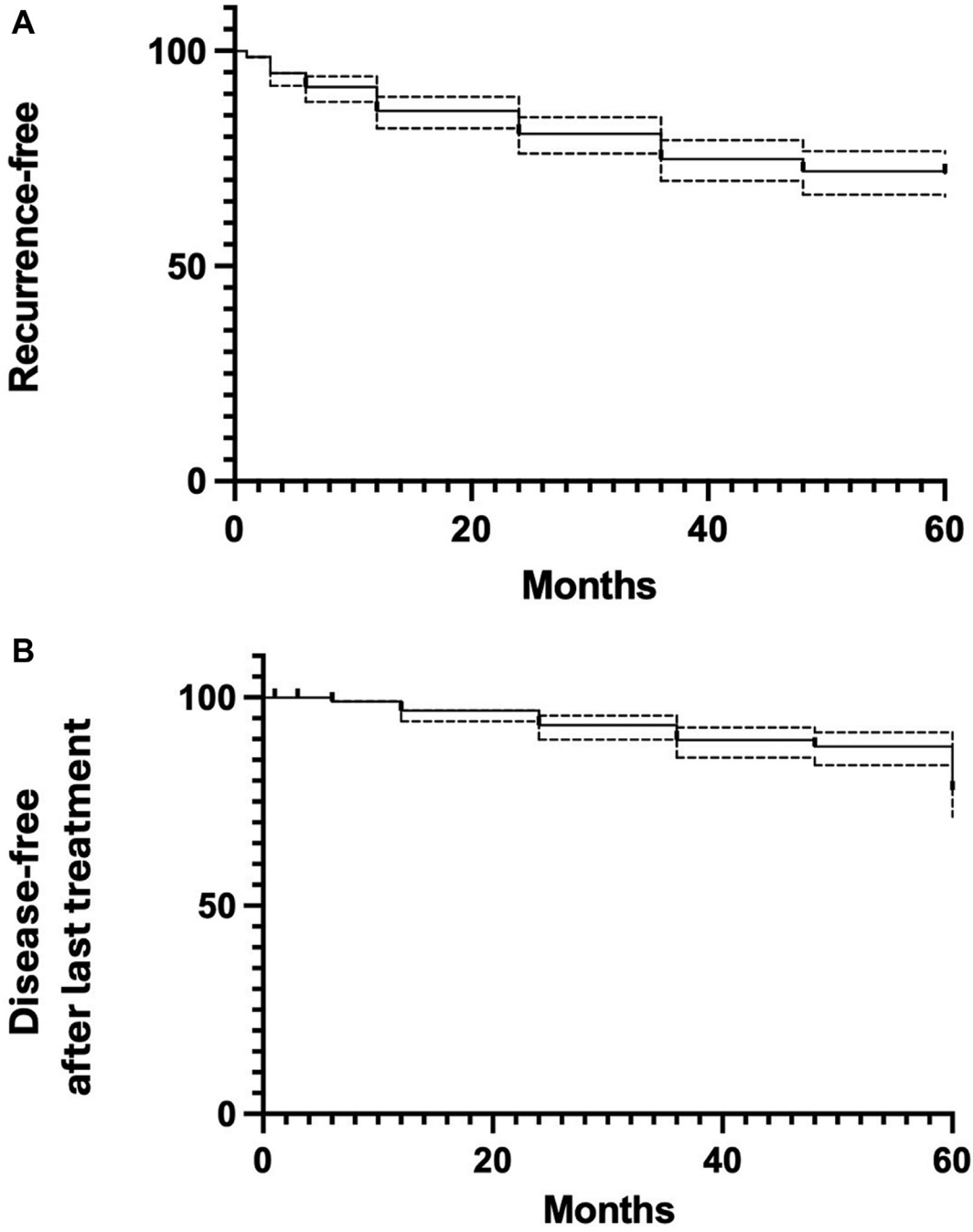

Fig 1. (A) recurrence-free time after first ultrasound-guided foam sclerotherapy (UGFS) treatment and **(B)** disease-free time in the entire cohort.

