

# Heparin prophylaxis in major sclerotherapy (the Prosclep study)

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## Abstract

### Objective

To study the incidence and the possibility of preventing thrombotic complications during major sclerotherapy for venous insufficiency of lower limbs.

### Methods

A total of 2489 sclerotherapy sessions were performed on 2010 patients. 1087 sessions (43.7%) were carried out without heparin prophylaxis while in 1402 sessions (56.3%) a prophylaxis with low molecular weight (LMWH) was used. Thrombotic complications were divided into a) post sclerotherapy transient extension (**POSTE**) if they consisted of a simple extension of sclerotherapy, and b) deep venous thrombosis (**DVT**) when the complication occurred in a location separate from that of sclerosis.

### Results

## Introduction

The role of sclerotherapy in the treatment of venous insufficiency of the lower limbs has been revolutionized by the introduction of sclerosing foam<sup>1</sup>. Since then the practice of saphenous sclerotherapy has greatly increased and in some guidelines it is now considered more appropriate than surgical treatment by stripping<sup>2</sup>.

One of the main objections to foam sclerosis is that there is the risk of thrombotic involvement of the deep circulation after sclerotherapy, especially when sclerosis is carried out in the proximity to the sapheno-femoral junction or sapheno-popliteal junction. Nevertheless, the largest study available on this topic has proved that sclerotherapy is associated with the lowest risk of deep vein thrombosis (DVT) or pulmonary embolism (PE)<sup>3</sup>.

Many reviews, however, do not show any difference in the incidence of post-treatment complications among the various techniques (surgery, radiofrequency, laser and

The overall incidence of a thrombotic complication was 0.52%. Out of 2489 sessions, 8 cases of POSTE (0.32%) and 5 thromboses of a gastrocnemius vein (0.2%) were diagnosed

The most significant figures were reached in the great saphenous vein (GSV) subgroup, where the incidence of complications was 1.91% without prophylaxis and 0.31% ( $p = 0.009$ ) with prophylactic heparin.

### Conclusions

In this study prophylaxis with LMWH significantly reduced the incidence of thrombotic complications when sclerotherapy of the great saphenous vein was performed.

**Keywords** Ultrasound guided foam sclerotherapy, heparin, thrombosis, varicose veins, sclerotherapy complications

sclerotherapy). It should be emphasized that in the various studies examined complications were evaluated in a very different way, thus making the comparison between the various studies difficult<sup>4</sup>. The guidelines of the European Society of vascular surgery calculate a risk of DVT between 0.3% and 7.8% considering that such risk does not increase after intravenous procedures<sup>5-6</sup>.

The purpose of this study named PROSCLEP (PROphylaxis in SCLerotherapy with hEParin) was to verify the incidence and characteristics of thrombotic complications during major sclerotherapy in the treatment of superficial venous insufficiency of the lower limbs and the possible prophylactic role of heparin.

The study involved 16 Italian phlebology centers with experience in sclerotherapy. In some centers antithrombotic prophylaxis was not carried out, while in others heparin prophylaxis was performed routinely.

tributaries (the latter only if the diameter was greater than 10 mm) were included in the study. Written informed consent was obtained for treatment for every patient. As this is a retrospective analysis of a database ethical committee approbation is not applicable.

Each center performed sclerosing treatment in their usual manner without any indication of technique, but only including in this report injections of polidocanol (POL) or tetradecyl sodium sulfate (STS) in concentrations greater than or equal to 1% in order to exclude minor sclerotherapy. For the production of the foam, all the centers used the Tessari method<sup>7</sup>. In addition, each AFI center followed the same protocol when performing duplex study of patients before and after treatment in order to make the evaluation

## Material and methods

Members of AFI (Associazione Flebologica Italiana, Italian Phlebological Association) use the same Excel file to collect data in patients submitted to sclerotherapy.

Sixteen AFI centers with experience in sclerotherapy for superficial venous insufficiency of the lower limbs were included in this study. A total of 2489 sessions out of 2010 patients ranging from CEAP class from C2 to C6 were performed over a period from December 2017 to June 2019 and the relevant data were stored in a common Excel file shared by all centers. As the data were originally collected for clinical use and not for a prospective study, we found incomplete informations on C class, age and gender.

