Single-center retrospective review of early outcomes of radiofrequency ablation versus cyanoacrylate ablation of isolated great saphenous vein insufficiency

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ABSTRACT

Objective: Data comparing radiofrequency ablation (RFA) with cyanoacrylate closure (CAC) treatment of isolated great saphenous vein (GSV) insufficiency are limited. In this study, we present our early outcomes of RFA vs CAC for the treatment of GSV insufficiency.

Methods: Between March 2015 and February 2017, a total of 159 patients underwent CAC (n = 75) or RFA (n = 84) for treatment of GSV insufficiency by a single surgeon. Medical data of the patients were retrieved from the institutional database and retrospectively analyzed. All patients underwent lower extremity venous color duplex ultrasound examination. The Venous Clinical Severity Score and Aberdeen Varicose Vein Questionnaire were used. Total closure rates of the GSV with RFA or CAC were recorded at 1 month, 6 months, and 12 months. Procedure-related adverse events and quality of life of the patients were also evaluated.

Results: The mean age was 46.33 ± 14.40 years in the CAC group and 48.09 ± 13.25 years in the RFA group ($P = .4$). The mean treated saphenous vein diameter was 7 mm in the CAC group and 7.25 mm in the RFA group ($P = .07$). The length of treated venous segment was 30 cm in both the CAC and RFA groups ($P = .66$). The mean duration of operation was 25 minutes in the CAC group and 35 minutes in the RFA group ($P < .001$). The incidence of adverse events was higher in the RFA group ($P < .05$). At 1 month, 6 months, and 12 months of follow-up, there was no statistically significant difference in the total closure rates between the CAC and RFA groups. There was no significant difference in the Venous Clinical Severity Score and Aberdeen Varicose Vein Questionnaire score between the groups ($P > .05$).

Conclusions: Our study results suggest that both RFA and CAC are effective in closure of the target GSV. Although the incidence of tumescent anesthesia-related and procedure-related complications is higher with the RFA technique, both techniques can be used safely with similar success rate and patient satisfaction. (J Vasc Surg: Venous and Lym Dis 2019;7:480-5.)

Keywords: Great saphenous vein; Cyanoacrylate closure; Radiofrequency ablation; Varicose vein

Venous insufficiency of the lower extremity affects about 40% to 50% of the population.[1] Although it is asymptomatic in only 10% of cases, it is a chronic and progressive condition that accounts for skin changes and healed or active venous ulcers in 6% of cases in Western countries.[2,3] It is also associated with a higher degree of loss of work productivity than peripheral artery disease is.[4]

Stripping of the great saphenous vein (GSV) combined with high ligation was the standard surgical procedure for treatment of GSV insufficiency in the past. However, in recent years, novel and less invasive methods, including endovenous thermal ablation, have been widely adopted thanks to fewer side effects and more rapid recovery.[5]

Radiofrequency ablation (RFA) is a minimally invasive technique using thermal energy for ablation of the affected veins. It is an ablative technique using radiofrequency-induced thermal energy to produce acute endothelial damage through bipolar electrodes or catheters.[6] The use of RFA is associated with side effects like tumescent anesthesia-related discomfort and ecchymosis, and there is also a risk of thermal nerve damage that can result in paresthesia.[7] To minimize such complications, the cyanoacrylate molecule, which was used for endoscopic and intravenous embolization of peptic varicose veins and intracranial arteriovenous malformation treatment in the past, has been considered an alternative for the treatment of GSV insufficiency in recent years.[8-10] In the *n*-butyl cyanoacrylate ablation

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technique, the cyanoacrylate tissue adhesive contacts the venous endothelium, thereby inducing an inflammatory process and fibrosis.[11]

In the literature, the number of studies comparing RFA and nonthermal cyanoacrylate closure (CAC) techniques for the treatment of GSV insufficiency is limited. Therefore, in this study, we aimed to compare these two techniques and to evaluate side effects, vein closure rates, symptom scores, and quality of life in patients with GSV insufficiency.