Some studies showed an 80% to 93% efficacy after the first treatment.[23] However, most studies did not distinguish between symptomatic and asymptomatic disease after treatment failure and highlighted a common preference for treating recurrences with open surgery or thermal ablation.[24] Approximately one-half of our patients showing residual or recurrent saphenous trunk incompetence were asymptomatic at the end of the study and did not require any treatments, whereas symptomatic cases (14.5%) treated again with the same technique resulted in an 80% success rate. A Dutch trial showed noninferiority in the recurrence rate of USGF treatment compared with surgical stripping with high ligation for reflux associated with venous symptoms (11.3% vs 9.0%), although follow-up was limited to 2 years after surgery.[25] The more recent re-analysis of their results described a low rate of symptomatic recurrence in the surgery group 8 years after treatment (72.1% vs

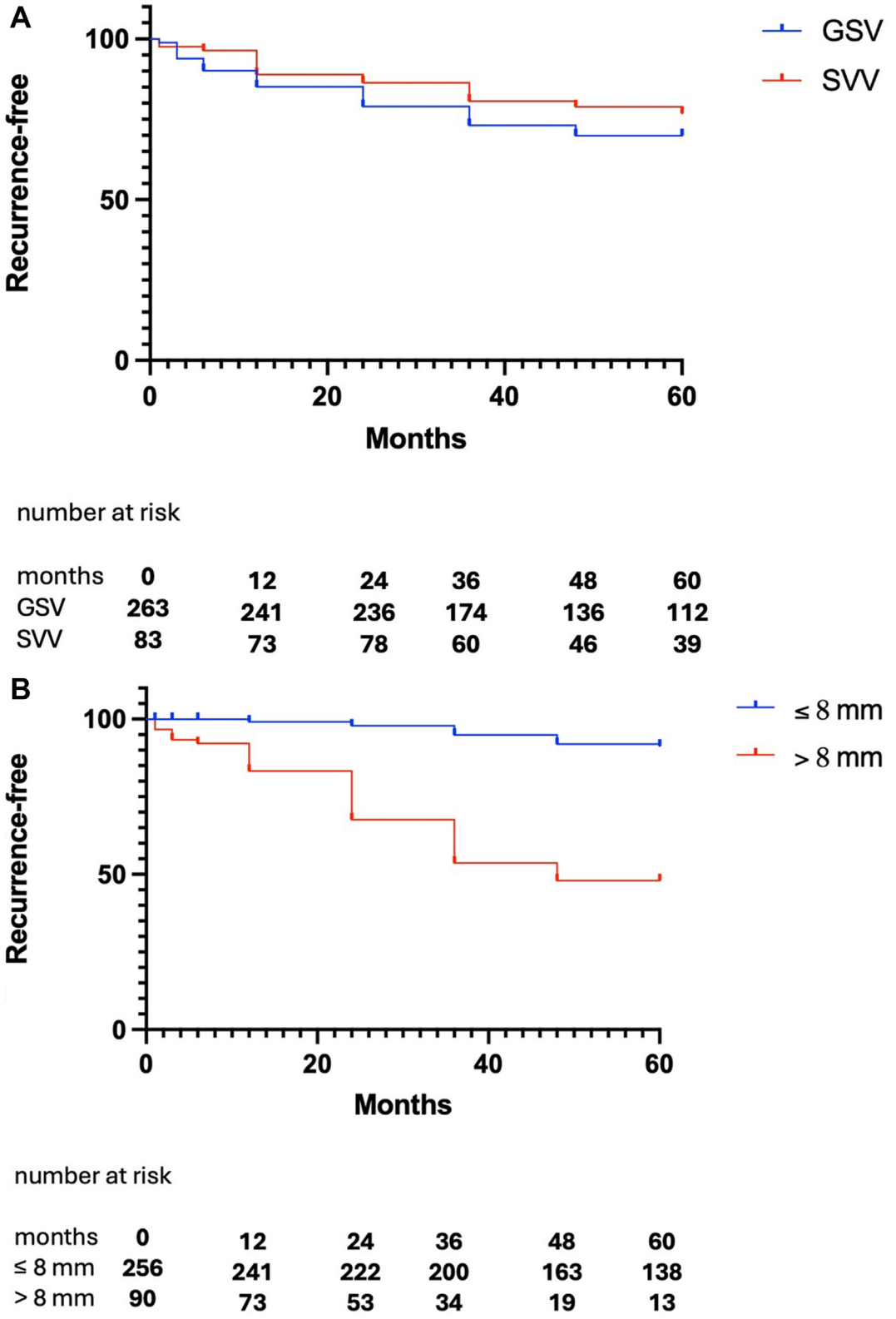

Fig 2. Recurrence-free time in patients: **(A)** with reflux in the great saphenous veins (*GSV*) vs small saphenous veins (*SSV*) and **(B)** with an insufficient vessel of ≤8 mm vs >8 mm in diameter.

