Catheter foam sclerotherapy of refluxing great saphenous vein combined with preterminal saphenous interruption and phlebectomy: 1-year clinical and ultrasound outcomes

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Objectives
To assess the efficacy and safety of catheter foam sclerotherapy of refluxing great saphenous vein (GSV) after preterminal saphenous interruption and phlebectomy.
Patients and methods
We describe the results of the first 80 patients who fulfilled the inclusion criteria. The study endpoints were procedural technical success, 1-year GSV recanalization by duplex, and its relation to clinical varicose veins' recurrence and disease severity by comparing the presclerotherapy venous clinical severity score with the postsclerotherapy values.
Results
Technical success was 100%. After 1 year, venous clinical severity score improved from 7.3±2.2 to 2.5±0.3 ($P<0.0001$), with no clinical recurrence. The total GSV occlusion rate was 90% and reflux-free GSV was 95%, with no major complications.
Conclusions
Catheter foam sclerotherapy after preterminal saphenous interruption and phlebectomy yielded good short-term duplex and clinical results. It is simple, effective, safe, and easily repeatable. Long-term comparative study is essential taking into account the greater importance of clinical than duplex response.

Keywords:
foam sclerotherapy, ultrasound-guided sclerotherapy, varicose veins, venous severity score

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Introduction

The importance of varicose veins (VVs) emerges from its high prevalence (25–40%) in adults [1], and frequent disabling manifestations, such as leg and foot edema, venous claudication, skin changes, and venous ulcers, which adversely affect the quality of life [2,3].

The traditional treatment for truncal VVs used to be flush ligation at the saphenofemoral junction (SFJ), stripping of the refluxing great saphenous vein (GSV), and stab avulsion of dispersed varicosities. Evolving endovenous procedures, such as endovenous thermal ablation (EVTA) of GSV by laser or radiofrequency, and endovenous foam sclerotherapy, are replacing classic surgery steadily. The guidelines recommended EVTA as the first-line treatment of VVs [4,5]. Ultrasound-guided foam sclerotherapy (UGFS) efficacy in axial vein ablation was a subject of debate in these guidelines, ranging from considering its evidence incomplete [4] to recommending it as the second-line treatment [5].

The major reason for treatment failure in UGFS compared with EVTA and surgery was assessed by some studies as venous recanalization [6,7]. The pathophysiology of this problem is the deactivation and dilution of the sclerosing foam by blood [8–11]. To solve this problem, several adjunctive measures were proposed with UGFS such as saline infusion in the GSV to replace blood, perisaphenous tumescence [12–14], high selective compression [15], mechanicochemical ablation [16], and laser-assisted foam sclerotherapy [17]. All these added measures aim at the reduction of venous diameter during foam injection and/or elimination of sclerosant dilution by blood. However, there is no consensus on the ideal adjunctive to UGFS, in addition to the fact that most of these techniques require additional devices or use of tumescence.

To achieve these targets in a simple way, without tumescence or additional technology, we described ultrasound-guided catheter foam sclerotherapy, which aids vein spasm, after phlebectomy of leg

veins and preterminal GSV division, both of which reduce the blood content of the GSV. The aim of this study was to assess technical success and clinical efficacy by the patient-reported venous clinical severity score (VCSS) and clinical recurrence of VVs as well as GSV recanalization after 1 year of UGFS augmented by these simple techniques.

Patients and methods

Study design

We describe the 1-year results of the first 80 patients who fulfilled our selective inclusion criteria. They were enrolled during the period from January 2017 to January 2018. All patients were offered catheter-directed GSV foam sclerotherapy and division ligation of the GSV about 3 cm below the SFJ after phlebectomy of leg varicosities.

An informed written consent was obtained from all patients participating in the study. The Local Faculty Ethical Committee approved this study under no. 31228/11/16.

