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Original Article

A comparison of cyanoacrylate closure to radiofrequency ablation techniques for treatment of truncal venous insufficiency

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Abstract

Aim: Cyanoacrylate closure (CAC) has become an alternative to endothermal ablative therapies for chronic venous insufficiency. In this study, we aimed to present our experience with CAC in comparison with radiofrequency ablation (RFA) and discuss the application techniques thereof.

Materials and Methods: A retrospective review was performed for adult patients who underwent CAC or RFA for great saphenous vein insufficiency during two years to identify baseline patient and disease characteristics, procedural details and outcomes. The primary outcome was a complete occlusion rate. Secondary outcomes were adverse events/complications and the quality of recovery.

Results: In this study, 36 patients (mean age 48.3 ± 11.2 years with 27 women) were treated with either CAC (n =19) or RFA (n = 17) during the defined period. At follow-up, after a mean duration of 8.5 ± 2.2 months, the closure rates were similar at 18/19 vs. 17/17, respectively. Apart from phlebitis and pigmentation, the incidences of bruising, skin burn and paresthesia were lower in the CAC group compared to the RFA group. The mean procedural times were shorter for CAC. In both groups, the Venous Clinical Severity Score significantly improved from baseline to last follow-up, somewhat better in the RFA group. The satisfaction level with the treatment was moderately higher among RFA patients than CAC patients, as well.

Conclusion: The findings suggest that while it shortens the procedural time and does not require postoperative stockings, CAC is not a miraculous alternative for those who can duly administer tumescent anesthesia.

Keywords: Cyanoacrylate closure; chronic venous insufficiency; endovenous procedure; outcome; radiofrequency ablation

INTRODUCTION

Improvements in interventional procedures, particularly the widespread use of endovenous thermal ablative therapies, such as laser ablation (EVLA) and radiofrequency ablation (RFA), have allowed safer and effective management of chronic venous insufficiency that has been traditionally treated with surgical high ligation and stripping (1,2). However, the need for tumescent anesthesia, perioperative sedation and postoperative compression stockings are the main downsides as to the implementation of endothermal modalities (3-5). Moreover, endothermal ablative therapies are not without complications, such as skin burns, deep vein thrombosis (DVT), paresthesia and pigmentation, which are mainly related to a thermal injury (6,7). Endovenous cyanoacrylate-based closure (CAC), a novel nonthermal nontumescent method, has become an alternative to treat incompetent varicose veins after the first human use in 2013 (8-14). Results of the recent studies comparing CAC with existing endothermal modalities are promising concerning safety, closure rate, device-related adverse events/complications and improvement of quality of life, as well as patient comfort (15-22).

We should note that this study is not the first study comparing the CAC with any of the endothermal modalities. However, to our knowledge, this is the first study conducted by a group of interventional radiologists who are experienced in imaging-guided catheter therapies. We hereby present not only a comparison of the effectiveness, safety and clinical outcomes of the treatments performed either with CAC or RFA for incompetent great saphenous veins (GSVs) but also question the implementation techniques thereof.

MATERIALS and METHODS

After obtaining ethical approval of the local Ethical Committee (Approval number, 2020/697), a retrospective chart review was conducted, including adult patients

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who underwent an endovenous procedure for saphenous vein truncal incompetence either with CAC or RFA, at our angiography unit during the period between September 2017 to December 2019. The patients who underwent such an intervention for the small saphenous vein or anterior accessory saphenous vein were excluded from this study. Patients' details, including age, gender, weight, height, clinical history, physical examination findings and color Doppler ultrasound (CDUS) results, were collected from the clinical notes that were written in paper charts during the primary evaluation. Preoperative clinical disease severity was graded using the Clinical, Etiological, Anatomical, and Pathophysiological (CEAP) classification and the Venous Clinical Severity Score (VCSS) as well.

