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A retrospective cohort study comparing two treatments for active venous leg ulcers

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Abstract

Endovenous laser ablation (EVLA) and ultrasound-guided foam sclerotherapy (UGFS) have largely replaced traditional surgery for treatment of varicose veins (VVs) with active venous leg ulcers (VLUs), and multiple combined modes have emerged. A retrospective cohort study was performed to compare the effect of traditional surgery (high ligation and stripping followed with compression [compression plus HL-S]) to high ligation-endovenous laser ablation-foam sclerotherapy followed with compression (compression plus HL-EVLA-FS) on the treatment of active VLUs.

Data of active VLUs treated in our center from 2008 to 2017 and followed up for 1 year were analyzed. The intervention measures in the first 5 years were compression plus HL-S, and in the following 5 years were compression plus HL-EVLA-FS. The primary outcome was ulcer healing time. The secondary outcomes were the VVs occlusion and clinical success as assessed by a change in venous clinical severity score (VCSS) and complications.

The study included 120 patients and 200 patients treated with HL-S and HL-EVLA-FS, respectively, during 2008 to 2017. The average ulcer healing time were 2.3 ± 2.4 and 1.7 ± 1.7 months, respectively. Significant difference was found in the cumulative ulcers healing rate between the two groups (Hazard ratio [HR] and 95% confidence interval [CI] was respectively 1.458 and 1.140–1.865, $P = .0002$), but no difference was found in the VVs occlusion (HR and 95% CI was respectively 1.005 and 0.774–1.3071, $P = .967$). Significant difference occurred in 6 months and 12 months post-operatively in the VCSS change and in the procedure data and some complications between the 2 groups.

In conclusion, the treatment of HL-EVLA-FS can accelerate the healing of VLUs, improve the VCSS and present superior procedure data. However, no advantage could be found in the VVs occlusion compared with control group.

Abbreviations: DVT = deep venous thrombosis, EVLA = endovenous laser ablation, FS = foam sclerotherapy, GSV = great saphenous vein, HL-S = high ligation and stripping, N-UGFS = non- ultrasound-guided foam sclerotherapy, SSV = small saphenous vein, VCSS = venous clinical severity score, VLUs = venous leg ulcers, VVs = varicose veins.

Keywords: endovenous laser ablation, foam sclerotherapy, high ligation, stripping, varicose veins, venous leg ulcer

1. Introduction

Venous leg ulcers (VLUs) are a considerable health problem because of their high incidence, slow healing, high recurrence rate and high cost of treatment.[1,2] In recent years, medical scientists have sought to uncover efficient methods to treat VLUs that result in quick healing and a low recurrence rate and that are minimally invasive. This effort has achieved good results.[3–9] To integrate various advantages and improve curative effects, some surgeons performed several methods of varicose veins (VVs) treatment simultaneously, such as traditional surgery, foam sclerotherapy or laser ablation, and achieved a better treatment effect.[10–14] However, the combined treatment of active VLUs (C6[15]) of the great saphenous vein (GSV) and/or the small saphenous vein (SSV) with high ligation (HL), of the stem of GSV and/or SSV with endovenous laser ablation (EVLA) and VVs of the branch of GSV or SSV with foam sclerotherapy (FS) is rarely reported.

This study was a retrospective cohort study to compare the effect of traditional surgery (high ligation and stripping followed with compression [compression plus HL-S]) to high ligation-endovenous laser ablation-foam sclerotherapy followed with compression (compression plus HL-EVLA-FS) on the healing time of VLUs, venous clinical severity score (VCSS) changes and the occlusion rate of VVs in 12 months after intervention.

2. Methods

This retrospective cohort study was approved by the medical ethics committee of Ganzhou People's Hospital. The methods were carried out in accordance with the approved guidelines.

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The authors report no conflicts of interest.

The data sets used and/or analyzed during the current study are available from the first author on reasonable request.

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2.1. Patients and groups

The study was based on a consecutive inpatient population with active VLUs and was conducted in a single center from 2008 to 2017. Patient with active VLUs in both limbs were counted as 2 patients.

1. Age ≥18 years;
2. Active venous ulcer of the lower extremity;
3. Patients with moderate to severe GSV reflux and perforating vein reflux.

The exclusion criteria were as follows:

1. Leg ulcers from other causes such as arterial ulcers, diabetic ulcers, malnutrition ulcers, malignant ulcers, etc.;
2. Healed ulcer (C5);
3. A history of surgery for VVs;
4. Diameter of VVs > 1 cm;
5. Serious systemic diseases.

The patients were divided into 2 groups based on surgical procedures, one was compression plus HL-EVLA-FS and the control group was compression plus HL-S. Patients satisfying the inclusion criteria had been fully informed about the HL-S and HL-EVLA-FS procedures and had given their written consent to undergo this specific treatment.

2.2. Methods of the venous reflux measurement[16]

GSV reflux time: with the patients in a supine position, GSV reflux time in the groin were measured during a Valsalva maneuver (holding breath after forced exhalation for at least 3 seconds). A reflux time <1.0 second was normal, and a reflux time continuing the entire Valsalva maneuver was considered persistent reflux. The reflux time ≥2.0 seconds was defined as moderate or severe reflux.