Inclusion criteria

The included patients had to have primary lower limb VVs with an incompetent SFJ terminal valve (SFJ reflux >0.5 s) and valves of GSV, but with competent SFJ junction tributaries, as documented by duplex. Patients had to have an ankle–brachial index of more than 0.8.

Exclusion criteria

Patients were excluded from the study if they had secondary VVs, markedly tortuous GSV, active or previous history of deep venous thrombosis (DVT), hypercoagulable states, pregnancy, known allergy to aethoxysklerol, and/or limited mobility. Patients with venous leg ulcers were excluded because of their inclusion in another study.

Study protocol

The demographic and clinical characteristics are shown in Table 1. CEAP classification (clinical, etiological, anatomical, and pathophysiological) was reported for the treated limb as well as VCSS for comparison with postoperative scores at follow-up visits for subjective clinical assessments. VCSS entails assessment of pain, venous edema, VVs pattern, and extent in the limb, skin changes including pigmentation, inflammation, induration, and venous ulcers number, duration and size, as well as use of compression therapy. Preprocedural venous duplex scan, in the standing position, was performed using an ATL HDI 5000 (Viamoo; Toshiba Medical Systems, Tokyo, Japan) with a 5–10 MHz transducer. Reflux was defined as retrograde flow lasting for more than 0.5 s in the target vein after manual calf compression and release (Fig. 1a, b). The diameter of the refluxing GSV 15 cm below the terminal valve was measured for comparison with the postoperative diameter (Table 2).

Table 1 Demographic and clinical baseline characteristics

Patient characteristics	Patients (*N*=80)
Females	64 (80)
Age (years)	37.3±10.8 (20–52)
Smoking	16 (20)
BMI	24.5±3 (21–29)
ABI	1.04±0.1 (0.9–1.2)
Laterality (left lower limb)	44 (55)
CEAP 2 (varicose veins)	40 (50)
CEAP 3 (edema)	32 (40)
CEAP 4a (pigmentation)	8 (10)
Preoperative GSV diameter (mm)	8.30±0.62 (7.2–9.2)

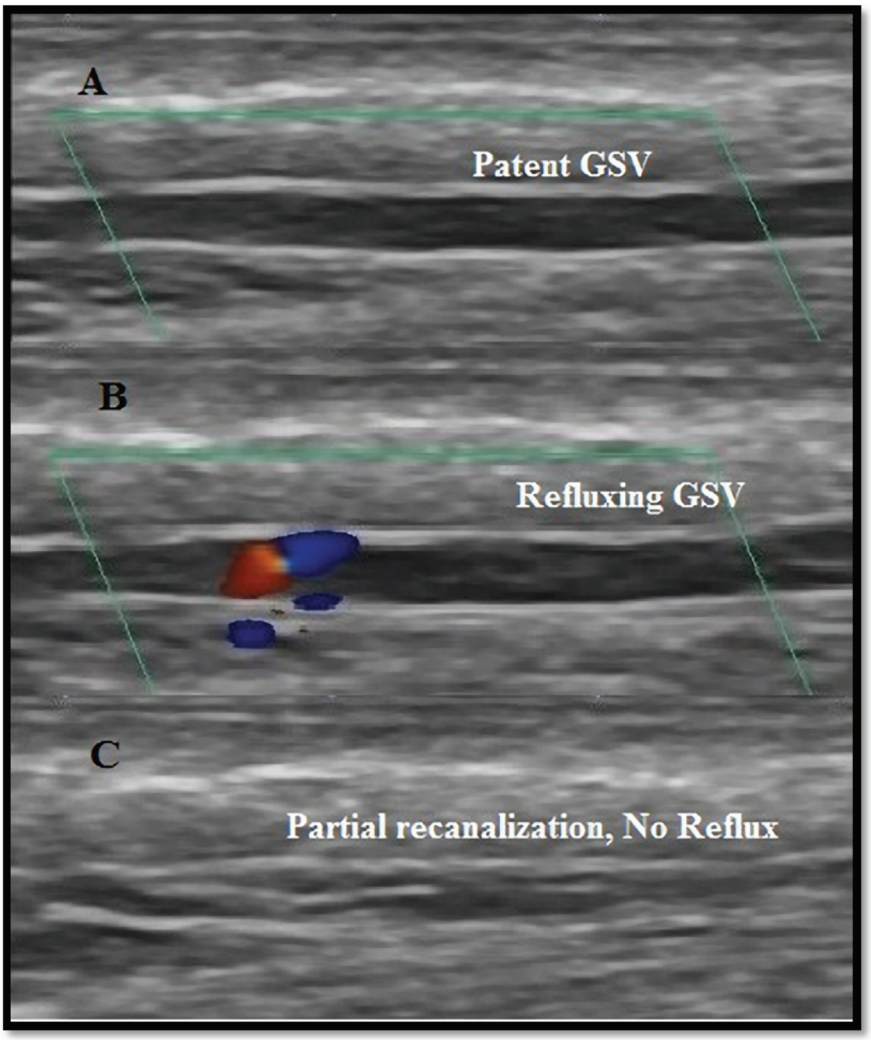
Data are presented as *n* (%) and mean±SD (range). ABI, ankle–brachial index; CEAP, clinical, etiological, anatomical and pathological classification; GSV, great saphenous vein.

