Duplex-guided foam sclerotherapy versus multiple-layer compression therapy in the treatment of chronic venous ulcers

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Background
Compression therapy is considered the gold standard of care for chronic venous disorder and venous leg ulcer treatment. Sclerotherapy is the treatment of choice for reticular varicosities and telangiectasia. Duplex ultrasonography improves the safety and efficacy of conventional sclerotherapy, gives a better evaluation of its results, and provides an understanding of the advantages of using sclerosant in the form of foam. The aim of our study was to compare the results of Duplex-guided foam sclerotherapy for the injection of incompetent perforators versus multiple-layer compression therapy in the treatment of chronic venous ulcer.
Patients and methods
The present study included 58 patients of chronic venous ulcers. Patients were divided randomly into two equal groups: group I (foam) comprising 29 patients treated by Duplex-guided foam sclerotherapy and group II (compression) comprising 29 patients treated by multiple-layer compression therapy. The statistical analysis was carried out using SPSS.
Results
There were statistically significant increases in the frequency of perforation among group I, while there was a statistically significant increase in the frequency of incomplete perforation among group II. There was a statistically significant increase in the frequency of complications among group I compared with group II. The most frequent complication was abscess.
Conclusion
Compared with multiple-layer compression therapy of incompetent perforators to treat venous ulcers, the use of foam injection sclerotherapy of incompetent perforators is feasible and effective, without serious complications and with easy repeated access and ablation of recanalized or new incompetent perforator veins.

Keywords:
chronic venous ulcers, foam sclerotherapy, multiple-layer compression therapy

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Introduction

Chronic venous disorder (CVD) is a term that describes the morphological and functional abnormalities of the venous system ranging from telangiectasia to venous ulcer. Chronic venous insufficiency (CVI) is a term describing advanced CVD associated with functional abnormalities of the venous system resulting in edema, skin changes, or venous ulcer [1].

Venous ulcer is defined as "an open skin lesion of the leg or foot that shows no tendency to spontaneous healing and occurs in an area affected by ambulatory venous hypertension and displaying other signs of CVI" [2].

The Comprehensive Classification System for Chronic Venous Disorders (CEAP) classification of CVDs (Table 1) is based on the following: clinical manifestations, etiological factors, anatomical distribution of the disease, and pathophysiological processes underlying the disease. The CEAP classification has evolved into a well-organized and meaningful basis for international communication and documentation of CVD [4].

The presence of a fan-shaped arrangement of several intradermal veins on the medial or lateral aspect of the foot or ankle, named inframalleolar ankle flare, is thought to be an early sign of advanced disease [5].

Suspicious ulcers of prolonged duration with features indicative of a mixed etiology should undergo a biopsy to exclude malignancy [6].

Protocols of CVI treatment support the hypothesis proposed by Bergan and Pascarella (Table 2). Compression treatment reduces ambulatory venous

pressure with secondary healing of venous leg ulcers (VLUs). Moreover, superficial vein surgery reduces ambulatory venous pressure, permits healing of VLU, and reduces the consequences of CVI. Finally, perforator vein (PV) interruption procedures reduce ambulatory venous pressure and decrease the chronic changes of CVI [8].

Compression therapy is a well-established effective treatment for ambulatory venous hypertension and hence considered the gold standard of care for CVD and VLU treatment. Compression reduces superficial vein distention during sedentary periods and assists the calf muscle pump during active episodes by preventing retrograde flow of blood; hence, it increases the venous return, resulting in reduced edema [9]. Sclerotherapy is the best treatment for reticular varicosities and telangiectasia. Duplex ultrasonography has improved the safety and efficacy of sclerotherapy, gives a better evaluation of its results, and provides an understanding of the advantages of using sclerosant as a foam. The superiority of foam over liquid sclerosant has been obviously established [10].

Table 1 The Comprehensive Classification System for Chronic Venous Disorders classification [3]

Anatomical classification	Pathophysiological classification
A s Superficial vein	P r Reflux
A p Perforating vein	P o Obstruction
A d Deep veins	P r,o Reflux and obstruction
A.n No venous location identified	P n No venous pathology identified
V	Venous anatomical segment classification
Superficial veins	Deep veins
1. Reticular veins	6. Inferior vena cava
2. GSV above knee	7.Common iliac vein
3. GSV below knee	8. Internal iliac vein
4. SSV	9. Exterval iliac vein
5. Nonsaphenous veins	10. Pelvic, gonadal, etc.
	11. Common femoral vein
	12. Deep femoral vein
	13. Femoral vein
	14. Popliteal vein
	15. Crural veins, anterior tibial, posterior tibial, peroneal
	16. Muscular veins, gastrocnemius, solus, etc.
	Perforating veins
	17. Thigh-perforating veins
	18. Calf-perforating veins

GSV, great saphenous vein; SSV, small saphenous vein.