PV reflux time around the ulcers: with the patients in a supine position, the pressure was relieved after pressing the calf muscle while measuring the reflux time of PVs around the ulcers. A reflux time <0.5 seconds was normal, and persistent blood flow from the deep to the superficial veins through the PVs was defined as persistent reflux. The reflux time ≥1.0 seconds was defined as moderate or severe reflux.

2.3. Variables

Data collected from the medical records included gender, age, duration of VVs, ulcer location, ulcer duration, ulcer diameter, come from countryside, and pre-operative VCSS.[17] The procedure data included HL applied to the SSV, operation duration, bleeding volume, the time of VVs occlusion and ulcer healing time. Data collected during the follow-up included complications such as saphenous nerve injury, deep venous thrombosis (DVT), pulmonary embolism, superficial phlebitis, and VCSS at 1, 6, and 12 months post-operatively. All recorded data and values were checked at least twice by a different person.

2.4. Surgical procedure

All the procedure of the patients with VLUs were performed by the same surgical team.

2.4.1. High ligation -stripping. The procedure was performed on an inpatient basis under lumbar or general anesthesia. After successful anesthesia, the patient was placed in the supine position, and the entire lower limb was disinfected. All the VVs were marked before surgery. An incision was made inside the femoral artery's pulsing point to dissect the trunk of the GSV and its branches. All the branches were ligated, followed by HL of the GVS 0.5 cm from the femoral vein. The whole GVS was stripped by VVs stripper. Then small incisions were made at the superficial VVs of the lower limbs and stripped VVs with small plier.

2.4.2. Endovenous laser ablation. The trunk of the GSV was punctured at the medial malleolus, and the laser fiber was inserted into the trunk of the GSV. The 810 nm-laser' machine (company: AngioDynamics) was activated using a pulse of 1 time/second, to close the trunk of GSV. The laser power used on the thigh was 15 W, and that on the calf was 10 to 12 W. For those patients who could not be inserted the guidewire upward from the ankle, we chose to downward insert the guidewire into the GSV at the inguinal incision, and the GSV was closed by laser retrograde. Cases' local GSV could not pass through the guide wire due to occlusion or stenosis, we would choose segmental laser cauterization of the GSV.

2.4.3. Foam sclerotherapy. Multi-point punctures were made on the VVs of the lower leg for the patients with HL-EVLA-FS treatment. Sclerosing foam was injected into the VVs separately under the non- ultrasound-guided foam sclerotherapy (N-UGFS) (1 ml lauromacrogol injection and 4 ml CO_2 was configured using the Tessari method into 4 ml sclerosing foam[18]). Approximately 4 ml of sclerosing foam was injected at each point. The total amount of lauromacrogol injected into each limb was no more than 10 ml. The collapse of the varicose vein was immediately visible after injection of sclerosing foam.

2.4.4. Post-procedure. Following cleansing of the ulcer, the wound was covered with a vaseline gauze and multilayer of alcohol gauze. The limb was pressurized with elastic bandages at the end of surgery, which were replaced with level 2 elastic stockings 3 days later. The time of bed rest was 6 hours after surgery. Continuous compressive therapy was administered during the first 2 weeks. After 2 weeks, the patients were instructed to wear level 2 elastic stockings during the day and to remove the compression at night, while elevating the limb at rest. The ulcer wounds were kept clean during compression treatment until they healed. Compressive therapy was maintained for at least 3 to 6 months, though some patients, the compressive therapy lasted up to more than 1 year.

2.5. Outcomes and follow-up protocol

Technical success was defined as the ability to advance a guidewire or stripper into the saphenofemoral junction or the saphenopopliteal junction and complete stripping or cauterization of the trunk of the GSV and/or SSV. Perioperative complications were mainly recorded during the hospitalization, and the data were collected based on the description in the medical records. The collection of data regarding some complications, such as saphenous nerve injury and superficial phlebitis, was delayed up to 1 month after surgery.

All patients were followed up on an outpatient basis with a physical examination and duplex ultrasonography follow-up. Patients were evaluated at 1, 6, and 12 months post-intervention. Data collected during the follow-up period included the ulcer healing time, the VCSS, and the VVs occlusion rate. Clinical

assessment based on the VCSS was completed prior to the procedure (day 0) and 1 month, 6 months, and 12 months thereafter.

The primary outcome was ulcer healing time.

The secondary outcomes were the VVs occlusion and clinical success as assessed by a change in VCSS (pre-operation, 1 month, 6 months and 12 months postoperatively), and safety of treatment based on the procedure data and assessment of minor or major complications during the perioperative period.

At the time of follow-up, a recurrence of an ulcer and a VV was defined as unhealed and unclosed, respectively.

2.6. Statistical analysis

Data analyses were performed using SPSS software (ver. 22.0; IBM Corp; USA). Continuous variables are described as the mean ± standard deviation (SD), and categorical variables are presented as percentages. An Independent-Samples *t* test was used to test the difference between the means of the VCSS in the 2 groups. Kaplan–Meier curves analysis were used to compare the rate of ulcers healing and VVs occlusion between the two groups. A value of $P < .05$ was considered statistically significant.

