Kocaeli Med J 2019; 8; 2:204-209

Büyük Safen Venin Siyanoakrilat ile Glue Ablasyon ve Radyofrekans ile Endovenöz Termal Ablasyon İşlemlerinin Varfarin Tedavisi Alan Hastalarda Verimliliği ve Orta Dönem Sonuçları

Efficiency and Midterm Results of Glue Ablation with Cyanoacrylate and Endovenous Thermal Ablation with Radiofrequency of Great Saphenous Vein Under Warfarin Therapy

Emir Cantürk

Bezmialem Üniversitesi, Tıp Fakültesi, Kalp ve Damar Cerrahisi Ana Bilim Dalı, İstanbul, Türkiye

ÖZ

GİRİŞ ve AMAÇ: *Varfarin tedavisi alan hastalarda kronik venöz yetmezliğinin perkütan tedavisi sonuçlarını araştıran çalışma sayısı özellikle glue ablasyon açısından yetersizdir. Çalışmamızın amacı, siyanoakrilat ile glue ablasyon veya radyofrekans ile endovenöz termal ablasyon tedavilerinin, erken ve orta dönem sonuçlarını değerlendirmek ve bu teknikleri varfarin tedavisi alan hasta grubunda karşılaştırmaktır.*

YÖNTEM ve GEREÇLER: *Ocak 2013 ile Ocak 2018 tarihleri arasında, kronik venöz yetmezliği tanısı ile büyük safen venin tümesan veya lokal anestezi altında, siyanoakrilat ile glue ablasyon veya radyofrekans ile endovenöz termal ablasyon tedavisi yapılan toplam 306 hasta çalışmaya dahil edildi. 306 hastanın 30'una (12 erkek, 18 kadın; ort. yaş 63,28 ± 3.46 yıl; dağılım 51-72 yıl) varfarin tedavisi altında glue ablasyon (11 hasta) veya endovenöz termal ablasyon (19 hasta) tedavisi uygulandı.*

BULGULAR: *Takip süresi içerisinde 5 hastada (% 16.6) rekanalizasyon gözlendi. Bu 5 hastadan 4'üne (% 21) radyofrekans ile endovenöz termal ablasyon, 1'ine (% 9) ise glue ablasyon tedavisi uygulanmıştı. Siyanoakrilat ile glue ablasyon ve radyofrekans ile endovenöz termal ablasyon tedavilerinin bir yıllık başarı oranları sırasıyla % 90,9 ve% 78,9 bulundu (P = 0,047). Rekanalizasyon gelişen beş hasta ise glue ablasyon ile % 100 başarı ile tedavi edilmiştir.*

TARTIŞMA ve SONUÇ: *İşlem sonrası kanama veya derin ven trombozu olmaksızın glue ablasyon işlemi varfarin tedavisi altında güvenli ve etkili bir şekilde yapılabilmekle beraber, radyofrekans ile endovenöz termal ablasyon tedavisine kıyasla orta dönem sonuçları daha üstün bulunmuştur.*

Anahtar Kelimeler: *Glue ablasyonu, termal ablasyon, Radyofrekans, büyük safen ven, kronik venöz yetmezlik.*

ABSTRACT

INTRODUCTION: *The number of articles examining the percutaneous treatment of chronic venous insufficiency in patients receiving warfarin therapy is insufficient especially for glue ablation. The aim of our study was to evaluate the early and midterm postprocedural outcomes of glue ablation with cyanoacrylate closure and endovenous thermal ablation with radiofrequency and to compare these techniques in a group of patients with uninterrupted warfarin therapy.*

METHODS: *From January 2013 to January 2018, a total of 306 patients who underwent glue ablation or endovenous thermal ablation with radiofrequency of the great saphenous vein under either tumescent or local anesthesia due to chronic venous insufficiency were included in this study. Of 306 patients, 30 patients (12 males, 18 females; mean age 63,28±3,46 years; range 51 to 72 years) underwent either glue ablation (11 patients) or endovenous thermal ablation (19 patients) under warfarin therapy.*

RESULTS: *Recanalization was observed in 5 patients (16.6%) during the follow-up period. Of these 5 patients, 4 patients (21%) underwent endovenous thermal ablation with radiofrequency and 1 patient (9%) underwent glue ablation. One-year success rate of glue ablation with cyanoacrylate closure and endovenous thermal ablation with radiofrequency were 90,9% and 78,9%, respectively (P=0.047). Five patients with recanalization have treated with glue ablation with 100% success.*

DISCUSSION and CONCLUSION: *Glue ablation could be safely and effectively performed in patients with uninterrupted warfarin therapy without postprocedural bleeding or deep vein thrombosis and, it was associated with superior mid and long-term results compared to the endovenous thermal ablation with radiofrequency.*