Procedures

Under local infiltration anesthesia, phlebectomies were performed for leg varicosities through minute 2 mm incisions. The GSV was accessed at its lowest point of reflux either percutaneously through duplex guidance above the knee or through one of the incisions for phlebectomy just below the knee. The GSV access was obtained by a 0.035 Terumo guidewire (Terumo, Japan) and a 5–6 Fr sheath (Fig. 2a-e). Under duplex visualization, the wire and an angiographic, BERN straight 5 Fr 100 cm (Cordis, CA) catheter were advanced upwards into the GSV until the preterminal valve (Fig. 3), 3–5 cm below the SFJ, where a 5 mm stab incision was performed under local infiltration anesthesia. Interruption of the GSV between the terminal and the preterminal valves was then performed without groin dissection or junction tributary ligation. In 20 cases with difficult wire introduction from below, this was accomplished from above through the distal GSV stump after proximal ligation (Fig. 4a,b). Before a sclerosant injection, the GSV was irrigated by saline and blood was aspirated through the sheath. Saline irrigation, blood aspiration, proximal GSV ligation, and distal phlebectomy all aimed to prevent blood pooling into the GSV to avoid dilution and deactivation of the sclerosant.

Sclerosant foam was generated, following the Tessari method, using Polidocanol (Aethoxysklerol 3%) and EasyFoam silicone-free syringes kit (Kreussler Pharma, Wiesbaden, Germany). Sclerosant and air were mixed

Figure 1



(A) Patent GSV before injection. (B) SFJ reflux into GSV before sclerosing foam injection. (C) Areas of the vein showing obliteration and others showing recanalization 6 months after injection. As there is no reflux; this should not be considered as a treatment failure.

Table 2 Venous clinical severity score for the study cohort and great saphenous vein residual diameter in recanalized cases