3. Results

3.1. General data of patients

A total of 375 patients with VLUs were treated in our single center from 2008 to 2017. In these patients, 146 patients were treated with compression plus HL- S in the first 5 years. Of them, 15 patients with healed ulcers (C5) and 14 patients with a surgical history of VVs were excluded. Of the remaining 117 patients, 3 had bilateral active VLUs resulting in a total of 120 limbs (counted as 120 patients) included in the study. Two and 3 patients were lost to follow-up at 6 months and 12 months post-operatively. Other 229 patients with VLUs were treated with a combination of compression plus HL-EVLA-FS from 2013 to 2017. 28 patients with healed ulcers (C5) and 8 patients with a surgical history of VVs were excluded. Of the remaining 193 patients, 7 had bilateral active VLUs resulting in a total of 200 limbs (counted as 200 patients) included in the study. 2, 3, and 5 patients were lost to follow-up at 1 month, 6 months and 12 months postoperatively. The number of patients treated and analyzed during follow-up is shown in the flow chart (Fig. 1). The baseline patient characteristics are shown in Table 1. The demographic characteristics of the 2 groups were essentially balanced and comparable.

HL-S was applied to GSV of 120 patients and to the SSV of 21 patients. HL-EVLA was applied to the GSV of 200 patients and to the SSV of 20 patients. N-UGFS injection was performed on the VVs of 200 patients. The technical success rate was 100%.

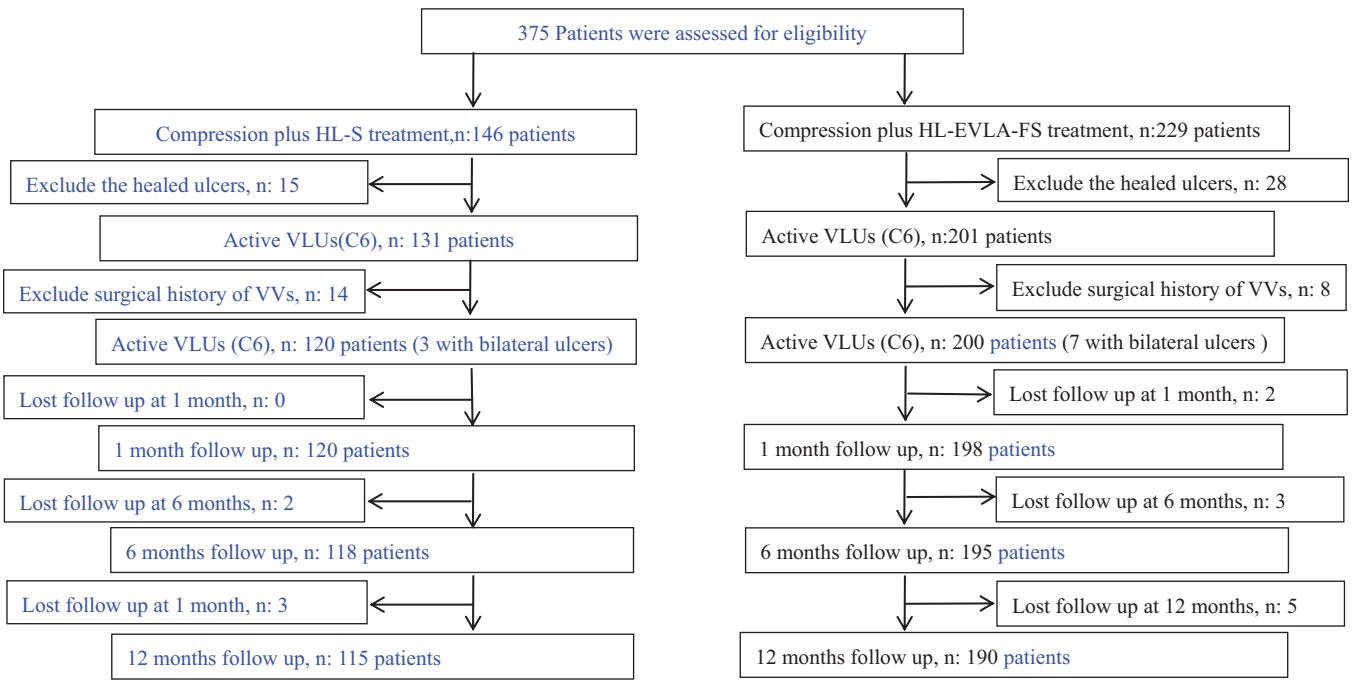
The average hospital stays time of the 2 groups were 11.2 ± 8.1 days and 7.1 ± 1.6 days, respectively ($P = .000$).

3.2. Primary outcome

The average ulcer healing time of the 2 groups were 2.3 ± 2.4 months and 1.7 ± 1.7 months, respectively (Table 2). Significant difference was found in the cumulative ulcers healing rate between the 2 groups (Hazard ratio [HR] and 95% confidence interval [CI] was respectively 1.458 and 1.140–1.865, $P = .0002$) (Fig. 2).

