Comparative Study of Outcome of Duplex Ultrasound-Guided, Catheter-Directed Foam Sclerotherapy and Radio-frequency Ablation in the Management of Great Saphenous Varicose Veins

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Abstract Chronic venous insufficiency of lower limbs is a common problem in adults. We compared the two modalities, namely duplex ultrasound-guided, catheter-directed foam sclerotherapy (UGFS) and radio-frequency ablation (RFA), in the management of great saphenous varicose veins using clinical assessment (Venous Clinical Severity Score, Venous Disability Score) and duplex imaging. Patients presenting with great saphenous vein (GSV) varicosity due to incompetent saphenofemoral junction (SFJ) were selected and randomly assigned in each arm, i.e., duplex UGFS group and RFA group. Patients were assessed on days 7, 30, and 90 both clinically and sonologically. Clinical assessment was based on the Venous Clinical Severity Score (VCSS) and Venous Disability Score (VDS). Obliteration of the treated GSV segment was noted in all the limbs of the RFA group (31/31) on duplex sonography on days 7, 30, and 90, while in the UGFS group, out of 30 limbs, obliteration was successful in 28 (28/30) and 2 had treatment failure. However, outcome of both the groups were statistically comparable (P value > 0.05). After the procedure, improvement in the VCSS was noted in both the study arms in every follow-up and both the modalities were found to be equally effective. Improvement in the Venous Disability Score was there on every follow-up, but maximum improvement was seen on the second visit, i.e., post-treatment day 30. Improvement was statistically significant and equal in both arms after the initial 1 week. Foam sclerotherapy, especially catheter-directed, is as effective as radio-frequency ablation in achieving anatomical obliteration

and yielding relief in clinical signs and symptoms in patients with GSV varicosity with SFJ incompetence.

Keywords Varicose veins · Foam sclerotherapy · Radio-frequency ablation · Venous Clinical Severity Score · Venous Disability Score

Introduction

Chronic venous insufficiency (CVI) of lower limbs is a common problem in adults. The Bonn Vein Study (2003), a general population-based study, has found that every sixth man and every fifth woman have CVI [1]. Valvular incompetency of the great or small saphenous vein is the most common cause [2]. Removal of such refluxing vein relieves the patient from its signs and symptoms.

Surgery has been the standard of care in the treatment of truncal varicose veins. The great saphenous vein (GSV) with an incompetent valve at the saphenofemoral junction (SFJ) is treated by high ligation followed by short stripping to the knee, while the varicose short saphenous vein (SSV) is addressed by ligation at the saphenopopliteal junction only. Although successful, its invasive nature is associated with post-operative morbidity and delay in return to normal activities [3, 4]. Minimally invasive newer endoluminal treatment modalities have been developed to treat great saphenous varicose veins, which include ultrasound-guided foam sclerotherapy, radio-frequency ablation (RFA), and endovenous laser therapy (EVLT), with a goal of achieving equal or better efficacy than conventional surgery, with reduced post-operative morbidity and faster recovery. Ultrasound-guided, catheter-directed foam sclerotherapy (UGFS) has been introduced recently, and its medium-term efficacy has been noted superior or equal to ultrasound-guided foam sclerotherapy [5, 6]. Foam

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sclerotherapy involves injection of varicosities with sclerosants in the form of foam [7]. RFA is a technique used for heat (radio-frequency waves) energy-induced obliteration of truncal varicose veins with excellent outcomes [8], but the disadvantages of this technique are high cost of treatment and lack of widespread availability. The Cochrane Database of Systematic Reviews (2014) of RCT data comparing foam sclerotherapy, radio-frequency ablation, and endovenous laser therapy to high ligation stripping for the treatment of great saphenous varicose veins suggested that all these endoluminal modalities are at least as effective as surgery [9].

In a developing country like India, ultrasound-guided foam sclerotherapy, especially catheter-directed, offers great promise not only because both Doppler and polidocanol are widely available but they are also relatively cheap. Comparing two minimally invasive modalities will help define their role as not many prospective studies have been done on the subject.

Aims and Objective

The aim of this study was to compare the outcome of duplex UGFS and RFA in the management of great saphenous varicose veins with saphenofemoral incompetence using clinical assessment (Venous Clinical Severity Score, Venous Disability Score) and duplex imaging.

Material and Methods

The proposed study was conducted in the Department of Surgery, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, in collaboration with the Department of Radiodiagnosis over a period of 18 months. Patients presenting in surgical outpatient department with GSV varicosity due to incompetent SFJ were selected on the basis of clinical history, physical examination and duplex ultrasound, then randomly assigned in each arm i.e. duplex UGFS group and radio-frequency ablation (RFA) group by a sealed envelope technique.