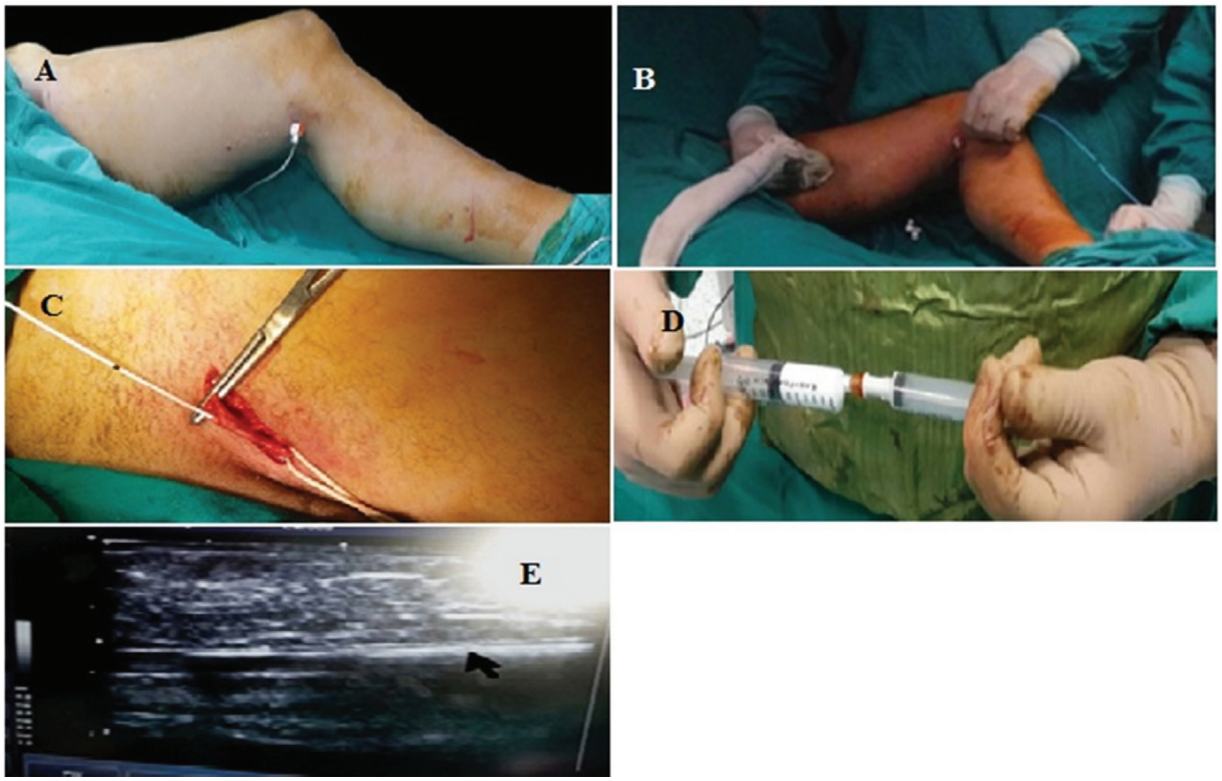
Variables	Preoperative	6 months	12 months	*P* value
VCSS (range)	5–9	2–4	2–3	*P*1=0.0001*
Mean±SD	7.3±2.2	3.2 ±0.9	2.5 ±0.3	*P*2=0.0001*
GSV diameter (mm) (range)	7.2–9.2	1.4–3	1.4–4	*P*1=0.001*
Mean±SD	8.3±0.6	2.6 ±0.4	2.9 ±0.8	*P*2=0.001*

GSV, great saphenous vein; VCSS, venous clinical severity score. *P* value more than 0.05 is considered significant. *P*1, for comparison between preoperatively and 6 months postoperatively. *P*2, for comparison between preoperatively and 12 months postoperatively. *Statistical significance.

at a 1 : 4 proportion, displacing the mix from one syringe to the other at least for 20 times to produce a homogenous and stable foam (Fig. 2d), which was then slowly and simultaneously injected at a rate of 1 ml every 5 cm of the GSV under ultrasound monitoring. The median volume of foam used was 8 ml, ranging between 7 and 10 ml, whereas the median length of the treated GSV was 44 cm, ranging between 28 and 50 cm. Injection was continued till all refluxing vein segments became full of foam (Fig. 2e). In case of deep passage of foam, the injection was stopped till it was completely cleared. Finally, duplex was used to ensure foam distribution and absence of DVT.