3.3. Secondary outcomes

There was no significant difference in the VVs occlusion (HR and 95% CI was respectively 1.005 and 0.774–1.3071, $P = .967$) between the 2 groups (Fig. 3).



HL-S = high ligation-stripping; HL-EVLA-FS = high ligation- endovenous laser ablation- foam sclerotherapy
VLUs = venous leg ulcers; VVs = varicose veins

Figure 1. Patient flowchart.

Table 1

Baseline characteristics of the study participants.

Variable	Compression plus HL-S treatment n (%) or Mean ± SD	Compression plus HL-EVLA-FS treatment n (%) or Mean ± SD	*P* values
Gender			.370*
Male	52 (43.3)	97 (48.5)	
Female	68 (56.7)	103 (51.5)	
Come from countryside	106 (88.3)	173 (86.5)	.635*
Age	59.0±12.4	60.6±10.3	.236†
Duration of VVs (years)	20.9±10.9	20.5±12.4	.748†
Ulcer duration (months)	24.4±78.4	25.3±71.0	.910†
Ulcer diameter (cm)	3.5±2.6	3.1±2.4	.181†
Preoperative VCSS	12.8±2.7	12.6±3.3	.470†
Location			.773*
Left medial malleolus	47 (39.2)	79 (39.5)	
Right medial malleolus	22 (18.3)	43 (21.5)	
Right lateral malleolus	3 (2.5)	8 (4.0)	
Left lateral malleolus	12 (10.0)	12 (6.0)	
Left foot boots area	21 (17.5)	35 (17.5)	
Right foot boots area	15 (12.5)	23 (11.5)	
BMI	28.4±2.68	28.4±2.7	.846†
Diabetes history	3 (2.5)	7 (3.5)	.749‡
Smoking history	37 (30.8)	61 (30.5)	.950*

BMI = Body mass index, HL-EVLA-FS = high ligation-endovenous laser ablation-foam sclerotherapy, HL-S = high ligation and stripping, HL-S = high ligation and stripping, SD = standard deviation, VCSS = venous clinical severity score, VVs = varicose veins.

* Pearson Chi-Square.

† Independent-sample *t* test.

‡ Fisher exact test.

Table 2

Independent-sample *t* tests of the VCSS between the 2 groups at the same time point (pre-operation, 1, 6, and 12 months post-operation).

	Compression plus HL-S treatment Mean±SD	Compression plus HL-EVLA-FS treatment Mean±SD	*P* values
Pre-operation	12.8±2.7	12.6±3.3	.470
1 month post-operation	9.4±2.9	9.8±3.6	.301
6 months post-operation	6.0±2.9	2.6±1.9	.000
12 months post-operation	5.3±2.5	2.1±1.7	.000

HL-EVLA-FS = high ligation-endovenous laser ablation-foam sclerotherapy, HL-S = high ligation and stripping, SD = standard deviation, VCSS = venous clinical severity score.

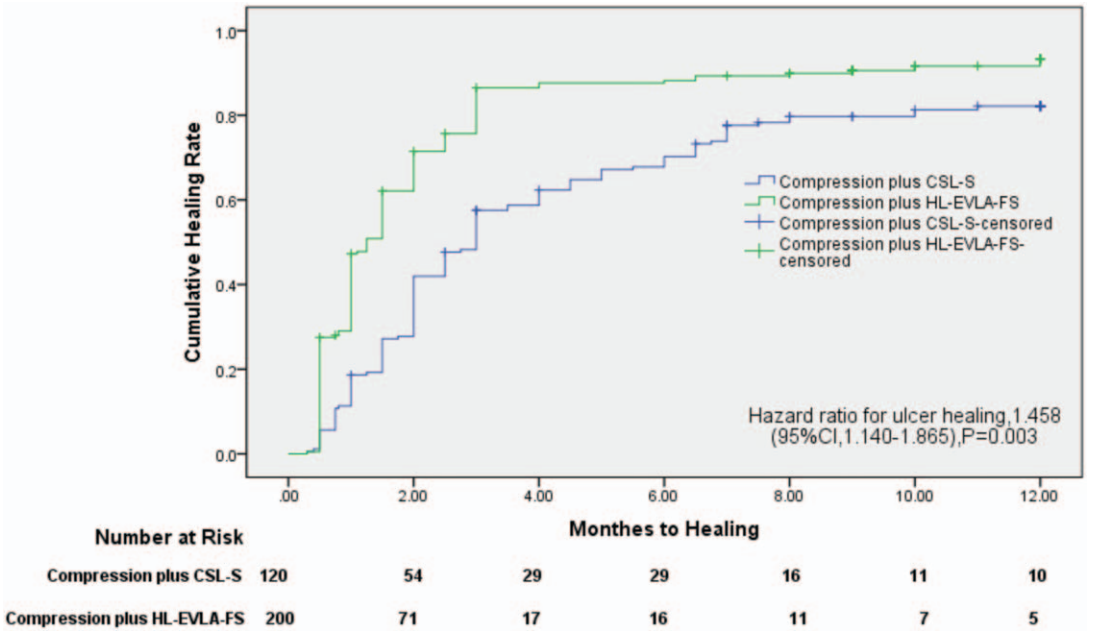


Figure 2. Kaplan–Meier curves for time to ulcer healing in the 2 groups.

