

Sclerotherapy as adjunctive therapy in remaining varicose veins after endovenous laser ablation therapy

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Abstract

EVLT and sclerotherapy are relatively new in the field of management of varicose veins and reflux. a two-step management of varicose veins by EVLT and subsequent sclerotherapy is not extensively studied in the literature. Thus, we aimed to evaluate and compare the clinical outcomes of one-step EVLT and two-step EVLT and sclerotherapy in treatment of below-knee varicose veins.

This prospective study was performed from October 2020 to October 2021 at Imam Khomeini Hospital of Tehran. Patients with proved varicose veins of lower extremity were recruited for the study. All patients underwent endovascular laser ablation in SFJ and GSV regions at first step. After 48 hours of EVLT, color Doppler ultrasonography was done to rule out DVT. After four weeks, they were evaluated by physical examination and Doppler ultrasonography. In cases with remaining clinical or paraclinical evidence of varicose veins in below-knee veins, foam sclerotherapy was performed. Patients who had undergone sclerotherapy in the second step then underwent physical examination and Doppler ultrasonography. Demographic and baseline parameters were recorded. Ultrasonographic parameters, CEAP and VCSS were evaluated at three time-periods of baseline, one month after EVLT and one month after sclerotherapy.

Mean age of patients was 46.67 ± 13.31 years. 43 limbs (52.4%) were for male patients while 39 limbs (47.6%) were for female participants. Pain and visible varicose veins were the most common complaints. Significant improvements in ultrasonographic parameters, CEAP and VCSS were seen after one-step EVLT and two-step combined EVLT and sclerotherapy ($p < 0.05$).

A two-step strategy with initial EVLT and deferred sclerotherapy in selected patients with below-knee varicose veins can yield remarkable results comparable to the results of treatments of above-knee varicose veins previously reported in the literature.

Keywords: EVLT, Sclerotherapy, Varicose, CEAP, VCSS

Introduction

Varicose veins in lower extremity are very prevalent; found in around 25% of general adult population around the world which impair patients' quality of life remarkably [1]. These varicose veins are superficial veins which become enlarged and dilated with tortuosity. The changes in venous vasculature cause clinical symptoms including feeling of heaviness in lower extremity, pain, pigmentation or ulceration [2]. The underlying reasons for development of varicose veins are reflux and accumulation of blood in superficial veins which occur due to multiple mechanisms such as venous hypertension, inflammation, etc [3, 4].

Main treatment options of open surgery, endovenous laser ablation therapy (EVLT), radiofrequency ablation (RFA) and foam sclerotherapy exist for management of incompetent great saphenous vein (GSV) [2, 4, 5]. Traditionally, open surgery (high ligation and stripping) has widely been used for treatment of GSV incompetency [6]. In recent years, EVLT and foam sclerotherapy methods has been introduced as newer methods of treatment of varicose veins. In sclerotherapy, closure of varicose vein is performed through injection of chemical agents. These agents impair the endothelial layer and expose collagen fibers which lead to coagulation and venous thrombosis [7]. In EVLT, radiofrequency

waves are delivered for destruction of endothelial layer and closure of incompetent valve [8]. EVLT and sclerotherapy approaches have led to higher levels of efficacy, reduced rates of recurrence, shorter recovery duration and diminished rates of complication compared to open surgery [9]. Remarkable pain and wound after open surgery has been a matter of concern in management of varicose veins while in EVLT and sclerotherapy, only 1% of patients have reported pain one month after intervention [10]. An important point is that studies available in the literature have reported that EVLT is superior to sclerotherapy in terms of rates of post-intervention residual reflux of GSV and occlusion rates [11, 12]. Some authors have used a combination approach with concomitant use of EVLT and sclerotherapy for reduction of complications and reoperations and improvement in patients' quality of life [13, 14]. Some other authors have also suggested an interval (about 4 weeks) between EVLT and sclerotherapy to allow the varicosities shrink over time after EVLT and increase the chance of sclerotherapy in full resolution of symptoms and abnormalities [15].

