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Di Gangi, Stefania ; Guillet, Carole ; Anzengruber, Florian ; Zechmann, Stefan ; Meier, Thomas O

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Original communication

Deep vein thrombosis after sclerotherapy and endovenous laser ablation of varicose veins – an observational study

Stefania Di Gangi[1,2], Carole Guillet[2,3], Florian Anzengruber[2,3,4], Stefan Zechmann[1,2,a], and Thomas O. Meier[2,5,a]

[1] Institute for Primary Care, University Hospital Zurich, Switzerland
[2] Medical Faculty, University of Zurich, Switzerland
[3] Department of Dermatology, University Hospital Zurich, Switzerland
[4] Department of Dermatology, Cantonal Hospital of Grisons, Chur, Switzerland
[5] Clinic for Angiology, University Hospital Zurich, Switzerland
[a] Shared last authorship

Summary: *Background:* The risk of developing deep vein thrombosis (DVT) after endovenous ablation of varicose veins varies in the literature. Little is known about the characteristics of this complication and associated factors. This study aimed: 1) to study the occurrence of DVT after ultrasound-guided foam sclerotherapy (UGFS) alone or combined with endovenous laser ablation (EVLA) for lower-limb varicose veins; 2) to identify factors associated with DVT. *Patients and methods:* The study included all outpatients aged 18 years or older who underwent UGFS and EVLA or UGFS alone at the University Hospital of Zurich between 2011 and 2015. Data were extracted from the hospital electronic medical record. Patients were surveyed about their level of pain after the procedure and their level of satisfaction with the procedure. Duplex ultrasound was used to assess the deep venous system 7–10 days and 6–8 months after the procedure. Regression analysis was used to examine the association of patient and procedure characteristics with the development of DVT. *Results:* A total of 334 patients (561 procedures performed in 393 different sessions) were included: 73% of the patients underwent combined UGFS and EVLA and 27% underwent UGFS alone. DVT occurred in 24 (7.2%) patients, of whom 88% underwent combined procedures and 17% underwent interventions involving both the great and small saphenous veins on the same session. DVT occurred in 8.2% of patients receiving thromboprophylaxis and in 9.5% of patients not receiving thromboprophylaxis. DVT occurred in 5.2% of women and 11.9% of men. No factors associated with a diagnosis of DVT after intervention were identified. Pain and satisfaction levels did not differ between patients with and without DVT. *Conclusions:* This study adds to the knowledge of the risk of DVT following UGFS alone or combined with EVLA. Further studies are needed to revise thromboprophylaxis.

Keywords: Varicose veins, sclerotherapy, endovenous laser ablation, compression ultrasound, deep vein thrombosis

Introduction

Minimally invasive endovenous treatments of varicose veins, i.e. incompetent saphenous veins and tributaries, are replacing conventional surgery. Ultrasound-guided foam sclerotherapy (UGFS) alone or in combination with endovenous laser ablation (EVLA) is often used as an endovenous treatment. The advantages of these methods are a quick return to normal activities and low complication rates. Following sclerotherapy there are systemic complications such as transient visual disturbances, acute migraines and local complications such as hyperpigmentation, superficial vein thrombosis and deep vein thrombosis (DVT) [1].

According to the literature, DVT is considered a rare complication of sclerotherapy and is reported in 0.2–1% of cases [1]. However, the risk of thromboembolic events after EVLA varies from 0 to 7.7% and the reason for this wide range is unclear and interpreted as investigation bias [2]. Little is known about the characteristics, nature and factors associated with thrombosis after sclerotherapy of varicose veins [3]. In particular, comparative studies of EVLA and UGFS, combined or alone, are scarce and it is not clear whether a combined procedure should be recommended, although the advantage is the possibility of treating all varicose veins in one session [4]. Furthermore, the management of post-interventional distal DVT is

controversial [5]. Treatment of distal DVT consists of compression therapy and anticoagulation for 3 months at the discretion of the physician [6].

The aim of this study was to describe the occurrence of DVT after UGFS, alone or combined with EVLA, performed for the treatment of lower limb varicose veins, and to identify factors associated with the diagnosis of DVT.

Patients and methods

Patients

This study used a convenient sample of patients enrolled in a specific time period: all outpatients aged 18 years or older who underwent UGFS of lower limb varicose veins with 1% polidocanol foam alone or together with EVLA using a 1470 nm radial laser system, at the University Hospital of Zurich between January 2011 and November 2015.

Patients with UGFS were included regardless of whether they had concomitant EVLA. Combined procedures were considered to assess the additional EVLA as a potential factor associated with DVT.

