

Healing and recurrence rates following radiofrequency ablation of the saphenous vein and ultrasound-guided foam sclerotherapy of perforator reflux in patients with venous ulceration

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Background

Chronic venous ulcer (CVU) is responsible for significant healthcare expenditure worldwide. Compression therapy is the mainstay of treatment, but long-term compliance with this therapy is difficult. Surgery for axial and perforator reflux has been used as an adjuvant to compression to fasten healing and reduce recurrence rates. The treatment of varicose veins has also undergone dramatic changes with the introduction of percutaneous endovenous ablation techniques, including radiofrequency ablation (RFA) and ultrasound-guided foam sclerotherapy (UGFS). The role of these techniques in the treatment of CVU is just beginning to be defined.

Patients and methods

Sixty-six patients with CVU with 71 active leg ulcers who presented at our vascular clinic were included in this study. All patients underwent duplex scanning for venous insufficiency. Ulcer dimensions at each visit were recorded and used to calculate healing rates. The presence or absence of ulcer recurrence at 1-year follow-up was recorded. Ulcers treated with compression alone (the 'compression group') were compared with those treated with compression and minimally invasive interventions, such as RFA of superficial axial reflux and UGFS of incompetent perforating veins and varicosities (the 'intervention group').

Results

The average age in the intervention and compression groups was 36.7 and 41 years, respectively ($P = \text{NS}$). Ulcers were recurrent in 41.7% of the patients in the intervention group and in 25.5% of patients in the compression group ($P = \text{NS}$). In the intervention group 14.7% underwent RFA of the axial reflux, 38.2% underwent UGFS of perforators, and 41.1% underwent both treatments. The only complication of intervention was a single case of cellulitis requiring hospitalization. No significant difference ($P = 0.73$) was seen in the proportion of ulcers that did not heal within 24 weeks (24.3% compression vs. 17.5% intervention). Within 1 year a significantly higher rate of recurrence was seen in the compression group compared with the intervention group (46 vs. 20.5%; $P = 0.004$).

Conclusion

Minimally invasive ablation of superficial axial and perforator vein reflux in patients with active CVU is safe and leads to faster healing and decreased ulcer recurrence when combined with compression alone in the treatment of CVU.

Keywords:

healing, radiofrequency, recurrence, ulcer, venous

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Introduction

It is well known that chronic venous ulceration places a major burden on the patient's lifestyle with a protracted course of healing and a high recurrence rate. The economic cost of this disorder was estimated at about 1% of the total healthcare costs in developed countries in 2000 [1].

Compression therapy alone can lead to healing of chronic venous ulcer (CVU) in most patients, and continued compliance with compression prevents ulcer recurrence [2–4]. However, despite the prescription of elastic compression stockings, 12-month ulcer recurrence rates of 26–28% [5–7] have been reported

and can be as high as 69% [8] and this is why simple superficial venous surgery — that is, saphenous vein ablation and/or perforator ligation — was thought to decrease the recurrence rate compared with compression therapy alone.

In a nonrandomized study, patients with isolated superficial venous reflux undergoing compression therapy alone were compared with those undergoing compression treatment and superficial venous surgery. Surgery did not confer any additional benefit in terms of venous ulcer healing, but recurrence was significantly reduced from 28 to 14% at 12 months [6].

In 2004, Barwell *et al.* [9] conducted a randomized control study comparing surgery and compression with compression alone (ESCHAR study). In this study, overall 24-week healing rates were similar in the compression and surgery and compression-alone groups but 12-month ulcer recurrence rates were significantly reduced in the compression and surgery group. Adverse events were minimal and almost equal in each group.

The treatment of varicose veins has undergone marked evolution since the introduction of percutaneous endovenous ablation techniques, including endovenous laser therapy (EVLA), radiofrequency ablation (RFA), and foam sclerotherapy [2]. These techniques are percutaneous office-based procedures that can be performed under local or tumescent anesthesia with nearly equal early and midterm results and with less discomfort to the patient, improved early quality of life, and earlier return to work [10–12].

The purpose of this study was to review patients with CVU presenting at our outpatient vascular clinic who were treated with compression only (the ‘compression group’) and compare them with patients treated with compression plus RFA of saphenous and/or perforator foam sclerotherapy (the ‘intervention group’).