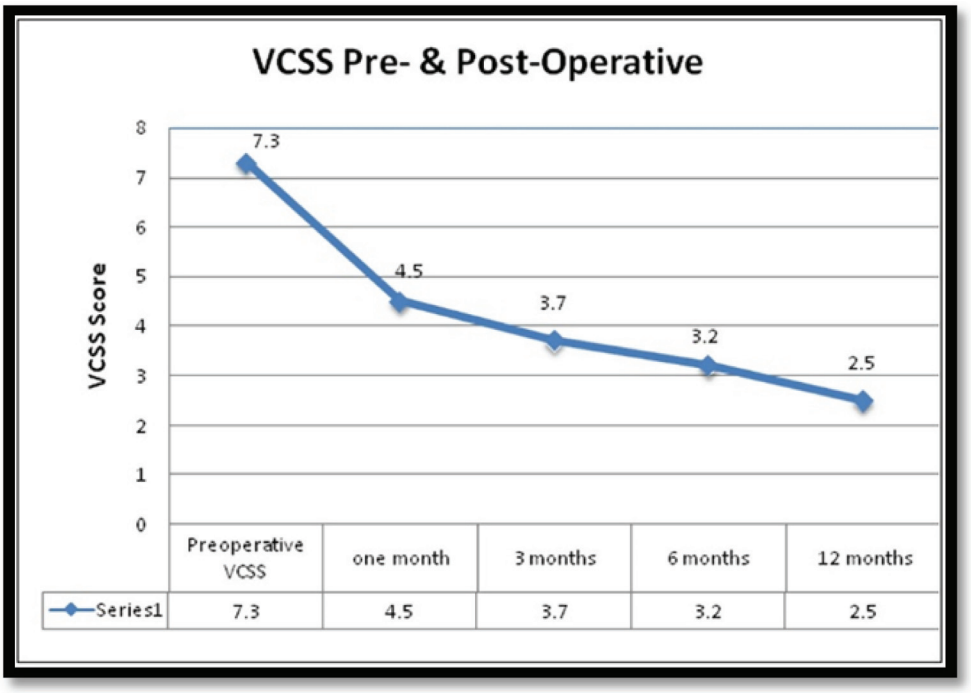
Two-layered compression bandage was prescribed for 1 week, which was replaced by class II elastic stocking for 3 months. Patients were instructed to ambulate regularly. Analgesia was prescribed (Ibuprophen 600 mg tablet twice daily for 2 days), with a prophylactic anticoagulant (enoxaparin 40 IU) on the day of the procedure.

Figure 2



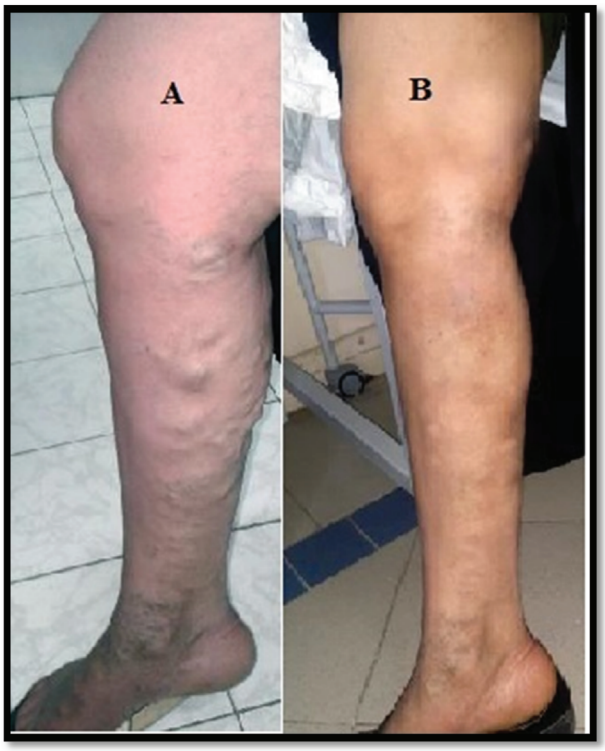
(A) Insertion of the sheath in the GSV just below the knee. (B) Insertion and advancing of the catheter into the GSV guided by duplex. (C) In some cases catheter insertion in the GSV was from the groin incision. (D) Generation of foam by Tessari method. (E) Foam filling the vain (black arrow) in duplex.