Aim

The aim of our investigation was to compare the results of Duplex-guided foam sclerotherapy for injection of incompetent perforators versus multiple-layer compression therapy in the treatment of chronic venous ulcer.

Our primary endpoints include the following (and they are):

(1) Anatomical success=effective perforator closure.
(2) Clinical success=proper ulcer healing after perforator closure.

Our secondary endpoints include the following (and they are):

(1) Procedural complications during and after ablation.
(2) Patient outcome evaluated using Venous Clinical Severity Score.

Patients and methods

This prospective, observational, and randomized controlled study was carried out between January 2017 and January 2019 with a mean follow-up period of 9.8±6.2 months. The study was conducted at the Vascular Surgery Department at Zagazig University Hospitals. The present study included 58 patients suffering from chronic venous ulcers. Patients were divided randomly into two equal groups: group I (foam) comprising 29 patients treated by Duplex-guided foam sclerotherapy and group II (compression) comprising 29 patients treated by multiple-layer compression therapy.

Inclusion criteria

(1) Both sexes, aged 18–70 years.
(2) Patients having chronic venous ulcers who had received optimal therapy with compression and

Table 2 Hypothesis explaining genesis of advanced chronic venous insufficiency [7]

1. Superficial vein valve incompetence[a] raises distal venous pressure.
2. Perforating vein valve incompetence[b] raises distal venous pressure.
3. Additive effects of superficial and perforating incompetence produce profound distal venous hypertension.
4. Venous hypertension produces venulectasia, edema, leukocyte-endothelial interaction, and the inflammatory response.
5. Inflammation produces hyperpigmentation, fibrosis, and ulceration

[a]Due to gravitational reflux-induced valve remodeling. [b]Due to muscle compartment pressure-induced valve remodeling.

wound care for at least 3 months (ulcers refractory to conventional treatment).
(3) Patients having active venous ulcers=CEAP (clinical–etiological–anatomical–pathophysiological) six classification at the time of intervention.
(4) Diagnostic ultrasonography confirmation of the absence of superficial axial reflux, and confirmation of the presence of significant incompetent perforator veins (ICPVs) related to the ulcer region, with reflux of more than or equal to 0.5 s and/or an intrafascia diameter of more than or equal to 3.5 mm.
(5) Patients were available for all the follow-up visits and in a physical condition allowing ambulation after the procedure.
(6) Patients understanding the study requirements provided written informed consent to participate.

Exclusion criteria

(1) Acute (within the prior 3 months) deep venous thrombosis (DVT) or phlebitis in either limb.
(2) Complete or near-complete deep venous obstruction documented by ultrasound.
(3) Patients having a medical condition, serious illness, or extenuating circumstance that would significantly decrease study compliance, including all required study follow-ups.
(4) Patients who had undergone major surgery, which may result in abnormalities of the target body area, reasonably suspected to compromise the study outcomes.
(5) Patients with known incompatibility, such as an allergic reaction to aethoxysklerol, which was to be used in the ICPV sclerotherapy.
(6) Patients with ankle–brachial pressure index less than or equal to 0.8.
(7) Patients receiving medications that interfere with normal mechanisms of wound healing, for example high-dose steroid, antineoplastic and immunosuppressive drugs, and others such as, colchicine and penicillamine.

The study was approved by the Faculty's Scientific and Ethics Committee, Institutional Review Board. All patients were informed about the details, benefits, and risks of the sclerotherapy, available alternative treatments, and the need for multiple treatment sessions and the follow-up protocol, and they signed an informed consent form before enrollment.

Preoperative evaluation

All patients with venous ulcers had received an initial evaluation in the form of the following.

History

The following information was recorded:

(1) A thorough history was taken about the personal data including habits and occupation.
(2) Past history of medical diseases.
(3) Duration of the CVI and its history.
(4) The detailed history of medical illness (diabetes and hypertensive states).
(5) Any trials for the treatment of the CVI, including the medical treatment duration, previous surgeries, and outcomes.

