

## Endovenous ablation technique using N-butyl cyanoacrylate in varicose veins

### Variköz venlerde N-bütül siyanoakrilat ile endovenöz ablasyon tekniği

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#### ABSTRACT

**Objectives:** This study aims to report the outcomes of a novel non-tumescence endovenous ablation technique using the N-butyl cyanoacrylate (NBCA) in patients with varicose vein.

**Patients and methods:** Between November 2014 and August 2017, a total of 292 patients (174 females, 118 males; mean age 42.6±17.9 years; range, 20 to 69 years) who were admitted with chronic venous insufficiency and diagnosed with saphenofemoral or small saphenous vein insufficiency by Doppler ultrasound (DUS) were included. The patients underwent endovenous ablation using the NBCA and DUS was performed before and after the procedure. The patients were evaluated using the Comprehensive Classification System for Chronic Venous Disorders (CEAP) and Venous Clinical Severity Score (VCSS).

**Results:** The great saphenous vein was ablated in a total of 264 patients and small saphenous vein was ablated in 28 patients. The mean CEAP score was 3.3. The mean diameter of the great saphenous vein was 7.8 mm, while the mean diameter of the small saphenous vein was 6.9 mm. The patients were scheduled for follow-up visits at one week and three months after the procedure. The total occlusion rate was 97.6%, as assessed by the post-procedural DUS examination. Of the patients, 4.7% had phlebitis-like events. The mean pre-procedural VCSS score was 9.2, which decreased to 3.4 at three months after the procedure.

**Conclusion:** Our study results show that endovenous ablation technique using the NBCA is a safe and simple method with successful results in the early period.

**Keywords:** Endovenous ablation; N-butyl cyanoacrylate; varicose veins.

#### ÖZ

**Amaç:** Bu çalışmada variköz venleri olan hastalarda N-bütül siyanokrilat (NBCA) kullanılarak yeni bir endovenöz ablasyon tekniğinin sonuçları sunuldu.

**Hastalar ve Yöntemler:** Kasım 2014 - Ağustos 2017 arasında kronik venöz yetmezliği ile başvuran ve Doppler ultrason (DUS) ile safenofemoral veya küçük safen ven yetmezliği tanısı konan toplam 292 hasta (174 kadın, 118 erkek; ortalama yaş: 42.6±17.9 yıl; dağılım, 20-69 yıl) çalışmaya alındı. Hastalara NBCA kullanılarak endovenöz ablasyon uygulandı ve işlem öncesi ve sonrası DUS yapıldı. Hastalar Kronik Venöz Bozukluklarda Kapsamlı Sınıflandırma Sistemi (CEAP) ve Venöz Klinik Şiddet Skoru (VCSS) ile değerlendirildi.

**Bulgular:** Toplam 264 hastada büyük safen vene ve 28 hastada küçük safen vene ablasyon yapıldı. Ortalama CEAP skoru 3.3 idi. Ortalama büyük safen ven çapı 7.8 mm iken, ortalama küçük safen ven çapı 6.9 mm idi. İşlem sonrası birinci hafta ve üçüncü ayda hastalara takip viziti planlandı. İşlem sonrası DUS değerlendirmesi ile toplam oklüzyon oranı %97.6 olarak bulundu. Hastaların %4.7'sinde flebit benzeri durum gelişti. İşlem öncesi ortalama 9.2 olan VCSS skoru, işlemten üç ay sonra 3.4'e düştü.

**Sonuç:** Çalışma sonuçlarımız, NBCA kullanılarak yapılan endovenöz ablasyon tekniği erken dönem sonuçları başarılı olan güvenli ve basit bir yöntemdir.

