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Original Article

Evaluation of mid-term results in our patients treated with N-Butyl cyanoacrylate embolization in saphenous vein insufficiency

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Abstract

Aim: The aim of this study is to present our mid-term results obtained from patients with advanced saphenous vein insufficiency treated with N-butyl cyanoacrylate embolization (CAE).
Material and Methods: In the present study, we included 1013 patients who were treated with CAE because of moderate and severe saphenous vein insufficiency in Eskişehir Osmangazi University Medical Faculty Hospital Cardiovascular Surgery Clinic between January 2015 and November 2019. The patients were rechecked at 1st, 6th, 12th, 24th and 36th months. Venous Clinical Severity Score (VCSS) and Aberdeen Varicose Vein Questionnaire (AVVQ) results recorded at preoperative and postoperativee period. Doppler ultrasonography (USG) was performed to all patients in all controls. The absence of re-canalized flow in Doppler USG was accepted as the success of the procedure.
Results: The mean age of 1013 patients was 51.27±14.30 years (448 men (44.2%) and 565 women (55.8%)). The average procedure time was 12.4±2.1 minutes, the average amount of CA used in the procedure was 1.6 ml (min: 1 ml - max: 2ml). In outpatient controls, complication rates was low, thrombophlebitis occurred in 17 patients (1.7%) and ecchymosis occurred in 9 patients (0.9%). The occlusion rate was 97.6% according to the 1-year follow-up results and 93.3% according to the 3-year follow-up results. The decrease in VCSS and AVVQ scores was statistically significant when the preoperative and postoperative period results compared ($p<.05$).
Conclusion: In the present study, we think that CAE is a safely and effective treatment method for saphenous vein insufficiency. It has low complication, high occlusion rates and provides better comfort to the patients.

Keywords: Venous insufficiency, glue ablation, saphenous

INTRODUCTION

Superficial venous insufficiency of the lower extremities is a common vascular pathology, which might cause many problems from telangiectasias to venous ulcers. The most common symptoms are pain, burning and tingling sensations in the lower extremities, heaviness and fatigue in the legs, itching, edema, and night cramps in patients [1]. The prevalence of venous insufficiency in the community was reported to be 20-40% in previous studies [2,3].

Traditional methods such as ligation and stripping can be used for the treatment of saphenous vein insufficiency; endovenous interventions such as Laser Ablation (EVLA), Radiofrequency

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Ablation (RFA), and n-butyl Cyanoacrylate Embolization (CAE) are also used widely for this purpose [4]. The target of these treatment methods is to eliminate the reflux flow at the saphenofemoral junction. The reason for the increasing popularity of endovenous interventions by moving away from traditional methods recently is the long recovery times in traditional methods [5].

The medical uses of Cyanoacrylate (CA) are quite wide. It is used in the closure of Type 1 and 2 endoleaks in the repair of abdominal aortic aneurysms, to treat varicocele, arteriovenous malformations, pelvic congestion syndrome, stopping the bleeding of gastric varices, and eliminating superficial venous insufficiency in the lower extremities [6-9]. Following the injection of N-Butyl Cyanoacrylate into the vein, it hardens rapidly with a polymerization reaction, occludes the vessel and causes a local inflammatory reaction in the vessel wall and surrounding tissues [10]. Cyanoacrylate also has elasticity and viscosity. With the polymerization that takes place in less than five seconds, the risk of embolization of deep veins is very low, and no limitation of movement is observed due to its elasticity feature [11,12].

Studies conducted on this subject have gained importance with the widespread use of CA in the treatment of saphenous vein insufficiency. It has great importance to conduct multicenter studies with large patient groups and to explain the long-term follow-up results of patients to assess the efficacy of the treatment. In the present study, the purpose was to present the mid-term results of the CAE treatment that was applied in a large group of patients with moderate and severe saphenous vein insufficiency.