Examination and investigations

The following were carried out:

(1) Full general examination.
(2) Photography of the ulcer with measurement of its vertical and horizontal axes and recorded as surface area.
(3) The ankle–brachial index measured when indicated.
(4) Full routine laboratory investigations were performed for every patient that included complete blood count, liver function tests, kidney function tests, bleeding profile, and hepatitis markers.
(5) Doppler ultrasound scanning using a logiq 5 machine (General Electric Medical Systems, Milwaukee, Wisconsin, USA) was performed in the upright position by a single experienced vascular radiologist before treatment.
(6) The patient's limb was examined for the presence of diseased deep, superficial and perforating veins, considering dilatation, reflux, detection of acute or chronic thrombosis, and the topographic relation to the ulcer area.
(7) Perforating veins were identified by cross-sectional scanning in real-time B-mode, starting from the medial malleolus and extending up to the knee.
(8) Photography of the ulcer area with the marked significantly ICPVs that were chosen for treatment to document their sites and allow the consequent follow-up examinations to differentiate recurrent perforators from newly developed ones.

Technique

Duplex-guided foam sclerotherapy technique

All treatments lasted less than 30 min and were carried out as office procedures in the operation room. Tessari's method was used to prepare the sclerosant foam: 2 cm^3 of sclerosing agent (aethoxysklerol 3%) in one syringe and 8 cm^3 of air in the other were mixed by applying 20 alternative movements from one syringe to

the other by using a stopcock to produce 10 cm^3 of foam.

The procedure involves the following (and they are):

(1) Mapping and drawing the venous network on the skin to choose the site(s) of injection, and to decide the section to be sclerosed.
(2) Preparing the skin and preparing the foam.
(3) Placing a needle into the perforating vein at its entry to the deep fascia under duplex guidance. Elevating the limb, with compression either at the saphenofemoral or the saphenopopliteal junction to avoid the entry of bubbles into the deep venous system and DVT incidence.
(4) Injecting the first bubbles.
(5) Verifying the bubbles inside the vein.
(6) Injecting the sclerosing foam progressively, followed by massaging it with the probe in the varicose network, and then ensuring that the foam fills all the desired veins.
(7) Checking the apparition of venous spasm.
(8) Removing the needle and placing a ball of cotton on the site of injection.
(9) Applying a bandage and grade 2 medical stockings, and keeping the stockings for 7 days and then for all day long only.
(10) Giving instructions to all patients with regard to walking and mobilizing early.
(11) Scheduling a follow-up after 2 weeks, either for duplex evaluation or for another injection.

Applying compression bandaging

(1) The leg is washed in warm water with emollient. Hyperkeratosis is removed with a soft cloth and further emollient applied, such as a 50% white soft paraffin mixture.
(2) The dressing of choice is applied to the limb. In most instances, a simple nonadherent dressing is sufficient. Tubular gauze can be applied if the wadding irritates the skin.
(3) The subbandage wadding is applied in a spiral fashion, toe to knee, for protection of bony prominences and exudate absorption. This is considered to be the first layer of the multilayer system. Subbandage wadding must always be used under compression bandages. The wadding protects the tibial crest or shin, and Achilles tendon. However, care must be taken not to use too much padding, as this will increase the limb width significantly.
    (a) The first layer of the compression therapy – the type 3a bandage – is applied using a figure of eight technique. Note ankle position and do not overextend the bandage. Check whether the tension is correct using two fingers.
    (b) The second layer of the compression therapy – the type 3b bandage – is then applied in a spiral fashion.
(4) The crepe bandage is applied in a spiral fashion, toe to knee; this will flatten the wadding layer. This is considered to be the second layer of the system.
(5) Next comes the compressive third and fourth layers.
    It is essential that the correct technique and pressure is used, ensuring 50% stretch and 50% overlap. Apply all bandages from the base of the toes to 1 cm below-knee space. The ankle should be dorsiflexed (toes to the nose) or at a 90° angle; this will prevent creasing of bandages over the dorsum or the front of the ankle, which is a common cause of pain and lack of compliance.
(6) Check that the calf is fully enclosed with the calf muscle covered completely.
(7) Now check for comfort and whether footwear can be worn.
(8) The patient should be aware of signs of poor perfusion and told to remove the top compression bandage and inform us if the following signs are present:
    (a) pins and needles sensation over toes.
    (b) numbness or discoloration of the toes.