Majority of studies have been conducted on above-knee segments in management of GSV incompetency. In addition, EVLT and sclerotherapy are relatively new in the field of management of varicose veins and reflux. Given these reasons, more studies are needed to clarify the clinical benefits and applications of these methods. Particularly, a two-step management of varicose veins by EVLT and subsequent sclerotherapy is not extensively studied in the literature. Thus, we aimed to evaluate and compare the clinical outcomes of one-step EVLT and two-step EVLT and sclerotherapy in treatment of below-knee varicose veins.

Materials and Methods

This prospective study was performed from October 2020 to October 2021 at Imam Khomeini Hospital of Tehran. Patients with proved varicose veins of lower extremity (confirmed by ultrasonography and physical examination) who presented to vascular surgery clinic of the hospital were recruited for the study. Patients underwent ultrasonography in case of presence of clinical evidence of varicose veins, visible varicose veins and symptoms of chronic venous insufficiency including pain, edema, ulcer, etc. After ultrasonographic confirmation of SFJ (saphenofemoral junction) and

SPJ (saphenopopliteal junction) incompetency and presence of reflux in these regions, visualization of superficial tortuous veins and pathologic diameters of veins, patients were enrolled in the study. Exclusion criteria included insufficiency of deep veins, history of deep vein thrombosis, previous surgery of varicose veins, anticoagulants' consumption, heart failure, current pregnancy and age <18 years. Patients were taken informed consent before undergoing interventions.

All patients underwent endovenous laser ablation therapy in SFJ and GSV regions at first step. After 48 hours of EVLT, color Doppler ultrasonography was done to rule out DVT. After four weeks, they were evaluated by physical examination and Doppler ultrasonography. In cases with clinical or paraclinical evidence of varicose veins in below-knee veins, foam sclerotherapy was performed. Main indications for undergoing sclerotherapy was presence of ultrasonographic evidence of varicose veins (reflux duration over 0.5 seconds in GSV and LSV or perforating veins, absence of reduction in size of superficial varicose veins in below-knee region and persistence of dilatation and tortuosity in superficial veins). Patients who had undergone sclerotherapy in the second step then underwent physical examination and Doppler ultrasonography. Treatment response was considered as resolution of clinical symptoms and ultrasonographic evidences indicative of improvement in dilatation of superficial veins and absence of pathologic reflux in GSV, LSV and perforating veins.

Demographic (age, gender) and baseline (BMI, family history, comorbidities, etiology, anatomic classification, involvement side and presenting complaints) parameters were recorded. Ultrasonographic parameters (SFJ reflux duration, SPJ reflux duration, GSV diameter, LSV diameter, insufficiency of perforating veins and presence of tortuous veins) were assessed at baseline, one month after EVLT and one month after sclerotherapy. For assessment of clinical severity and varicose veins, CEAP (clinical, etiological, anatomical and pathophysiological) and VCSS (venous clinical severity score) systems were evaluated at three time-periods of baseline, one month after EVLT and one month after sclerotherapy.

Data analysis was performed by IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, N.Y., USA). To compare two groups in terms

of categorical data, chi-square test was used. Comparison of quantitative variables between groups was performed by t-test. To evaluate the trend of changes in groups, ANOVA repeated measures was used. Statistical significance threshold was considered as p-value <0.05.

Results

Initially, 78 patients were selected for our study. One patient with chronic venous insufficiency, one patient with previous varicose veins' surgery, two patients with heart failure and three patients with age of <18 years old were excluded from the study. In total, 71 patients (82 limbs) were evaluated in our study which included 60 unilateral (84.50%) cases and 11 bilateral cases (15.49%). 63 limbs were treated with EVLT and 19 limbs underwent a combination two-step procedure of EVLT and sclerotherapy due to permanent below-knee varicose veins after EVLT.

Baseline characteristics

Mean age of patients was 46.67±13.31 years. 43 limbs (52.4%) were for male patients while 39 limbs (47.6%) were for female participants. 52 patients (63.4%) had visible varicose veins, 30 patients (36.6%) had foot edema, 8 patients (9.8%) had foot ulcer, 23 patients (28%) felt heaviness in their lower extremities, 60 patients (73.2%) experienced foot pain, 2 patients (2.4%) reported leg restlessness and 13 patients (15.9%) underwent intervention for cosmetic indications. Baseline characteristics are compared between two treatment groups in Table 1.