Keywords: *Glue ablation, thermal ablation, radiofrequency, great saphenous vein, chronic venous insufficiency.*

İletişim / Correspondence:
Dr. Emir Cantürk
Bezmialem Üniversitesi, Tıp Fakültesi, Kalp ve Damar Cerrahisi Ana Bilim Dalı, İstanbul, Türkiye
E-mail: mehtapakbalik@hotmail.com
Başvuru Tarihi: 19.08.2019
Kabul Tarihi: 25.08.2019

INTRODUCTION

Chronic venous insufficiency is a common disorder with an incidence of 21% in the general population. [1] Edema, pain, skin changes, hyperpigmentation, and ulcerations are considered as the main symptoms of chronic venous insufficiency. [2] Endovenous thermal ablation of great and small saphenous vein has become the treatment of choice among most of the patients with superficial vein reflux. The main mechanism of endovenous thermal ablation (with either laser or radiofrequency) is to injure the venous endothelium to obliterate the vein lumen. The early thrombosis of the vein constitutes the initial mechanism of the thermal ablation before the venocontraction and fibrosis.[3] On the other hand, new generation minimally invasive treatment modalities including glue ablation with cyanoacrylate closure, foam therapy and mechanochemical ablation (MOCA) are less invasive, reduce pain and provide fast recovery.[4-6] The volume of patients under anticoagulation therapy due to several diseases has recently increased among patients who underwent great saphenous vein ablation due to chronic venous insufficiency however, it is still a therapeutic dilemma. The studies investigating and comparing the success of ablation and postprocedural outcomes in mid-term and long-term follow-up of glue ablation with cyanoacrylate closure (nonthermal, nontumescent) and endovenous thermal ablation (with either laser or radiofrequency) for the treatment of chronic venous insufficiency are scarce. Continuation of sodium warfarin therapy during procedure may increase the bleeding and reduce the success rate of ablation.[7] The aim of our study was to evaluate the early and midterm postprocedural outcomes of glue ablation with cyanoacrylate closure and endovenous thermal ablation with radiofrequency, and to compare these techniques in a subgroup of patients with uninterrupted warfarin therapy.

MATERIALS and METHODS

Study population

From January 2013 to January 2018, a total of 306 patients who underwent glue ablation or endovenous thermal ablation with radiofrequency of the great saphenous vein under either tumescent or local anesthesia due to chronic venous insufficiency were included in this study. Of 306 patients, 30 patients (12 males, 18 females; mean age 63,28±3,46 years; range 51 to 72 years) underwent either glue ablation (11 patients) or endovenous thermal ablation with radiofrequency (19 patients) under warfarin therapy. Pain, aching, cramping, heaviness, edema, and restless leg were observed as preoperative symptoms. Patients' demographics, physical examination findings including CEAP classification, laboratory tests, etiological factors, medical history, comorbidities, Venous Clinical Severity Score, Aberdeen Varicose Vein Questionnaire and postprocedural outcomes were evaluated. The primary endpoint was complete closure of great saphenous vein and the secondary endpoint was the development of postprocedural adverse events including bleeding and thromboembolism. Before the intervention, duplex ultrasound scanning was performed to all patients at the standing position, which examined both superficial and deep venous system of the limbs. Interventional treatment indications were accepted as more than 2 seconds of reflux and more than 5,5 mm and less than 10 mm in diameter of the great saphenous vein. Patients with a history of deep venous thrombosis (DVT), pulmonary embolism, severe deep venous insufficiency, more than 10 mm in diameter of the great saphenous vein and simultaneous small saphenous vein reflux were excluded from the study. Patients were divided into two groups according to the type of intervention; as group 1: glue ablation (cyanoacrylate closure) and group 2: endovenous thermal ablation (with radiofrequency). All patients were evaluated at 1st week, 1st, 6th and 12th months, and annually with Duplex ultrasound in terms of the patency of the veins and venous reflux. More than 5 cm patency in length, residual reflux more than 0.5 second were defined as the procedural failure.[8]

Procedural technique

Endovenous thermal (Radiofrequency) ablation

After a 6F sheath was introduced with the guidance of Duplex ultrasound, the 5F catheter (ClosureFAST, Medtronic, USA) was inserted into the great saphenous vein, which was positioned 2 cm distal to the saphenofemoral junction under local

anesthesia with appropriate sedation. Tumescent anesthesia solution that contains 0.1% lidocaine, sodium bicarbonate and epinephrine was subcutaneously administered to prevent the thermal injury owing to the procedure. Ablation was performed for every 7 cm segment of the great saphenous vein with 15 seconds durations by using a special catheter, which reached to 120 C degree bove the knee level. Compression was done by using an ultrasound probe during the ablation.