Postoperative care

Graduated compression stockings with strengths of 20–30 mmHg (class I) or 30–40 mmHg (class II) should be worn the first night and then daily for 1–3 weeks, depending on the vessel size treated.

After treatment, an elastic compression bandage was applied across the whole lower limb, with a cotton roll over the treated site. Patients are asked to carry out lower extremity exercises instantly after sclerotherapy and then on a daily basis. Patients were given directions with regard to pain control and the use of multilayered compression dressing. Patients were also instructed about the methods of ulcer dressing and wound care.

Follow-up

All patients were followed-up at 7 days and 2, 4, and 6 months after treatment. At the first visit, the bandages were removed and a duplex was performed to look specifically for DVT.

In each visit treatment-related complications were recorded after Duplex-guided sclerotherapy, and the fate of ablated PVs and the patency of lower limb deep veins were evaluated using Duplex ultrasound to

evaluate anatomical outcome; the targeted ulcers were measured with calculation of the surface area to assess ulcer healing rate, and the date of complete healing was recorded to measure the ulcer healing time and the ulcer recurrence after healing points to evaluate clinical outcomes.

After attaining complete healing of their ulcers, patients were advised to stick to the compression therapy and return if any new symptoms developed. Ulcer healing was defined as complete epithelialization. PV recurrence was defined by the appearance of recanalized PV at the site previously treated.

Sample size calculation

Assuming that the percentage of complete ulcer healing after 12 weeks of foam sclerotherapy technique is 81%, and that of multiple compression layer therapy is 42%, the sample size was calculated to be 58 patients "29 in each group" using Epi with power 80% 95% confidence interval.

Statistical analysis

Individual data were summarized using frequencies or percentages for categorical variables and the mean±SD for normally distributed continuous variables. Kaplan–Meier estimation was used to calculate survival time of ulcer healing and survival time of perforator closure. Paired *t* test was used to compare pretreatment and posttreatment VCSS. *P* value less than 0.05 was considered statistically significant. All data were analyzed using Statistical Package for Social Science for Windows version 20.0 (IBM, Armonk, New York, USA).

Results

In the present study, 58 patients were included in this randomized prospective observational trial. In each study group (foam vs. compression), there were 29 patients. The duplex findings among the two studied groups are presented in Table 3, wherein there were statistically significant increases in the frequency of perforation among group I (foam), while there were statistically significant increases in the frequency of incomplete perforation among group II (compression). The baseline patient characteristics between the compared groups in this study are presented in Table 4.

The size and number of ulcers are presented in Table 5, wherein there were statistically significant increases in

Table 3 Duplex findings among the two studied groups

Variables	Group I (foam) (*N*=29) [*n* (%)]	Group II (compression) (*N*=29) [*n* (%)]	χ^2	*P*
Duplex				
DVT	9 (31)	6 (20.7)		
INC. SFJ	9 (31)	6 (20.7)		
Incomplete perforation	3 (10.3)	14 (48.3)		
3	0 (0)	5 (17.2)		
4	0 (0)	3 (10.3)		
5	0 (0)	3 (10.3)	10.91	0.01*
6	3 (10.3)	3 (10.3)		
Perforation	26 (89.7)	15 (51.7)		
1	0 (0)	3 (10.3)		
3	6 (20.7)	6 (20.7)		
4	17 (58.6)	3 (10.3)		
5	0	3 (10.3)		
6	3 (10.3)	0		

DVT, deep venous thrombosis; SFJ, saphenofemoral junction. **P* value less than 0.05, significant.

Table 4 Sociodemographic data of the two studied groups

Variables	Group I (foam) (*N*=29)	Group II (compression) (*N*=29)	*t*	*P*
Age (year)	35–50			
Mean±SD	39.17±4.43	42.21±7.81	1.82	0.07
Range		28–52		NS
Variable	*n* (%)	*n* (%)	χ^2	*P*
Sex				
Female	18 (62.1)	9 (31)	5.61	0.02*
Male	11 (37.9)	20 (69)		

NS, nonsignificant (*P*>0.05); *t*, independent *t* test. *Means that the value is significant since *P*-value is less than 0.05.