Treatments for insufficiency of the great saphenous vein, small saphenous vein, perforators, cavernomas.

of results uniform<sup>8</sup>. Specifically, the echocolordoppler examination was done with the patient in standing position; the compression ultrasound (CUS) was performed on deep and superficial veins according to the known modalities<sup>8</sup>.

All patients with major contraindications to sclerotherapy with POL or STS (allergy, concomitant treatment with disulfiram, uncontrolled systemic disease or severe infection, pregnancy, breast feeding, recent surgical intervention and evolutive malignancy) and those who underwent sclerotherapy in association with thermal ablation, glue closure or saphenous surgery, were excluded from this study.

Antithrombotic prophylaxis was performed with nadroparin 3800 UI or enoxaparin 4000 UI started before treatment and continued for a period ranging from 3 to 6 days.

Some of the centers performed a thrombosis prophylaxis, while others did not, according to their own protocol. Thus the study was not randomized, as it generally occurs in a retrospective analysis. All patients underwent post-sclerosis compression with Class 1 or Class 2 stockings and were asked to walk at least one hour a day during the period following the sclerosis.

Out of a total of 2489 sessions, 1087 (43.7%) were performed without prophylactic heparin while in 1402 (56.3%) prophylaxis was carried out at the doses described above.

A sclerosing foam was used in 99% of cases and the average volume per session was 4.9 ml. POL was used in 88.3% of treatments and only in 11.6% sclerotherapy was done with STS.

As regards the treated veins, refer to Table I.

In the ultrasound evaluation of the results, which was aimed at identifying possible thromboses of the deep venous circulation, we considered two different entities: 1) direct progression of the effect of sclerotherapy in the deep venous circulation, which we called POSTE (post sclerotherapy transient extension); and 2) deep vein thrombosis not in direct continuity with the area subjected to sclerotherapy.

Thrombotic complications of the superficial venous circulation were not included in the study as they were not easily differentiated from the normal reaction to sclerotherapy nor were they the object of interest in this study.

**Statistical analysis**

Age quantitative data were presented. The qualitative data were displayed through contingency tables. Fisher's exact test was used to measure the statistical independence of quantitative variables.

A P value of <0.05 was considered as statistically significant.

All statistical analyses were performed using the SAS System for Windows (release 9.4; SAS Institute Inc., Cary, North Carolina, USA).

**Table I**  
Description of treated veins

Treated Vein	With prophylaxis (%)	Without prophylaxis (%)
GSV	956 (38.4%)	314 (12.6%)
SSV	150 (6%)	106 (4.2%)
PERF	66 (2.6%)	24 (0.9%)
RVV	184 (7.3%)	132 (5.3%)
AASV	103 (4.1%)	54 (2.1%)
Tributary		40 (1.6%)
<b>Total</b>	<b>1459</b>	<b>670</b>

*GSV: Great Saphenous Vein; SSV: Small Saphenous Vein ; PERF:Perforator Vein; RVV: Recurrent Varicose Vein; AASV: Anterior Accessory Saphenous Vein*

*§Please note: 1. the treated veins are less than the sessions, i.e. each vein was treated in several sessions; 2. some patients had more than one vein treated (2010 patients out of 2129 veins and 2489 sessions)*

## Results

Patients were treated with a variable number of sessions: in 1888 cases (75.8%) only one treatment was required, two sessions were needed in 551 (22.1%) and three sessions in 45 (1.8%). Only in 5 cases (0.2%) were 4 or more sessions necessary.

Out of 2489 sessions, 13 thrombotic complications occurred (0.52%), among which 8 (0.32%) were identified as POSTE and 5 (0.20%) as thrombosis of a gastrocnemius vein.

Neither total thrombosis of the common or popliteal femoral veins nor pulmonary embolism (PE) was observed.

## Discussion

Some studies on patients undergoing varicose surgery have concluded that DVT prophylaxis is not required in these cases<sup>9-10</sup>.

The SIGN guidelines state that pharmacological prophylaxis is not required in non-surgical treatments of venous insufficiency except in cases where associated risk factors are present<sup>11</sup>.

Conversely, some surveys have shown a lack of consensus on the need to perform antithrombotic prophylaxis in the case of venous ablation<sup>12</sup>.

In a cohort of patients with post thrombotic syndrome (PTS), Reich-Schupke found no DVT after sclerotherapy performed with heparin prophylaxis<sup>13</sup>.