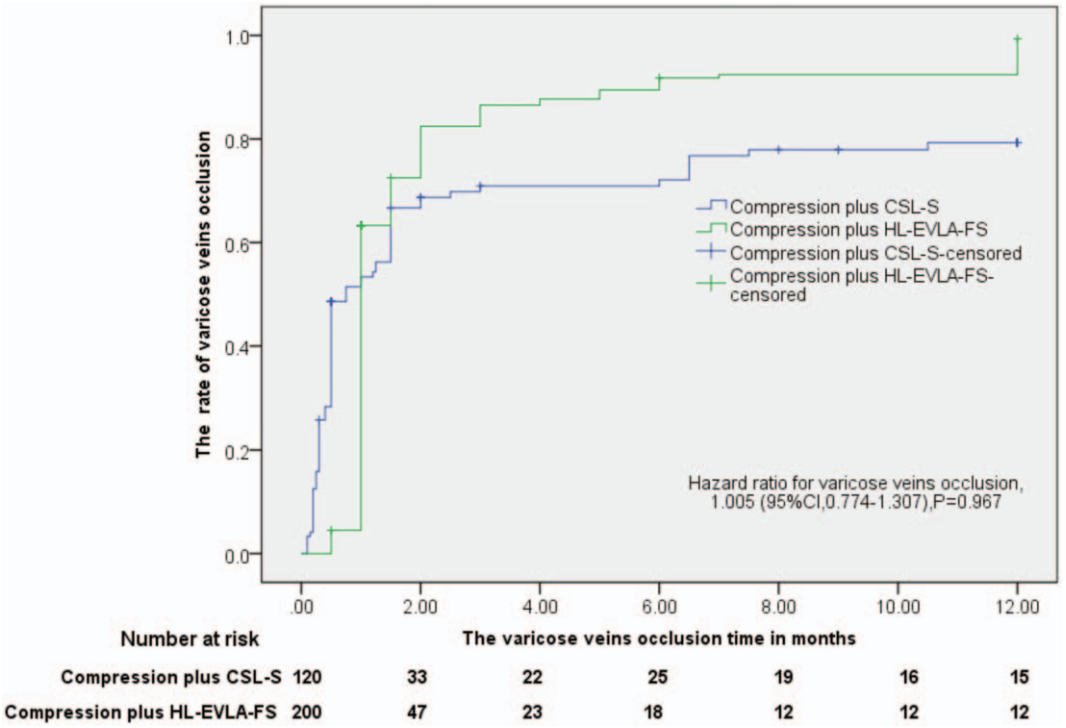


Figure 3. Kaplan–Meier curves for time to varicose veins occlusion in the 2 groups.

The VCSS changes of the 2 groups in 6 months ($P=.000$) and 12 months ($P=.000$) post-operatively were significant difference (Table 2).

Significant difference occurred in the procedure data such as operation duration ($P=.000$) and bleeding volume ($P=.000$) (Table 3). HL-S group had longer operative time and more intraoperative bleeding volume than that of HL-EVLA-FS group.

A major adverse event of DVT occurred 1 patient in each group, though the thrombus disappeared in 3 months and 4.5 months after anticoagulation therapy and compression treatment, respectively.

No major complication of pulmonary embolism occurred in either group.

Several minor adverse events occurred in the 2 groups. The post-operative complication of saphenous nerve injury was significantly higher in the HL-S group, with an incidence of 31.3% ($P=.000$), while the complication of superficial phlebitis was higher in the HL-EVLA-FS group, with an incidence of 7.5% ($P=.023$) (Table 3).

Laser burn of the skin occurred in 6 patients (3.0%) in the HL-EVLA-FS group, but the symptoms were mild and resolved within 1 week.

4. Discussion

Our retrospective cohort study indicate that HL-EVLA-FS treatment can accelerate the healing of VLUs, improve the VCSS of 6 months post-operatively and present superior procedure data. However, no advantage could be found in the VVs occlusion compared with the control group and the risk of

Table 3

Procedure data and complications.

Variable	Compression plus HL-S treatment n (%) or Mean ± SD	Compression plus HL-EVLA-FS treatment n (%) or Mean ± SD	*P* values
HL applied to the SSV	21 (17.6)	20 (10.0)	.048*
Operation duration (min)	104.8±15.8	59.9±8.1	.000†
Bleeding volume (ml)	58.6±18.6	11.3±4.3	.000†
Ulcer healing time (month)	2.3±2.4	1.7±1.7	.013†
Complications			
Saphenous nerve injury	36 (31.3)	11 (5.8)	.000‡
DVT	1 (0.9)	1 (0.5)	1.000‡
Pulmonary embolism	0 (0)	0 (0)	NA
Superficial phlebitis	2 (1.7)	15 (7.5)	.023*

DVT = deep venous thrombosis, HL-EVLA-FS = high ligation-endovenous laser ablation-foam sclerotherapy, HL-S = high ligation and stripping, SD = standard deviation, SSV = small saphenous vein.

* Pearson Chi-Square.

† Independent-sample *t* test.