All participants gave informed consent. First treatment and recurrent interventions were included to better characterize the risk of developing DVT after endovenous treatment.

After 48 hours and after a week from the procedure, patients were asked about their level of pain and after 6 months from the procedure about their level of satisfaction with the procedure, the resolution of venous symptoms, the cosmetic result and whether they would choose the procedure again.

Ethics

The study was approved by the local ethics committee (BASEC 2019-00971).

Pre-operative Duplex

Pre-operative duplex ultrasound was performed to assess lower limb venous disease, which could be located in the great saphenous vein (GSV), small saphenous vein (SSV) or both. The diameter of the GSV was measured 3 cm from the junction and mid-thigh in the standing position using toe movements, manual compression and decompression and Valsalva maneuvers to assess orthograde flow and reflux. The diameter of the SSV was not measured.

Endovenous treatment of varicose veins

Treatment was performed by two specialists using standard techniques. Thermal ablation of incompetent saphenous veins using EVLA has been described elsewhere [7]. In the EVLA technique used, the tip of the laser fiber was placed 1.5 cm distal to the sapheno-femoral junction or in the horizontal part of the small saphenous vein respectively. A 6-F introducer sheath was placed into the great saphenous vein above or below the knee or into the small saphenous vein above the Achilles tendon. A radial 600 µm fiber connected to a 1470 nm diode laser (Biolitec AG, Jena, Germany) was advanced under duplex scanning control to the groin or to the popliteal fossa. Laser energy was delivered at a power of 10 W to achieve a linear energy dose of 60-90 J per cm of the treated vein. The tumescent solution consisted of 1000 ml saline solution 0.9%, 50 ml lidocaine 1%, 1 mg adrenaline and 10 ml potassium bicarbonate 8.4% and was cooled to approximately 5° C. Approximately 500 ml of this anaesthetic solution was injected around the target vein using a long 20 G x 23/16 needle under ultrasound guidance. The tumescent anesthesia was introduced in the saphenous compartment or the perivenous space in case of extrafascial vein segments. One puncture was required approximately every 10 cm along the vein. An infiltration pump (DP 20 Nouvag NP60, Goldach, Switzerland) with a flow rate of 60 ml/min was used to obtain sufficient volume.

The varicose tributaries were treated with UGFS during the same session. Foam of 1% polidocanol solution (Sclerovein®, Resinag AG, Zug, Switzerland) and 30% oxygen-70% carbon dioxide (PanGas AG, Dagmarsellen, Switzerland), in a ratio of 1:4 was used as sclerosant. Peripheral venous catheters for UGFS were placed just before the tumescent anesthesia (TA). The median volume of foam used per treatment session was 8 ml (range 3–16 ml). Eccentric compression with focal enhancement and compression stockings were applied at the end of the treatment.

Prophylactic antithrombotic measures

All patients were required to walk for one hour immediately after the procedure. They were also required to wear class 2 (25–15 mmHg) full-leg compression-stockings for 3 weeks after the procedure, day and night for the first 72 hours, then daytime only. Patients at high risk of thrombosis, such as those with a medical or family history of thrombophilia, were required to take low-molecular-weight heparin (LMWH) (dalteparin 5000 units subcutaneously per day, enoxaparin 40 or 60 mg subcutaneously per day) or rivaroxaban 10 mg per day for two weeks immediately after the endovenous intervention.

Off-label prophylaxis with rivaroxaban, a direct oral anticoagulant (DOAC), was used instead of LMWH in patients who were unwilling to receive a subcutaneous injection, after consultation with the patient, risk-benefit assessment, and exclusion of contraindications. Verbal informed consent was obtained instead of written consent. In the case of pre-existing anticoagulation, the decision to discontinue the treatment for the intervention was made on an

individual basis after patient assessment, in accordance with internal guidelines for perioperative management, which recommend stopping anticoagulation therapy one to two days before surgery for patients taking a DOAC and two to five days before surgery for patients taking VKA (vitamin K antagonist).

Follow-up with clinical examination and complete compression ultrasound

A complete compression ultrasound of the treated leg (thigh and calf) and a clinical examination were performed on all patients before the procedure, between 7 and 10 days and between 6 and 8 months after the procedure. If DVT was detected the treatment consisted of compression stockings and therapeutic doses of LMWH or DOAC for 4 to 6 weeks, depending on the risks of bleeding and patient comorbidities. Before stopping treatment, a follow-up examination was performed.