Table IV. Symptoms after great small saphenous (*GSV*) vs small saphenous vein (*SSV*) treatment

Characteristics	GSV (n = 162)	SSV (n = 51)	*P* value
After treatment CEAP			ns[a]
≤2	156	47	
>2	6	4	
After treatment symptoms	7	1	ns[a]
r-VCSS (mean)	2	1.3	**.006**[a]
CIVIQ-14 (median)	17.5	15	**.016**[a]

CEAP, Clinical-Etiology-Anatomy-Pathophysiology classification system; *CVD,* chronic venous disease; *GSV,* great saphenous veins; *SSV,* small saphenous veins; *r-VCSS,* revised Venous Clinical Severity Score; *CIVIQ-14,* short Chronic Venous Disease Quality of Life Questionnaire.
Boldface entries indicate statistical significance.
[a]Data available for 213 patients.

55.1%). Major failures have been described in the SFJ and above-knee GSV between patients treated with UGFS. Nevertheless, only patients with GSV disease were treated and there was a 50% dropout rate, which prevents a realistic view of the failure rate in the general population.[26] We speculate that careful assessment of symptoms and close monitoring will allow the patient to be directed to early treatment of possible relapses and prevent deterioration in QoL. The CLASS trial, which involved 798 participants with primary varicose veins, showed that minimally invasive techniques (UGFS and EVLA) were associated with a faster return to normal activities than surgery. In addition, UGFS was superior to EVLA in terms of return to full-time work and short and long distance walking.[27] In our cohort, both questionnaires showed a significant improvement in QoL after UGFS, further demonstrating its long-term safety and patient acceptance.

The incidence of nonsaphenous recurrences after first treatment of the saphenous trunks was not analyzed. The available evidence suggests that surgical and endovenous ablative treatments have similar recurrence rates.[10,28] A reduction in invasiveness, an increase in accuracy, and selectivity in the treatment of endovenous techniques have been associated with a decrease in varicose recurrence, particularly at the SFJ or SPJ levels, where the occurrence of new vessels is virtually eliminated.

Table V. Univariate analysis

Variables	Univariable Cox	
	HR	*P* value
Sex, male/female	0.53 [0.30-0.97]	**.030**
Age, ≤65/>65 years old	0.84 [0.55-1.27]	.404
Vessel diameter, ≤8 mm/>8 mm	4.80 [2.82-8.23]	**<.0001**
CEAP class, 2/3-4	0.85 [0.52-1.38]	.506
Sodium tetradecyl sulphate (first session), 1%/3%	1.32 [0.74-2.33]	.345
Injected foam, ≤6 mL/>6 mL	0.86 [0.46-1.59]	.642
Total sessions, 1-2/>2	2.50 [1.26-5.0]	**.009**

CEAP, Clinical-Etiology-Anatomy-Pathophysiology classification system; *HR,* hazard ratio.
Boldface entries indicate statistical significance.

It has been hypothesized that certain factors, such as the preparation and the concentration of the foam sclerosant, the lifecycle of the foam plug, the injection technique, the degree of vasospasm generated, or the postsclerotherapy compression regimen, may influence clinical outcomes.[20,29] Other factors can influence the filling of a vein with foam and the resulting venous spasm: the position of the lower limb, the diameter of the vein, the venous flow rates (shear stress and shear rate), and the presence of any turbulence in the trunk, as well as the outlets and diameters of the tributary veins (varicose veins and/or normal veins) and/or perforating veins, the sites of the foam injection. Foam biophysic studies and duplex ultrasound scans show that, at high shear rates, the injected foam loses stability and the foam structure is disrupted. This means that, after the foam has been injected, it loses its effectiveness at the SFJ-SPJ owing to the presence of epigastric and common femoral or popliteal flow. At the saphenous outlet of tributaries or perforating veins with a diameter of >1 mm, the foam becomes inactive and affects the outcome of the treatment; because of this, the sites of the injection points should be close to the outlets of the major tributaries and perforating veins along the saphenous trunks. The foam injection rate must be fast to allow the foam plug to spread better. Current biophysical methods of foam characterization can help to optimize therapeutic efficacy, although there remains a lack of knowledge about the flow behavior of foam plugs in the venous environment during treatment.[30] The addition of catheter-directed foam sclerotherapy with or without perisaphenous tumescent infiltration collapses the vein, increasing surface contact and the degree of venous filling. Although long-term results are not yet available, it seems to offer a higher success rate than UGFS in the short term and in the treatment of saphenous trunks >8 mm in diameter.[31] However, our approach consisted of a direct injection into the vein, which represents the least invasive and the most cost-effective option. Furthermore, this method allowed to inject fresh foam in a shorter time frame and at multiple locations along the saphenous trunk, thereby enhancing the efficiency and precision of the procedure.