Figure 3



VCSS; Venous clinical severity score pre and post operative.

Figure 4



Patient pre-operative; veins along GSV distribution are prominent. (B) Patient post-operative; the same veins were obliterated.

Study endpoints

The primary endpoints were technical success (defined as complete obliteration of the refluxing GSV as documented by duplex on the first postoperative day) and the 1-year clinical response assessed by VCSS and clinically visible recurrence of VVs. The secondary endpoints were the recanalization rate of the previously occluded GSV and procedure-related complications.

Statistical analysis

Statistical analysis was carried out using GraphPad Prism, version 6 (San Diego, California, USA). Continuous variables were expressed as mean±SD or median and range, and were analyzed using standard Student's test (*t* test) or Mann–Whitney's test. Categorical variables were expressed as number and percentage and were analyzed using the χ^2 test. A two-sided *P* value less than 0.05 was considered statistically significant.

Follow-up

Follow-up visits were scheduled at 1 week, 1, 3, and 6 months, and 1 year following treatment. The initial visit was scheduled to confirm vein obliteration and to detect early complications such as DVT, superficial thrombophlebitis, skin necrosis, pigmentation, or ecchymosis. The following visits were scheduled to evaluate the degree of GSV occlusion, recanalization and reflux, clinical recurrence, and the need for further treatment sessions.

Postprocedure duplex response

The treated GSV vein was classified at ultrasound examination as (a) occluded: the vein had no identifiable patent lumen and/or no compressibility, with no detectable blood flow along at least 80% of its length; (b) partially occluded without reflux (obliterated): the vein had a small remaining lumen and partial compressibility with only antegrade flow in less than 80% of the treated segment (Fig. 1c); (c) partially occluded with reflux: as in 2, but with both antegrade and retrograde flows; and (d) patent: the treated vein had remaining reflux flow more than 0.5 s throughout its length with complete compressibility.

Results

Patients had a history of VVs for a mean of 5.3±1.2 years and a range of 9 months to 10 years. The mean operative time was 32±5 min (range, 30–55 min). The mean return to normal activity was 2±0.5 days (range, 2–7 days).

Primary endpoints

Technical success

The technical success was 100%. GSV obliteration by foam sclerosant was successful in all cases whether the catheter was introduced from the distal GSV near the knee or from the upper thigh at the distal saphenous stump.

Clinical improvement

The mean preoperative VCSS was 7.3±2.2 (Table 2). It was reduced significantly at all follow-up visits, reflecting the clinical subjective improvement (Fig. 3). At 1 year of follow-up, the mean VCSS became 2.5±0.3, *P*=0.0001. Scars from phlebectomy and saphenectomy incisions were satisfactory to patients. All patients showed improvements in their venous symptoms, with no visible recurrence of varicosities at all follow-up visits (Fig. 4a,b).

Secondary endpoints

Rate of recanalization

Four (5%) cases had patent segments in the GSV 1 week after the procedure; two were 4 cm in length related to incompetent above-knee perforators, another one was 3 cm in length at the mid-thigh, and the fourth one was about 7 cm in length also at the mid-thigh. The recanalized segments were obliterated after reinjection sclerotherapy guided by duplex.

Table 3 Great saphenous vein occlusion and recanalization rate

Time	Total occlusion	Recanalization
1 week	76 (95)	4 (5) total recanalization
1 months	80 (100)	0
3 months	76 (95)	4 (5) partial recanalization with no reflux
6 months	72 (90)	8 (10) partial recanalization with no reflux
12 months	72 (90)	8 (10) partial recanalization, 4 with no reflux, 4 refluxing

Data are presented as *n* (%).

