Superficial thrombophlebitis: epidemiology, physiopathology, diagnosis and treatment

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ABSTRACT
Superficial thrombophlebitis of the lower limbs is a commonly occurring disease, and it is associated with various clinical and surgical conditions. Historically considered to be a benign disease due to its superficial location and easy diagnosis, its treatment was, for a long time, conservative in most cases. Nevertheless, recent reports of high frequency and associated thromboembolic complications, which vary from 22 to 37% for deep venous thrombosis and up to 33% for pulmonary embolism, have indicated the need for broader diagnostic and therapeutic approaches in order to diagnose and treat such possible complications. The possibility of coexistence of these and other systemic disorders (collagenosis, neoplasia, thrombophilia) interferes with evaluation and influences therapeutic conduct, which may be clinical, surgical or combined. However, due to a lack of controlled clinical assays as well as to a series of uncertainties regarding its natural history, the diagnosis and treatment of superficial thrombophlebitis remain undefined. A literature review was performed analyzing the epidemiology, physiopathology and current status of the diagnosis and treatment of superficial thrombophlebitis.

Keywords: Pulmonary embolism, prevention and control, thrombophlebitis, superficial thrombophlebitis, deep venous thrombosis.

RESUMO
A tromboflebite superficial de membros inferiores é doença de ocorrência comum, estando associada a diversas condições clínicas e cirúrgicas. Historicamente considerada doença benigna, devido à sua localização superficial e ao fácil diagnóstico, o tratamento foi conservador durante muito tempo, na maioria dos casos. Entretanto, relatos recentes de freqüências altas de complicações tromboembólicas associadas – 22 a 37% para trombose venosa profunda e até 33% para embolia pulmonar – alertaram para a necessidade de abordagens diagnósticas e terapêuticas mais amplas, visando diagnosticar e tratar essas possíveis complicações. A possibilidade da coexistência dessas e
de outras desordens sistêmicas (colagenoses, neoplasias, trombofilias) interfere na avaliação e influencia a conduta terapêutica, que pode ser clínica, cirúrgica ou combinada. No entanto, devido à falta de ensaios clínicos controlados e às incertezas quanto a sua história natural, o diagnóstico e o tratamento da tromboflebite superficial continuam indefinidos. Neste trabalho, foi feita uma revisão da literatura analisando-se a epidemiologia, fisiopatologia e estado atual do diagnóstico e tratamento da tromboflebite superficial.

Palavras-chave: Embolia pulmonar, profilaxia, tromboflebite, tromboflebite superficial, trombose venosa profunda.

Introduction

Superficial thrombophlebitis (ST), also called superficial venous thrombosis, is a pathological condition characterized by presence of a thrombus in the lumen of a superficial vein, followed by inflammatory reaction of its wall and adjacent tissues. It presents with a palpable, hot, painful and hyperemic cord through a superficial vein. This thrombosis has variable amplitude, reaching from small tributaries until large extension of saphenous trunks in the lower limbs. In more severe cases, it can be extended to the deep venous system (DVS); it can also cause pulmonary embolism, and there are indications of an association with recurrent episodes of venous thromboembolism. The incidence of ST ranges between 125,000 cases/year (USA) and 253,000 cases/year (France), and is more frequent when more accurate diagnostic methods are used, such as duplex scan (DS). In our country, Von Ristow et al., in a retrospective survey of patients submitted to varicose vein surgery, found signs of previous thrombophlebitis in 16% of cases.

Physiopathology

ST physiopathology, similarly to deep venous thrombosis (DVT), is also related to Virchow's triad (1856). ST more frequently occurs in varicose veins, since they can have morphological changes in their wall that predispose to stasis, and consequently to the development of the thrombotic process. A large number of ST cases is secondary to chemical intimal lesion, by injections of infusions of different solutions, with diagnostic or therapeutic purposes, and/or mechanical lesions, such as, for example, venous catheterization. ST can be prodromic of several known systemic diseases, such as neoplasms, arteriopathies and collagenosis, in addition to following a series of other disease and syndromes:

-Trousseau's syndrome: characterized by episodes of recurrent superficial migratory thrombophlebitis with impairment of veins, both in the upper and lower limbs, associated with mucin-producing adenocarcinomas of the gastrointestinal tract (stomach, pancreas and colon), lung, breast, ovary, and prostate.