Patients and methods

This study was conducted between July 2010 and January 2014, and including 66 patients with 71 active lower-limb venous ulcers. All patients attended our vascular clinic of Zagazig university hospital with diagnosis for venous stasis ulcer of the lower extremity (Fig. 1). They were then assessed for healing rates and 1-year recurrence rates associated with compression alone versus compression plus minimally

invasive intervention to correct superficial axial and/or perforator reflux.

Inclusion criteria

- (1) Any patient with an open ulcer between the knee and the malleoli who had a CVU as judged on the basis of clinical criteria of ulcer location, stasis change, and edema.
- (2) Doppler study confirming reflux at the superficial and/or perforator veins with no reflux at the popliteal vein.
- (3) The ulcer had not been treated before with standard compression therapy.

Exclusion criteria

- (1) Clinical features associated with iliac vein obstruction (diffuse lower-limb pain and edema) confirmed by venography finding of iliac vein obstruction.
- (2) Vein diameter less than 5 mm or more than 13 mm.
- (3) Positive investigations for vasculitis or thrombophilia.
- (4) Absent pedal pulsation with ABI less than 0.8.
- (5) Generalized severe cellulitis of the limb that must be treated before intervention.
- (6) Unable to give informed written consent.
- (7) Advanced irreversible scarring of the skin from multiple recurrent ulcers.
- (8) Loss to follow-up.

Treatment protocol

Demographic data, complete patient history, and treatment data were collected at first patient visit. At each weekly visit, the length and width of the ulcers were measured and multiplied to calculate the wound surface area (Fig. 2). Healing rates were calculated as

Figure 1



Active venous ulcer.

Figure 2



Ulcer that has begun to heal.

change in wound surface area per week until complete healing. In patients with bilateral ulcers, one ulcer from each leg was recorded and tracked separately. Data collection and analysis was performed by leg. When multiple ulcers were present on a leg, only the largest was analyzed.

At each visit, selective sharp debridement of the wound was performed when appropriate. Antibiotics were used selectively based on wound culture data and clinical assessment. Wound dressings were selected on the basis of wound characteristics, such as amount of drainage, presence or absence of infection, pain level, and amount of remaining nonviable tissue post debridement.

Our primary endpoints were 24-week ulcer healing and 12-month ulcer recurrence for patients in both arms of the study. We defined ulcer healing as complete epithelialization, and ulcer recurrence as epithelial breakdown anywhere between the knee and the malleoli of the study leg.

Venous duplex scanning was performed on all patients to assess reflux and/or obstruction in the superficial, perforator, and deep veins using compression release and/or valsalva to induce reflux in standing position. Special care was paid to the area around the ulcer to detect refluxing perforators. Reflux duration of greater than 0.5 s in the saphenous vein and perforators and 1 s in deep veins was considered significant [2]. Anatomy of reflux was categorized as superficial, perforator, or combinations thereof.

Obstructive pathology in the deep vein system was considered present only if an occluded segment in the femoral, superficial femoral, or popliteal vein was identified.

Compression was initiated at the first clinic visit and modified in response to patient tolerance of the dressing and wound response at subsequent visits. Compression with multilayer semirigid dressings from the forefoot to the knee was applied with three-layer and four-layer systems until the ulcer healed, and then class 2 community-grade elastic support stockings (Medi, Hereford, UK) were prescribed, which constituted the standard treatment for prevention of ulcer recurrence [5,7]. All participants were given standard advice sheets and encouraged to exercise and raise the affected leg as much as possible. The approach to compression therapy was the same throughout the study period, at each visit. Patients were generally seen every week. After ulcer healing patients were reviewed monthly for 1 year.

The decision to use minimally invasive intervention to correct superficial and/or perforator incompetence

was made by the treating vascular surgeon and was also based on patient preference.

Interventions included RFA of the great and small saphenous veins, foam sclerotherapy of incompetent perforators and varicosities with duplex guidance (2% and 3 sodium tetradecyl sulfate foam using the Tessari method) [13], and stab phlebectomies. In some patients, more than one of these interventions was performed. As a general rule, axial reflux was corrected before perforator incompetence (Fig. 3).

During radiofrequency we used the closure fast catheter, which was inserted about 2 cm distal to the saphenofemoral junction with US guidance. We used an RFG2 generator to achieve the required temperature (120°C) during 20 s cycles. The closure fast catheter treats a 7 cm vein segment in every cycle (20 s). Two cycles were performed in the position 2 cm below the saphenofemoral junction, and then at every 7 cm distal segments were ablated by one cycle.

After ulcer healing all patients were followed up for 1 year at monthly intervals to monitor for recurrence (Fig. 4).