**Anabtar sözcükler:** Endovenöz ablasyon, N-bütül siyanoakrilat; variköz ven.

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Chronic venous insufficiency (CVI) of the lower limb and associated varices are a common health problem which impair the quality of life of individuals with occasional severe complications. Its incidence ranges between 20 and 40%.<sup>[1-3]</sup> It primarily affects the superficial veins or perforating veins up to 95%. It can be successfully treated by the removal of these veins (ablation) or surgery.<sup>[4]</sup> Its etiology is multifactorial including genetic predisposition, age, sex, obesity, pregnancy, intra-abdominal malignancies, thrombophlebitis, previous leg injury, and standing for long-periods.<sup>[4]</sup>

Over the past decade, treatment paradigm has been shifted from conventional surgery to endovenous thermal ablation (EVTA) and ultrasound-guided foam sclerotherapy (UGFS).<sup>[5]</sup> In 2001, Navarro et al.<sup>[6]</sup> performed a successful thermal endovenous ablation using laser in the treatment of varicose veins, suggesting an alternative modality to standard surgery. Since then, several reports have been published on thermal ablation procedures using varying wavelengths and radiofrequency catheters. With the paradigm shift toward thermal ablation, mechanical ablation techniques have been assessed. Ultrasound-guided foam sclerotherapy is one of these techniques which contains polidocanol (Aethoxysklerol®). However, studies on UGFS reported relatively lower efficacy rates according to the EVTA in multiple centers with interim results of one randomized clinical trial showing a great saphenous vein occlusion rate of only 67.4%.<sup>[7,8]</sup> On the other hand, these methods require the use of tumescent anesthesia, which may cause some adverse effects, such as post-procedural pain, ecchymosis, hematoma, and sensory nerve damage.<sup>[9-11]</sup> Therefore, mechanochemical ablation techniques have been developed.<sup>[12]</sup>

N-butyl cyanoacrylate (NBCA) glue was approved by the United States (US) Food and Drug Administration for the treatment of brain aneurysms and arteriovenous malformations.<sup>[13-15]</sup> In addition, this agent can be used in the treatment of gastrointestinal bleeding, bone cysts, cecal resection, and venous dilatations such as varicose or mesenteric varices.<sup>[16,17]</sup> As a relatively novel treatment option, NBCA can be used as an endovenous ablation technique for the affected veins. Therefore, Variclose® vein sealing system (Biolas, FG Group, Ankara, Turkey) has been developed. The colorless NBCA liquid becomes solid via polymerization reaction following the intravascular injection, and activates an inflammatory reaction in the vein wall.<sup>[18]</sup>

In this study, we report the outcomes of a novel non-tumescence endovenous ablation technique using the NBCA in patients with varicose vein.

## PATIENTS AND METHODS

Between November 2014 and August 2017, a total of 292 patients (174 females, 118 males; mean age 42.6±17.9 years; range, 20 to 69 years) who were admitted with CVI and diagnosed with saphenofemoral or small saphenous vein insufficiency by Doppler ultrasound (DUS). Exclusion criteria were as follows: previous history of deep vein thrombosis, immobilization, systemic infections, secondary varices, prior interventions using any other technique, congenital vascular malformations, deep venous valvular insufficiency, focal aneurysmal dilatations, and severe arterial insufficiency. All patients underwent endovenous ablation using the NBCA, and DUS was performed before and after the procedure. The patients were evaluated using the Comprehensive Classification System for Chronic Venous Disorders (CEAP) and Venous Clinical Severity Score (VCSS). The patients were also scheduled for further clinical and DUS examination at one week and three months after the procedure. The study protocol was approved by the institutional ethics committee. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

After providing adequate antisepsis of leg, the saphenous vein was cannulated under the ultrasound guidance with the local anesthesia of the entrance site. Then, the introducer was inserted into the saphenous vein and the catheter marker was inserted 3-cm behind the saphenofemoral or saphenopopliteal junction. The NBCA (BiolasVariclose® FG Group, Turkey) was inserted into the injector and placed into the injection gun. The microcatheter was mounted into the tip of the injector and the air was removed from the injector. Then, it was placed into the catheter marker to deliver NBCA into the vessel. Before the procedure was initiated, the proximal vein was compressed using the DUS probe. The injector gun was held in a certain position and 0.1 mL polymer was injected. After a three-second interval, the catheter was retrieved 3-cm backwards. The procedure was repeated until all vein segments were occluded. The saphenous vein was examined by DUS, after the procedure was completed.

### Statistical analysis

Statistical analysis was performed using the IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed in mean  $\pm$  standard deviation (SD) and range (min-max) values. Pre- and postoperative continuous variables were compared using the independent *t*-test. A *p* value of  $<0.05$  was considered statistically significant.