Partial recanalization without reflux was found in 4/80 (5%) patients on the third month, which was increased to 8/80 (10%) patients by the sixth month (Table 3). Further sclerotherapy was not recommended for these cases. Four of these cases remain as such till the last follow-up visit at 1 year, whereas the remaining four patients developed retrograde flow (reflux) in GSV segments without visible varicosity. These four patients were instructed to undergo a second sclerotherapy session; however, they reported satisfaction with the result, absence of symptoms, and refused further sclerotherapy. The eight patients with partially recanalized GSV segments had a residual GSV diameter of 2.9±0.8 mm, with a range of 1.4–4 mm, P=0.001 (Table 2). At 1 year of follow-up, the total GSV persistent obliteration rate was 90%, whereas the reflux-free GSV was 95%.

Postoperative complications

No major complications were encountered. Postoperative ecchymosis, at sites of phlebectomies, was observed in 16 (20%) patients, which resolved in 3 weeks, and 12 (15%) patients had postoperative superficial thrombophlebitis at sites of phlebectomies, treated by analgesics and antiplatelets, and that resolved within 4 weeks. Postoperative mild groin edema was observed in four (5%) patients, which was treated by antiedematous medications and prophylactic antibiotic. Finally, scattered skin pigmentations were encountered in eight (10%) cases at the sites of foam injection, which resolved spontaneously within two months.

Discussion

Our study shows that catheter-directed UGFS preceded by preterminal ligation of the GSV and varicosities phlebectomy yielded a high total occlusion rate of 90% and a low recanalization rate with reflux (5%), with no clinical recurrence of ablated VVs after 1 year of follow-up. Our results are comparable to EVTA, the first-choice treatment for GSV reflux according to guidelines, which had a 1-year total occlusion rate of around 90% [6,18,19]. Patients' reported quality of life and subjective clinical assessment were significantly improved at all stages of follow-up.

Foam sclerotherapy techniques for axial veins are diverse. In older studies, foam injection was carried out through single or multiple cannulae inserted into the GSV at some distance from each other [20,21]. Blood dilution of the sclerosant and skip areas missed without sclerosant coverage within larger diameter veins yielded inferior results to EVTA. These results probably had a passive impact on the American Venous Forum recommendations in 2011, which considered recanalization as a major problem after foam sclerotherapy of the axial veins [4]. Despite this, UGFS was recommended by the American Venous Forum as a second option for axial vein ablation with some advantages over classic surgery. Further refinements in the sclerotherapy techniques targeted the dilution, diameter, and recanalization problems [22,23].

Therefore, we performed foam injection through a catheter and a sheath whose manipulations help GSV spasm, and deliver foam consistently along the vein without skip areas which may be perceived as treatment failure or recanalization. Phlebectomy and saphenous ligation in the Trendelenburg position, before foam injection, induce a decrease in the blood pooled in the superficial veins including the axial veins. Saphenous ligation helps to decrease foam spillage into the deep system during foam injection, thus reducing the risk of DVT. At the same time, it prevents blood reflux from the incompetent SFJ with dilution of the sclerosing activity even postoperatively when the patient moves. This is in contrast to the technique of SFJ compression during injection, which leads to foam washout to the deep system after release of compression.

Saphenectomy without junction dissection or tributary interruption is now preferred by some authors than the classic flush saphenofemoral disconnection with wide dissection, which is believed to lead to neovascularization and recurrence [24–26]. Ricci *et al.* [26] reported a simple technique of preterminal saphenous ligation, provided that the junction tributaries have been proven to be competent. Leo *et al.* [23] reported 93% persistent total GSV occlusion at 1 year of follow-up on applying this technique with phlebectomy and UGFS using a cannula.