All treatments were performed by a single operator (F.U.) after having confirmed that the criterion for the therapy had been met for each patient, symptomatic moderate to severe varicosities and venous reflux in the GSV >0.5 second in standing position. The CACs were conducted using the VenexTM Cath Sealing System (Gama Medikal, Ankara, Turkey), of which standard disposable kit consists of a short 6 Fr introducer sheath, a 0.035-inch x 150 cm PTFE-coated guidewire and a total of 2 mL of high-viscosity n-butyl cyanoacrylate (NBCA) glue divided into two sterile bottles of 1 mL, as well as a delivery system formed by assembling two components: a 4 Fr coaxial catheter and a dispenser gun. All procedures were started by cannulation of the GSV with an 18 G Seldinger needle under ultrasound guidance at the most distal point of reflux. In all except for two procedures, the whole amount of NBCA glue within the disposable was injected via the delivery system as per the current instruction for use. However, in two procedures, a total of 3 mL of NBCA glue had to be injected considering the longer thigh length of the patients. After CACs, the treated limb was wrapped with elastic bandages, 15 cm in width, for 12 hours post-intervention. The RFAs were performed using the VenefitTM (Medtronic, Dublin, Ireland) as per the current instruction for use. Unlike in the CACs, it was paid attention not to insert the needle below the knee not to lesion the saphenous nerve while performing RFAs. The vast majority of the procedures were performed using a 7 mm radiofrequency probe. When it was not available, a 3 mm probe had to be used, which slightly extended the procedure time. After all RFAs, the treated limb was wrapped as in the CACs for 12 hours and then changed to wear the class-2 compression stockings (thigh-high) for 14 days post-treatment. To prevent probable inflammatory response due to the closure of the GSV, all patients treated either with CAC or RFA were prescribed 100 mg of flurbiprofen, a non-steroidal anti-inflammatory drug, twice a day for ten days after the treatment, whether they would feel pain or not. In case of any gastric problem, they were advised to take 30 mg of lansoprazole, a proton-pump inhibitor, once or twice daily. Following each session, the length of the embolized or ablated segment of the GSV, as well as the period between the first introduction of the Seldinger needle and withdrawal of the introducer sheath, were noted.

All follow-up examinations were conducted by the same operator having performed the procedures. The primary outcome measure was complete occlusion on CDUS, defined as occlusion of the entire treated vein segment with no discrete segments of patency exceeding 5 cm (4,9-11) at last follow-up within one year of the treatment. Secondary outcomes that were assessed were the following: all adverse events/complications and the quality of recovery. Bruising, phlebitis, skin burn, paresthesia, pigmentation, DVT and access site wound were the clinically significant events that were observed. At the last follow-up, the VCSS was calculated once again to identify the degree of clinical improvement. In addition, the patients were asked to rate their overall level of satisfaction with the treatment (Grade 1: worsened; Grade 2: poor; Grade 3: slightly satisfied; Grade 4: satisfied; and Grade 5: very satisfied).

Statistical Package for Social Sciences for Windows, version 21.0 (SPSS, Chicago, IL, USA) was used for statistical analysis. For continuous variables, data summaries were expressed as mean ± standard deviation. For categorical variables, frequencies (percentage) were reported. To analyze whether the variables assessed in this study could cause a difference in the outcome, the Mann-Whitney U test or the Wilcoxon signed-rank test were used for continuous variables or the chi-square test for categorical variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

In this study, 67 patients underwent endovenous varicose vein treatment during the defined period. Particularly, there were 36 patients with GSV insufficiency, wherein the treatment was performed either with CAC or RFA. Out of these 36 patients, 19 patients were treated using CAC, whereas 17 patients received RFA. No patient underwent a bilateral intervention. The mean age of the patients was 48.3 ± 11.2 years (range, 29–71), with the majority being female (75%).