## RESULTS

Of a total of 292 patients, the great saphenous vein was ablated in 264 and small saphenous vein was ablated in 28. The mean CEAP classification was  $3.3 \pm 0.8$  (range, 2 to 5). The mean diameter of the great saphenous vein was  $7.8 \pm 2.3$  mm (5.8 to 17 mm), while the mean diameter of the small saphenous vein was  $6.9 \pm 1.9$  mm (4 to 42 mm). The total procedural duration was  $13.3 \pm 2.1$  min (4 to 28 min). The mean pre-procedural VCSS score was  $9.2 \pm 1.3$  (6 to 12), which decreased to  $3.4 \pm 1.7$  (2 to 10) at three months ( $p < 0.001$ ). A partial patency was observed in only five patients following the procedure with a total occlusion rate of 97.6%, as assessed by the post-procedural DUS examination. At the end of three weeks and three months, venous closure rates were same as early post-procedural rates. A total of 26 patients (8.9%) had transient pain during the procedure. Of the patients, 14 (4.7%) had phlebitis-like events at one week. There was no complication or further pathology after application, such as allergenic reactions, infection, deep venous thrombosis and hematoma, except for small-size ecchymosis in the puncture site. All patients were instructed to wear medium-pressured (Class II) compression socks for the first two weeks. Phlebectomy was applied for small superficial varicosities after two months of postoperative glue application period. Post-procedural hospitalization duration changed between one and three hours.

## DISCUSSION

Chronic venous insufficiency is a progressive disease which may impair the quality of life of the individuals with high treatment costs.<sup>[19]</sup> It is estimated that CVI affects more than 25 million adults in the US and more than six million with severe venous disease.<sup>[1]</sup> Over the past decade, minimally invasive techniques such as EVTA, radiofrequency or laser ablation and UGFS have been widely adopted as an

alternative to conventional surgical interventions.<sup>[5]</sup> However, as EVTA has been associated with skin burns and superficial nerve injury, tumescent anesthesia is performed to avoid these complications, which, however, prolongs the duration of procedure with an increased rate of hematomas.<sup>[20]</sup> In addition, tumescent anesthesia may also induce ecchymosis, hematoma, pain, and sensory nerve injury.<sup>[9-11]</sup> Furthermore, UGFS has been associated with an increased rate of deep vein thrombosis, pulmonary embolism, inflammation, skin discoloration, and visual disturbances with lower venous occlusion rates, compared to EVTA.<sup>[7,8,21,22]</sup>

The utilization of NBCA in the treatment of venous insufficiency was first described by Almeida et al.<sup>[23]</sup> The authors performed NBCA in 38 patients and reported a total occlusion rate of 92% at 24 months with a post-procedural complication rate of 16%. In another study, Toonder et al.<sup>[24]</sup> performed embolization using the NBCA into the perforated vein and reported a success rate of 76% at three months. In a multi-center study including 70 patients with saphenous vein insufficiency, the total occlusion rate was reported to be 93% with a phlebitis-like complication rate of 25% at 12 months.<sup>[25]</sup> In another study, Yasim et al.<sup>[26]</sup> conducted a survey for five months and found venous closure rates to be 100%. In the present study, the total occlusion rate was 96.5%, although we observed patency in a very short segment between the proximal and distal portion of the saphenous vein in five patients. At three months, three patients had persistent partial patency, while the saphenous vein was occluded (thrombosed) in the remaining two patients. With the introduction of novel delivery systems, post-procedural saphenous patency can be occluded through NBCA injection under the guidance of DUS. Furthermore, we believe that total occlusion of the saphenous vein and prevention of pain and phlebitis can be achieved using more fluid glues. This can be also achieved avoiding the injection of the agent from the entrance site to the skin and avoiding excessive amount of agent into the saphenous veins proximal to the skin tissue. The distance between the saphenous vein and the skin and the diameter of the vein can be also calculated to estimate the agent amount before the procedure.

In conclusion, our study results show that endovenous ablation technique using the NBCA is a safe and simple method with successful results in the early period. However, further large-scale and long-term randomized studies are required to establish a conclusion.

### Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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