CLINICAL STUDY

Predictors of Recanalization for Incompetent Great Saphenous Veins Treated with Cyanoacrylate Glue

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ABSTRACT

Purpose: To determine predictors of recanalization in patients treated with endovenous cyanoacrylate.

Methods: Follow-up by serial clinical and duplex examinations was performed at 1 week, 1 month, 6 months, 12 months, and 24 months of 108 legs in 55 patients (21 men, median age 65 y) with primary varicose veins treated with endovenous cyanoacrylate. Cox regression analysis was used to examine venous characteristics before the procedure: diameter of great saphenous vein (GSV), treatment length of GSV, presence of incompetent perforators, clinical severity of varicose vein, and experience of operator as predictors of recanalization. With the patient in supine position, GSV diameter was measured at 3 levels (proximal thigh 1 cm from saphenofemoral junction, midthigh, and distal thigh above knee).

Results: Of 108 legs, 2 had minimal extension of thrombus to deep vein, and 4 had superficial thrombophlebitis. Kaplan-Meier analysis showed GSV closure rates were 97.2%, 92.3%, 89.2%, and 75.7% at 1 week, 1 month, 6 months, and 12 months after the procedure. With a median follow-up period of 5 months (range, 0–18 months), 4 legs had clinical recurrence. Mean GSV diameter $\geq$ 6.6 mm was the only significant predictor for recanalization (hazard ratio 12.1; 95% CI, 1.6–92.7; $P = .016$).

Conclusions: The use of endovenous cyanoacrylate to treat varicose veins caused by incompetent GSV was safe. GSVs $<$ 6.6 mm in diameter had a closure rate of 90.0% at 12 months. Despite 97.2% closure rates at 1 week, recanalization was observed in GSVs with larger diameter.

ABBREVIATIONS

AVVQ = Aberdeen Varicose Veins Questionnaire, CEAP = Clinical-Etiology-Anatomy-Pathophysiology, GSV = great saphenous vein, SF-36 = 36-item short form health survey, SFJ = saphenofemoral junction, VCSS = Venous Clinical Severity Score

Recently developed nonthermal endovenous treatment modalities are minimally invasive, do not require tumescence anesthesia, and can be performed as office-based procedures (1). There are to date 4 commercially available nonthermal endovenous ablation systems without the need of tumescence anesthesia, including mechanochemical ablation (ClariVein; Vascular Insights, Quincy, Massachusetts), VariClose (Biolas, Ankara, Turkey), polidocanol endovenous microfoam (Varithena; BTG International, London, United Kingdom) (2), and VenaSeal Closure System (Medtronic, Gorway, United Kingdom). Both VariClose and VenaSeal use cyanoacrylate, but with different formulations and methods of delivery. In the US VeClose trial, in the 108 legs treated with endovenous cyanoacrylate, the 3-month closure rate was 99% (3). From the demographic and baseline characteristics of the VeClose VenaSeal cohort [Table II in Morrison et al (3)], the mean diameter of the mid great saphenous vein (GSV) was 4.9 mm (range, 0–9 mm), and the mean diameter of the proximal GSV was 6.3 mm (range, 3–12 mm), which are smaller than GSVs in the general treatment population in Asia. This study evaluated predictors of recanalization with longer follow-up after

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None of the authors have identified a conflict of interest.

http://dx.doi.org/10.1016/j.jvir.2017.01.011

treatment of incompetent GSVs with cyanoacrylate in a cohort of patients (including those from our pilot study) (4).