Ultrasonographic parameters during the course of study

Ultrasonographic examinations revealed that all parameters were similar between two groups at baseline except for insufficiency of perforating veins which was significantly higher in the group who needed additional treatment of sclerotherapy later in the course of follow-up (p=0.010). Significant improvements by EVLT was observed in both groups (p-value <0.05). In addition, sclerotherapy could yield substantial improvements in patients who could not reach satisfactory treatment response by EVLT alone (p-value <0.05). The details of ultrasonographic findings are presented in Table 2.

Table 1. Baseline characteristics in two treatment groups

Parameter	EVLT alone	EVLT and sclerotherapy	p-value
Age	47.84±13.09	42.78±13.62	0.148
Gender			
Male	32 (50.8%)	31 (49.2%)	0.587
Female	11 (57.9%)	8 (42.1%)	
BMI	25.26±4.30	24.35±4.90	0.442
Family history	23 (36.5%)	7 (36.8%)	0.979
Comorbidities			
Diabetes mellitus	7 (11.1%)	2 (10.5%)	0.943
Hypertension	11 (17.5%)	3 (15.8%)	0.865
Hyperlipidemia	7 (11.1%)	1 (5.3%)	0.451
Etiology			
Primary	2 (3.2%)	1 (5.3%)	0.609
Secondary	14 (22.2%)	5 (26.3%)	
Congenital	4 (6.3%)	3 (15.8%)	
Hereditary	22 (34.9%)	4 (21.1%)	
Not identified	21 (33.3%)	6 (31.6%)	
Anatomic classification			
Superficial veins	63 (100%)	19 (100%)	-
Perforator veins	25 (39.7%)	16 (84.2%)	0.001
Deep veins	9 (14.3%)	3 (15.8%)	0.871
Side			
Left	35 (55.6%)	11 (57.9%)	0.171
Right	28 (44.4%)	7 (36.8%)	
Presenting complaints			
Visible varicose veins	40 (64.5%)	12 (63.2%)	0.914
Edema	22 (35.5%)	8 (42.1%)	0.601
Ulcer	5 (7.9%)	3 (15.8%)	0.312
Heaviness	18 (29%)	5 (26.3%)	0.818
Pain	47 (75.8%)	13 (68.4%)	0.520
Restlessness	2 (3.2%)	0 (0%)	0.428
Cosmetic	12 (19.4%)	1 (5.3%)	0.143

Clinical severity of varicose veins and response to treatment

Two CEAP and VCSS scoring systems have been used for assessment of clinical severity of varicose veins. CEAP did not reveal any significant difference between two groups (p=0.761) at baseline. EVLT significantly improved CEAP in both groups (p=0.000) as majority of CEAP classes were C2 and C3 (80.9%) at baseline which turned into C0 and C1 (95.2%) after 4 weeks in EVLT alone group (p=0.033). In the combination group, C2 and C3 majority (73.7%) were downgraded to C1 and C2 (63.15%) (p=0.012). Sclerotherapy in the combination group significantly

improved the CEAP after 4 weeks with only Co (84.21%) and C1 (15.78%) cases ($p=0.003$). The details of CEAP in both groups during study are presented in table 3 and figure 1.

VCSS at baseline showed that cases with moderate levels of severity have been more prevalent

in combination EVLT and sclerotherapy group while mild cases were more prominent in EVLT alone group ($p=0.039$). Significant improvements in both groups after EVLT were seen (p -values of 0.012 and 0.44 in EVLT and combination groups, respectively). Sclerotherapy was significantly efficacious in terms of VCSS in patients with partial response to EVLT. The details of VCSS are shown in Table 4.