Glue ablation (N-Butyl-2-Cyanoacrylate)

After a 6F sheath was introduced with the guidance of Duplex ultrasound, the catheter was delivered to the 2 cm distal to the saphenofemoral junction and 2 mL cyanoacrylate glue (VariClose®, Biolas, Turkey) was intravenously administered during the glue ablation procedure. Compression was done by using an ultrasound probe under local anesthesia.

Intravenous sedation was applied if necessary. Venous occlusion was confirmed by Duplex ultrasound. Simultaneous miniphlebectomy was performed after the ablation. A compression bandage was applied to all patients after the procedure. No particular priority was given to any surgical technique according to surgeon's preference and the anatomical status of the affected vein. All procedures were performed by the same surgeon (E.C.) and all patients were discharged on the same day.

Statistical analysis

The Statistical Package for the Social Sciences Windows Version 21 (IBM Corp., Armonk, NY, USA) was used to assess the data. The Kolmogorov-Smirnov test was used to analyze normally distributed continuous variables. Categorical variables were presented as percentage and frequency. Continuous variables were presented as mean ± standard deviation (SD). The continuous variables were compared using the Student / independent sample T-test and the Mann-Whitney U test while the categorical data were compared using the Chi-square test or Fisher's exact test. A p-value of <0.05 was considered as statistically significant.

RESULTS

Sample sizes and demographic features

Of the 30 patients, glue ablation was applied to 11 patients (36.7%) while endovenous thermal ablation with radiofrequency was applied to the remaing 19 patients (63.3%). The clinical, demographic and laboratory features of patients are shown in Table 1. Simultaneous miniphlebectomy was applied to 76.6% of patients (23 patients). Warfarin therapy was continued to all patients before and after the procedure. Atrial fibrillation (in 12 patients) and a metallic heart valve (in 18 patients) were the main indications of the oral warfarin therapy. The mean international normalized ratio (INR) was 2.76±0.56 (range: 2.02-3.05). The mean body mass index (BMI) was 26.3±2.2 (range: 23.4-32.7). Seventeen patients (56.6%) were in CEAP 2 while the remaing 13 patients (43.4%) were in CEAP 3 classification. The mean diameter of the treated great saphenous vein was 7.7±1.8 mm (range: 5.5-10 mm). No technical failure and device-related complications were observed during the procedure. The mean follow-up duration was 3.43±0.70 years (range: 1-5 years) and no patient was lost to follow-up at first year. No major bleeding, abundant bruising, nerve injury and deep vein thrombosis occurred on postprocedural period. Recanalization was observed in 5 patients (16.6%) during follow-up period. Of these 5 patients, 4 patients (21%) underwent endovenous thermal ablation with radiofrequency ablation and 1 (9%) underwent glue ablation. One-year success rate of glue ablation with cyanoacrylate closure and endovenous thermal ablation with radiofrequency were 90,9% and 78,9%, respectively (P=0.047). Five patients with recanalization were treated with glue ablation with 100% success. There was a significant difference in terms of the intervention time in favor of glue ablation (21.3±3.7 min for glue ablation vs 32.5±5.1 min for endovenous thermal ablation, P<0.05). Venous Clinical Severity Score and Aberdeen Varicose Vein Questionnaire results were found to be better in patients who underwent glue ablation (P<0.01).

Table 1: The clinical, demographic and laboratory features of patients

	Group 1 Glue ablation, n=11 patients			Group 2 Radiofrequency ablation, n=19 patients			Total		
	n	%	Mean±SD	n	%	Mean±SD	n	%	P
Age			62,9±5,1			63,5±6,3			0,79
Gender									
Male	4	36,3		8	42,1		12	40	1
Surgical Side									
Right	5	45,5		9	47,3		14	46,6	1
CEAP 2	6	54,5		11	57,8		17	56,6	1
CEAP 3	5	45,5		8	42,1		13	43,3	1
Current smoking	3	27,7		3	15,7		6	20	0,641
Hypertension	1	9		2	10,5		3	10	1
DM	1	9		1	5,2		2	6,6	1
BMI			26,5±4,1			26,2±2,7			0,810
Surgery time			21,3±3,7			32,5±5,1			*0,001*
Recanalization	1	9		4	21		5	16,6	*0,047*

DISCUSSION

The number of articles examining the percutaneous treatment of chronic venous insufficiency in patients uninterrupted warfarin therapy is insufficient. This is the first study, which investigated and compared the mid/long term outcomes of glue and radiofrequency ablation in patients under warfarin therapy. The main finding of this study was, recanalization rate on mid/long term follow up with glue ablation was found lower in patients under warfarin therapy and, it can be safely and effectively applied.