MATERIALS AND METHODS

Study Population

This study had local institutional review board approval (reference UW 15-212). This was a retrospective review of a prospectively collected database, and the method of recruitment of patients and preoperative assessment have been described before (4). From September 2014 to June 2016, 108 legs in 55 consecutive patients (34 women) with duplex ultrasound–proven saphenofemoral junction (SFJ) and/or GSV incompetence were included in this study. The first patient was treated on September 3, 2014, and the last included patient was treated on June 2, 2016. Bilateral lower limb varicose veins were present in 53 patients. Bilateral cases were preferentially chosen because of the cost of the cyanoacrylate. All treatments were done as outpatient procedures, and all patients returned for the scheduled follow-up visits. Using the CEAP (Clinical-Etiology-Anatomy-Pathophysiology) classification, 65 legs were classified as C3 venous disease, 32 legs were classified as C4a, 5 legs were classified as C4b, 3 legs were classified as C5, and 3 legs were classified as C6. The predominant symptoms were leg pain, cramps, and aching. The Venous Clinical Severity Score (VCSS) and the Aberdeen Varicose Veins Questionnaire (AVVQ) score were consistent with mild to moderate venous reflux disease at baseline (**Table 1**).

All duplex ultrasound scans were performed by certified vascular sonographers using ACUSON Sequoia 512 (Siemens Medical Solutions USA, Inc, Ultrasound, Mountain View, California) or Philips iU22 (Philips Healthcare Solutions, Bothell, Washington) machines. Saphenous vein incompetence was defined by the presence of retrograde flow of $\geq$ 0.5 second detected by duplex scan over the SFJ with the patient examined in the standing position (5). With the patient in the supine position, the diameters of the GSV were measured at 3 levels (proximal thigh 1 cm from SFJ, midthigh, and distal thigh above the knee) and then averaged. The duplex ultrasound scans documented the presence or absence of SFJ and perforator incompetence (**Fig 1**).

Table 1. Patient and Varicose Vein Characteristics

Characteristics	Values
Patients (n = 55)	
Median age, y	65
IQR	17
Range	39–86
Male/female patients	21/34
Comorbidities, n (%)	
Diabetes mellitus	5 (9.1%)
Hypertension	15 (27.3%)
Cardiac	8 (14.5%)
Renal	2 (3.6%)
Respiratory	0 (0%)
Side, n (%)	
Unilateral	2 (3.6%)
Bilateral	53 (96.4%)
Varicose veins (n = 108)	
CEAP clinical classification, n (%)	
C3	65 (60%)
C4a	32 (30%)
C4b	5 (5%)
C5	3 (3%)
C6	3 (3%)
Median diameter of GSV, mm	6.6
IQR	2.3
Range	2.3–11.4
Median treatment length of GSV, cm	28
IQR	6
Range	15–41

CEAP = Clinical-Etiology-Anatomy-Pathophysiology; GSV = great saphenous vein; IQR = interquartile range.

Study Procedure

The endovenous procedures were performed as outpatient cases in the minimally invasive surgical center under local anesthesia in the presence of an anesthetist. Percutaneous ultrasound-guided puncture of the GSV was performed using a micropuncture set (Angiodynamics, Inc, Latham, New York). The 0.035-inch proprietary guide wire was passed to the SFJ and then exchanged to the proprietary 5-F long sheath. The proprietary guide wire and the long sheath were from the VenaSeal set. The VenaSeal cyanoacrylate was prepared and attached to the delivery catheter. With the patient in head-down position, the tip of the 5-F introducer sheath/cyanoacrylate catheter was advanced to the SFJ and positioned 4.0 cm distal to the SFJ under ultrasound guidance. With occlusive compression at the SFJ by the ultrasound probe, cyanoacrylate was injected endovenously with 2 injections of 0.09 mL given 1 cm apart at this location followed by a 3-minute period of local compression and then repeated at 3-cm intervals with 30-second ultrasound probe compression sequences until the entire length of the target vein was completed. GSV obliteration and the lack of deep vein thrombosis (with compressibility) were confirmed by duplex ultrasound intraoperatively. Small stab avulsions of varicosities under local anesthesia were performed simultaneously in all patients. The study protocol with the catheter starting point at 4 cm from the SFJ and compression at the SFJ was different from the US instructions for use with the catheter tip 5 cm from the SFJ and compression at 2–2.5 cm. Patients were discharged after the procedure from the vascular ward on the same day. All patients were advised to wear full-length compression stockings (SIGVARIS; Ganzoni & Cie AG, St. Gallen, Switzerland) for at least 1 month.