METHODS

This study included a total of 159 patients who underwent CAC (n = 75) or RFA (n = 84) for the treatment of isolated GSV insufficiency between March 2015 and February 2017 by a single surgeon. Medical data including baseline demographic and clinical characteristics of the patients, Clinical, Etiology, Anatomy, and Pathophysiology (CEAP) class, and clinical variables were retrieved from the institutional database and retrospectively analyzed. A written informed consent was obtained from each patient. The study was approved by the institutional Ethics Committee and conducted in accordance with the principles of the Declaration of Helsinki.

Inclusion criteria were as follows: age ≥20 years to ≤76 years, vein diameter at GSV of ≥5.5 mm to ≤9.5 mm, reflux in GSV of >0.5 second, and CEAP class C2 to C4. Exclusion criteria were as follows: prior pulmonary embolism, deep venous thrombosis, or superficial venous thrombosis; tortuous GSV; pregnancy; immobilization; presence of malignant neoplasms; known sensitivity to cyanoacrylate adhesives; prior GSV treatment; symptomatic peripheral artery disease history, ankle-brachial index <0.9, severe femoral or popliteal venous insufficiency, and perforator vein insufficiency; and presence of varicose veins (>1 cm in diameter).

All patients underwent lower extremity venous color duplex ultrasound (DUS) examination. The Venous Clinical Severity Score (VCSS) and Aberdeen Varicose Vein Questionnaire (AVVQ) were used.

Procedural techniques. In all patients, the procedure was performed using local anesthesia under sterile conditions in the operating room. In the CAC technique, a disposable sterile VariClose ampule using the VariClose Vein Sealing System (Biolas, Ankara, Turkey), each containing 1 mL of VariClose polymer-based cyanoacrylate, and a delivery catheter were inserted. The VariClose set consisted of a 6F introducer sheath, a 0.035-inch guidewire, a 3-mL injector, an injection gun, an injection adaptor, a labeling 5F catheter, and a 4F microcatheter. The saphenous vein was percutaneously cannulated at above-knee level under the guidance of DUS. The introducer sheath was inserted in the saphenous vein, and the labeling catheter was pushed 3 cm distal to the saphenofemoral junction. The delivery catheter was prepared, and *n*-butyl cyanoacrylate solution was placed into the injection gun. The microcatheter was then pushed through a 5F catheter and locked to be 3 cm distal to the saphenofemoral junction. The location of the catheter was confirmed through DUS, and precipitation was applied twice for 1 second in the microcatheter system for priming by applying compression into the proximal segment with the DUS probe to prevent the bolus polymer from escaping into the deep venous system before the solution was given. The catheter was then pulled back 2 cm/s by pushing the trigger system of the gun for 5 seconds. Pressure was applied with the DUS probe simultaneously, and for each 5-second triggering of the gun, 0.3 mL of polymer was given to the vein (0.03 mL/cm). The procedure was continued until all saphenous vein segments were embolized.

In the RFA technique, the GSV was percutaneously cannulated from above-knee level under local anesthesia by guidance of DUS. A 6F introducer sheath (Input introducer sheath; Medtronic Ireland, Galway, Ireland) was inserted into the saphenous vein, and a ClosureFast RFA catheter (VNUS ClosureFast; Covidien, Dublin, Ireland) was pushed 3 cm distal to the saphenofemoral junction. Tumescent anesthesia (500 mL of 0.9% saline, 50 mEq of $NaHCO_3$, 50 mg of bupivacaine 0.5%, and 0.5 mL of epinephrine 1:1000) was infiltrated into the perisaphenous compartment under the guidance of DUS. Each segment of the treated saphenous vein was exposed to a two-cycle radiofrequency pulse. Compression was also applied simultaneously to the treated segment through the DUS probe. After the procedure, the saphenous vein segments that were treated were controlled through DUS. No additional attempt for phlebotomy or sclerotherapy was applied. All patients were uneventfully discharged on the day of the procedure. The visual analog scale scores were also recorded. All patients were mobilized in the early period. To follow a standard follow-up protocol, all patients were instructed to wear compression stockings (open toe, thigh high, 20-30 mm Hg) for 7 days.