Endovenous thermal ablation with radiofrequency has been used for the treatment of superficial veins reflux of the lower limb. Compared to stripping surgery, this approach can be used in elderly patients with several comorbidities.[9] The reported treatment success rate of glue and radiofrequency ablation without warfarin therapy was 100% and 99%, respectively.[10] Bozkurt et al. [11] reported that the one-year success rate of endovenous thermal ablation with laser and glue ablation was 92.2% and 95.8%, respectively (P=0.138) in patients without warfarin therapy. In addition, Park [5] reported that the VenaSeal system was found to be safe and efficient for the treatment of reflux of small saphenous vein with 100% patient's satisfaction. The main advantages of glue ablation over endovenous thermal ablation are including less pain, hematoma, and ecchymosis.[5]

Due to potential postprocedural hemorrhage, the majority of authors are recommended to discontinue warfarin therapy prior to procedure.[9] However, some authors advocated that continuation of anticoagulant therapy does not affect the success rate of endovenous thermal ablation and foam sclerotherapy.[6] Furthermore, conversion to low molecular weight heparin therapy prolongs the preoperative duration and may increase the risk of pulmonary thromboembolism in this subgroup of patients.[12,13] Low-molecular-weight heparin mostly preferred as a bridging anticoagulant therapy that can be applied to reduce the thromboembolism unless warfarin cessation.[13] Due to the advances of ultrasound-guided minimally invasive endovenous interventions, patients under anticoagulation or antiplatelet therapy constitute a lower rate of bleeding.[14]

Sharifi et al.[6] compared 60 patients (88 limbs) who underwent endovenous thermal ablation with radiofrequency (48 limbs) or laser (EVLA) (40 limbs) under warfarin or antiplatelet therapy with 65 patients (92 limbs) without anticoagulant or antiplatelet therapy. They investigated the recanalization of the great saphenous vein. None of the patients had postprocedural major bleeding while minor bleeding was significantly higher in patients underwent endovenous thermal ablation with radiofrequency (P < 0.001). However, minor bleeding rate was not statistically different among

the same subgroup of patients underwent EVLA.[6] They revealed a 100% success rate after 1 year follow-up without adverse effect of anticoagulant therapy. [6] Anticoagulants may be considered to prevent thrombotic occlusion however, EVLA did not affect the thrombotic occlusion and thermal ablation in patients under warfarin therapy without bleeding complications.[9,12] In addition, Gabriel et al.[15] reported a 37 patient-study which investigated the endovenous thermal ablation with radiofrequency under warfarin therapy and, they found good long term results. Our one-year success rate was similar to previous studies after glue ablation in patients under warfarin therapy (90,9%) while, the success rate of radiofrequency was found lower (78,9%).

Theivacumar et al.[12] reported a study including 24 limbs that underwent EVLA under warfarin therapy, and they found an 83% success rate without a statistically significant difference with the control group without extensive bruising or hematoma. Additionally, Delaney et al. [16] reported a 15 patient study that EVLA under anticoagulant therapy reveals a 93% (14 of 15 patients) success rate after 12 months follow-up with minor complications. Riesenman et al. [9] reported a 5 patient study that EVLA was applied with a precise success rate without any adverse affect including bleeding and deep venous thrombosis during 8 weeks early follow up. Furthermore, they reported that without interruption of warfarin therapy, EVLA therapy can be safely and effectively performed with reasonable outcomes and can be considered as an alternative to open surgery.[9,12]

The incidence of superficial phlebitis under glue and endovenous thermal ablation with radiofrequency was 5% and 16%, respectively.[10] Our results were lower than the previous studies that no superficial phlebitis was observed in our study.

This study has a number of limitations worth noting. First, we conducted a retrospective study. Second, the number of patients, which were included in our study, may seem relatively small compared to other studies. Third, it's a single-center design. Fourth, perforating veins were not assessed. Confirmation of our findings will require randomized controlled prospective studies, which investigates the impact of warfarin on Glue and radiofrequency ablation.

In conclusion, the results of the present study demonstrate that glue ablation can be considered as an alternative therapy to open surgery for chronic venous insufficiency under warfarin therapy. It can be safely and effectively applied without postoperative major bleeding and deep vein thrombosis. In addition, glue ablation was associated with superior results on the midterm and long-term follow-up compared to endovenous thermal ablation with radiofrequency.

Declaration of conflicting interests
None
Funding
None

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