Data description

Data were extracted from the hospital electronic medical record system KISIM®. The following information was collected: baseline characteristics (sex, patient age, body mass index (BMI), family and medical history of venous insufficiency treatment or thrombophilia), classification of venous insufficiency according to the CEAP (Clinical Etiology Anatomy Pathophysiology) [8], treatment information (date of intervention or session; limb treated: left or right; type of procedure: UGFS and EVLA or UGFS alone; length and diameter of the vein treated; localisation: GSV, SSV or both), prophylactic anticoagulation before and after the treatment (yes/no; type of drug; duration), data on complications after intervention (DVT: yes/no; localisation of thrombosis: muscular veins, posterior tibial veins, tibiofibular trunk, popliteal vein, femoral vein, common femoral vein; whether recanalisation occurred at 6 months after DVT).

The date of intervention identified a single session, first or subsequent for each patient, in which more than one procedure could have been performed in the case of treatment of both legs or treatment of both veins. UGFS and EVLA combined were considered as a single procedure. A subsequent intervention (session) in the same leg was defined as a secondary intervention. For each procedure, the main outcome (development of DVT) was recorded, but the date on which it occurred was not recorded.

In addition, information about pulmonary embolism was found in the post-interventional medical history and clinical examinations, but no further screening was performed.

The subjective experience of pain was assessed as in another study [9]. Patient survey data on reported pain and satisfaction were defined as a scale: 0 = not at all, 10 = very much. Information on the use of pain medication and whether the patient was unable to work after the procedure was also self-reported.

Statistical analysis

Patient and procedure characteristics, pain medication and patient satisfaction scales, were compared between patients who did or did not develop DVT. On the other hand, the occurrence of DVT was compared within each characteristic. Categorical or dichotomous variables were summarized as count (proportion %) and continuous variables as mean (SD). Available case analysis was performed, and the number of non-missing observations was reported. Patient satisfaction scores were considered as continuous variables. Chi-square test was used for categorical or dichotomous variables and t-test for continuous variables. Logistic regression mixed model analysis, univariable and multivariable, was carried out at intervention level to identify factors (fixed effects) associated with the development of DVT after correction for repeated measures in patients (random effects). Patient and procedure characteristics were considered as fixed effects. For the multivariable analysis, possible clinically relevant factors were taken into account if they did not substantially reduce the number of observations analysed (i.e. if less than 15% of the total observations were missing). Factors were removed if the model had collinearity problems. The results of the regression analysis were reported as odds ratio (OR) (95% confidence interval [CI]) and the number of observations. Life-table analysis (Kaplan-Meier) of DVT after the primary intervention was also performed for patients with more than one intervention in the same limb. Time to event (DVT or DVT-free) was defined as the difference (in days) from the last intervention (session), as the date of DVT was not recorded. All test results were considered statistically significant at p-value ≤ 0.05. All analyses were performed with the statistical software R version 4.1.0 [10].

Results

Patient and procedure characteristics

Patient and procedure characteristics were reported in Table I. Of the 334 patients included, with a total of 561 procedures performed in 393 single sessions, the majority (57.8%) were classified by CEAP as symptomatic C2 (varicose), followed by C3 (edema) (25.6%). A family history of venous insufficiency or thrombophilia was reported by the majority (71.5%) of patients and a previous history of venous insufficiency treatment or thrombophilia at study start was reported in 35.5% of patients. The mean age of the patients at the time of the intervention was 49.1 (SD 15.3) years. Females were more likely to be treated (69.8%). A total of 242 (72.5%) patients underwent combined procedures (UGFS and EVLA) and 92 (27.5%) UGFS alone. Most of the patients 279 (83.5%) had no subsequent

Table I. Diagnosis of deep vein thrombosis after endovenous intervention by patient and procedure characteristics