‡ Fisher exact test.

superficial phlebitis post-operatively may be higher than HL-S treatment.

The principle underlying the treatment for VVs of the lower extremities is to block venous reflux, reduce superficial venous high pressure and prevent skin damage such as calf skin rash, pigmentation and ulceration. The conventional surgery involves HL of GSV and/or SSV and stripping of the stem of GSV and/or SSV and VVs. This method removes the VVs directly, eliminates the target reflux vessels, and cures the skin damage caused by venous hypertension. However, traditional surgical methods have certain drawbacks, such as the use of multiple skin incisions, slow recovery, and long hospital stay.[19]

In our retrospective study, the hospital stay of HL-S treatment was 11.2 ± 8.1 days, which was obviously longer than that of the HL-EVLA-FS treatment. And the HL-S group had longer operative time and more intraoperative bleeding volume than that of HL-EVLA-FS group. The traditional surgery (HL-S group) shew slightly worse results on the procedure data.

In recent decades, minimally invasive treatments such as laser, radiofrequency of thermal ablation[8,20–25] and foam sclerotherapy[5,26–30] of chemical ablation have appeared. The aim of these treatments is to destroy the VV endothelial cells, close the VV, and finally eliminate venous reflux, reduce venous hypertension and heal the skin damage caused by the VVs.[31–33] However, minimally invasive treatment also has some complications, such as skin burn and damage to the saphenous nerve.[33] In addition, foam sclerosing may cause superficial phlebitis and induce DVT.[34] Closed VVs can also recanalize.[35,36] Thus, there has been no consensus about the best method to employ.[37–40]

According to the extent of the lesion and for better treatment effects, combined treatment modalities have been constantly appearing.[41] Combined treatments such as EVLA-FS,[10,12] HL-FS,[14] and HL-EVLA[13] have been introduced successively. Comprehensive treatments can draw on their respective strengths to achieve the best effect, especially when treating severe or recurrent VVs.[12,14,42] However, the comprehensive treatment of active VLUs with HL-EVLA-FS has rarely been reported.

The comprehensive method of applying HL-EVLA-FS is feasible for the treatment of VLUs because it conforms to the treatment principle of VVs. First, the reflux of the GSV/SSV is blocked by high ligation of these vessels and their branches. Second, the GSV/ SSV are closed with EVLA, which blocks the veins themselves. Finally, FS is used to close the VV, which handles the offending vessels, eliminates the reflux target vessels of the PVs and narrows them. FS also directly acts on the endothelial cells of the PVs, causing their occlusion. All these strategies help to eliminate venous reflux, reduce superficial venous compression and promote ulcer healing. A variety of treatments have been used to eliminate total superficial vein reflux in treating venous ulcers, and good results have been achieved.[43]

Combined HL-EVLA-FS can accelerate healing of the ulcer. In our study, the average ulcer healing time was 1.7 ± 1.7 months, while that of the control group was 2.3 ± 2.4 months. Through Kaplan-Meier curves analysis the cumulative ulcers healing rate between the 2 groups, we found the HR was 1.458 (Fig. 2), which meant that the healing time of VLUs in HL-EVLA-FS group was significant shorter than that of HL-S group. Abdul-Haqq et al[3] used EVLA alone to close the GSV and PV to improve the healing of venous ulcers and found that the average ulcer healing time was 3.4 months.

The occlusion rate is another important index for the treatment of VVs. Devereux et al[44] conducted a randomized controlled trial of catheter-guided foam sclerosing treatment of GSVs. One group applied tumescent local anesthesia, while the other did not. At 1, 6, and 12 months of follow-up, the GSV occlusion rate in group 1 was 93%, 90.5%, 73.9%, respectively, compared with 90%, 82%, 75%, respectively, in the other group. Furthermore, the diameter of the GSV was reduced. Venermo et al[45] conducted a randomized controlled trial to compare the effect of surgery, EVLA (with phlebectomies) and UGFS on the GSV occlusion rate 12 months after surgery and found at 1 year that the occlusion rates were 97%, 97%, and 51%, respectively. The authors concluded that the occlusion efficiency of traditional surgery and EVLA is higher than that of FS.

However, in our retrospective cohort study, the results of the VVs occlusion was good in both groups and there was no significant difference. HR of the Kaplan–Meier curves for time to VVs occlusion in the 2 groups was 1.005 (Fig. 3), which may be largely related to the surgical procedure methods. In the HL-S group, most of the superficial VVs had been removed, HL eliminated the reflux of the GSV, and the remaining few VVs gradually close under the continuous compression. While in the HL-EVLA-FS group, the superficial VV's endothelium is destroyed by sclerotherapy and most venous reflux was abolished by EVLA and FS, furthermore the VVs gradually closes under the continuous function of late compression.