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center retrospective cohort study
- **Key Findings:** In 159 patients, radiofrequency ablation and cyanoacrylate closure treatment were equally safe, with similar occlusion rates, clinical success, and patient satisfaction at 1 year.
- **Take Home Message:** Radiofrequency ablation and cyanoacrylate closure techniques can be used safely with similar success rate and patient satisfaction at 1 year after intervention.

Table I. Baseline and demographic characteristics of patients

	CAC (n = 75)	RFA (n = 84)	*P* value
Sex, female/male	42 (56)/33 (44)	44 (52.4)/40 (47.6)	.648[a]
Age, years	46.33 ± 14.40 (20-70)	48.09 ± 13.25 (22-76)	.423[b]
Target lower extremity, right/left	47 (62.7)/28 (37.3)	49 (58.3)/35 (41.7)	.577[a]
BMI, kg/m^2	26.69 ± 2.80 (20-34)	27.13 ± 3.12 (21-34)	.356[b]
Main symptom			
Pain	29 (38.7)	34 (40.5)	.745[a]
Swelling	29 (38.7)	30 (35.7)	
Heaviness	15 (20)	15 (17.9)	
Itching	2 (2.7)	5 (6)	
GSV diameter, mm	7 (5.5-9)	7.25 (5.5-9.5)	.072[c]
CEAP class			
C2	49 (65.3)	54 (64.3)	.865[a]
C3	19 (25.3)	20 (23.8)	.865[a]
C4	7 (9.3)	10 (11.9)	.865[a]

BMI, Body mass index; *CAC*, cyanoacrylate closure; *CEAP*, Clinical, Etiology, Anatomy, and Pathophysiology; *GSV*, great saphenous vein; *RFA*, radiofrequency ablation.
Data are presented as mean ± standard deviation (minimum-maximum), median (minimum-maximum), or number (%).
[a] χ^2 test.
[b] Independent samples *t*-test.
[c] Mann-Whitney *U* test.

Follow-up protocol. Preprocedural and postprocedural data were evaluated. Before the procedure and at 1 month, 6 months, and 12 months after the procedure, lower extremity venous DUS was performed for all patients by a single radiologist using the SonoScape S40 ultrasound device (SonoScape Medical Corp, Shenzhen, China). Total closure rates of the GSV with RFA or CAC were recorded. Procedure-related adverse events and quality of life of the patients were also evaluated.

Statistical analysis. Statistical analysis was performed using the SPSS version 22.0 statistical software (IBM Corp, Armonk, NY). Descriptive data were presented as mean ± standard deviation, median (minimum-maximum), or frequency (%). According to the normality test results, independent samples *t*-test or Mann-Whitney *U* test was used to compare the groups. For the CAC and RFA groups, preprocedural and postprocedural VCSS and AVVQ scores were analyzed using the Wilcoxon signed rank test. The χ^2 and Fisher exact tests were used to compare categorical variables. A *P* value of <.05 was considered statistically significant.

RESULTS

Of a total of 159 patients, 84 underwent RFA and 75 underwent CAC. Of the patients, there were 42 women (56%) and 44 women (52.4%) in the CAC and RFA groups, respectively. The mean age was 46.33 ± 14.40 years in the CAC group and 48.09 ± 13.25 years in the RFA group ($P = .4$). According to the CEAP classification, 65.3% of the patients (n = 49) were C2, 25.3% (n = 19) C3, and 9.3% (n = 7) C4 in the CAC group and 64.3% (n = 54) were C2, 23.8% (n = 20) C3, and 11.9% (n = 10) C4 in the RFA group ($P = .865$). The median GSV diameter was 7 mm in the CAC group and 7.25 mm in the RFA group ($P = .07$). Main symptoms included pain (n = 63), swelling (n = 59), itching (n = 7), and feeling of heaviness (n = 30) in both groups. There was no statistically significant difference between the groups. Demographic and baseline characteristics of the patients are shown in Table I.