Vein recanalization was considered by most authors and guidelines as a treatment failure and was frequently used for outcome comparison among various methods of venous ablation. However, a normal individual without VVs has a patent GSV, yet without reflux. Therefore, the appropriate determinants of treatment success or failure should be the duplex detection of refluxing valves and their clinical implication if they develop varicosities (clinical recurrence), rather than partial recanalization with antegrade flow. The European guidelines in 2014 [27] considered clinical improvement, even in the presence of a short recanalized segment with reflux, as a treatment success. In parallel, the US Food and Drug Administration [28] recommended that patient-reported outcomes, as described by severity scores and quality-of-life questionnaires, should be the cornerstone for the assessment of treatment failure for VVs. This discrepancy between duplex and clinical response after venous ablation was proved in our study and in several studies [6,19,29].

Rasmussen *et al.* [6], in a randomized clinical trial comparing surgery, endo venous laser ablation (EVLA), UGFS, and radiofrequency ablation for GSV incompetence, reported 1-year treatment failure, as a duplex response, in 16% of UGFS patients. However, there were no clinical implications of this response as proven by VCSS, Chronic Venous Insufficiency Questionnaire, and nonstatistically different VV recurrence among the groups. Moreover, UGFS was associated with the least expenses, postoperative pain, and time off work. Similarly, Williamson *et al.* [29] performed a single session of catheter-directed UGFS without SFJ interruption in 100 patients with GSV reflux. After 1 year, the total occlusion rate was only 70%, partial occlusion was 14%, and recanalization was 15%. Clinically, 84% of the patients were satisfied with the treatment. The authors did not assess the direction of flow in the recanalized veins.

In another randomized clinical trial by van der van der Velden *et al.* [19] evaluating the long-term outcomes of conventional surgery, EVLA, and UGFS for GSV varicosity, duplex results were against UGFS, where GSV obliteration at 5 years was 85, 77, and 23%, respectively. Partial recanalization with antegrade flow (without reflux) was considered a treatment failure. Moreover, the mean amount of foam was only 4.4 ml injected through a cannula at the knee level as a single shot. This inevitably caused a relatively significant blood dilution of this relatively low amount of foam and little if any uniform foam distribution along the whole GSV, especially at the proximal thigh. However, there were no significant differences between EVLA and UGFS in the clinical outcome. In addition, new reflux in above-knee tributary veins was more after EVLA than UGFS: 35 versus 30%, respectively.

In our study, eight (10%) cases underwent partial recanalization after 6 months, but without reflux; thus, they were not offered additional foam sclerotherapy. After 1 year, four of these cases developed retrograde flow (reflux) without visible varicosity. This recanalization with reflux is surely considered by the treating physician as a treatment failure; however, as no recurrence of symptoms occurred, the patients refused to undergo further sclerotherapy sessions. Similarly, Biemans *et al.* [18] reported that 11 patients with residual reflux after UGFS refused to undergo further sclerotherapy because of the absence of venous symptoms. This strengthens the consideration of clinical outcome rather than the duplex one. VCSS was reduced significantly in our patients with an obliterated and partially recanalized GSV, indicating clinical and quality of life satisfaction. This is in agreement with the previous UGFS studies [22,23]. VCSS postprocedural improvement was only related to improved venous symptoms such as pain, edema, extent of VVs, and pigmentation as venous ulcers were not included in the study and there was a single compression protocol for all cases.

The adverse events in our study were minor. Superficial thrombophlebitis was observed in 15% of the phlebectomy sites, although it was resolved rapidly by medical treatment and local compression. Similar results were obtained in a study by Ali *et al.* [30], in which, also, no major adverse events were encountered, whereas GSV thrombophlebitis was observed in 2% and skin pigmentation in 7.8%.

Our study is not without limitations. The principal one is that the follow-up was limited to short term. Further follow-up and inclusion of a comparative group are currently ongoing on the basis of these promising short-term results.

Conclusions

Catheter foam sclerotherapy after preterminal saphenous interruption and phlebectomy yielded good short-term duplex and clinical results. It is simple, effective, safe, and easily repeatable. A long-term comparative study is essential taking into account the greater importance of the clinical than the duplex response.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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