Table 2. Ultrasonographic parameters during the study

Ultrasonographic parameters	EVLT alone	EVLT and sclerotherapy	p-value
SFJ reflux duration (s)			
Baseline	1.62±2.30	2.40±2.85	0.220
4 weeks after EVLT	0.31±0.17	0.73±0.49	0.036
4 weeks after sclerotherapy	-	0.26±0.11	-
SPJ reflux duration (s)			
Baseline	1.26±0.31	1.40±0.32	0.346
4 weeks after EVLT	0.25±0.16	0.84±0.20	0.029
4 weeks after sclerotherapy	-	0.28±0.09	-
GSV diameter (mm)			
Baseline	7.35±2.79	11.96±4.34	0.033
4 weeks after EVLT	5.13±1.82	8.73±2.01	0.012
4 weeks after sclerotherapy	-	5.98±1.44	-
LSV diameter (mm)			
Baseline	3.00±1.06	4.35±1.97	0.026
4 weeks after EVLT	1.97±0.72	3.08±1.13	0.041
4 weeks after sclerotherapy	-	2.17±0.65	-
Insufficiency of perforating veins			
Baseline	32 (50.8%)	16 (84.2%)	0.010
4 weeks after EVLT	7 (11.11%)	12 (63.15%)	0.000
4 weeks after sclerotherapy	-	1 (5.26%)	-
Presence of tortuous veins			
Baseline	50 (79.4%)	16 (84.2%)	0.640
4 weeks after EVLT	9 (14.28%)	11 (57.89%)	0.002
4 weeks after sclerotherapy	-	1 (5.26%)	-

Correlation of study parameters with outcomes

Univariate analysis revealed that insufficiency of perforating veins ($p=0.001$), GSV diameter ($p=0.033$) and LSV diameter ($p=0.026$) were associated with treatment response (the need for sclerotherapy) but multivariate regression analysis rejected the probable independent and significant impact of these parameters on study outcomes (p -values >0.05).

Discussion

In this study we aimed to evaluate and compare the clinical outcomes of one-step EVLT and two-step EVLT and sclerotherapy in treatment of below-knee varicose veins. We found out that while one-step EVLT is highly efficient in improving patients' symptoms and clinical conditions, addition of sclerotherapy is so beneficial in patients who had not responded well to the EVLT.

It is expected that diameter of involved veins decreases with successful treatment of varicose veins. To evaluate the diameters of varicose veins, ultrasonography is used as a non-invasive and inexpensive method with excellent sensitivity and specificity in evaluation of venous reflux (95% and 100%, respectively) [16]. Ultrasonographic evaluations in our study revealed significant reductions in diameters of GSV and varicose veins, as well as durations of SFJ reflux by EVLT at first step and sclerotherapy in the second step. EVLT significantly reduced frequency of insufficient perforating and tortuous veins but in severe cases which needed additional treatment, sclerotherapy proved to be highly efficacious. De Oliveira reported a significant 33% decrease in GSV diameter during 90 days after sclerotherapy [17]. The point is that the diameter rapidly and remarkably decreased at immediate phase of post-sclerotherapy and then increased gradually. A study by Proebstle et al [18], also showed that pretreatment GSV diameter of $5.8±2.2$ decreased to around $4.6±1.7$ mm at 6 weeks after treatment. In our