MATERIAL AND METHODS

Eskişehir Osmangazi University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee Approval was obtained for the study (approval date: 17.01.2023 and approval number: E-25403353-050.99-2300020649). The files of 1472 patients who were treated with CAE because of moderate and severe saphenous vein insufficiency in Eskişehir Osmangazi University Medical Faculty Hospital Cardiovascular Surgery Clinic between January 2015 and November 2019 were scanned retrospectively and a total of 1013 patients who had regular postoperative follow-up data for 3 years were included in the study. Pathological venous reflux was defined as the reverse flow response for 2 seconds to the release of the compression in the thigh or calf following the valsalva maneuver in a standing patient. A great saphenous vein (GSV) diameter greater than 5.5 mm and a reflux for more than 2 seconds on Doppler Ultrasonography (USG) were accepted as an indication for the procedure. Among these patients, those who were over the age of 18, those with a vessel diameter of less than 15 mm, those between C2-6 according to the CEAP clinical classification, those who lived independently, and those who came to follow-ups regularly were included in the study. Having a history of rheumatology, peripheral artery disease, deep vein thrombosis, pregnancy, a pathology leading to hypercoagulability, GSV with a tortuous course, active infection, varicose veins because of abdominal or pelvic mass, those who were obese, patients with small saphenous vein (SSV) insufficiency, perforating vein insufficiency, GSV diameter over 15 mm, dense packing, immobility, a history of cancer, thrombophlebitis, and those who did not attend regular follow-ups were excluded from the study. All patients who met these criteria during the specified date range were treated in this way.

The preoperative CEAP clinical classifications (Clinical severity, Etiology, Anatomy, Pathophysiology) were made by looking at the data in the files of the patients who were included in the study. Venous Clinical Severity Score (VCSS) Clinical Scoring and Aberdeen Varicose Vein Questionnaire (AVVQ) Quality of Life Questionnaire results, which were recorded at the preoperative and postoperative 1st month, 6th month, 12th month, 24th and 36th months, were assessed. The assessment of pain, varicose veins, venous edema, skin pigmentation, inflammation, induration and number of active ulcers was made in VCSS with a scoring that ranged between 0 and 30 points, and 30 points describe the most severe findings [13]. In the AVVQ, there are 13 questions defined by Andrew Garratt to question the symptoms affecting the life of patients with venous insufficiency (duration of pain, effect on clothing selection, effect on hobbies, effect on business life, etc.) and a score is made between 0 and100 [14]. A score of zero indicates the best quality of life, and higher scores indicate a decrease in quality of life. The endpoints were the disappearance of post-operative pain, the disappearance of reflux, the resolution of edema, the occurrence of recurrence, and the resolution of hyperpigmentation. Doppler USG results performed by the same radiology team in all follow-ups were compared. The absence of re-canalized flow in Doppler USG was accepted as the success of the procedure.

Although ecchymosis, pain, induration, paresthesia, superficial thrombophlebitis and skin changes in the operation area in the postoperative follow-up of the patients are considered minor complications, conditions such as artery and vein injuries, leakage of CA to deep vein, skin burn, Deep Vein Thrombosis (DVT), pulmonary thromboembolism, and motor defect were accepted as major complications.

All patients underwent the procedure in the operating room setting under local anesthesia. During the procedure, a puncture was made to the GSV at the level of the knee using the Seldinger Technique under USG guidance and a 7F sheath was placed. A 0.035 inch J guide wire was advanced through the sheath to the SFJ. Then, the catheter was advanced up to 3 cm distal to the SFJ over the guide wire and the patient was placed in the