Variable	Description	Number of patients	DVT		p-value
			No	Yes	
		334	310 (92.8)	24 (7.2)	
Patient characteristics					
Sex n (%)	female	233 (69.8)	221 (94.8)	12 (5.2)	0.050
	male	101 (30.2)	89 (88.1)	12 (11.9)	
Age (years)	mean (SD)	49.1 (15.3)	49.0 (15.3)	50.4 (15.8)	0.658
BMI	mean (SD)	25.0 (4.4)	25.0 (4.4)	24.8 (4.6)	0.903
		N = 118	N = 109	N = 9	
Previous history of venous insufficiency treatment or thrombophilia at study start n (%)	yes	103 (35.5)	92 (89.3)	11 (10.7)	0.290
		N = 290	N = 267	N = 23	
Family history of venous insufficiency or thrombophilia n (%)	yes	198 (71.5)	182 (91.9)	16 (8.1)	0.757
		N = 277	N = 253	N = 24	
Prophylaxis					
Anticoagulant used before treatment n (%)		N = 146	N = 122		
	no	135 (92.5)	111 (82.2)	24 (17.8)	0.268
	yes	11 (7.5)	11 (100.0)	0 (0.0)	
	VKA	9 (6.1)	9 (100.0)	0 (0.0)	0.363
	DOAC	2 (1.4)	2 (100.0)	0 (0.0)	1.000
Antiplatelet use before treatment n (%)		N = 146	N = 122		
	no	131 (89.7)	110 (84.0)	21 (16.0)	0.714
	yes	15 (10.3)	12 (80.0)	3 (20.0)	
	Aspirin	13 (8.9)	10 (76.9)	3 (23.1)	0.449
	Clopidogrel	2 (1.4)	2 (100.0)	0 (0.0)	1.000
Prophylaxis after the procedure n (%)		N = 289	N = 265		
	no	21 (7.3)	19 (90.5)	2 (9.5)	0.689
	yes	268 (92.7)	246 (91.8)	22 (8.2)	
	LMWH (dalteparin)	258 (89.3)	238 (92.2)	20 (7.8)	0.305
	VKA	10 (3.5)	10 (100.0)	0 (0.0)	0.700
	DOAC	6 (2.1)	3 (50.0)	3 (50.0)	0.009
Duration of prophylaxis (weeks)*	mean (SD)	1.8 (0.6)	1.8 (0.6)	1.8 (0.6)	0.971
Procedures					
CEAP n (%)		N = 180	N = 162	N = 18	
	C1: reticular	4 (2.2)	4 (100.0)	0 (0.0)	1.000
	C2: varicose	104 (57.8)	91 (87.5)	13 (12.5)	0.291
	C3: edema	46 (25.6)	40 (87.0)	6 (13.0)	0.608
	C4: pigmentation-eczema	27 (15.0)	27 (100.0)	0 (0.0)	0.126

(Continued on next page)

Table I. (Continued)

Variable	Description	Number of patients	DVT		p-value
			No	Yes	
	C5: healed ulcer	6 (3.3)	5 (83.3)	1 (16.7)	1.000
	C6: active ulcer	2 (1.1)	2 (100.0)	0 (0.0)	1.000
Subsequent interventions n (%)	yes	55 (16.5)	47 (85.5)	8 (14.5)	0.043
Secondary interventions in the same leg n (%)	yes	40 (12.0)	36 (90.0)	4 (10.0)	0.509
Total number of procedures n (%)	1	156 (46.7)	146 (93.6)	10 (6.4)	0.895
	2	147 (44.0)	136 (92.5)	11 (7.5)	
	3–6	31 (9.3)	28 (90.3)	3 (9.7)	
Type of procedure n (%)	UGFS and EVLA	242 (72.5)	221 (91.3)	21 (8.7)	0.140
	UGFS only	92 (27.5)	89 (96.7)	3 (3.3)	
Localisation (for UGFS and EVLA procedure) n (%)	GSV	203 (84.6)	184 (90.6)	19 (9.4)	1.000
	SSV	42 (17.5)	41 (97.6)	1 (2.4)	0.167
	GSV and SSV	14 (5.8)	10 (71.4)	4 (28.6)	0.034
Limb treated in the same session/intervention n (%)	both	135 (40.8)	128 (94.8)	7 (5.2)	0.625
	right	144 (43.5)	131 (91.0)	13 (9.0)	0.126
	left	84 (25.4)	75 (89.3)	9 (10.7)	0.100
Length treated (cm)		N = 273	N = 251	N = 22	0.167
	mean (SD)	46.7 (18.6)	46.3 (18.3)	52.0 (21.3)	
Diameter (mm) of the vein treated		N = 272	N = 248	N = 24	0.962
	mean (SD)	6.8 (3.2)	6.8 (3.1)	6.8 (4.2)	

Notes. Data were evaluated at patient level and results stratified by patient and procedure characteristics. Percentages were calculated per row to evaluate the occurrence of deep vein thrombosis in each subgroup. Comparisons of occurrence of DVT within each strata were performed using chi-square test or t-test as appropriate. *Patients with no prophylaxis were included with duration 0. BMI: body mass index; CEAP: Clinical Etiology Anatomy Pathophysiology; DOAC: direct oral anticoagulant; DVT: deep vein thrombosis; EVLA: endovenous laser ablation; GSV: great saphenous vein; LMWH: low-molecular-weight heparin; NSAID: nonsteroidal anti-inflammatory drug; SSV: small saphenous vein; UGFS: ultrasound-guided foam sclerotherapy; VKA: vitamin K antagonist.