Details of interventions are summarized in Table 1. All patients receiving intervention also continued with compression therapy. Some, but not all, patients received a single dose of intravenous cefazolin immediately before thermal ablation.

Statistical analysis

Demographic and ulcer information was compared between the compression and intervention groups. Descriptive statistics are displayed as means and SDs

Figure 3



Foam sclerotherapy.

for continuous variables, and as number and percentage with characteristics for categorical variables. For continuous variables with skewed distributions (healing times, ulcer size) data are summarized with medians and interquartile ranges. The χ^2 or Fisher's exact test was used for categorical data, and *t*-tests or Wilcoxon's rank-sum tests were used for continuous data. Time zero for ulcer healing in patients recruited with open ulcers was at first compression or after intervention. Time zero for ulcer recurrence was at ulcer healing; therefore, ulcer recurrence analyses only included patients with healed ulcers. A *P* value of less than 0.05 was considered significant. All statistical calculations and plotting were performed using SPSS, version 20.

Results

The demographic criteria of our patients and ulcer data are summarized in Table 2.

The mean age in years in the compression and intervention groups was 36.7 ± 11.6 and 41.4 ± 12.2 , respectively ($P = 0.323$), with a ratio of women to men of 1 : 1.5.

Diabetes and a history of deep vein thrombosis were not significantly different between treatment groups.

The initial ulcer size was nearly identical between groups. Although in the intervention group a trend was seen toward more frequent recurrence of the ulcers, the differences were not significant.

Table 3 shows the anatomy type of venous incompetence – that is, the location of reflux or contributing to ulcer. Significantly more ulcers with only superficial venous incompetence were treated with intervention, and significantly more ulcers with only perforator incompetence were treated with compression only ($P = 0.031$).

Table 4 shows healing rates and recurrence rates in the compression and intervention groups. Decrease in actual wound size (measured in cm^2) was faster in the intervention group but the difference was not statistically significant.

Patients treated with intervention healed in less time compared with those treated with compression only (10 vs. 20 weeks; $P = 0.011$). Time spent before an intervention was not included in healing time.

No significant difference ($P = 0.55$) was seen in the proportion of ulcers that did not heal within 24 weeks (nine ulcers, 24.3% compression vs. six ulcers, 17.5% intervention).

Figure 4



Healed ulcer.

Table 1 Distribution of interventions

Intervention	N (%)
RFA of GSV and/or SSV	5 (14.7)
Sclerotherapy of perforator	13 (38.2)
RFA + sclerotherapy	14 (41.1)
RFA + phlebectomy	1 (2.9)
RFA + sclerotherapy+stab phlebectomy	1 (2.9)

GSV, great saphenous vein; RFA, radiofrequency ablation; SSV, small saphenous vein.

Table 2 Comparison of demographic and ulcer data between intervention and compression groups

Healing rate	Intervention (n = 34)	Compression (n = 37)	<i>P</i>
Age [mean (SD)] (years)	36.7 ± 11.6	41.4 ± 12.2	0.323
Male [n (%)]	23 (67.6)	25 (67.5)	0.131
BMI [mean (SD)] (kg/m^2)	35.4 ± 8.5	38.6 ± 11.8	0.353
Diabetes (%)	8 (23.5)	11 (29.7)	0.294
Initial ulcer size [median (IQR)] (cm^2) ^a	4.3 (8.5)	4.5 (11.5)	0.725
History of DVT [n (%)]	4 (11.7)	7 (18.9)	0.311
Recurrent ulcer [n (%)]	9 (26.4)	7 (18.9)	0.079

DVT, deep vein thrombosis; ^aTest performed using the Wilcoxon rank-sum test.

A significantly higher rate of recurrence was seen in the compression group. Seventeen patients experienced recurrence within 1 year compared with seven in the intervention group (46 vs. 20.5%; $P = 0.002$).

Table 5 shows the complications that occurred in the intervention group. Six limbs (17.6%) presented with bruises and ecchymosis (without distinction between those due to treatment itself and those due to tumescent injection or foam sclerotherapy), two limbs (5.8%) showed prolonged ecchymosis and local edema for 1 month, and three limbs (8.8%) showed paraesthesia.

