

Comparison of foam sclerotherapy versus radiofrequency ablation in the treatment of primary varicose veins due to incompetent great saphenous vein: Randomized clinical trial



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Background and Objective: Minimally invasive procedures such as foam sclerotherapy and radiofrequency ablation (RFA) have gained attention for treatment of incompetent great saphenous vein (GSV). The objective of this study was to compare recurrence rate and quality of life between foam sclerotherapy and RFA in patients with incompetent GSV varicose veins.

Methods: In this parallel single-blinded randomized clinical trial, 60 adult patients with primary varicose veins due to incompetent GSV (CEAP classes C2-4EPAsPr) were included and randomly divided to receive RFA or foam sclerotherapy. Health-related quality of life (HRQOL) was assessed by the Short Form 36, and the Aberdeen Varicose Vein Questionnaire (AVVQ) was applied to assess the impact of varicose veins on quality of life of the patients. In addition, pain severity after the procedures was investigated by a visual analog scale (VAS) (range, 0 to 10). The patients were followed at 1 week, 1 month, 3 months, and 6 months postoperation. GSV reflux and recurrence was assessed by color Doppler ultrasound examination after 6 months.

Results: Twenty-eight patients in RFA and 27 patients in foam sclerotherapy remained for the final analyses. The time interval from the procedure and recovery to daily normal activities was 1 day in both groups. Mean ($\pm$ SD) pain VAS score in RFA group decreased from preintervention score of 7.35 ($\pm$ 3.28) to 1.21 ($\pm$ 0.68); $P < .0001$. Likewise, this score decreased from 6.64 ($\pm$ 2.04) to 1.29 ($\pm$ 0.91) in foam sclerotherapy group. HRQOL scores increased gradually at 1, 3, and 6 months after the intervention. AVVQ scores decreased significantly 1 week postintervention in both groups. After 6 months, 17.9% (5 patients) in RFA group and 14.8% (4 patients) in foam sclerotherapy group had recurrence of GSV reflux ($P = .52$).

Conclusion: Both foam sclerotherapy and RFA were effective in treatment of GSV reflux. Comparable findings were observed between the 2 groups regarding postoperative pain, recovery time, HRQOL, and AVVQ scores. (J Vasc Nurs 2019;37:226-231)

INTRODUCTION

Varicose veins of the lower extremity can affect about one-fourth of adult population and accompany significant comorbidities. This condition can adversely affect quality of life of the patients. Conventional surgeries including high ligation and stripping have been recognized as standard treatment options

and performed for long time for treatment of great saphenous vein (GSV) incompetence.¹ However, introduction of endovascular therapy and ablation techniques has yielded satisfactory results regarding efficacy (especially lower recurrence rate), recovery time, and lower complication rates, as well as lower costs.² For example, it has been shown that conventional surgery is associated with significant postoperative pain and wound

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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complications.³ But, endovascular ablation techniques such as foam sclerotherapy and radiofrequency ablation (RFA) are associated with less frequent pain, reported as 1% after 1 month in a report after using RFA.⁴ Various chemical agents (liquid or foam preparations) may be injected during sclerotherapy to close varicose veins. In foamed sclerotherapy, the chemical agent achieves direct contact with the epithelial layer of the vein because the gas mixture inside the foam causes expulsion of the blood.⁵ In RFA, thermal energy is produced using radiofrequency waves which damages the endothelial layer and seals the valve which is incompetent.⁶

Currently, minimally invasive procedures have become acceptable alternatives to surgical interventions for treatment of incompetent GSV. Not only minimally invasive procedures can be done as office-based procedures without the need for hospitalization, they are also associated with fewer complications and shorter recovery time when compared with more conventional open surgical approaches.⁷ Several studies have shown that foam sclerotherapy is inferior to open surgery and endovenous laser ablation (EVLA) regarding occlusion rate and residual reflux of great saphenous varicose veins.⁷⁻⁹ In a study which followed the patients for 5 years, EVLA and open surgery achieved higher rates of GSV obliteration in comparison to foam sclerotherapy.¹⁰ Faster recovery after minimally invasive procedures is one of the important advantages contributed to popularity of such techniques in the management of varicose veins.¹¹

As stated above the evidence currently favors endovascular laser ablation and RFA as comparable to conventional surgery regarding efficacy, yet, with fewer complications. This has been demonstrated in a recent systematic review.¹²

The purpose of this clinical trial was to determine the efficacy of 2 minimally invasive methods, foam sclerotherapy and RFA, in the treatment of patients with primary varicose vein due to incompetent GSV. In our opinion, the findings of this study would add substantial evidence to the current knowledge of the field and would enable clinicians to choose the most suitable treatment to manage the condition.