Table II. Risk factors for the development of deep vein thrombosis after endovenous intervention

	Univariate analysis		Multivariable analysis	
	OR (95% CI)	Number of observations	OR (95% CI)	Number of observations
Male (ref. female)	2.35 (1.03, 5.40)	393	2.01 (0.86, 4.72)	342
Age (years)	1.00 (0.98, 1.03)	393	1.00 (0.97, 1.03)	342
BMI	1.00 (0.86, 1.17)	143		
Previous history of venous insufficiency treatment or thrombophilia (ref. no)	1.87 (0.77, 4.44)	349		
Family history of venous insufficiency or thrombophilia (reference no)	0.82 (0.34, 1.99)	329		
Aspirin use before intervention (ref. no)	1.64 (0.43, 6.31)	174		
No prophylaxis after intervention (ref. yes)	1.07 (0.24, 4.79)	342	1.17 (0.25, 5.44)	342
Prophylaxis duration (weeks)	1.01 (0.50, 2.05)	342		
CEAP C2 (ref. other)	1.61 (0.58, 4.47)	215		
Subsequent intervention (ref. first intervention)	1.54 (0.55, 4.28)	393	2.43 (0.72, 8.21)	342
Secondary intervention in the same leg (ref no)	1.21 (0.35, 4.24)	393		
UGFS only (ref. EVLA and UGFS)	0.46 (0.17, 1.25)	393	0.36 (0.11, 1.18)	342
Both SSV and GSV treated in the same session (ref. no)	3.53 (0.90, 13.9)	251		
Both legs treated in the same session (reference one leg)	0.50 (0.18, 1.39)	390		
Length treated (cm)	1.01 (0.99, 1.03)	313		
Vein diameter (mm)	1.01 (0.89, 1.14)	315		

Notes. Mixed logistic regression analysis results were evaluated at intervention level with patients as random effects. Previous history of venous insufficiency was defined at study start for the first intervention and as "yes" at subsequent interventions. BMI: body mass index; GSV: great saphenous vein; CEAP: Clinical Etiology Anatomy Pathophysiology; DOAC: direct oral anticoagulant; DVT: deep vein thrombosis; EVLA: endovenous laser ablation; Ref: reference category; UGFS: ultrasound-guided foam sclerotherapy; SSV: small saphenous vein.

intervention sessions but the majority 178 (53.3%) underwent more than one procedure.

Deep vein thrombosis after the endovenous intervention

The proportions of patients with DVT after endovenous procedures were compared by patient and procedure characteristics in Table I. DVT was diagnosed in 24 patients (7.2%) after endovenous intervention, corresponding to 28 procedures (5.0% of all procedures). DVT occurred in 5.2% of the women and 11.9% of the men. There was no difference in age between the DVT and no-DVT group. The mean BMI was 25.0 (SD 4.4) which was not significantly different between the groups. Most DVT cases (80%) were located in one of the two posterior tibial veins. No proximal DVT (femoral or popliteal) could be found. Therefore, no patient had an endothermal heat-induced thrombosis (EHIT). Most of the patients who developed DVT, 21 (88%), underwent UGFS and EVLA. In the group of patients who underwent UGFS and EVLA, DVT occurred in 21 (8.7%) patients and in the group who underwent UGFS alone DVT occurred in 3 (3.3%) patients, p = 0.140. DVT occurred in 28.6% of the patients who had both saphenous veins, GSV and SSV, treated in the same session. Of all DVT patients, only one had history of previous DVT at study start. No pulmonary embolism occurred during follow-up.

Prophylaxis

No antithrombotic medication was given prior to treatment to most patients 135 (92.5%) and to all DVT patients (see Table I). VKA was given to 9 (6.1%) patients and DOAC to 2 (1.4%) patients. DVT was diagnosed in 23.1% of the patient's using aspirin. The most commonly used post-treatment prophylactic anticoagulant was dalteparin (LMWH), administered in 258 (89.3%) patients. DVT was diagnosed in 8.2% of the patients with any post-treatment prophylaxis (7.8% of the patients using LMWH) and in 9.5% of the patients without post-treatment prophylaxis. Patients who were taking a VKA or a DOAC prior to treatment continued to receive prophylaxis with a VKA or a DOAC after treatment. The mean duration of prophylaxis was 1.8 (0.6) weeks, which was not significantly different between the DVT and no-DVT groups, p = 0.971.