Inclusion Criteria

- Symptomatic patients belonging to $C_{2-5}E_pA_{s,p}P_r$ based on the Clinical-Etiology-Anatomy-Pathophysiology (CEAP) classification with incompetent SFJ
- Between 12 and 70 years of age at the time of enrolment

Exclusion Criteria

- Patients belonging to $C_{0,1,6}$ of CEAP classification
- History of deep venous thrombosis

- Pregnant ladies
- Allergic to polidocanol or anesthetic agent
- Greatly tortuous GSV
- Peripheral arterial insufficiency
- Locoregional infection
- Immobility
- Severe co-morbidities
- History of previous treatment for varicose vein
- Patent foramen ovale (on echocardiography)

Study protocol was approved by a local ethical committee. All patients were informed about the intervention technique, and written informed consent was taken. Study visits took place at baseline, time of the procedure, and 1 week, 1 month, and 3 months following the procedure. Follow-up visits included clinical and sonological assessments.

Procedures

To perform Duplex ultrasound-guided, catheter-directed foam sclerotherapy, foam was created by connecting two Luer-Lok syringes using a three-way stopcock. One of the syringes was filled with 2 ml of 3 % polidocanol (Asklerol 3 %, Samarth Life Sciences Pvt. Ltd., Goregaon, Mumbai) and the other with 8 ml of carbon dioxide. A local anesthetic cream was applied at the site of cannulation. The GSV was cannulated with a 6-Fr ureteric catheter at the level of knee under ultrasound guidance up to 3 cm below the SFJ, while the patient was in horizontal position. Post-cannulation patient was put in reverse Trendelenburg position with the limb raised. A pressure was applied at the SFJ by thumb, foam was injected slowly, and simultaneously, a catheter was steadily pulled out. An average volume of foam solution used in all the patients was 8–10 ml. A maximum of 10 ml of solution was used at a time as per European guidelines. External compression was applied over the treated segment manually. After injection, cotton wool was wrapped over thigh and compression bandage was done. The patient was advised to walk for 15–20 min post-procedure. Compression therapy was recommended for a period of 1 week.

Radio-frequency ablation was done using the VNUS Radiofrequency Generator (model RFG2) by Vnus Medical Technologies, Inc., CA, USA. While performing radio-frequency ablation, the patient was placed in reverse Trendelenburg position. A local anesthetic cream was applied along the course of the GSV. Under ultrasound guidance, a 7-F venous catheter sheath was cannulated over a 0.18 guidewire in the GSV trunk just above the knee. A radio-frequency catheter was placed through the sheath, and its tip was positioned 3 cm distal to the SFJ. Under USG guidance, perivenous tumescent fluid was injected to reduce treatment-related pain and vein diameter as well as to protect perivenous tissues from heat damage. The heating element was activated

Table 1 Number of limbs, gender composition, mean age, and mean C value (CEAP classification) in the study groups

	Number of limbs	Male patients (%)	Female patients (%)	Mean age (years) $\pm$ standard deviation	Mean C value $\pm$ standard deviation
RFA group	31	26 (83.9)	05 (16.1)	42.48 $\pm$ 13.73	3.97 $\pm$ 0.875
UGFS group	30	19 (73.1)	07 (26.9)	41.90 $\pm$ 12.82	3.73 $\pm$ 1.230
<i>P</i> value	–	–	–	0.864	0.416

with radio-frequency energy to 120 °C for 20-s heating cycles. External compression was achieved during treatment by manual compression. Ablation was started in incremental steps of 6.5 cm till the total length of the great saphenous vein was closed up to the knee. The catheter was pulled out with a 7-F sheath, and the access site was closed with sterile adhesive dressing. A crepe bandage was applied from the foot to the groin immediately after the procedure.

Below-knee varicosities, including varicosities due to incompetent perforators (usually above ankle), were treated by foam sclerotherapy in both the treatment groups in the same sitting.

Treatment Assessment

Post-procedure patients were assessed on days 7, 30, and 90 both clinically and sonologically. Clinical assessment was based on the Venous Clinical Severity Score (VCSS) and Venous Disability Score (VDS), taking into consideration the presence of pain, residual varicosity, edema, inflammation, pigmentation, induration, need of compression therapy, and ability to carry out usual activities. Side effects and complications of the treatment were also looked for.

Sonological assessment was done by duplex ultrasound of the treated GSV trunk. End points were vein occlusion (no blood flow in the treated segment of the great saphenous vein)

and absence of reflux. Flow in the GSV stump up to 3 cm below the SFJ was considered normal.

Statistical Analysis

The data was fed into Microsoft Excel format in a computer and was analyzed using SPSS statistical software, version 16. Categorical variables were presented as numbers, and continuous data was presented as mean $\pm$ standard deviation or median (min–max) as appropriate. The comparison between qualitative data was determined by applying chi-square or Fischer's exact test. The continuous data was compared by Student's *t* test/Mann-Whitney *U* test wherever required. The comparison over period of time was done by applying the Friedman test followed by post hoc comparison by the Wilcoxon signed-rank test after adjusting the probability. A *P* value less than 0.05 was considered significant.