Trendelenburg position. The saphenofemoral junction was collapsed by pressing with the USI probe. VenaBLOCK (RD Global Health Inc, Invamed) venous embolization material that contained N-Butyl cyanoacrylate was injected continuously along the saphenous vein trace. After the injection, external pressure was applied to the saphenous vein trace for 60 seconds. The material in the vein and the patency of the deep femoral vein were checked with Doppler USG following the termination of the compressions. Accompanying varicose veins and telangiectasias were not intervened during the first 6 months. After 6 months, phlebotomy was performed for varicose veins (68 patients (6.7%)) and sclerotherapy was performed for telangiectasias (49 patients (4.8%)). The legs of the patients were put in an elastic bandage to stay for 1 day and the patients were transferred to the ward. A single dose of Low Molecular Weight Heparin (LMWH) was administered to the patients who were transferred to the ward for deep vein thrombosis prophylaxis. All patients were discharged on the same day. The patients were prescribed antibiotics, venoprotectants and analgesics at discharge. None of the patients were made to put on compression stockings. Mobilization restriction was not applied to any of the patients.

Statistical Analysis

The IBM SPSS version 21.0 program (IBM Corp. 2012. Windows IBM SPSS Statistics, Version 21.0, Armonk, NY: IBM Corp) was used for statistical analysis. For continous variables, suitability to normal distribution and homogeneity were tested using the Kolmogorov-Smirnov test and the Levene test, and data were classified accordingly. Continuous variables were expressed as mean±Standard Deviation (SD). Categorical data were given as percentages (%). Shapiro Wilk test was used to investigate the suitability of the data for normal distribution. The comparisons between groups were performed with Pearson Chi Square and Fischer exact tests for categorical variables. Wilcoxon signed rank test was used to compare the preoperative and postoperative AVVQ and VCSS values of the patients. The p value <.05 was considered statistically significant.

RESULTS

The clinical and demographic characteristics of the patients are summarized in Table 1. The mean age of the patients was 51.27±14.30 years (448 men (44.2%) and 565 women (55.8%)). According to the CEAP Clinical Classification, 347 patients (34.3%) were operated in Class C2, 284 patients (28.1%) in Class C3, 215 patients (21.2%) in Class C4a, 72 patients in Class 4b (7.1%), 54 patients in Class 5 (5.3%), and 41 patients in Class 6 (4%). The mean GSV diameter of the patients who underwent intervention was 7.8±1.6mm. In the preoperative assessments, the mean VCSS score of the patients was 8.2±1.4 and the mean AVVQ score was 21.46±7.3.

Table 1: The clinical and demographic characteristics of the patients

Characteristics	Number (n) / (Mean±SD / %)
Age	51.27±14.30
Gender	
Male	448 (44.2)
Female	565 (55.8)
Side	
Right	471 (46.5)
Left	542 (53.5)
CEAP-Clinical Classification	
C2	347 (34.3)
C3	284 (28.1)
C4a	215 (21.2)
C4b	72 (7.1)
C5	54 (5.3)
C6	41 (4)
Comorbidity	
DM	128 (12.6)
HT	113 (11.1)
COPD	51 (5)
GSV diameter	7.8±1.6mm
VCSS score	8.2±1.4
AVVQ score	21.46±7.3
Smoking	374 (36.9)
Family History	410 (40.4)

DM: diabetes mellitus, HT: hypertension, COPD: chronic obstructive pulmonary disease, GSV: great saphenous vein, VCCS: venous clinical severity score, AVVQ: aberdeen varicose vein questionnaire

Intraoperative data of the procedure and complications in the postoperative period are summarized in Table 2. Although the average procedure time was 12.4±2.1 minutes, the average amount of CA used in the procedure was 1.6 ml (min: 1 ml - max: 2ml). The mean discharge time was 2±1.2 hours. All patients were operated under local anesthesia. In the post-procedure Doppler USG, CA material was detected in the deep vein in 2 patients. An incision was made in the femoral region under the local anestesia and the saphenofemoral junction was found and bleeding control was achieved with the help of a side clamp. Then, an incision was made to the saphenous vein and the CA material was removed from the deep vein in these 2 patients. Complete closure of the GSV was observed in Doppler USI that was performed while on the operating table after the procedure in all patients.