MATERIALS AND METHODS

Trial design

This study was a single-blinded parallel randomized clinical trial.

Participants

The study population was selected from patients aged 18–75 years with primary varicose veins due to incompetent GSV referred to our university hospital in 2017.

Inclusion criteria

Inclusion criteria were primary varicose veins due to incompetent GSV, symptomatic varices Clinical Etiologic Anatomic Pathophysiologic classes (C₂₋₄E_pA_sP_r), diameter of the GSV 3 cm below sapheno-femoral junction of 10–20 mm by color Doppler ultrasound, no duplication of the saphenous vein, no current or previous history of deep venous thrombosis (DVT), not taking anticoagulant or antiplatelet medications by the patients, no indirect GSV, and no varicose vein recurrence. Exclusion criteria were pregnant pa-

tients as well as those who died after the intervention or they did not cooperate for following visits.

Sample

A total of 60 patients were selected consecutively. Then, they were randomly assigned to foam sclerotherapy or RFA groups.

Assessment

For all patients, initially color Doppler ultrasound (UGEO WS80 A, Samsung, South Korea) was performed by a board-certified radiologist to examine the diameter of the vein and the presence of the GSV reflux. Clinical Etiologic Anatomic Pathophysiologic grades were determined according to Doppler ultrasound and clinical examinations. At this step, in addition to documenting the demographic data of the patients, the Short Form Health Survey (SF-36) questionnaire was used to assess the health-related quality of life (HRQOL)¹³ and the Aberdeen Varicose Vein Questionnaire (AVVQ) was applied to assess the varicose veins.¹⁴ The AVVQ was introduced in 1993 as a tool to measure quality of life in patients with lower extremity varicose veins.¹⁵ This contains 13 questions and a diagram that the patient can mark location of varicose veins. This questionnaire has been used widely in assessing the efficacy of interventions performed for varicose veins, and its reliability has been verified.¹⁴ The total score of the AVVQ ranges from 0 (no impact on QOL) to 100 (great impact on QOL); lower scores indicate better QOL. The purpose of the SF-36 questionnaire is to evaluate the health status (both the physical and mental health), which is obtained by combining the scores of the health domains. The questionnaire has 36 questions and assesses 8 different areas of health. An average score of the 8 domains is calculated. In addition, postintervention pain severity was documented using a visual analog scale with a range of 0 (no pain) to 10 (most severe pain experienced). The patients were blinded to the treatment groups.

Interventions

Radiofrequency ablation. In this method, heat was deployed to the GSV via a 7-cm catheter or heating element (Covidian, Costa Rica). The catheter was advanced up to 2 cm below the sapheno-femoral junction. In each segment, the heat was delivered (120°C) for 20 seconds.¹⁶

Foam sclerotherapy. The sclerosant foam was prepared by sclerosing solution (Fibrovein solution, United Kingdom) to air ratio of 1:5. Then, the foam was injected to the varicose vein under ultrasound guidance. The injection was done until the foam reached to the point nearly 2 cm below the sapheno-femoral junction.¹⁷ In both procedures, hair clipping of the surgical site of the leg was done before the procedures, and the area was cleansed with povidone iodine. The antiseptic agent used (ie, povidone iodine) was similar in both procedures.

Postprocedure care

The patients were instructed to wear class 2 compression stockings that cover the leg up to the thighs for 2 weeks. The patients were asked to wear the stockings day and night in the first 72 hours post-intervention. After this time, the patients were instructed to wear the stockings only when doing daily routine activities. They were asked not to take bath in the first 72 hours. All patients were encouraged to start their routine daily activities as soon as possible.