Moreover, our study demonstrated a significantly low recurrence rate when treating saphenous trunks ≤8 mm in diameter (5-year rate of 91.3%), thus extending the availability of USGF to a larger number of patients than recommended by the most recent guidelines (OR, 4.80; 95% CI, 2.82-8.23; $P < .0001$).[11,32] We speculate that,

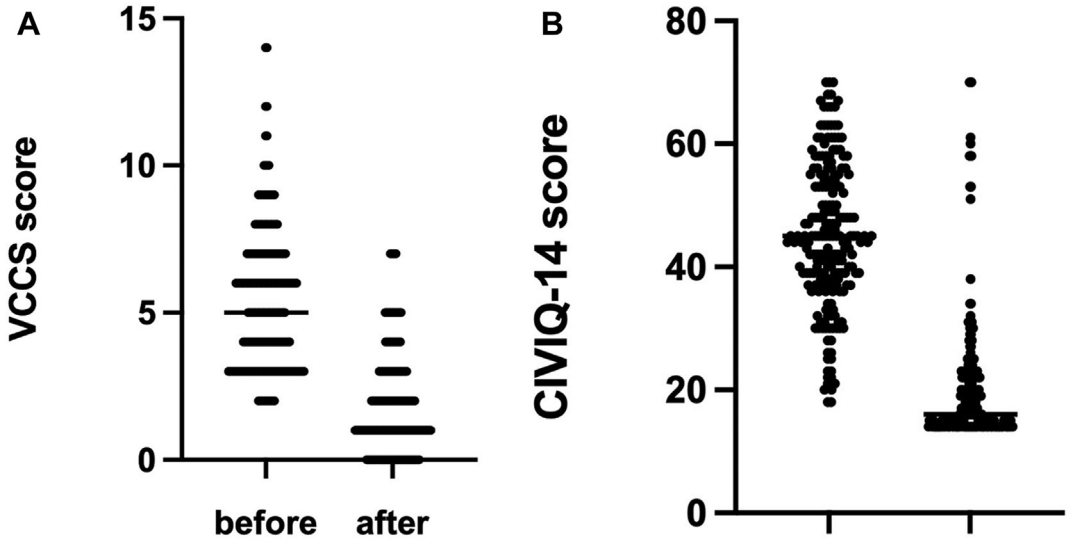

Fig 3. Boxplot showing patients satisfaction using **(A)** revised Venous Clinical Severity Score (*VCSS*) score ($P <$ .001) and **(B)** short Chronic Venous Disease Quality of Life Questionnaire (*CIVIQ-14*) score ($P <$ .001).

for a larger diameter of the saphenous trunk, early treatment of varicose tributaries could result in a reduction of the diameter of the saphenous trunk, ultimately improving long term outcomes. More studies are needed. Male sex (OR, 0.53; 95% CI, 0.30-0.97; $P = .030$) and more than two treatment sessions (OR, 2.5; 95% CI, 1.26-5.0; $P = .009$) were also identified as significant prognostic factors for recurrence, suggesting that these patients were treated for more clinically severe disease.

Another interesting issue is the morbidity rate of UGFS and other ablation treatments compared with open surgery. We observed a negligible amount of both immediate (<4%) and delayed (<3%) postprocedural complications. Some patients developed redness and pain over the treated veins, even with adequate compression, particularly in the case of large extrafascial varicose veins close to the skin. In these patients, needle puncture of the semifluid sclerothrombus was performed during the first 2 weeks after treatment, which provided symptomatic relief and reduced skin pigmentation in most cases. Endovenous foam-induced thrombosis was the only major complication detected and was treated with fondaparinux 5 mg/day until the thrombosis resolved (mean, 10 days), with no DVT and/or pulmonary embolism. In the Dutch trial, thrombophlebitis as an adverse event of UGFS occurred in 7.4% of patients, with one case of DVT and one case of pulmonary embolism, both treated with oral anticoagulant therapy. Other early complications, such as groin infection, hematoma, or paresthesia, were more common after surgery and improved overall hospital costs.[25]

Given the retrospective nature of the study, the available data may not be representative of the whole population, and randomized groups need to be analyzed in further studies.