Table 3 Comparison of venous reflux anatomy between intervention and compression groups

Anatomy type [n (%)]	Intervention (n = 34)	Compression (n = 37)	P
Superficial	11 (32.3)	4 (10.8)	0.031
Perforators	10 (29.4)	20 (54)	
Superficial and perforators	13 (38.2)	13 (35.1)	

Table 4 Chronic venous ulcer healing and recurrence rates between intervention and compression groups

Healing rate	Intervention (n = 34)	Compression (n = 37)	P
Healing rate [median (IQR)] (cm ² /week) ^a	0.34 (0.59)	0.19 (0.39)	0.154
Ulcer healed without recurrence for 1 year (%)	21 (61.6)	11 (29.7)	0.012
Ulcer healed and recurred within 1 year (%)	7 (20.5)	17 (46)	0.002
Ulcer not healed within 24 weeks (%)	6 (17.5)	9 (24.3)	0.55
Time in weeks until healed [median (IQR)] ^{a,b}	10 (8.1)	20 (31.7)	0.011

^aTest performed using the Wilcoxon rank-sum test; ^bOnly healed ulcers were included.

Table 5 Complications in the intervention group

Complications	N (%)
Perforation of SFJ	0 (0)
Bruises and Ecchymosis	6 (17.6)
Nerve injury	3 (8.8)
Erythema	4 (11.7)
DVT	0 (0)
Pulmonary embolism	0 (0)

DVT, deep vein thrombosis; SFJ, saphenofemoral junction.

Skin burn occurred in the form of mild erythema in four limbs (11.7%), which might be due to insufficient tumescent anesthesia and very superficial veins. All patients improved with conservative management.

In the compression-only group, four patients suffered from ulcers due to bandaging; another two patients were hospitalized for cellulitis, which improved after medical treatment and continued our compression therapy.

Discussion

Compression therapy remains the standard of care for patients with advanced chronic venous disease (CVD) and venous ulcers (class C3–C6). Compression therapy improves calf muscle pump function and decreases reflux in vein segments in patients with chronic venous insufficiency (CVI) [14,15]. In patients with venous ulcers, graded compression is effective as the primary treatment to aid healing of venous ulceration and as adjuvant therapy to interventions to prevent recurrence of venous ulcers [3].

The main drawback in compression therapy is its dependence upon patient's compliance. Mayberry *et al.* [3] conducted a cohort study of venous ulcer treatment in 113 patients treated over 15 years. Ulcer healing with local care and compression was 97% in compliant patients and 55% in noncompliant patients ($P = 0.0001$). Ulcer recurrence was 16% in compliant patients and 100% in noncompliant patients.

Surgical correction of superficial and perforator incompetence to reduce local venous hypertension and assist healing of CVU is by no means new. Great and small saphenous vein stripping [16] and subfascial endoscopic perforator surgery (SEPS) [17] have been used for this purpose, but the effect on healing rates has been unclear.

In 2004 the ESCHAR study [9] randomized 500 patients from three centers with leg ulcers, who had isolated superficial venous reflux or mixed superficial and deep reflux, to compression treatment alone or to compression combined with superficial venous surgery. Surgery included high ligation, division, and saphenous stripping. Rates of healing at 24 weeks were similar in both groups (65 vs. 65%; hazard ratio, 0.84; 95% confidence interval, 0.77–1.24; $P = 0.85$), but 12-month ulcer recurrence rates were reduced in the compression with surgery group (12 vs. 28%; $P = 0.0001$).

After 4 years of follow-up in the ESCHAR study, the long-term results of the difference in ulcer recurrence rates between the two groups was still significant [18].

After introduction of minimally invasive procedures to superficial venous surgery, which offer obvious advantages over traditional surgical methods by avoiding incisions and tissue disruption in areas of significant inflammation and infection, several reports have examined the effect of minimally invasive correction of axial incompetence and perforator incompetence on ulcer healing [19].

Pang *et al.* [20] described the effect of using ultrasound-guided foam sclerotherapy (UGFS) on ulcer healing. They did not treat perforator reflux, although they comment that perforators were often incidentally occluded after UGFS. In 83 C6 patients, the healing rate was 81% at 6 months, with a 5% recurrence rate at 2 years.

Harlander-Locke *et al.* [21] quantitates the effect of RFA of axial and perforator reflux in patients with CVU that failed to heal with compression alone. They showed significant improvement in healing rates after application of these minimally invasive therapies. The

effect of minimally invasive therapy is particularly impressive, given that the ulcers had been present for almost 5 years on average and the fact that all patients had shown failure to reduce ulcer size for a minimum of 5 weeks with intensive compression treatment by dedicated wound nurses in a wound clinic environment before undergoing intervention.