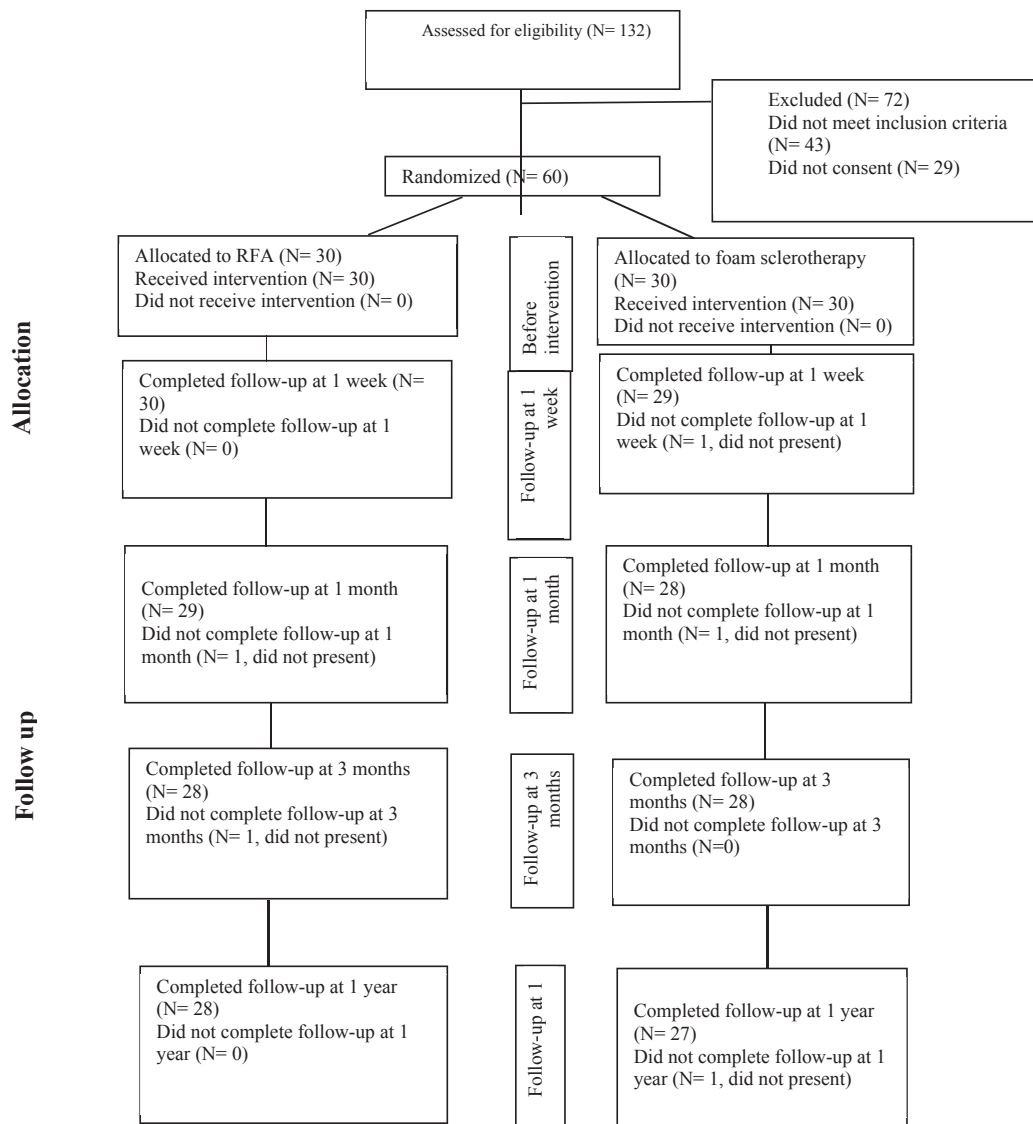


Figure 1. CONSORT diagram for the trial. RFA = radiofrequency ablation.

Follow-up and outcomes

The patients were visited at the following time points: 1 week, 1 month, 3 months, and 6 months after the procedures. At the first visit, the patients filled out the AVVQ, the SF-36, and VAS for measuring postintervention pain. Also, color Doppler ultrasound of the GSV was performed. The patient was asked about the time interval between the procedure and recovery to normal routine daily life. The treatment costs were also documented. At the successive follow-up visits, the SF-36 forms were completed, and color Doppler ultrasound examinations (to assess GSV incompetence recurrence) were performed. The successful treatment was defined as no blood flow in the GSV based on Doppler ultrasound examination. The possible complications were categorized as minor (those that did not require intervention) and major complications (those that required intervention).

Sample size

Considering the probability of recurrence in foam sclerotherapy group as 0.9 (P1) and in the RFA method as 0.5 (P2) and power (C)

as 10.5 and 10% drop, the sample size was calculated as 30 patients in each intervention group, using the following formula:

$$m(\text{size per group}) = c \times \frac{\pi_1(1 - \pi_1) + \pi_2(1 - \pi_2)}{(\pi_1 - \pi_2)^2}$$

where $c = 7.9$ for 80% power and 10.5 for 90% power, π_1 and π_2 are the proportion estimates.