The VCSS changes of the 2 groups in 6 months ($P = .000$) and 12 months ($P = .000$) post-operatively were significant difference, which indicates that HL-EVLA-FS treatment has certain advantages over HL-S treatment for patients with active VLUs. The attribute indexes of VCSS values include pain, VVs, venous edema, skin pigmentation, inflammation, induration, number of active ulcers, active ulcer size, ulcer duration, and compression. The decrease of VCSS indicates improvement of lower limb symptoms.[17] The decrease of VCSS values in this group was mainly attributed to the closure of the VVs and the healing of ulcers. At present, the value of the VCSS is widely used to evaluate the severity and therapeutic effect of VVs.[14,41,46–48]

Nevertheless, the major adverse event of DVT occurred 1 patient in each group. The DVT incidence was low in the 2 groups and recovered after anticoagulation therapy. No pulmonary embolism occurred in either group. However, in the previous literature, UGFS has been reported to be associated with the risk of severe pulmonary embolism.[49]

Several minor adverse events occurred in the 2 groups. The complication of saphenous nerve injury was significantly higher in the HL-S group, with an incidence of 31.3% ($P = .000$). Because of the anatomical location of saphenous vein and saphenous nerve, most saphenous nerve injury caused by stripping is permanent, while caused by thermal damage of EVLA is temporary. Saphenous nerve injury has long been one of the complications of VVs surgery. In the previous literature, saphenous nerve injury was often reported in traditional surgery.[50,51]

While the complication of superficial phlebitis was higher in the HL-EVLA-FS group, with an incidence of 7.5% ($P = .023$) (Table 3). Phlebitis is primarily caused by FS treatment, which was reported in many similar literatures[14,27,52,53] in the past and the incidence ranged from 15.4% to 20%. However, the symptoms of the patients in our study are not serious, and disappeared within 3 months after compression treatment, elevation of the affected limbs and application of mucopolysaccharide polysulfonate cream.

Laser burn of the skin occurred in 6 patients (3.0%) in the HL-EVLA-FS group, but the symptoms were mild and resolved

Table 4

Details in the characteristics of the enrolled patients among the main literatures.

First author, year, country	Type of study	Treatment and control	Patients Age Male (%) CEAP classification C6 (n [%])	Primary endpoint	Patients (treatment/ control)	Follow-up time	Results
Kanchanabat B,[43] 2015 Thailand	prospectively collected and retrospectively reviewed	Total superficial vein reflux eradication	Age: 60.4 (27–80) Male: 8 (23) C6: 3.8 (0.4–10)	Wound healing	39	22 months (3–82 months)	Venous ulcer could be satisfactory treated by the total removal of the peri-ulcer reflux.
Abdul-Haqq R,[3] 2013, American	retrospective review	EVLA of GSV without IPV vs EVLA of GSV with untreated IPV vs EVLA of GSV and IPV	Age: 59.4±15.5 vs 57.2±11.6 vs 54.4±12.6 Male: 23 (56) vs 22 (51) vs 13 (76) C6: 108 (100)	Ulcer healing	46 45 17	16.9 weeks 19.2 weeks 14.0 weeks	Ulcer healing was accomplished to a significantly greater degree using EVLA of the GSV and IPV compared to GSV ablation alone for the treatment of active VSU in patients with combined reflux.
Devereux N,[44] 2014, Germany	prospective blinded RCT	CDFS +TA vs CDFS	Age: 52.7 (20–83) vs 55.1 (26–80) Male: 9 (36) vs 8 (32) C6: 0 (0) 1 (4)	Occlusion rates of GSV	25 25	1-, 6-, and 12 months follow-up.	No benefit could be found using additional TA to reduce the vein diameter before the treatment.
Venermo M,[45] 2016 Finland	RCT	Surgery vs EVLA vs UGFS	Age: 47.3 (27–75) vs 47.0 (20–73) vs 48.3 (23–74) Male: 10 (15.4) vs 18 (24.7) vs 18 (23.7) C6: NA	Occlusion rates of GSV	65 73 76	1-month and 1-month	In comparison with open surgery and EVLA, UGFS resulted in equivalent improvement in quality of life but significantly higher residual GSV reflux at 12-month follow-up.
Cicek MC,[50] 2016 Turkey	Single-center non-random trial	Group A (big olive heads) vs Group B (big olive heads) vs Group C (big olive heads)	Age: 36.16±12.31 vs 36.14±11.00 vs 40.18±17.01 Male: 26 (52) vs 25 (50) vs 23 (55.5) C6: NA	The incidence of nerve injury	50 50 50	6 months	Saphenous nerve injury complications of group C were significantly lower than group A and B
Papakostas JC,[51] 2014 Greece	RCT	Group A (upwards stripping) vs group B (downwards stripping)	Age: 44.6+11.45 vs 46.4+11.48 Male: 12 vs 12	Saphenous nerve injury	25 25	2 weeks and 12 weeks	Saphenous nerve injury was equally observed after downwards or upwards total stripping of the GSV
Yin H,[14] 2017 China	Prospective Randomized Study	GSV high ligation and UGFS vs traditional surgery	Age: 53.2 (29–74) vs 54.8 (25–77) Male: 36.6% vs 38.9% C6: 10 (12.2%) vs 11 (11.6%)	Reflux recurrence rate	73 90	12 months	UGFS combined with GSV high ligation was safe and effective for severe lower extremity varicosis.
Neto FC,[27] 2015 Brazil	Retrospective study	A two-year series in a single center	Age: 53 (27–79) Male: 25 (28%) C6: 57 (65.5%)	Clinical improvements, ulcer-healing rates	87	3 months	An outpatient, low-cost and high-resolution technique showed to be a safe and effective alternative for the treatment of severe varicose.
Baeshko A,[53] 2016 Belarus	Controlled clinical trial	A series of patients	Age: <30, 25 (7.7%) 31–40, 183 (56.1%) 41–49, 99 (30.4%) 50–59, 12 (3.7%) >60, 7 (2.1%) Male: 20 (6.1%) C6: 2 (0.5%)	GSV occlusion	326	5-year	An improved technique of foam sclerotherapy allows improving immediate and long-term results.
Bush.R.[4] 2013 USA	Case report	Case report	Age: 67 Male: 1 (100%) C6:1 (100%)	Ulcer healing	1	8 weeks	The technique of FS directed injected at the distal most vessels without ultrasound, with excellent penetration into the underlying venous network.
Camillo O,[55] 2018, Italy	retrospective study	Group A (long-catheters) vs B (short catheters or direct needle injection)	Age: 62.3 (36–82) vs 60.5 (30–84) Male: 18 vs 61 C6: NA	GSV occlusion	46 231	52.1 months (1–174 months)	In this long-term experience, foam-guided sclerotherapy of the GSV with a long-catheter turned out to be more effective than the usual foam-guided sclerotherapy.
Gohel MS,[56] 2018, UK	RCT	The deferred intervention group vs the early intervention group	Age: 67.0±15.5 vs 68.9±14.0 Male: 127 (56.7) vs 120 (53.1) C6: 100%	The time to ulcer healing	226 224	12 months	Early endovenous ablation of superficial venous reflux resulted in faster healing of venous leg ulcers and more time free from ulcers than deferred endovenous ablation.