Alden *et al.* [22] retrospectively reviewed 86 patients with CVU with 95 active ulcers. Ulcers treated with compression alone (compression group) were compared with those treated with compression and minimally invasive interventions, such as thermal ablation of superficial axial reflux and UGFS of incompetent perforating veins and varicosities (intervention group). Compared with the compression group, the ulcers in the intervention group healed faster (9.7 vs. 4.2% per week; $P = 0.001$) and showed fewer recurrences at 1-year follow-up (27.1 vs. 48.9%; $P < 0.015$).

Our patients, as in the other studies, were challenging. The patients were old, obese, and had advanced venous disease; more than 26% of the ulcers were recurrent. These demographics of our patient population are comparable to those of other reports evaluating the use of SEPS for the treatment of CVU [23], and to the more recent reports of Lawrence *et al.* [24], Harlander-Locke *et al.* [21], and Pang *et al.* [20], except that our patients were younger; this may be due to the exclusion of any patient treated with compression before.

Our review shows a significant improvement in the ulcer healing rates and recurrence rates when minimally invasive techniques are used to treat superficial and perforator vein reflux in conjunction with compression. Patients treated with intervention healed in less time compared with those treated with compression only (10 vs. 20 weeks; $P < 0.01$). No significant difference ($P = 0.73$) was seen in the proportion of ulcers that did not heal within 24 weeks (nine ulcers, 24.3% compression vs. six ulcers, 17.5% intervention). A significantly higher rate of recurrence was seen in the compression group. Seventeen patients experienced recurrence within 1 year compared with seven in the intervention group (4 vs. 20.5%; $P = 0.002$).

In the study by Harlander-Locke *et al.* [21], 23.6% failed to heal. This is a bit higher than the 17.5% failure to heal in our report and may be explained by a higher percentage of patients with deep system reflux (36.3%) in the study by Harlander-Locke *et al.*, whereas any patient with reflux at the popliteal vein was not included in our study.

The ESCHAR study clearly showed the value of surgical correction of the superficial reflux in preventing

ulcer recurrence, but no improvement in healing rates occurred with surgical correction of the superficial axial reflux [9]. Our experience and that of the investigators cited earlier indicates that early minimally invasive treatment of superficial reflux and perforator incompetence is safe in the presence of an active ulcer.

Contrary to the ESCHAR study [9], in which 653 of 1418 patients screened were unsuitable for surgery because of comorbidity, anatomy, and other factors, these minimally invasive techniques allow safe treatment of even the most infirm patients as long as they have suitable venous anatomy.

In our study, none of the patients in either group were identified with obstructive physiology, despite a history of deep vein thrombosis in 11.7 and 18.9% of the compression and intervention groups, respectively. We as a rule avoided using these minimally invasive therapies in patients with obstructive physiology, given reports of relatively poor effectiveness of SEPS in these patients [25,26].

The study does not separate the effects of treatment of axial reflux from those of treatment of perforator or varicose reflux. The question of which reflux is more important in the care of CVU has been a topic of much discussion in evaluating the results of treatment using SEPS [25]. In this study the concept was to treat the axial reflux first, followed by perforator treatment if the axial treatment did not lead to ulcer healing, as minimally invasive methods in patient care have significantly less morbidity compared with surgical approaches. We treated a perforator first only if it was the most relevant source of reflux and was not receiving reflux from an axial vein.

This study adds additional evidence that minimally invasive treatment of axial and perforator incompetence is a valuable adjunct to the use of compression in the treatment of CVU. However, a subset of ulcers remains truly recalcitrant and will not heal despite these measures. This rate was 23.6% in the rigorously selected group reported by Harlander-Locke *et al.* [21] and 17.5% in the current series. Whether a subset exists in whom minimally invasive correction of superficial axial and perforator incompetence should be avoided is unclear, but it is fair to suggest that this treatment will not always be effective.

The complications in our study were, as expected, relatively low in comparison with that of the ESCHAR study [9], which may be due to the use of minimally invasive intervention on a younger group of patients with exclusion of patients with reflux below the femoral vein level.

Our study has modified our CVU treatment approach. We now perform minimally invasive interventions in appropriate patients soon after initiation of compression treatment without waiting for the ulcer to heal.

Conclusion

In the presence of venous stasis ulcers, early treatment with minimally invasive ablation of the superficial axial and perforator reflux in addition to standard compression therapy is associated with faster ulcer healing and lower recurrence rate with minimal risk.

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Conflicts of interest

None declared.

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