Table 5 The size and number of ulcers among the two studied groups

Variables	Group I (foam) (*N*=29)	Group II (compression) (*N*=29)	Test	*P*
Ulcer number [*n* (%)]			χ^2	
1	17 (58.6)	26 (89.7)		
2	9 (31)	3 (10.3)		0.02*
3	3 (10.3)	0 (0)	7.88	
Size (cm)	(*n*=44)	(*n*=32)	MW	**
Mean±SD	1.14±0.53	1.86±0.85	3.98	<0.001
Median	1	2		
Range	0.5–2	1–3.5		

MW, Mann–Whitney test. *Significant ($P<0.05$). **Highly significant ($P<0.01$).

Table 6 Frequency of complications among the two studied groups

Variables	Group I (foam) (*N*=29) [*n* (%)]	Group II (compression) (*N*=29) [*n* (%)]	χ^2	*P*
Complication				0.002**
No	21 (72.4)	29 (100)	9.28	
Yes	8 (27.6)	0		
Abscess	4 (13.8)			
Skin gangrene	2 (6.9)	–		
Thrombophlebitis	2 (6.9)			

NS, nonsignificant ($P>0.05$).

Table 8 Frequency and healing time among the two studied groups

Variables	Group I (foam) (*N*=29)	Group II (compression) (*N*=29)	Test	*P*
Healing [*n* (%)]				
No	0	9 (31)	10.65 (χ^2)	<0.001**
Yes	29 (100)	20 (69)		
Time of healing (week)	*N*=29	*N*=20	Test	*P*
Mean±SD	9.72±3.17	11.4±3.63	2.12 (MW)	0.04*
Range	9.5–16	12.6–16		

MW, Mann–Whitney test. **P* value less than 0.05, significant. ***P* value less than 0.01, highly significant.

Table 7 Correlation between healing time and age and ulcer diameter among the two studied groups

Variables	Group I: healing time (*N*=29)		Group II: healing time (*N*=20)	
	r	*P*	*r*	*P*
Age (years)	0.25	0.20 (NS)	0.37	0.11 (NS)
Number of ulcers	0.65	<0.001**	0.08	0.70 (NS)
Ulcer size (cm)	0.42	0.04*	0.76	<0.001**

NS ($P>0.05$); *r*, Pearson's correlation coefficient. *Significant ($P<0.05$). **Highly significant ($P<0.01$).

the number of ulcers among group I, but there were statistically significant increases in ulcer size among group II. The frequency of complications among the two studied groups are presented in Table 6, wherein there were statistically significant increases in the frequency of complications among group I (foam) compared with group II. The most frequent complication was abscess. Correlation between healing time and age and ulcer diameter among the two studied groups are presented in Table 7, wherein there were positive significant statistical correlations between healing time and ulcer size in both groups. Frequency and healing time among the two studied groups are presented in Table 8, wherein there were statistically significant increases in the duration of healing among group II (compression) (Figs 1–3).

Discussion

Conservative treatment in the form of leg elevation and multilayered compression dressings have been the main treatment for venous ulcer for thousands of years. Although proved to be an effective method for the promotion of ulcer healing in up to 70% of treated ulcers, the recurrence rate is depressive if this compression is not maintained, reaching up to 25% in the first year and maybe as high as 100% with longer follow-up [11].

An important large randomized controlled trial (RCT), the Effect of Surgery and Compression on ulcer Healing and Recurrence trial, was carried out to compare the efficacy of surgical intervention (saphenous stripping

Figure 1

Case treated with foam injection sclerotherapy; (a) before 3 months and (b) after 3 months.

Figure 2

Case treated with foam injection sclerotherapy; (a) before 3 months; (b) after 1.5 months; and (c) after 3 months.

±phlebectomies) plus compression with compression alone in the management of venous ulcer. Although it showed no difference between the two groups concerning ulcer healing rate (overall 65% in both groups), it showed a significant reduction in ulcer recurrence (surgery 28% vs. compression 12%, $P<0.0001$) at 1-year follow-up [12]. This reduction was also maintained in the surgical group (surgery 31% vs. compression 55%) at the 4-year follow-up and, most importantly, the surgical group experienced half the number of ulcer episodes than the compression group (81 in the compression group vs. 41 in the surgical group) [13]. This trial proved the superiority of surgical treatment to compression and establishes a grade 1A

Figure 3

Case treated with multiple layer compression therapy; (a) before 4 months and (b) after 4 months.

recommendation that ligation and stripping of the great saphenous vein (GSV) is associated with ulcer recurrence prevention in the absence of multilevel deep venous pathology. It should be noted that in the Effect of Surgery and Compression on ulcer Healing and Recurrence study, ICPVs were not treated actively, and only half of the patients had duplex verified ICPVs, which may explain the early good results with saphenous surgery alone.