CONCLUSIONS

We suggest that UGFS treatment of the GSV/SSV is safe and effective in the long term. The results are strictly dependent on the therapeutic indications, the accuracy of the diagnosis, the vein mapping, and the appropriate UGFS technique. Saphenous trunks with a diameter of ≤8 mm have a low recurrence rate, similar to that of endovenous thermal and other nonthermal procedures. For recurrent disease, a further treatment has a high success rate, but because patients are at risk of developing recurrences, they should be kept under surveillance. Moreover, UGFS results in significant improvements in symptoms and QoL, with high levels of patient satisfaction and a rapid return to normal activities. Although further work is needed to optimize the UGFS technique, our study shows that there is no significant difference in clinical outcomes between UGFS and other ablation techniques. Because UGFS is less expensive and less invasive, it is likely to be a more cost-effective option for most patients.

AUTHOR CONTRIBUTIONS

Conception and design: FM, GS, MB
Analysis and interpretation: LC, EA
Data collection: FM, GS, RM, VB, MB
Writing the article: FM, LC, EA
Critical revision of the article: GS, RM, VB, MB
Final approval of the article: FM, LC, GS, RM, EA, VB, MB
Statistical analysis: Not applicable
Obtained funding: Not applicable
Overall responsibility: GS

FUNDING

None.

DISCLOSURES

None.