Despite these data, several observations referable to thrombotic progression at the level of the saphenous femoral junction after thermal ablation have been recorded since the introduction of new forms of saphenous ablation<sup>14-17</sup>.

Additionally, in a very large number of procedures O'Donnell's study showed that the incidence of thrombotic complications of the deep venous system ranges from 4.4% in RFA (radiofrequency ablation) to 3.1% in laser ablation, to 2.4% after surgery for varicose veins and finally only 0.8% after sclerotherapy. Considering pulmonary embolism (PE), all procedures carried a risk of 0.3% excepting sclerotherapy with a risk of 0.2%<sup>3</sup>.

Therefore, recent literature shows that the thrombotic risk after major sclerotherapy is extremely low, with lower complication rates than by the other methods for the treatment of venous insufficiency.

Analyzing the various subgroups, it was shown that for the treatment of the greater saphenous vein the risk of thrombotic complications was 0.31% using prophylaxis, while the same risk rose to 1.91% without prophylaxis. This difference is statistically significant ( $p = 0.009$ ).

In the other veins where a smaller number of cases was treated the difference was not significant (SSV 2% without prophylaxis / 1.88% with prophylaxis - perforators 0% without prophylaxis / 1.5% with prophylaxis).

No thrombotic complications were observed for treatment of AASV, recurrences and large-caliber tributaries.

Despite this, the enormous spread of sclerotherapy with sclerosing foam poses the problem of whether DVT prevention through heparin prophylaxis is indicated.

Several clinical conditions have been proposed in order to identify thrombotic complications after saphenous ablation (EFIT, EHIT, PASTE, X-PASTE)<sup>18-21</sup>.

This study analyzes the possibility of preventing post-sclerotherapy thrombotic complications in a large number of treatments.

Two different clinical entities have been identified in this study: post-sclerotherapy transient extension (**POSTE**) when the sclerotherapy process directly progresses in the deep system provoking a partial occlusion of the deep system itself, and deep venous thrombosis (**DVT**) not in continuity with the area where sclerotherapy has been performed. These complications must be kept separate because in our study the clinical behavior was very different.

Indeed, POSTE could represent a simple progression of sclerotherapy in the deep circulation through an open junction or a perforator and in our series this complication was always partially occluding, asymptomatic and resolved spontaneously or after a short treatment with low molecular weight heparin (LMWH) similar to what happens in EHIT (Endovenous Heat Induced Thrombosis) described for thermo-ablative endovascular techniques.

On the other hand, isolated deep venous thrombosis was always localized in a gastrocnemius vein in our patients and could perhaps be explained by the stagnation of some quantity of sclerosing agent in these deep veins with low flow for a certain period of time resulting in important endothelial damage or independent thrombosis. In these cases, thrombosis was generally painful and complete recanalization of the vessel could not be achieved.

Clearly, more studies are necessary to understand such complications.

The study demonstrates that the incidence of thrombotic complications after major sclerotherapy is 0.52%. Of these, 0.32% are referable to POSTE and only 0.20% are represented by gastrocnemius thrombosis.

## Conclusions

In our opinion two different entities could be regarded as post-sclerotherapy thrombotic complications: POSTE and isolated deep vein thrombosis. These clinical conditions should be distinguished since in our patients they were different from a clinical and a prognostic point of view. More investigation on this topic is needed, possibly a histologic study, in order to prove a different composition of the thrombus from the thrombotic reaction to sclerotherapy.

Major sclerotherapy with foam results in a very low risk of thrombotic complications and prophylaxis with

In this series we have shown that prophylaxis with LMWH for 3-6 days after GSV sclerotherapy succeeds in significantly reducing the risk of thrombotic complications (0.31% vs 1.91% -  $p = 0.009$ ).

Due to study limitations this protective effect could not be demonstrated for SSV and perforators. There were no thrombotic complications in the other veins.

LMWH for 3-6 days has significantly reduced this risk in the treatment of GSV in our patients. Due to the limited number of cases, it was not possible to demonstrate this effect in the treatment of SSV and perforators while there were no thrombotic complications in the treatment of recurrences, the AASV and larger tributaries.

This study confirms that thrombotic complications after major sclerotherapy are a rare and minor event.

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