Factors associated with DVT

In Table II, the results of univariable and multivariable logistic regression analysis were reported, corrected for correlation between repeated measures for re-interventions. Being male was positively associated with the development of DVT in univariable analysis, but in multivariable analysis, after adjusting for age, prophylaxis after intervention, having undergone subsequent interventions or combined procedures, no significant factor associated with

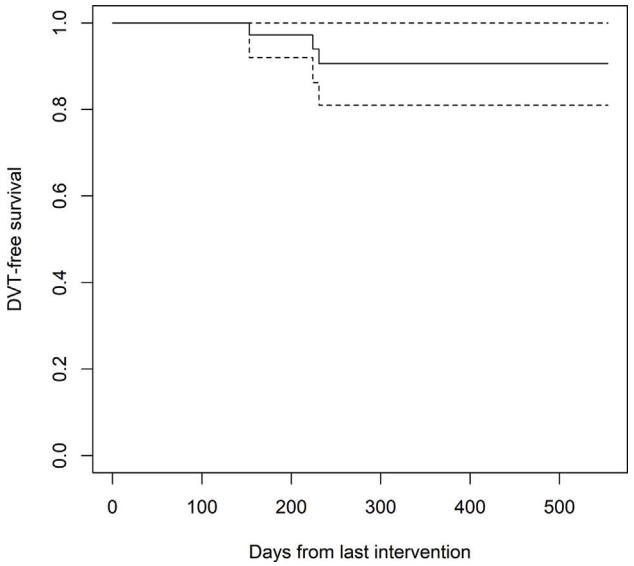

Figure 1. Life table (Kaplan Meier) of DVT after re-intervention in the same limb. A total of 3 DVT cases over 56 re-interventions occurred within one year after the last intervention in the same limb. DVT-free survival probability was 91%.

DVT was identified. In Figure 1 Kaplan Meier analysis for the absence of DVT after re-intervention is shown. For the patients who underwent more than one intervention in the same limb, the probability of developing DVT within one year of the last intervention was 9%.

Patient satisfaction

The post-intervention questionnaire was completed by 113 (33.8%) patients, of which 6 were in the DVT group (see Table III). Patients with DVT were not significantly less satisfied with the treatment compared to patients without DVT, 8.0 (2.4) vs. 8.8 (1.8), p = 0.313. Patients with DVT were not less satisfied with venous problems or with cosmetic results. Procedures were recommended with a lower scale by DVT patients compared to the others, but this was not statistically significant, 6.8 (2.6) vs. 8.5 (2.4), p = 0.097. There was no significant difference in pain between the groups although DVT patients took pain medications for longer than the others, 4.7 (5.5) days vs. 1.1 (1.9) days, p<0.001.

Discussion

The main findings of this single-centre study were: i) DVT after UGFS alone or combined with EVLA occurred in 7.2% of patients, 5.0% of all procedures, mainly in the two posterior tibial veins, especially in those undergoing UGFS and EVLA, and of these, those who had both the GSV and the SSV treated in the same session; ii) most patients, 93%, received post-interventional antithrombotic prophylaxis, mainly with LMWH and for an average of about 2 weeks; iii) no factor associated with the development of DVT was identified in multivariable analysis; iv) for the patients who underwent more than one intervention in the same limb, the probability of developing DVT within one year of the last intervention was 9%; v) post-interventional pain did not differ between the DVT and no-DVT groups.

Patient characteristics

In this study, 70% of the patients were women. This is consistent with the fact that varicose veins affect more women than men [11, 12]. The mean age of the patients was 49.1 (15.3) years, also in line with other studies [13]. The mean BMI was 25.0 (SD 4.4), also in agreement with other publications [14, 15, 16]. CEAP C2 class was found in 57.8% of patients, in agreement with other studies [13]. The majority of patients in our study had a family history of venous insufficiency or thrombophilia, which is consistent with a recent study [12].

Development and location of DVT

We found that DVT after UGFS alone or combined with EVLA occurred in 7.2% of patients, or 5.0% of all procedures, the latter allows comparison with the literature where results are often reported in terms of limbs treated or procedures rather than patients. This proportion is within the published range of the risk of developing DVT after endovenous ablation, the highest being 7.7% [2, 17, 18, 19].

The variability in the rates reported in the literature might be due to the fact that the complete compression ultrasound of the calf veins is neither consistent nor standardised in follow-up reports. In addition, the rates depend on the use of thromboprophylaxis, the type of endovenous ablation and the combination of treatment methods used [20, 21].

We found no cases of endothermal heat-induced thrombosis (EHIT). This might be due to our EVLA technique, which is described in the Methods section. This is lower than the previously reported risk of EHIT after EVLA (5.3%–6.4%) [22, 23].

The predominant site of DVT was the posterior tibial veins. This might be because these veins are often connected to the posterior accessory saphenous vein by perforator veins, allowing the sclerosant to enter the deep venous system. In addition, the posterior tibial veins may have less drainage, resulting in prolonged contact with the sclerosant compared to other deep calf veins [24].