Complications were detected in 54 (5.3%) patients in the postoperative period, and these complications were divided into 2 as major and minor complications (Table 2).

Table 2: The intraoperative data of the procedure and complications in the postoperative period	
Data	**Number (n) (Mean/%)**
Procedure time (minutes)	12.4±2.1
Amount of CA used (ml)	1.6±0.4
Discharge time (hours)	2±1.2
Type of anesthesia	
Local	1013 (100)
General	-
Patients with deep vein CA material on Doppler USG after the procedure	2
Patients with complete closure of the GSV in the Doppler USG after the procedure	1013
Minor Complications	
Pain on GSV trace	14 (1.4)
Ecchymosis	9 (0.9)
Superficial thrombophlebitis	17 (1.7)
Induration	12 (1.2)
Paresthesia	0
Major Complications	
CA escape into deep vein	2 (0.19)
Arterial injury	0
Skin burn	0
Deep Vein Thrombosis	0
Pulmonary Thromboembolism	0
Motor Defect Occurrence	0

CA: cyanoacrylate, USG: ultrasonography, GSV: great saphenous vein

As a major complication, only 2 patients had a small amount of CA leakage into the deep vein, and in these 2 patients, an incision was made from the femoral region under local anesthesia and the polymerized CA material was removed from the deep vein. Among the minor complications, pain was detected in 14 patients (1.4%), ecchymosis in 9 patients (0.9%), superficial thrombophlebitis in 17 patients (1.7%), and induration in 12 patients (1.2%). Patients with pain associated with the procedure described the GSV trace above the knee as the localization of their pain, which disappeared in all patients in 10 days with non-steroidal anti-inflammatory treatment. Antibiotic and anti-inflammatory treatment was prescribed for 17 patients with superficial thrombophlebitis, and thrombophlebitis regressed in all patients.

The data of the preoperative and postoperative symptoms of the patients are summarized in Table 3. It is seen in the table that the symptoms in the patients in the preoperative period reduced significantly in the postoperative period. It was also found that there were edema and pain symptoms in 68 (6.7%) patients in the 36th month follow-ups of the patients who underwent the procedure, and all of these patients were those with re-canalized flow in Doppler USG controls.

Re-canalized flow and SFJ reflux levels were determined from the postoperative 1st, 6th, 12th, 24th and 36th month Doppler USG reports of the patients (Table 4). In the follow-ups, recanalization was detected in 1 patient (0.01%) at the postoperative 1st month, in 6 patients (0.6%) at the 6th month, in 17 patients (1.7%) at the 12th month, in 41 patients (4%) at the 24th month, and in 68 (4%) patients at the 36th month (6.7%). In 100 of these patients who had reflux of 2 seconds or more, the patients were re-intervened, SFJ was explored, and GSV was ligated. In other words, 9.8% of the patients needed re-intervention.

Clinical evaluations of the patients in their postoperative follow-ups were made by assessing their VCSS and AVVQ scores, and these scores were compared with the preoperative scores (Table 5). Although an increase was detected in the mean scores of VCSS and AVVQ as the control period progressed, the decreased scores after the procedure were statistically significant when the preoperative and postoperative period results were compared ($p<.05$).

Table 3: The data on patient symptoms

Symptom	Preoperative Symptom Number of Patients (%)	Postoperative Symptoms (%)				
		1st month	6th month	12th month	24th month	36th month
Pain	1013 (100)	2 (0.2)	20 (2)	28 (2.7)	33 (3.2)	68 (6.7)
Numbness	785 (77.5)	1 (0.1)	12 (1.1)	14 (1.4)	23 (2.3)	27 (2.6)
Night cramp	672 (66.3)	3 (0.3)	9 (0.9)	11 (1)	12 (1.2)	17 (1.7)
Edema	973 (96)	18 (1.8)	26 (2.6)	34 (3.4)	57 (5.6)	68 (6.7)
Itching	573 (56.6)	6 (0.6)	8 (0.8)	13 (1.3)	25 (2.5)	32 (3.2)
Burning sensation	612 (60.4)	5 (0.5)	7 (0.7)	12 (1.2)	29 (2.9)	36 (3.6)
Restless leg	273 (27)	1 (0.1)	4 (0.4)	5 (0.5)	11 (1)	11 (1)