Table 1. Demographics and baseline characteristics of patients

	CAC (n=19)	RFA (n=17)	p
Age, yrs	46.3 ± 11.5	50.6 ± 10.8	0.25[a]
Sex, female	11 (57.9)	16 (94.1)	**0.03**[b]
BMI, cm/kg^2	27.7 ± 4.0	27.1 ± 4.7	0.70[a]
CEAP class			
C2	12 (63.2)	13 (76.5)	0.27[b]
C3	3 (15.8)	4 (23.5)	
C4	3 (15.8)	N/A	
C5	1 (5.3)	N/A	
Preprocedural VCSS	5.0 ± 3.0	5.9 ± 2.9	0.32[a]

BMI = body mass index, CAC = cyanoacrylate closure, CEAP = clinical, etiological, anatomical, pathological classification, RFA = radiofrequency ablation, VCSS = venous clinical severity score Categorical variables are presented as number (%). Continuous variables are presented as mean ± standard deviation (range). [a]The p-value is calculated using the Mann-Whitney U test.[b]The p-value is calculated using the chi-square test. Boldface type indicates statistical significance

The average body mass index (BMI) was 27.4 ± 4.3 cm/kg^2 (range, 18.7–35.5). The average diameter of the GSVs before the intervention was 7.6 ± 1.6 mm (range, 5–13). Out of 36 patients, 25 patients (69.4%) had CEAP class 2 disease with an average VCSS of 5.4 ± 2.9 (range, 1–14). Age, body mass index (BMI), vein diameter, the target leg for the procedure, CEAP classification and preprocedural VCSS were similar in both groups, while most of the patients who underwent RFA were female (Table 1).

The mean last follow-up within one year of the treatment was 8.5 ± 2.2 months (range 3 to 12 months). Complete closure was noted in all except for one patient at the time of all follow-ups. In the patient who was treated with CAC, the CDUS examination at one-month post-operation revealed a partial recanalization concerning the proximal one-third of the GSV distal to the SFJ. Upon detecting incomplete closure, the recanalized segment was closed with foam sclerotherapy using 3 mL of polidocanol 2% after a while, and there was no residual patent lumen on subsequent follow-ups. In seven patients, four embolization patients and three ablation patients, foam sclerotherapy was subsequently applied to varicose tributaries. The overall success rates were 18/19 (94,7%) and 17/17 (100%) in the CAC and RFA groups, respectively (p = 0.34). The procedure duration was significantly shorter in the CACs. The most frequent patient complaint following the procedures was bruising (27.7%), which was followed by superficial phlebitis with the rate of 25%. None of the patients experienced DVT. None of the patients were prescribed antibiotics, and none developed any problems with wound infection. There was a significant improvement in the overall mean VCSS post-intervention (5.4 ± 2.9 vs. 1.5 ± 1.3, p = <0.001). The average overall satisfaction level with the treatment experience was 4.4/5. The procedural details and treatment outcomes, as well as the means of the scorings used for estimating the quality of recovery, are summarized in Table 2.

Table 2. Procedural characteristics and treatment outcomes

	CAC (n=19)	RFA (n=17)	p
Target leg, left	13 (68.4)	10 (58.8)	0.80[a]
GSV diameter, mm	7.5 ± 1.8	7.7 ± 1.4	0.64[b]
GSV treatment length, cm	35.5 ± 6.1	35.2 ± 4.5	0.93[b]
Procedure duration, min	15.2 ± 2.5 (10–19)	29.2 ± 5.6 (22–36)	**0.01**[b]
Occlusion rate	18 (94.7)	17 (100)	0.34[b]
Bruising	3 (15.7)	7 (41.1)	0.09[a]
Phlebitis	5 (26.3)	4 (23.5)	0.84[a]
Skin burn	N/A	1 (5.9)	0.95[a]
Paresthesia	1 (5.3)	2 (11.7)	0.48[a]
Pigmentation	1 (5.3)	N/A	1.00[a]
DVT	N/A	N/A	-
Access site wound	N/A	N/A	-
Preprocedural VCSS	5.0 ± 3.0	5.9 ± 2.9	0.32[b]
Postprocedural VCSS	1.7 ± 1.3	1.3 ± 1.3	0.47[b]
	0.01[c]	**<0.001**[c]	
Score of satisfaction level	4.3 ± 0.9	4.5 ± 0.7	0.75[b]

CAC = cyanoacrylate closure, DVT = deep vein thrombosis, GSV = great saphenous vein, RFA = radiofrequency ablation, VCSS = venous clinical severity score. Categorical variables are presented as number (%). Continuous variables are presented as mean ± standard deviation (range).
[a]The p-value is calculated using the chi-square test.
[b]The p-value is calculated using the Mann-Whitney U test.
[c]The p-value is calculated using the Wilcoxon signed-rank test.
Boldface type indicates statistical significance