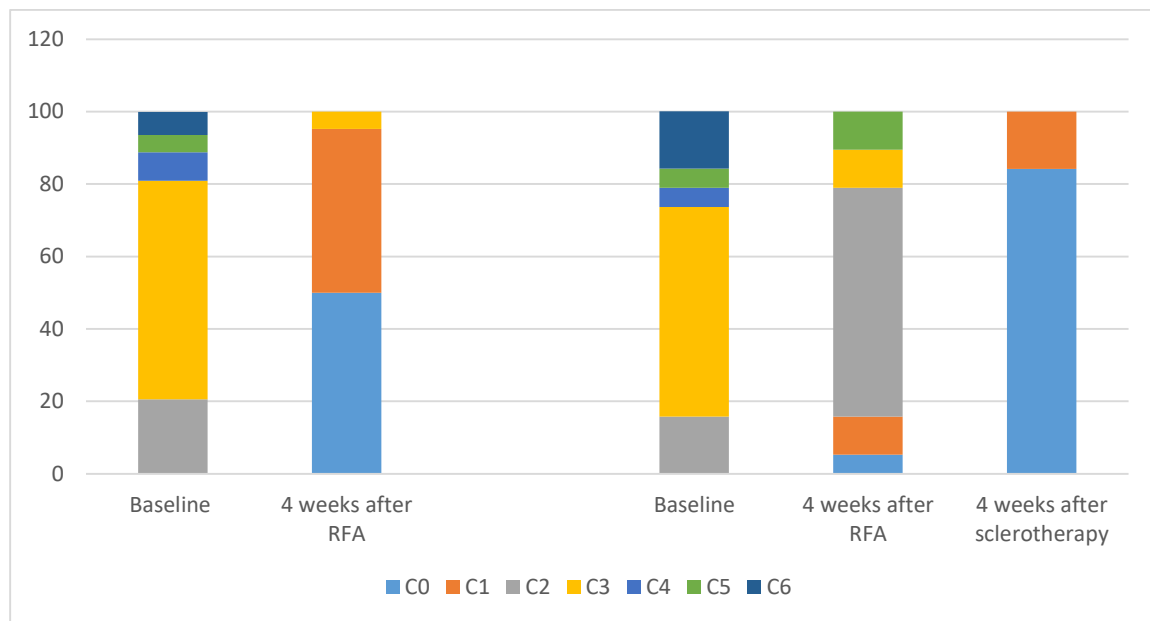


Figure 1. Distribution of CEAP classes in three time periods (A: EVLT alone, B: combined EVLT and sclerotherapy)

study, EVLT alone reduced frequency of insufficient perforating veins from 50.8% to 11.11% (EVLT one-month occlusion rate of 88.89%) while combination therapy of EVLT and sclerotherapy led to reduction of these rates from 84.2% to 63.15% at first step and then to 5.26% with sclerotherapy (combination therapy two-month occlusion rate of 94.74%). Tortuous veins were also decreased from 79.4% to 14.28% in EVLT and from 84.2% to 5.26% in the combination EVLT and sclerotherapy group. Thus, post-treatment residual varicose veins were relatively lower in combination treatment after second step compared to EVLT alone. Woo et al reported that at least 98.9% reached occlusion after EVLT [19]. Venermo et al also reported a 1-year occlusion rate of 97% after EVLT and 51% after sclerotherapy [11]. Studies have reported that sclerotherapy has been inferior to EVLT for resolution of varicose vein and its symptoms [11, 12]. To cover this issue, combination treatments have been introduced. For instance, Poschinger-Figueiredo et al reported that simultaneous EVLT and foam sclerotherapy leads to a 90.9% occlusion rate at first week which decreases to 69.7% at 3 years' post-intervention [20]. Pihlaja et al also reported 100% occlusion rate in concomitant EVLT and foam sclerotherapy [21]. We used interval EVLT and sclerotherapy in our patients to detect patients who have not responded well to EVLT alone. Partial-responders to EVLT then underwent sclerotherapy in

our study and yielded excellent results which were comparable to the available successful studies.

Clinical severity of varicose veins was assessed by two CEAP and VCSS systems in our study. CEAP at baseline was comparable between two groups but then after first step, patients with higher levels of CEAP needed an additional second step of sclerotherapy. Following sclerotherapy yielded very satisfactory results comparable or better than patients who had responded well to EVLT at first step. VCSS also showed exactly the same pattern as CEAP. Many studies have indicated that reduction of CEAP and VCSS is a suitable indicator of improvement in varicose veins. Rasmussen et al reported significant improvement in VCSS after EVLT or sclerotherapy without any difference between groups [22]. Choi et al reported reduction of CEAP from 2.33 ± 0.78 at preoperative period to 1.29 ± 0.96 at postoperative phase [23]. VCSS also showed decreases from 3.48 ± 0.98 to 0.63 ± 1.16 . Poschinger-Figueiredo et al reported reduction of VCSS from 8 at preoperative phase to 4 at six months after intervention by combination of EVLT and foam sclerotherapy [20]. Gameel et al also showed significant improvement in VCSS after undergoing combined EVLT and sclerotherapy [24]. The latter study was similar to our study regarding the study design and deferring sclerotherapy after EVLT at first step. Our results indicate that clinical severity and status of varicose veins improve significantly with performing delayed