Table 4: The postoperative doppler USG control data

Follow up Time	Recanalized Flow (n)	0-2 sec SFJ reflux (n)	2-4 sec SFJ reflux (n)	>4sec SFJ reflux (n)
Postop 1st month	one	one	0	0
Postop 6th month	6	4	2	0
Postop 12th month	17	8	6	3
Postop 24th month	41	11	23	7
Postop 36th month	68	9	17	42

Table 5: The clinical evaluation follow-up results

Scoring	Time of Scoring					
	Preoperative	Postoperative				
		1st month	6th month	12th month	24th month	36th month
VCSS	7.3±1.40	1.10±0.82 (p<0.05)	1.21±0.90 (p<0.05)	1.54±0.98 (p<0.05)	1.89±1.10 (p<0.05)	2.1±1.13 (p<0.05)
AVVQ	23.79±7.67	5.12±1.33 (p<0.05)	5.29±1.41 (p<0.05)	6.12±1.71 (p<0.05)	6.33±1.83 (p<0.05)	6.88±1.92 (p<0.05)

DISCUSSION

Saphenous vein insufficiency is a pathology that affects the quality of life and aesthetic appearance of patients significantly and requires effective treatment. Ligation, stripping, RFA, EVLA and CAE Methods can be used in the interventional treatment of saphenous vein insufficiency. Ligation and stripping may lead to longer recovery times, longer duration of the procedure, and higher incidence of additional complications because they are surgical procedures [5,15]. Also, Tumescent Anesthesia (TA) is used in RF and EVLA Methods, and conditions such as pain and ecchymosis can be seen more frequently in the postoperative period because of multiple interventions for the use of TA [16]. In a study that was conducted with 318 patients who underwent CAE in 2020, thrombophlebitis was detected in 1.9% of the patients, ecchymosis in 3.8%, and pain in 7.5% [17]. In another study conducted by Koramaz et al. in 2017, pain was reported in 4.7% of 150 patients who underwent CAE in the postoperative period, and phlebitis in 2.1% [18]. In the present study, postoperative pain was detected in 1.4% of the patients, thrombophlebitis in 1.7%, and induration in 0.9%, and these rates were consistent with the literature data. All of our patients who had thrombophlebitis were weak and had weak muscle tissue in the thigh region. The saphenous vein segment that developed thrombophlebitis was the section where the saphenous vein was superficial under the skin. For this reason,

we think that it is more appropriate to start from the section where the saphenous vein runs under the fascia in performing CAE. Also, the leakage of CA into the deep femoral vein, which was found in 2 patients in our study and which was specified as a major complication, shows the importance of the pressure that should be applied to the SFJ during the treatment of CAE. We did not use medical compression stockings for any of our patients in the postoperative period. When the literature was reviewed, it was found that medical compression stockings are not required after CAE, and there is no recommendation about their use in the guidelines [19,20]. In a systematic review conducted by Dimech et al. in 2020, it was reported that occlusion rate after CAE is not influenced by the use of postoperative compression stockings and occlusion is retained even without postoperative compression stockings and elastic bandages [21]. In another study comparing EVLA and CAE, it was stated that there was no need for the use of compression stockings after CAE [18].

Although CAE is the preferred treatment modality in the vast majority of patients with saphenous vein insufficiency, it is necessary to avoid it or to be careful in some cases. For example, acute deep vein thrombosis, being septic and allergy to CA are absolute contraindications, and the tortuous course of the vascular structure is reported to be a relative contraindication [22]. We think that CAE should not be preferred because the possibility of skin-related complications increases in the postoperative period in patients with GSV close to the skin surface. Also, the application of classical methods may yield more successful results because the possibility of complete closure is low in applications made to GSVs of 15 mm and above.