DISCUSSION

The findings obtained in this study revealed a comparable success rate in patients undergoing CAC or RFA for the treatment of insufficient GSV despite a relatively small sample size. Apart from phlebitis and pigmentation, the incidences of remaining adverse events, including bruising, skin burn and paresthesia, were lower in the CAC group compared to the RFA group. As expected, the mean procedural times were shorter for CAC. However, the improvement in VCSS was more prominent in RFA compared to CAC treatments. Furthermore, the ratings showed a somewhat higher mean level of satisfaction with the treatment in those who received RFA.

Previous studies have demonstrated higher closure rates reaching as high as 100% for CAC, especially in short- and mid-term follow-ups (23-27). Among them, the closure rate after CAC was compared with any of the endothermal modalities in only few studies. For example, Bozkurt and

Yilmaz (5), as well as Koramaz et al. (4), used EVLA as the comparator, whereas Morrison et al. (16), Yang et al. (19) and Kolluri et al. (20) preferred RFA for this purpose. In Eroglu and Yasim's (3) study, both EVLA and RFA were used for comparison therein. The comparative results of these studies as to the 12 months closure rates of CAC vs. EVLA or RFA were the following: 95.8% vs. 92.2% (5), 98.6% vs. 97.3% (4), 97.2% vs. 97% (16), 100% vs. 99% (8 weeks follow-up!) (19), 99.0% vs. 96.2% (6 months follow-up!) (20) and 94.7% vs. 94.2%/92.5% (3), respectively. In all these studies, the findings showed that CAC was not superior to EVLA or RFA concerning closure rate, like in our study.

As the previous studies reported, we have found a lower incidence of bruising in CAC compared to RFA treatments (3,4,16). The incidence of bruising was not reported in Yang et al.'s study (19). The studies conducted by Koramaz et al. (4) and Bozkurt and Yılmaz (5) reported a lesser incidence of bruising after CACs. Substantially, all trials concerning CACs indicate a lower incidence of bruising (15,16,23). It is easy to understand the reason behind the more extensive bruising in endothermal therapies. Repeated injections that are required for tumescent anesthesia puncture surrounding small vessels (2,15,23). In addition, we have found a higher incidence of phlebitis (mostly as an erysipeloid phlebitic skin reaction) in the CACs compared to RFAs, unlike most of the previous studies. In fact, only one study (16) reported a consistent result with ours, wherein the incidence of phlebitis in the CAC group was higher than that of in the RFA group, despite not being statistically significant. Their explanation for this phenomenon was the mechanism of action of the NBCA. As expected, no skin burn was encountered with the administration of CAC in our study. As the previous studies argued, paresthesia was temporary and less frequent in our patients treated using CAC (4,5,15,17,19,23). One of our patients experienced pigmentation at the treatment site after CAC, which resolved in time. The two studies comparing CAC with RFA (16,19) did not report the incidence of pigmentation among the adverse events. Nevertheless, in the study conducted by Bozkurt and Yilmaz (5), the incidence of pigmentation was higher, although not statistically significant, in the EVLA group than in the CAC group. Similarly, Koramaz et al. (4) reported that pigmentation after treatment was only observed in EVLA-treated subjects, which was statistically significant and was temporary. In our study, there was a statistically significant decline in VCSSs in both groups, and the decline achieved in RFA-treated subjects was more prominent. This was opposite to what was reported in the study conducted by Eroglu and Yasim (3). In the other aforementioned studies, although an improvement was observed in VCSS post-intervention in all groups, the difference was not significant (4,5,16). The level of satisfaction with the treatment was moderately higher in the RFA group compared to the CAC group, which was in line with the improvement in VCSS. Finally, although we could not evaluate it statistically, it was deduced that the treatment success was not affected by the site, diameter and length of the target vein in the CACs as in the RFAs.