Ethics

After assessing patients in terms of the inclusion criteria, complete descriptions of the main goals of the study, the interventions descriptions, the possible complications, and follow-up conditions of the patients were delivered to the patients, and written informed consent were obtained. It was assured to the patients that their participation in the study was on a voluntary basis and their information would be completely kept confidential and will be used only for scientific purposes. The study protocol was registered at the Iranian Registry of Clinical Trials (IRCT20180223038837N1). In addition,

TABLE 1

COMPARISON OF AGE AND GENDER DISTRIBUTION BETWEEN RADIOFREQUENCY ABLATION AND FOAM SCLEROTHERAPY GROUPS

Demographic Character	RFA (N = 28)	Foam Sclerotherapy (N = 27)
Gender		
Male	13 (48.1%)	14 (51.9%)
Female	15 (53.6%)	13 (46.4%)
Age, mean ($\pm$ SD)	43.65 ($\pm$ 10.78)	40.07 ($\pm$ 15.88)

RFA = radiofrequency ablation.

the study protocol was approved by the Ethics Committee of our university (IR.KUMS.REC.1397.493).

RESULTS

A total of 132 patients were assessed for inclusion into the study. Of this, 43 patients did not meet the inclusion criteria, and 29 cases did not consent to participate at the study. Finally, a total of 55 patients were treated with 28 in the RFA group and 27 in the foam sclerotherapy group. Others who dropped out were not accessible despite contacting them several times and did not present for follow-up visits (Figure 1).

Table 1 presents gender distribution and comparison of mean age between the 2 groups. As observed, no difference was seen between the study groups regarding the 2 variables.

Great saphenous vein reflux recurrence

At 1 week and 1 month following the interventions, no GSV reflux was detected in any group using color Doppler ultrasound. At 3 months, 2 patients (2 out of 27, 7.4%) in foam sclerotherapy group showed evidence of GSV reflux recurrence. At 6 months, 5 patients in RFA group (17.9%) and 4 patients in foam sclerotherapy group (14.8%) had recurrence of GSV reflux ($P = .52$).

Recovery to daily routine activities

The time interval from the procedure and recovery to daily normal activities was 1 day in both groups. None of the patients in either group developed infection at the surgical site.

Pain score and Aberdeen varicose vein questionnaire

Table 2 presents postintervention pain score and AVVQ in the study groups. In both groups, pain score decreased significantly 1 week after the procedures. No difference was detected regarding pain severity between the groups postintervention. As observed, improvement was seen in the AVVQ scores in both groups which was statistically significant.

Health-related quality of life

Table 3 presents mean (SC) scores of the SF-36 form at baseline and measured time points. HRQOL scores increased gradually at the time points. No statistically significant differences were seen between the 2 groups at any time points assessed after the interventions.

TABLE 2

COMPARISON OF PAIN SCORE AND ABERDEEN VARICOSE VEIN QUESTIONNAIRE (PREINTERVENTION AND POSTINTERVENTION) IN RADIOFREQUENCY ABLATION AND FOAM SCLEROTHERAPY GROUPS

Type of Treatment (Pain Score)	Preintervention Pain Score	1 Week Postintervention Pain Score	P Value*
RFA (N = 28)	7.35 ($\pm$ 2.38)	1.21 ($\pm$ 0.68)	<.0001
Foam sclerotherapy (N = 27)	6.64 ($\pm$ 2.04)	1.29 ($\pm$ 0.91)	<.0001
P value		.73 [†]	
Type of Treatment (AVVQ Score)	Preintervention AVVQ Score	1 Week postintervention AVVQ Score	P Value*
RFA (N = 28)	33.57 ($\pm$ 6.64)	19.46 ($\pm$ 5.15)	<.0001
Foam sclerotherapy (N = 27)	34.62 ($\pm$ 6.03)	16.66 ($\pm$ 4.8)	<.0001
P value		.73 [†]	

RFA = radiofrequency ablation.

*Wilcoxon signed rank test.

[†]Mann-Whitney U-test.

TABLE 3

HEALTH-RELATED QUALITY OF LIFE IN RADIOFREQUENCY ABLATION AND FOAM SCLEROTHERAPY GROUPS

<i>Type of Treatment</i>	<i>Preintervention</i>	<i>1 Week Postintervention</i>	<i>1 Month Postintervention</i>	<i>3 Months Postintervention</i>	<i>6 Months Postintervention</i>
RFA	42.32 (± 6.46)	63.53 (± 4.06)	68.43 (± 1.87)	68.75 (± 2.31)	69.21 (± 2.15)
Foam sclerotherapy	41.22 (± 4.29)	64.29 (± 4.11)	68.56 (± 1.87)	69.18 (± 2.11)	69.41 (± 2.21)
<i>P</i> value	.29	.5	.75	.33	.53

RFA = radiofrequency ablation.