Table 3. CEAP during study in both groups

CEAP	EVLT alone	EVLT and sclerotherapy	p-value
Baseline			
C0	0 (0%)	0 (0%)	0.761
C1	0 (0%)	0 (0%)	
C2	13 (20.6%)	3 (15.8%)	
C3	38 (60.3%)	11 (57.9%)	
C4	5 (7.9%)	1 (5.3%)	
C5	3 (4.8%)	1 (5.3%)	
C6	4 (6.3%)	3 (15.8%)	
4 weeks after EVLT			
C0	31 (50%)	2 (10.52%)	0.000
C1	28 (45.2%)	6 (31.57%)	
C2	0 (0%)	6 (31.57%)	
C3	3 (4.8%)	3 (15.78%)	
C4	0 (0%)	0 (0%)	
C5	0 (0%)	2 (10.5%)	
C6	0 (0%)	0 (0%)	
4 weeks after addition of sclerotherapy			
C0	-	16 (84.21%)	-
C1	-	3 (15.78%)	
Mean CEAP			
Baseline	3.15±1.01	3.47±1.30	0.273
4 weeks after EVLT	0.59±0.73	2.21±1.18	0.000
4 weeks after sclerotherapy	-	0.17±0.39	0.668

Table 4. VCSS during study in both groups

VCSS	EVLT alone	EVLT and sclerotherapy	
Baseline			
Absent (0)	3 (4.8%)	2 (10.5%)	0.039
Mild (1)	34 (54%)	4 (21.1%)	
Moderate (2)	26 (41.3%)	13 (68.4%)	
Severe (3)	0 (0%)	0 (0%)	
4 weeks after EVLT			
Absent (0)	56 (88.88%)	2 (10.52%)	0.000
Mild (1)	7 (11.11%)	13 (68.42%)	
Moderate (2)	0 (0%)	4 (21.05%)	
Severe (3)	0 (0%)	0 (0%)	
4 weeks after sclerotherapy			
Absent (0)	-	17 (89.47%)	-
Mild (1)	-	2 (10.52%)	
Mean VCSS			
Baseline	1.36±0.57	1.57±0.69	0.180
4 weeks after EVLT	0.11±0.03	1.01±0.37	0.002
4 weeks after sclerotherapy	-	0.09±0.02	-

sclerotherapy in patients treated with EVLT at first who could not reach appropriate treatment response.

Below-knee varicose veins are a challenge in surgery due to relatively lower occlusion rates and higher recurrences. Shoab et al has reported that 46% of patients who need retreatment after initial EVLT suffer from varicose veins in below-knee veins which means that residual varicose segments are prevalent in below-knee regions [25]. Another study by Chan et al adds that 40.7% require sclerotherapy within 6 months after initial EVLT [26]. Our study findings indicate that in below-knee varicose veins which do not respond well to EVLT, retreatment with sclerotherapy yields significantly successful outcomes. Thus, a delayed sclerotherapy in patients with below-knee varicose veins undergoing EVLT at first can be a good strategy for managing patients with poor response to initial treatments. This strategy could

obviate the need for stab avulsion or microphlebectomy of varicose veins.

Our study had some limitations. The main limitation in our study was relatively short duration of follow-up. Longer follow-up durations in studies has yielded more comprehensive results which can aid surgeons in choosing the proper treatment strategy. Our second limitation was lack of sole sclerotherapy group for a better and more precise comparison between EVLT, sclerotherapy and their combination.

Conclusion

A two-step strategy with initial EVLT and deferred sclerotherapy in selected patients with below-knee varicose veins can yield remarkable results comparable to the results of above-knee varicose veins' treatments previously reported in the literature.

Author contribution

Study conception: M N, Data collection: all authors, Analysis: B G, Investigation: all authors, Manuscript preparation: all authors

Critical review and revision: all authors, Final approval of the article: all authors, Accountability for all aspects of the work: all authors

Conflict of Interest

The Authors declares that there is no conflict of interest

Ethical declaration

This study was performed in line with the principles of the Declaration of Helsinki

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