Thromboprophylaxis

With regard to prophylaxis, 92.5% had no previous antithrombotic treatment and 92.7% received post-interventional antithrombotic prophylaxis, mainly with LMWH, for an average of approximately 2 weeks. These figures appear to be in line with the literature, although there is variation in clinical practice and a lack of prescriptive

Table III. Patient survey data on reported pain and satisfaction

Variable	Description	Number of patients	DVT		p-value
			No	Yes	
		334	310 (92.8)	24 (7.2)	
Survey and patient satisfaction					
Survey participant n (%)	yes	113 (33.8)	107 (34.5)	6 (25.0)	0.468
Pain 48 hours after the procedure (scale 0-10)		N = 88	N = 82	N = 6	0.116
	mean (SD)	2.3 (1.9)	2.2 (1.9)	3.5 (1.5)	
Pain 1 week after the procedure (scale 0-10)		N = 83	N = 77	N = 6	0.224
	mean (SD)	1.7 (1.6)	1.7 (1.7)	2.5 (1.4)	
Pain medication use n (%)		N = 89	N = 83	N = 6	0.183
	yes	32 (36.0)	28 (33.7)	4 (66.7)	
Type of pain medication n (%)	Paracetamol	12 (13.5)	12 (14.5)	0 (0.0)	0.702
	NSAID	6 (6.7)	5 (6.0)	1 (16.7)	0.872
	cold spray	2 (2.2)	2 (2.4)	0 (0.0)	1.000
	Ibuprofen	6 (6.7)	5 (6.0)	1 (16.7)	0.872
	other	6 (6.7)	4 (4.8)	2 (33.3)	0.065
Duration of pain medication (days)		N = 87	N = 81	N = 6	<0.001
	mean (SD)	1.3 (2.5)	1.1 (1.9)	4.7 (5.5)	
Unable to work after the procedure n (%)		N = 113	N = 107	N = 6	1.000
	yes	17 (15.0)	16 (15.0)	1 (16.7)	
Satisfaction with the procedure (scale 0–10)		N = 105	N = 99	N = 6	0.313
	mean (SD)	8.7 (1.9)	8.8 (1.8)	8.0 (2.4)	
Satisfaction with the relief of venous problems (scale 0–10)		N = 102	N = 96	N = 6	0.845
	mean (SD)	8.7 (2.1)	8.7 (2.1)	8.5 (2.8)	
Satisfaction with the cosmetic results (scale 0–10)		N = 100	N = 94	N = 6	0.145
	mean (SD)	7.7 (2.6)	7.8 (2.6)	6.2 (2.7)	
Procedure recommendation (scale 0–10)		N = 76	N = 70	N = 6	0.097
	mean (SD)	8.4 (2.4)	8.5 (2.4)	6.8 (2.6)	

Notes. Data are evaluated at patient level and results stratified by diagnosis of deep vein thrombosis (DVT) after endovenous intervention. Percentages are calculated by column. Comparisons of each outcome within DVT (yes/no) groups were performed using chi-square test or t-test as appropriate.

guidelines for thromboprophylaxis in endovenous varicose vein interventions [20]. It should also be noticed that 13% of DVT patients used aspirin before the intervention, compared with 8% in no-DVT patients. This result, although not statistically significant, suggests the higher presence in DVT group of patients that were already at higher risk before the treatment, as aspirin use is associated with cardiovascular diseases or chronic comorbidities like diabetes.

Factors associated with DVT

Our results suggest a higher risk of developing DVT in patients who underwent the combined procedure UGFS and EVLA compared to those who underwent UGFS alone, although this finding was not statistically significant. Other studies [21, 25] found a trend toward increased venous thromboembolic events in patients undergoing EVLA. There are two possible clinical explanations for this. The first is that the tumescent anesthesia reduces the diameter of the epifascial accessory veins and the foam may spread through perforating veins in the deep venous system of the calf. This occurs in the first few seconds after the injection, as polidocanol is bound to the endothelial cells, blood cells and plasma components within few seconds [26, 27]. The second reason is that the extend of varicose veins in patients with EVLA was greater than in patients treated with UGFS alone.

In line with other studies [23, 28, 29] we did not identify age or the laterality of the affected limbs as factors associated with DVT. On the other hand, DVT after endovenous treatment of varicose veins was less common in women than in men in our study (5.2% vs. 11.9%) and the risk of developing DVT was more than twice as high in men than women in regression analysis. However, gender was not identified as a factor associated with DVT in multivariable analysis. This is consistent with another study [30]. Nevertheless, in other studies male sex was associated with a significantly increased risk of DVT after thermal ablation [31, 32], and in another study [23] female sex was associated with an increase in EHIT. Aurshina et al. [28] showed that vein type was an independent statistically significant predictor of thrombotic complications when nested for within-person correlation.