Cost

RFA was more costly than foam sclerotherapy. Mean ($\pm$ SD) costs (intervention and hospitalization costs) without insurance coverage in RFA and foam sclerotherapy groups were 3.05 (± 0.0068) and 0.8 (± 0.0074) Million Tomans ($P < .0001$); 1 US\$ = 11,000 Tomans.

DISCUSSION

Considering the recent advances in the treatment of patients with primary varicose veins with incompetent sapheno-femoral junction failure and the introduction of new minimally invasive techniques, this clinical trial was designed to compare foam sclerotherapy and RFA regarding efficacy and pain alleviation and recurrence rate. It is of great clinical importance to select the best available minimally invasive method. Hence, conduction of appropriate studies are required to make clear the advantages and limitations of each technique. According to the obtained findings, the studied methods achieved comparable outcomes. After 6 months of follow-up, similar percentages suffered recurrence. Pain alleviation and improvement of HRQOL were also similar in both groups. However, the only difference lowers hospitalization and intervention costs of foam sclerotherapy.

In a previous clinical trial,¹ the researchers compared 4 surgical approaches for the treatment of GSV varicose. These 4 treatments included EVLA, RFA, foam sclerotherapy, and conventional surgery. According to the obtained findings, higher number of patients in foam sclerotherapy group (16.3%) had GSV reflux compared with RFA group (4.8%) after 1-year post-intervention. This is inconsistent with the current findings. In a separate study,¹⁸ after 5 years of follow-up, recurrent varicose was reported in 19 patients of RFA group (125 patients) and 28 patients of foam sclerotherapy group (125 patients). Although most studies have reported higher rate of recanalization of patients who were treated by foam sclerotherapy when compared with conventional surgery or other endovenous techniques, this was not seen in our study. The current follow-up time at 1 year was sufficient to observe any differences. In a systematic review of surgical treatment of short saphenous vein varicosity, EVLA was found to have lower rate of reflux persistence when compared with conventional surgical intervention.¹⁹ AVVQ score was not reported in all studies included in the systematic

review. There were inconsistent results in other studies when comparing EVLA versus open surgery. In a recent long-term randomized trial, laser ablation and surgery had lower AVVQ scores (reflecting better QOL) in comparison to foam sclerotherapy, even though improvement in QOL was seen in all 3 groups.²⁰ The mentioned study showed that QOL improvements were comparable between laser ablation and conventional surgery groups.²⁰ This finding is in agreement with the results of another long-term follow-up study showed similar outcomes regarding patient-reported QOL but superiority of laser ablation over surgery in terms of recurrence.²¹

Similar to GSV reflux rate which was similar in the 2 groups, sustained improvement of AVVQ scores was observed in both groups which is compatible with a previous study.⁸ Likewise, HRQOL improved in both groups. These findings suggest that both methods were successful in alleviating pain and improving quality of life of the patients.

The cost of treatment in RFA group was higher than that of foam sclerotherapy group. In a former study,¹ the average cost of treatment in RFA group was 1,436 Euros which was higher than foam sclerotherapy at 994 Euros. As per findings of this study, the 2 methods were comparable, in our opinion; foam sclerotherapy may be a better option when health-related expenses are a major concern. We did not study EVLA, but in a study to compare cost-effectiveness of this method as well as foam sclerotherapy and surgery,² it was reported that EVLA was the most cost-effective 1 among these 3 techniques.

We had some limitations in performing the study. Although the patients were blinded to the treatments, the surgeon was not blinded as it was impossible. In addition, the follow-up time is relatively short, and it is suggested to monitor the patients for longer times in the future studies.

CONCLUSION

Both foam sclerotherapy and RFA were effective in treatment of GSV reflux, and comparable findings were observed between the groups regarding pain, recovery time, HRQOL, and AVVQ scores. Foam sclerotherapy is more cost effective compared with RFA and vein ligation. The studied minimally invasive procedures do not require general anesthesia; however, anesthesia is necessary in ligation and stripping of GSV varicose. This

increases the cost of treatment with ligation/stripping. RFA and ligation/stripping have nearly similar costs of treatment.

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