Although the application of CAC seems straightforward, all stages thereof need to be handled quite carefully. The first stage is the positioning of the delivery catheter. The tip of the catheter should be positioned at an appropriate distance away from the SFJ not to cause the media to flow into the deep vein, which may result in DVT and even in pulmonary embolism. Due to heat generation, DVT is also a risk of RFA, but not pulmonary embolism. The second (final) stage, the injection stage of the NBCA glue, should also be carried out meticulously. Once the setup is completed, the withdrawal of the delivery catheter should be conducted as continuously as possible while applying simultaneous pressure over the target vein by the CDUS probe without releasing the pressure from the SFJ so that a thin layer of NBCA in each millimeter of the venous lumen can be obtained, thereby having a safe and effective sealing effect. At the same time, this pulling back should be done as quickly as possible to prevent sticking of the catheter tip to the vessel wall, especially in case a low-viscosity NBCA is used, which has a polymerization time of shorter than five seconds (4,28). To aid delivery, some additives that increase viscosity and slow down the polymerization are included in the NBCA by the manufacturers (1,25). However, the longer-lasting the polymerization is the higher risk of leakage into a nontarget vessel. As for an RFA procedure, the setup is followed by tumescent anesthesia that is still the greatest challenge to only the ones who are not good at ultrasound-guided interventions (2); thereafter, the withdrawal of the radiofrequency probe takes its part as the most stress-free stage. As a third issue, the delivery catheter needs to be advanced with the assistance of a guidewire while performing CAC. If the target vein is not tortuous, tracking the path is not a problem. However, if dealing with a serpentine vessel, many times, it is actually the case, the navigation of the catheter may be challenging because of the square-edged tip thereof. Such a tip may be intercepted at the points where the vein shows a kink. On the other hand, a radiofrequency probe has a blunt-edged and smooth tip that facilitates navigation even within tortuous vessels. Moreover, the preferred radiofrequency probe has an inner lumen that enables introducing a 0.018-inch micro guidewire, if required. At the kink points, it is possible to manipulate the direction of the tip of this probe by applying pressure with fingers over the skin. In brief, the implementation technique is the merit as well as the soft underbelly of CAC. Such a technique requires experience and training, as well as the assistance of a second hand to ensure procedural safety and success. The similar results in this study concerning the treatment success and the complication rate for both methods are partly due to the operator's experience in catheter manipulations and his familiarity with the intravascular glue injections. Although Kolluri et al. (20) suggest that a CAC procedure can be rapidly learned, in our opinion, this suggestion is not acceptable for operators who are not familiar with endovascular procedures.

LIMITATIONS

There are some limitations to this study that need to be addressed. Firstly, this is a single-center retrospective study, wherein the sample size is pretty small. We did not have 1-year outcomes in all patients; thereby, our follow-up period remained relatively shorter. Actually, this limitation may cause to underestimate the denouement of the treatment in some patients because the trajectory of occlusion rate over the first and second year after the intervention is known to be favorable (15). Intra- and postprocedural pain and discomfort were not evaluated, which would more objectively reflect patient satisfaction with the procedure. We did not assess the disappearance rate of varicose veins following the treatments in that we mainly concentrated on the closure rate. In addition to the aforementioned limitations, it would be better if the improvement in the quality of life could have been scored with a detailed survey like the Aberdeen varicose vein questionnaire.

CONCLUSION

In conclusion, this study comparing CAC with RFA indicated no difference between the two methods concerning treatment success. In addition, CAC did not show an obvious advantage over RFA concerning adverse events/complications. The improvement in the severity of venous disease was better in favor of RFA procedures, as well. While CAC offers several benefits that can improve patients' comfort, such as shorter procedural time thanks to obviating tumescent anesthesia and no need for compression stockings post-intervention, it does not seem to replace endothermal ablative therapies because of its challenging aspects. Briefly, we consider that CAC is not a revolutionary innovation for those who are good at imaging-guided interventional procedures. However, CAC is potentially a viable option for patients for whom sedation is risky.

Competing Interests: The authors declare that they have no competing interest.

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Ethical Approval: This study was conducted under the approval of the Ethical Committee of the Ondokuz Mayis University. (number, 2020/697)

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