The possible relation between ICPVs and venous ulcer pathophysiology was first addressed by John Homans – the Boston surgeon – in 1917, as he stated that "As the valves in these veins become incompetent, venous reflux and hypertension develops, exacerbating CVI." His advice was eradication of both the GSV and particularly the ICPVs for venous ulcer treatment [14].

Although debatable, the fact that interrupting the ICPVs reduces the venous ulcer recurrence is well proven by recent studies [15–17] and by a meta-analysis of literature that concluded that "these findings confirm the importance of ligating all ICPVs, as ulcer healing was never achieved when residual perforating veins were found at follow-up" [18].

The opponents of this fact depend on two arguments against ICPV treatment. The first is that the deep vein reflux has more importance than the ICPVs in patients with venous ulcers, which was defeated by Iafrati *et al.* [19], by proving that "deep system reflux as measured with duplex scan valve closure times did not correlate with the rate of ulcer healing or recurrence, whereas the treatment of ICPVs was of clear benefit." The other argued that there was no benefit of ICPV interruption, as their competence was restored by saphenous surgery alone, which was proven to occur in less than 50% of ICPVs with even lower figures in venous ulcer patients [20].

Two RCTs addressed this issue: the first evaluated subfascial endoscopic perforator surgery (SEPS) after GSV stripping, which found that ICPVs do not remain closed after standard saphenous surgery when followed-up for a long enough period, as the majority of the immediately closed ICPVs reopened at 1 year; they concluded that adding SEPS reduces the number of ICPVs without added morbidity [21].

The other RCT compared GSV surgery alone versus GSV plus SEPS in venous ulcer patients and found that saphenous surgery alone rarely treats ICPVs, as only seven of the 37 treated limbs appeared free form original ICPV, and concluded that "If the goal is to obliterate ICPVs, they should be dealt with individually, rather than depending on treating associated saphenous incompetence" [22].

The most common site of perforator incompetence and associated venous ulcer was demonstrated by O'Donnell [23] in his systematic review to be the posterior tibial perforators 10–15 cm above the medial malleolus (the typical Cockett 2/3 area), which join the posterior accessory GSV with the posterior tibial veins, and this may explain why incompetence of these perforators is rarely treated by saphenous surgery alone.

Although it might be difficult to establish a causative relationship between ICPVs and skin changes associated with CVI, it had been proven that worsening of the CVI status was associated with the development of new ICPVs and increase in the diameter of ICPVs [24]. Several studies support the clinical benefits obtained by interruption of ICPVs in patients with advanced CVI [15].

The most recent guidelines by the Society for Vascular Surgery and the American Venous Forum (2014) recommend ablation of perforating veins located near healed or active venous ulcers in C5 and C6 classes, and, in contrast, they recommend against their treatment in C1 and C2 classes, while the value of perforator interruption in C3 and C4 classes is still unclear [25]. On the basis of these recommendations, our study included only CEAP 6 class patients (active venous ulcers) to assess the effect of ICPV closure by radiofrequency (RF) energy on ulcer healing rates.

Determining the parameters of detecting perforator incompetence implies a diagnostic dilemma, and there is no universal agreement in the literature for this issue. In his fabulous study, Yamamoto *et al.* [26] tried to correlate the ICPV diameter–reflux relationship by comparing the preoperative duplex ultrasound criteria with the intraoperative evaluation test, "Turner-Warwick bleed-back test", which concluded that a sensitivity of 87.7% and a specificity of 75.3% of duplex determined reflux more than or equal to 0.5 s. The author emphasizes that the sensitivity of reflux times was not sufficient to confirm perforator incompetence.

In another study carried out by Sandri *et al.* [27], the positive predictive value of PV diameter more than 3.5 mm was 90% in diagnosing incompetence, while a diameter less than 2.2 mm predicted the absence of reflux in 92% of PVs. The most recent clinical practice guidelines adopted a reflux time more than 0.5 s and a diameter more than 3.5 mm as the criteria to diagnose PV incompetence [25], the criteria that we applied in our study.