Results

Between November 2013 and January 2015, 62 patients were enrolled and 66 limbs were treated in the Department of Surgery at Safdarjung Hospital using UGFS and RFA (33 limbs in each treatment arm). Four patients had a bilateral disease. Five patients were lost to follow-up. Finally, we had 30 limbs (26

Fig. 1 Number of patients belonging to the C class in the RFA and UGFS groups

Fig. 2 Improvement in mean VCSS values post-intervention on days 0, 7, 30, and 90

patients) in the UGFS group and 31 limbs (31 patients) in the RFA group. The mean age of presentation was 42.19 years with a male preponderance (M:F ratio of 4.1:1) (Table 1).

Baseline characteristics were comparable in both the study groups. The mean value of C in the CEAP classification for lower extremity venous disease was 3.97 for the RFA group and 3.73 for the UGFS group. Though the mean C score was higher in the RFA group, yet both the groups were comparable (Table 1). Most subjects presented late, i.e., with complications (C₄ and C₅ stage of CEAP classification) (Fig. 1).

Improvement in Venous Clinical Severity Score

The presentation of patients with a varicose vein disease was late (baseline mean VCSS value for the RFA group=11.0, mean VCSS value for the UGFS group=9.70), with a minimum score being 1 representing an uncomplicated disease to a maximum score of 20 representing healed ulcers with lipodermatosclerosis. The baseline VCSS was higher for the RFA group, yet both the study groups were comparable. After the procedure, improvement was noted in both the study arms in each follow-up and both the modalities were found to be equally effective (mean VCSS value at 90 days: RFA group=03.90, UGFS group=03.53) (Fig. 2).

The improvement in VCSS value was uniform over different time intervals and was significant in every follow-up, $P<0.01$ (Table 2).

Table 2 Improvement in mean VCSS values over different time intervals (Wilcoxon signed-rank test)

	VCSS0– VCSS7	VCSS0– VCSS30	VCSS0– VCSS90	VCSS7– VCSS30	VCSS7– VCSS90	VCSS30– VCSS90
<i>P</i> value (RFA)	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
<i>P</i> value (UGFS)	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

Improvement in Venous Disability Score

The baseline VDS ranged from a minimum score of 0 to a maximum value of 3, with a mean value of 1.48 for the RFA group and 1.40 for the UGFS group. Both the treatment arms were comparable. Following intervention, the improvement was there on every follow-up but maximum improvement was seen on the second visit, i.e., post-treatment day 30 (mean VDS value 0.77 in the RFA group and 0.50 in the UGFS group) (Fig. 3).

During the initial first week, the improvement in both the groups was insignificant ($P>0.05$), but after that, the improvement was seen in every follow-up visit and was significant ($P<0.05$) (Table 3).

Truncal (GSV) Obliteration on Duplex Ultrasound

Obliteration of the treated GSV segment was noted in all the limbs of the RFA group (31/31) on duplex sonography on days 7, 30, and 90, while in the UGFS group, out of 30 limbs, obliteration was successful in 28 (28/30) while 2 had treatment failure. In these two patients, the baseline mid-thigh diameter of the GSV trunk was more than 10 mm (12 and 13 mm) and they required multiple sessions (three sessions) of foam sclerotherapy. However, outcome of both the groups was statistically comparable (P value>0.05).

Fig. 3 Improvement in mean VDS values post-intervention on days 0, 7, 30, and 90

Complications

None of the patients had serious complications like deep vein thrombosis, thromboembolic episodes, and anaphylaxis. The most common side effect noted was post-procedural pain in either of the groups (45.16 % in the RFA group versus 50 % in the UGFS group), which persisted for 3–4 days in RFA-treated patients and required analgesics, while intensity of pain as well as duration were shorter (1–2 days) in UGFS-treated patients. Of the RFA group patients, 09.68 % (03/31) complained of cannulation site numbness which did not resolve in the follow-up period. Mild skin burn along the GSV was reported in three patients (09.68 %) in the RFA group. Fifty percent (15/30) of the patients of the UGFS group had cord-like induration along the GSV, which spontaneously resolved without sequelae over 4–6 weeks. Thrombophlebitis occurred in 26.67 % (8/30) of the patients in the UGFS group.

Discussion

Varicose vein is an often overlooked disease because of an under-appreciation of the magnitude and impact of the problem. In the Vein Consult Program, more than 91,000 subjects in various geographic regions were evaluated and worldwide prevalence of clinically significant chronic venous insufficiency of ≈ 60 % was found. Prevalence was higher in developed

countries [10]. According to a western study, approximately 23 % of US adults had varicose veins, a disease being commoner in women and older adults (40–80 years) [11]. However, in the latest Edinburgh Vein Study (2014), there was no age or sex difference when a large population size was followed up for 13 years for the incidence of venous reflux [12].