We reported some differences between the DVT and no-DVT groups in prophylaxis before or immediately after the procedure. However, prophylaxis was not associated with a lower risk of DVT. This is not consistent with the literature, where anticoagulant prophylaxis was associated with a significantly lower risk of asymptomatic DVT compared with placebo [6]. However, the therapeutic benefits

of anticoagulant prophylaxis appear to outweigh the risks of bleeding, but prescribing of thromboprophylaxis is still inadequate and further research and interventions are needed to raise awareness of venous thromboembolism among healthcare professionals [33].

Life table analysis of DVT after re-intervention

We found that the probability of DVT within one year after the last intervention in the same limb was 9%. To our knowledge, there are no data in the literature to compare this with. This could be related to the failure rate of EVLA within 24 months which was found to be 10% [16] but further research is needed.

Pain scores and patient satisfaction

Overall, self-assessed pain scores at 48 hours and one week after the procedure were 2.3 (1.9) and 1.7 (1.6) respectively. This was below the levels seen in some studies [14, 34, 35] but above the levels seen in another study [9]. Patient satisfaction with the treatment was high with an average score of 8.7 (1.9) which is in line with other studies [36, 37, 38]. In this study, patients with and without DVT were similarly satisfied with the relief of venous problems and with the cosmetic results. These results may support the clinical impression of many angiologists that patients are satisfied with the outcome of intervention in terms of improvement of venous problems, regardless of the occurrence of post-interventional DVT. More research is needed on patients' post-interventional thoughts and satisfaction.

Limitations

A strength of this study is the sample size of 334 patients with a total of 561 procedures, which is large compared to other studies [13]. In addition, we examined not only clinical data and patient characteristics, but also patient satisfaction and a self-reported pain score. Furthermore, all procedures were performed by the same specialist, which differs from many other studies where the procedure was performed by several clinicians.

Nevertheless, this study has several limitations. First, the design of the study did not allow causality to be investigated, but only the association with DVT. Second, as the majority of the patients had a family history of venous insufficiency or thrombophilia, our results may not be free from selection bias and therefore should be interpreted with caution. In addition, we were not able to analyse the history of venous insufficiency and thrombophilia separately, and we did not have information on comorbidities such as cardiovascular diseases, which are associated with chronic venous insufficiency [11], or on patients' occupational history and activity, which are important diagnostic tools that could help with preventive measures [39]. Third, the number of missing observations could limit the validity of our findings. Fourth, data on some patients' history of thromboembolic disease or other factors associated with thrombosis, e.g. hyper-coagulable risk factor, were missing. Finally, we did not use validated quality of life scores or standardised scores such as the venous clinical severity score (VCSS) as patient outcomes. Instead, we used self-reported pain and satisfaction, in line with another study [9]. In addition, data on reported hyperpigmentation after UGFS and the effect of the use of anticoagulant would have been interesting to evaluate, as further research is needed [40].

Conclusions

Although this study could not identify factors associated with DVT after UGFS alone or combined with EVLA of varicose veins, it contributes to the evaluation of the risk of post-interventional DVT. Our results suggest that the type of thromboprophylaxis used in our patients might be insufficient or inadequate. Further studies are needed to assess the effect of thromboprophylaxis in preventing DVT. Furthermore, although this study did not use standardised tools to assess patients' post-interventional outcomes, and even with a low response rate, its results are still interesting to provide insights into patients' post-interventional thoughts and satisfaction, as there is limited research on this topic that needs further investigation.

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Publication ethics
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Authorship
All authors contributed to the conception and design of the study. Material preparation was performed by Stefan Zechmann, Thomas Meier and Carole Guillet, statistical analysis by Stefania Di Gangi. Data collection was performed by Florian Anzengruber and Thomas O. Meier. Supervision was provided by Thomas O. Meier and Stefan Zechmann. The first draft of the manuscript was written by Stefania Di Gangi and all authors commented on earlier versions of the manuscript. All authors read and approved the final version of the manuscript.

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ORCID
Stefania Di Gangi
https://orcid.org/0000-0002-2847-6399
Carole Guillet
https://orcid.org/0000-0003-3809-0526
Stefan Zechmann
https://orcid.org/0000-0001-5012-0068

Correspondence address
Stefania Di Gangi, Pd.D.
Institute for Primary Care
University Hospital Zurich
Pestalozzistrasse 24
8091 Zurich
Switzerland

stefania.digangi@usz.ch