As long as the ICPV can be detected by duplex ultrasound imaging, it can be cannulated and treated minimally invasively regardless of its location. Several techniques are available, including ultrasound-guided foam sclerotherapy and percutaneous thermal ablation of perforators, describing endovenous radiofrequency and endovenous laser ablation procedures [28].

Ultrasound-guided foam sclerotherapy is a widely performed technique due to its low cost, ease of use, good patient tolerability plus the benefits gained from the associated occlusion of the varicosity network related to the ulcer area, with a reported 54% perforator closure rate and 3% DVT of calf veins. Although cannulation and foam injection of the feeding varicosities appears simpler than the percutaneous thermal ablation of perforator technique, foam may show rapid washout in high-flow systems before spasm and thrombosis occur, and, also, larger veins require larger volumes of the sclerosant with higher concentration for successful closure, which may affect the complication rates [28].

In a recent study carried out by Rueda *et al.* [15], they evaluated the efficacy of ICPV interruption by both SEPS and RF ablation techniques on 64 patients with CVI stage C5 or C6 and concluded that RF ablation had low recurrence rates and fewer complications than SEPS; moreover, it can be performed under local anesthesia as an outpatient procedure, making it an attractive technique to be used in patients with multiple comorbidities. Thus, he recommended aggressive treatment in patients with advanced CVI stage concerning RF of associated ICPVs.

In our study, foam sclerotherapy was used in 29 patients and multiple layer compression therapy in 29. Our patients' demographics showed two differences from previous similar published studies. First, the age range of our patients was much younger (range, 23–67years), and the second is the sound male predominance (86.7%); this could be attributed to the greater life span in western countries if compared with that in Egypt. As for male predominance, we usually observed that early stages of varicose veins are more frequent in female individuals than in male individuals, as in western countries, but the advanced stages of CVI (CEAP classes C4–C6) are more common in male individuals mostly because of the working style of these patients, as most of them are manual workers who stand for long hours, and they usually do not have the facilities to change their jobs, as recommend in these situations.

Foam sclerotherapy was technically successful with a 100% initial success rate in all treated perforators, as all the cannulated ICPVs were successfully closed, as confirmed by the intraoperative duplex ultrasound; however, we could repeat access in nine limbs in which residual flow was observed after first access. At subsequent follow-up, duplex ultrasound examination revealed recurrent patent PVs in seven (24.1%) patients at periods ranging from 4 to 9 months with a mean of 1.97 months. This causes the overall perforator closure rate to become 76.7%. Two cases developed skin gangrene limited to 2 cm diameter that healed by debridement and follow-up over 4 weeks.

Twenty-nine limbs with 45 ICPVs were treated by multiple-layer compression therapy of incompetent perforators. Twenty-one cases healed completely at a mean of 4 months, with two cases with minimal response to treatment (6.8%). The other six cases felt marked discomfort with multiple layer compression therapy and refused to complete treatment by that method (20.6%). The overall healing rate was 72%, with six (20.6%) patients discontinuing treatment.

Procedure-related complications were low (20%; 6/78 injections) in the form of minor complications, with no major complications occurring at the follow-up period. There were two (6.7%) cases of skin gangrene, which

resolved within 4 weeks. There were no cases of deep vein thrombosis.

There was associated improvement in the patient outcome and quality of life after ablation, as measured by the VCSS scale.

Although there are some limitations in this study, it provides good evidence with regard to the value of perforator interruption in patients with venous ulcers and proved the relative simplicity and reproducibility of the duplex-guided foam sclerotherapy and multiple-layer compression therapy. These limitations include the relatively small patient cohort, which does not permit correlating various patients variable to the perforator or ulcer recurrence on conducting a regression analysis, the relatively short follow-up period of about 6 months in seven (24.1%) of our cases that may demonstrate different outcomes on longer follow-up and finally lack of precise preintervention data concerning wound care technique, surgical interventions, and type and gradient of compression therapy.

Conclusion

This study proved the significant role of interrupting ICPVs in patients with active venous ulcers (CEAP 6 classification) and demonstrated the feasibility and effectiveness of foam injection sclerotherapy of incompetent perforators over multiple layer compression therapy of incompetent perforators to treat venous ulcers in a selected group of patients after failure of other methods with the advantages of freedom from serious complications and easy repeated access and ablation of recanalized or new ICPVs.

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Conflicts of interest

There are no conflicts of interest.

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