REFERENCES

1. Gawas M, Bains A, Janghu S, Kamat P, Chawla P. A Comprehensive review on varicose veins: preventive measures and different treatments. *J Am Nutr Assoc*. 2022;41:499–510.
2. Farah MH, Nayfeh T, Urtecho M, et al. A systematic review supporting the Society for Vascular Surgery, the American Venous Forum, and the American vein and Lymphatic Society guidelines on the management of varicose veins. *J Vasc Surg Venous Lymphat Disord*. 2022;10:1155–1171.
3. Davies AH. The Seriousness of chronic venous disease: a review of real-world evidence. *Adv Ther*. 2019;36:5–12.
4. Nijsten T, van den Bos RR, Goldman MP, et al. Minimally invasive techniques in the treatment of saphenous varicose veins. *J Am Acad Dermatol*. 2009;60:110–119.
5. Gao RD, Qian SY, Wang HH, Liu YS, Ren SY. Strategies and challenges in treatment of varicose veins and venous insufficiency. *World J Clin Cases*. 2022;10:5946–5956.
6. Davies HO, Popplewell M, Darvall K, Bate G, Bradbury AW. A review of randomised controlled trials comparing ultrasound-guided foam sclerotherapy with endothermal ablation for the treatment of great saphenous varicose veins. *Phlebol J Venous Dis*. 2016;31:234–240.
7. Venermo M, Saarinen J, Eskelinen E, et al. Randomized clinical trial comparing surgery, endovenous laser ablation and ultrasound-guided foam sclerotherapy for the treatment of great saphenous varicose veins. *J Br Surg*. 2016;103:1438–1444.
8. Bradbury AW, Bate G, Pang K, Darvall KA, Adam DJ. Ultrasound-guided foam sclerotherapy is a safe and clinically effective treatment for superficial venous reflux. *J Vasc Surg*. 2010;52:939–945.
9. Gloviczki P, Lawrence PF, Wasan SM, et al. The 2022 Society for Vascular Surgery, American venous Forum, and American vein and Lymphatic Society clinical practice guidelines for the management of varicose veins of the lower extremities. Part I. Duplex Scanning and treatment of superficial truncal reflux. *J Vasc Surg Venous Lymphat Disord*. 2023;11:231–261.e6.
10. de Ávila Oliveira R, Riera R, Vasconcelos V, Baptista-Silva JC. Injection sclerotherapy for varicose veins. *Cochrane Database Syst Rev*. 2021;12:CD001732.
11. Naylor R, Rantner B, Ancetti S, et al. Editor's choice – European Society for Vascular Surgery (ESVS) 2023 clinical practice guidelines on the management of Atherosclerotic Carotid and Vertebral Artery disease. *Eur J Vasc Endovasc Surg*. 2023;65:7–111.
12. Baldazzi G, Tessari M, Zamboni M, Pagani A, Zamboni P. The sex prevalence of lower limb varicose vein networks. *J Vasc Surg Venous Lymphat Disord*. 2024;12:101944.
13. Cappelli M, Molino Lova R, Pinelli M, Franceschi C. Factors affecting the evolution of type III shunts of the greater saphenous vein after the first step of the CHIVA 2 strategy. *Veins Lymphat*. 2024;13. https://doi.org/10.4081/vl.2024.13043.
14. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Int J Surg*. 2014;12:1495–1499.
15. Mariani F, Marone EM, Gasbarro V, et al. Multicenter randomized trial comparing compression with elastic stocking versus bandage after surgery for varicose veins. *J Vasc Surg*. 2011;53:115–122.
16. O'Flynn N, Vaughan M, Kelley K. Diagnosis and management of varicose veins in the legs: NICE guideline. *Br J Gen Pract*. 2014;64:314–315.
17. Lurie F, Passman M, Meisner M, et al. The 2020 update of the CEAP classification system and reporting standards. *J Vasc Surg Venous Lymphat Disord*. 2020;8:342–352.
18. Vasquez MA, Rabe E, McLafferty RB, et al. Revision of the venous clinical severity score: venous outcomes consensus statement: Special communication of the American Venous Forum Ad Hoc outcomes working group. *J Vasc Surg*. 2010;52:1387–1396.
19. Biemans AAM, van der Velden SK, Bruijninckx CMA, Buth J, Nijsten T. Validation of the chronic venous insufficiency quality of life questionnaire in Dutch patients treated for varicose veins. *Eur J Vasc Endovasc Surg*. 2011;42:246–253.
20. Gloviczki P, Lawrence PF, Wasan SM, et al. The 2023 Society for Vascular Surgery, American Venous Forum, and American Vein and Lymphatic Society clinical practice guidelines for the management of varicose veins of the lower extremities. Part II. *J Vasc Surg Venous Lymphat Disord*. 2024;12:101670.
21. de-Abreu GCG, Camargo Júnior O, de-Abreu MFM, de-Aquino JLB. Ultrasound-guided foam sclerotherapy for severe chronic venous insufficiency. *Rev Col Bras Cir*. 2017;44:511–520.
22. Carman TL, Al-Omari A. Evaluation and management of chronic venous disease using the foundation of CEAP. *Curr Cardiol Rep*. 2019;21:114.
23. Darvall KAL, Bate GR, Adam DJ, Silverman SH, Bradbury AW. Duplex ultrasound outcomes following ultrasound-guided foam sclerotherapy of symptomatic recurrent great saphenous varicose veins. *Eur J Vasc Endovasc Surg*. 2011;42:107–114.
24. Figueiredo M, Araújo S, Barros N, Miranda F. Results of surgical treatment compared with ultrasound-guided foam sclerotherapy in patients with varicose veins: a prospective randomised study. *Eur J Vasc Endovasc Surg*. 2009;38:758–763.
25. Shadid N, Ceulen R, Nelemans P, et al. Randomized clinical trial of ultrasound-guided foam sclerotherapy versus surgery for the incompetent great saphenous vein. *Br J Surg*. 2012;99:1062–1070.
26. Lam YL, Lawson JA, Toonder IM, et al. Eight-year follow-up of a randomized clinical trial comparing ultrasound-guided foam sclerotherapy with surgical stripping of the great saphenous vein. *Br J Surg*. 2018;105:692–698.
27. Brittenden J, Cotton SC, Elders A, et al. A randomized trial comparing treatments for varicose veins. *N Engl J Med*. 2014;371:1218–1227.
28. Nesbitt C, Bedenis R, Bhattacharya V, Stansby G. Endovenous ablation (radiofrequency and laser) and foam sclerotherapy versus open surgery for great saphenous vein varices. *Cochrane Database Syst Rev*. 2014;7:CD005624.
29. Carugo D, Ankrett DN, Zhao X, et al. Benefits of polidocanol endovenous microfoam (Varithena) compared with physician-compounded foams. *Phlebology*. 2016;31:283–295.
30. Meghdadi A, Jones SA, Patel VA, Lewis AL, Millar TM, Carugo D. Foam-in-Vein: characterisation of blood displacement efficacy of liquid sclerosing foams. *Biomolecules*. 2022;12:1725.
31. Lim SY, Tan JX, D'Cruz RT, Syn N, Chong TT, Tang TY. Catheter-directed foam sclerotherapy, an alternative to ultrasound-guided foam sclerotherapy for varicose vein treatment: a systematic review and meta-analysis. *Phlebol J Venous Dis*. 2020;35:369–383.
32. Toniolo J, Chiang N, Munteanu D, Russell A, Hao H, Chuen J. Vein diameter is a predictive factor for recanalization in treatment with ultrasound-guided foam sclerotherapy. *J Vasc Surg Venous Lymphat Disord*. 2018;6:707–716.

Submitted Dec 9, 2024; accepted Feb 12, 2025.