The severity of the clinical condition of the patient is evaluated with the VCSS Scoring, and the quality of life standards with the AVVQ Scoring. In a study conducted by Chan et al. in 2017, patients with an average VCSS score of 6.9 had a mean VCSS score of 1.7 at the 12th month follow-up after the procedure. It was also reported that the mean AVVQ score, which was 23.7 before the procedure, was 4.1 at the 12th month follow-up following the procedure [23]. In the VeClose Study that was conducted in the United States, the mean VCSS score was reported to be 5.5 before the procedure and the mean AVVQ score was 18.9, and after the procedure, the mean VCSS score was less than 2 and the AVVQ score was 9 after a 1-year follow-up [24]. In the eSCOPE Study that was conducted in Europe in 2015, although the mean VCSS score was 4.3 and the AVVQ score was 16.4 in the preoperative period, the mean VCSS score was 1.1 and the AVVQ score was 6.7 at the postoperative 1st year [25]. In the present study, the VCSS score, which was 7.3±1.40 before the procedure, was found to be 1.54±0.98 at the 12th month after the procedure, and 2.1±1.3 at the 36th month. Likewise, in our study, the AVVQ score that was 23.79±7.67 in the preoperative period was found to be 6.12±1.71 at the postoperative 12th month and 6.88±1.92 at the 36th month. These results show that the reduction effect of the procedure on symptoms and its positive effects on quality of life are consistent with the literature data.

The most important criterion for success in endovenous treatment of saphenous vein insufficiency is complete closure and absence of re-canalized flow. In the study conducted by Biemans et al., 1-year results of EVLA, classical surgical treatment and foam sclerotherapy were compared and the success rates were found to be 88.5%, 88.2%, and 72.2%, respectively [26]. In another study, the postoperative 1-year results of CAE and EVLA Methods were compared, and the success rates were found to be 98.8% in CAE and 97.6% in EVLA [27]. In the study conducted by Bozkurt et al., according to the 1-year results of the patients who underwent EVLA and CAE, the occlusion rates were 92.2% and 95.8%, respectively [28]. The American Venous Forum recommends the application of CAE in diameters below 12 mm and states that post-procedure recanalization will be more common over this size [29]. In the present study, CAE treatment was used for all patients, and the occlusion rate was 97.6% according to the 1-year follow-up results and 93.3% according to the 3-year follow-up results. These results are consistent with the results of CAE treatment found in other studies in the literature, and when the results of patients treated with other methods were assessed, it was found that the success of the CAE treatment was not different from that of the treatments with other methods.

Although the study was conducted with a high patient population, the limitations of the study were that it had a single-center design, the CAE method was not applied to patients with too many varicose veins and perforating vein insufficiency in the selection of patients. Similarly, another limitation of the study was that only the occlusion rates were taken as the basis for the success of the procedure and the conditions of the varicose veins that were visible before and after the procedure were not compared.

In conclusion, in light of the data obtained in the present study, we think that CAE in the treatment of superficial saphenous vein insufficiency is an advantageous treatment modality for patients, considering its success in relieving symptoms and improving the quality of life of patients, having low complication and high occlusion rates, need for short-term hospitalization, and not restricting the daily life of patients. We think that not using compression stockings increases the patient's quality of life and has positive effects on the results of postoperative AVVQ scoring. CA leakage into the deep venous system is due to insufficient pressure applied to the saphenofemoral junction area with the USI probe. We think that to prevent this complication, it is necessary to make sure that the saphenous vein has collapsed by visualizing it on USI before starting the procedure.

Ethics Committee Approval: The study protocol was approved by the Eskişehir Osmangazi University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee (date/no: 17.01.2023 / E-25403353-050.99-2300020649).

Patient Consent for Publication: A written informed consent was obtained from all patients.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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