CDFS = catheter-directed foam sclerotherapy, CEAP = Clinical-Etiology-Anatomy-Pathophysiology, EVLA = endovenous laser ablation, FS = foam sclerotherapy, GSV = great saphenous vein, IPV = incompetent perforator vein, RCT = randomized clinical trial, TA = tumescent application, UGFS = ultrasound-guided foam sclerotherapy, VCSS = Venous Clinical Severity Score.

within 1 week. We also found that the reduction in laser power on the calf reduce the chance of skin burn and saphenous nerve injury; the laser power we used on the thigh was 15 W, and that on the calf was 10 to 12 W. However, some researchers found that late outcomes following EVLA were superior for the 14 W continuous power settings achieving better long-term venous occlusion and lowered recurrence rates without increasing post-operative morbidity,[54] which may be related to the characteristics of the enrolled patients and the laser machine.

Moreover, we directly injected foam sclerosing agent into VVs without ultrasound or catheter guidance with no resultant serious complications, such as PE. To achieve ulcer healing, Bush et al[4] used a percutaneous approach of non-ultrasound guided injection of foam sclerosing directly into the VVs around the ulcer to close the VVs and PVs surrounding the ulcer. During our early surgery, we found that the injection of foam sclerosing agent into the superficial veins could discharge from the distal part of the detached GSV at the SFJ, which has also been demonstrated by ultrasound during surgery. We speculate it is the pressure of the deep veins and the reflux of PVs of the patients that led to the backflow of sclerosing agent injected into the VVs without reaching into the deep veins. Consequently, HL of the GSV may help prevent the foam sclerosing agent from flowing back into the deep vein through the GSV, which supports the need for HL of the GSV and the safety of N-UGFS. To study the effect of different injection methods on GSV closure, Orsini Camillo compared catheter-directed foam sclerotherapy with direct injection with a needle or a short catheter (butterfly needle or peripheral i.v. cannula). He found that catheter-directed foam sclerotherapy was more effective than direct injection of foam sclerosing. The former approach attained better distribution of the foam in the GSV without any substantial spasm of the vein.[55] However, the object of his study was the GSV. In fact, insertion of the catheter into the VVs is, in general, quite difficult. In the future, the method of direct injection of foam sclerosing agent needs to be verified with a larger sample size and longer follow-up.

There is no denying that some patients whose venous reflux is milder, the ulcer duration is not longer and the ulcers are smaller, may heal by the conservative treatment like pressure treatment, elevating limbs and so on. However, if early endovenous ablation of superficial venous reflux as an adjunct to compression therapy may be associated with a shorter time to healing of VLUs than compression therapy alone.[56]

Some details in the characteristics of the enrolled patients among the main literatures are shown in the Table 4.

This study has some limitations. First, it is not a randomized controlled trial and is therefore more subject to bias, which may diminish the strength of our conclusions. In addition, the follow-up time is short, and a longer follow-up time is needed.

5. Conclusions

In summary, in this retrospective cohort study, comprehensive treatment of active VLUs with HL-EVLA-FS yields good results in terms of ulcer healing rate, the VCSS improvements in 6 and 12 months post-operatively and superior procedure data. However, no advantage could be found in the VVs occlusion compared with the control group and the risk of superficial phlebitis post-operatively may be higher than HL-S treatment. Prospective and comparative studies are needed to further confirm these results and to determine whether the interest of the HL-EVLA-FS technique as a first-line strategy is reasonable.

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