None of the patients experienced any major complication after the procedure, including death, deep venous thrombosis, and pulmonary embolism. The mean duration of operation was longer in the RFA group than in the CAC group ($P < .001$; Table II). In the early period, paresthesia was not seen in any of the patients in the CAC group, indicating a statistically significant difference between the groups ($P < .02$). In all patients with paresthesia, clinical symptoms spontaneously resolved within 3 months. In addition, the patients with phlebitis were treated with nonsteroidal anti-inflammatory drugs and antibiotherapy for a week. There was no statistically significant difference in the other adverse effects, postprocedural pain scores, diameter of treated veins, and body mass index between the groups ($P > .05$). Adverse events are summarized in Table II.

Closure rates of the GSV were evaluated at 1 month, 6 months, and 12 months through venous DUS in both groups. In the CAC group, the closure rate was 100% (n = 75) at 1 month, 96% (n = 72) at 6 months, and 94.7% (n = 71) at 12 months. These rates were as follows in the RFA group: 98.8% (n = 83) at 1 month, 95.2%

Table II. Procedural data and adverse events

	CAC (n = 75)	RFA (n = 84)	*P* value
Length of treated segment, cm	30 (25-36)	30 (21-39)	.66[a]
Duration of procedure, minutes	25 (20-36)	35 (29-51)	<.001[a]
Pain score	5 (2-8)	4 (2-8)	>.05[a]
Adverse events			
Phlebitis	4 (5.3)	5 (6)	>.05[b]
Skin pigmentation	2 (2.7)	3 (3.6)	>.05[b]
Ecchymosis	2 (2.7)	3 (3.6)	>.05[b]
Paresthesia	0	1 (1.2)	<.02[b]

CAC, Cyanoacrylate closure; *RFA*, radiofrequency ablation.
Data are presented as median (minimum-maximum) or number (%).
[a]Mann-Whitney *U* test.
[b]Fisher exact test.

(n = 80) at 6 months, and 92.8% (n = 78) at 12 months. No statistically significant differences in recanalization rates were seen (Table III).

In addition, both groups were evaluated in terms of clinical symptoms and quality of life through the VCSS and AVVQ. There were no statistically significant differences in the VCSS and AVVQ scores between the groups ($P > .05$). However, we found that both VCSS and AVVQ scores significantly decreased after the procedures compared with baseline values. The VCSS and AVVQ scores of both groups are presented in Table IV.

DISCUSSION

In our study, we evaluated early outcomes of RFA and CAC for the treatment of GSV insufficiency and showed that both RFA and CAC are effective in closure of the target GSV.

Although several studies using RFA and CAC in the treatment of GSV insufficiency are available in the literature, there is a limited number of head-to-head studies comparing these two techniques. Morrison et al[12] first compared RFA and CAC for the treatment of GSV insufficiency and found that the total closure rate of the GSV was 95% in the RFA group and 96% in the CAC group at the first postoperative year. Similarly, in this study, we found that total closure rate of the GSV was 92% and 94% in the RFA and CAC groups, respectively, at the first postoperative year. In this study, there was no significant difference in the total closure rate at 1 month and 6 months between the groups.

Table III. Postprocedural total closure rates of treated great saphenous vein (GSV)

	CAC (n = 75)	RFA (n = 84)	*P* value
Total closure rates			
1 month	75 (100)	83 (98.8)	.34[a]
6 months	72 (96)	80 (95.2)	.81[a]
12 months	71 (94.7)	78 (92.8)	.64[a]

CAC, Cyanoacrylate closure; *RFA*, radiofrequency ablation.
Data are presented as number (%).
[a]Mann-Whitney *U* test.

With use of the RFA technique, tumescent anesthesia-related paresthesia has been decreased over the years.[13] In our study, the incidence of paresthesia was statistically significantly higher in the RFA group, detected in only one patient, so this may be negligible; none of the patients experienced paresthesia in the CAC group. Similarly, Koramaz et al[14] compared thermal and nonthermal ablation methods and reported that none of the patients undergoing CAC ablation had paresthesia. We had double-treated segments with RFA; this may have been a risk of postprocedure paresthesia, but there was only one case of paresthesia in the RFA group. Adequate tumescent anesthesia in an appropriate manner should prevent paresthesia even with the double treatment technique.