In our study, the mean age of presentation is 42.19 years with a male preponderance. Though there seems to be no clear explanation for this finding, this might well be accounted for by the fact that most of the patients suffering from the disease were involved either in strenuous labor or need to stand or walk for long periods in their work field, as more males are involved in heavy work. Also, females seek help late and probably dependent on males for medical care in a hospital especially from lower socioeconomic background.

The usual presenting complains are visible dilated veins of the lower limb, heaviness in the leg, swelling around the ankle, hyperpigmentation, and recurrent/non-healing ulcers in the gaiter area.

A duplex study of the venous system tells about patency of deep veins; incompetency of the SFJ, SPJ, and perforators, if any; and GSV diameter at the mid-thigh level.

The present study compared the outcome of GSV truncal obliteration using the two minimally invasive methods: RFA and ultrasound-guided, catheter-directed foam sclerotherapy. Anatomical success was high and statistically comparable in

Table 3 Improvement in mean VDS values over different time intervals (Wilcoxon signed-rank test)

	VDS0– VDS7	VDS0– VDS30	VDS0– VDS90	VDS7– VDS30	VDS7– VDS90	VDS30– VDS90
<i>P</i> value (RFA)	0.083	<0.01	<0.01	<0.01	<0.01	0.014
<i>P</i> value (UGFS)	0.317	<0.01	<0.01	0.046	<0.01	<0.01

Table 4 Cost comparison of two modalities

Radio-frequency ablation	
1. VNUS Radiofrequency Generator	688,000
2. Radio-frequency catheter	46,000
3. Introducer kit	450
Total (2 + 3)	46,450.00 ^a
Ultrasound-guided, catheter-directed foam sclerotherapy	
1. Luer-Lok syringes with 3-way stop cock	100
2. Polidocanol 3 % (1 ampoule)	100
3. Ureteric catheter	600
Total (1 + 2 + 3)	800

All figures are in Indian National Rupee

^a Without considering the price of the radio-frequency generator

both the study groups maintained over the 90-day follow-up (100 % in the RFA group and 93.3 % in the UGFS group).

The important observation was that GSVs with a mid-thigh diameter up to 10 mm were successfully obliterated in a single session while higher diameters required multiple sessions of sclerotherapy to achieve the goal.

Studies have already proven the high occlusion rates of RFA maintained in short and middle terms [8, 13, 14]. There are relatively lesser studies on ultrasound-guided, catheter-directed foam sclerotherapy of varicose veins; however, they prove it to be safer and more efficacious when compared with the standard ultrasound-guided foam sclerotherapy [5, 6, 15]. Studies on ultrasound-guided foam sclerotherapy have reported around 75 % success rate at 1 year [16, 17] and 65 % at 5 years [18] in maintaining truncal occlusion when assessed sonologically, while on clinical assessment, the result was comparable to that of endothermal modalities [9, 18]. The improvement in subjective complaints, as assessed by the VCSS and VDS, was significant and comparable at every visit, suggesting excellent clinical results and high patient satisfaction.

Relatively more post-procedural pain, ecchymosis, and persistent cannulation site numbness of the skin were reported in some patients of the RFA treatment arm of the study, which seem inherent to heat-based therapies [19]. Sclerotherapy arm subjects had self-limiting mild post-procedural pain and cord-like induration along the GSV with slightly higher incidence of thrombophlebitis as reported in previous studies [13]. Deep vein thrombosis, pulmonary embolism, and anaphylaxis have been reported as serious complications of these endoluminal treatment modalities [20–22], but none of the patients in our study groups had these complications.

When we compared the cost of treatment of these two modalities, the expenditure of foam sclerotherapy was approximately 50 times less than RFA even after discounting the initial cost of an RFA machine (Table 4).

This study has some limitations like small sample size and short duration of follow-up. But still, the results are very

encouraging especially with ultrasound-guided, catheter-directed foam sclerotherapy. A longer follow-up with a larger number of patients will definitely help in establishing it as a treatment of choice in developing countries.

Conclusion

Foam sclerotherapy, especially catheter-directed, is as effective as radio-frequency ablation in achieving anatomical obliteration and yielding relief in clinical signs and symptoms in patients with GSV varicosity with SFJ incompetence. It represents an ideal and cheaper substitute of RFA, especially in developing countries like India, with almost the same benefits, where cost, training, and availability of RFA remain a major problem in the government setup.

Compliance with Ethical Standards

Ethical Approval All procedures performed in the study were in accordance with the ethical standards of the institution, and the study was approved by an institutional ethical committee.

Conflict of Interest The authors declare that they have no conflict of interest.

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