Although ecchymosis secondary to multiple punctures is more common in patients treated with the RFA technique,[15] in this study, we found no significant difference between the groups. This can be attributed to the fact

Table IV. Venous Clinical Severity Score (*VCSS*) and Aberdeen Varicose Vein Questionnaire (*AVVQ*) score of patients

	CAC (n = 75)	RFA (n = 84)	*P* value
VCSS			
Baseline	7 (4-14)	8 (5-14)	.07
1 month	3 (2-6)	3 (2-6)	.06
6 months	2 (1-5)	2 (1-5)	.19
12 months	1 (1-4)	1 (1-4)	.72
AVVQ score			
Baseline	17 (15-21)	17 (11-21)	.85
1 month	7 (6-9)	8 (5-13)	.10
6 months	5 (4-7)	6 (3-10)	.84
12 months	4 (3-6)	4 (1-9)	.61

CAC, Cyanoacrylate closure; *RFA*, radiofrequency ablation.
Numerical data were compared using Mann-Whitney *U* test. Data are presented as median (minimum-maximum). A *P* value less than .05 ($P < .05$) was considered statistically significant.

that we applied RFA with tumescent anesthesia to the intersaphenous compartment at an effective dose with fewer punctures under the guidance of DUS to prevent complications such as ecchymosis, paresthesia, skin pigmentation, skin burns, and postprocedural pain. Consistent with the literature,[12] we found no significant difference in the postprocedural pain scores between the groups.

On the other hand, the duration of operation is longer with endovenous thermal ablation techniques, as these techniques use tumescent anesthesia under the guidance of DUS for the treatment of isolated GSV insufficiency.[14] Similarly, we found that the duration of operation was statistically significantly shorter with CAC than with RFA in our study.

In addition, we recorded the VCSS and AVVQ scores before and after the procedures. We found a significant improvement in the VCSS and AVVQ scores with both techniques. However, neither technique was superior to the other.

Currently, compression stockings are recommended after medical or interventional treatments in patients with chronic venous insufficiency. In this study, we also recommended compression stockings for 1 week after the procedure in both groups. In the literature, there is evidence that wearing of compression stockings for 1 week after endovenous truncal ablation reduces postoperative pain and facilitates regaining of physical functions.[12] However, there is no consensus in the literature on the use of compression stockings after CAC, although there are some studies using compression stockings.[14,16] We therefore believe that the decision for the use of compression stockings should be made by the treating physician for each individual patient. The glue material used in our clinic (VariClose Vein Sealing System) is used in many centers in Turkey and Europe. The active ingredient of the glue is identical to the VenaSeal Closure System (Sapheon, Inc, Morrisville, NC) that is used in the United States, and therefore it is expected to have a similar efficacy.

Limitations. This study has some limitations. Small sample size and the lack of long-term follow-up are the main limitations. In addition, this is a retrospective study, limited to patients with primary isolated GSV insufficiency, so we were unable to investigate the indirect effects of RFA and CAC on varicose veins. Furthermore, this is a single-surgeon, nonblinded, nonrandomized study, but strict elimination criteria were applied in inclusion and exclusion to avoid randomization bias, but patient selection may still have the possibility of unintended bias. Therefore, further large-scale and long-term studies are needed to establish a conclusion.

CONCLUSIONS

Our study results suggest that both RFA and CAC are effective in closure of the target GSV. Although the incidence of tumescent anesthesia-related and procedure-related complications is higher with the RFA technique, both techniques can be used safely with similar success rate and patient satisfaction.

AUTHOR CONTRIBUTIONS

Conception and design: MB, EA
Analysis and interpretation: MB, MA, NB, EA
Data collection: MB, CK, EY, AO
Writing the article: MB, CK, MA, EY, AO, NB
Critical revision of the article: MB, EA
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