-Mondor's disease: thrombophlebitis of rare occurrence, more frequent in the female population and affecting the veins of the anterolateral thoracic wall. Most of the times, its etiology is unknown. In some cases, it is associated with local trauma, use of oral contraceptives, protein C deficiency, and presence of anticardiolipin antibodies. Farrow et al. observed an association with breast neoplasms.
- **Lemierre's syndrome**: described for the first time in 1936, it is characterized by septic thrombophlebitis of the internal jugular vein concomitant to oropharynx infection, and may progress with metastases, especially for the pulmonary territory, but also liver and spleen. Other causes related to its occurrence are central venous catheterization and infection of other cervical sites.\(^{17,18}\) The most prevalent etiologic agent is the gram-negative anaerobic germ *Fusobacterium necrophorum*\(^ {19}\).

- **Buerger's disease (Thromboangiitis obliterans)**: in this case, ST has a migratory character and may precede or be concomitant with arterial impairment.\(^ {20}\) Its presence reinforces diagnostic of Buerger's disease.

### Pathology

From the histopathological perspective, vein and thrombus in ST, in its initial stage, have predominance of leukocyte infiltrate (flogistic) (Figure 1 – HP blade), and this inflammatory process is extended to neighboring tissues, especially skin and subcutaneous cell tissue, thus explaining characterization of its clinical status, as well as less friability and more thrombus consistency.\(^ {21}\)

![Figure 1 - Histological section of thrombosed vein after chemical induction of superficial thrombophlebitis (there is accumulation of leucocytes)](image)

### Topographic aspects

In general, the left lower limb (LLL) seems to be more affected than the right lower limb (RLL). Upper limb veins are also often affected, as a complication of venous catheterization, and are found in up to 51.5% of cases in a survey conducted in our institution\(^ {22}\); the cephalic and basilic veins are the most frequently affected.\(^ {23}\)

In a retrospective survey, performed by Lutter et al., of 1,143 confirmatory DS for ST, 56% occurred in the LLL, whereas 51% in the RLL. However, such difference was not significant.\(^ {24}\) Gillet et al., in a prospective study of 100 patients, observed that the LLL was affected in 50% of cases, while the RLL was affected in 49%; in 1% there was bilateral impairment. In the same study, the great saphenous vein (GSV) territory was more affected (75% of cases) than the small saphenous
vein territory (24.3%), and in 0.7% (two cases) both territories were involved.\textsuperscript{25}

**Thromboembolic complications**

*Deep venous thrombosis*

Since 1964 reports have been published on this complication in patients with ST\textsuperscript{10,26-28}. It is estimated that the occurrence of a spontaneous episode of ST increases in about 10 times (odds ratio = 10.3; 95%CI: 2.0-51.6) the risk of developing DVT over the 6 subsequent months and absolute risk of 2.7% when compared with a population that never had a previous episode of ST.\textsuperscript{29} Simultaneous impairment of DVS usually occurs due to thrombus extension through the perforating veins or aortic arch, but it is possible that there is a given anatomical connection (associated DVT), strengthening the possible condition of hypercoagulability following ST. However, extension of the thrombus into the superficial venous system and/or its proximity to the DVS had no significant correlation with DVT occurrence according to some authors.\textsuperscript{30,31} In many series, the frequency of association between ST and DVT ranged between 22.7 and 36%.\textsuperscript{3,10,24,32} This association also seems to be more frequent in patients with varicose veins, probably due to the morphological changes that are characteristic of this disease, which favor both stasis and bidirectional blood flow in perforating veins and arches.\textsuperscript{33} However, in a study conducted in our service,\textsuperscript{34} the absence of varicose veins increased more than nine-fold the chances of an individual having DVT (odds ratio = 9.09; 95%CI: 1.75-50.0), a fact that was seen by other authors, who showed that presence of varicose veins was related to a more benign evolution of venous thromboembolic disease.\textsuperscript{30} In the study by Gillet et al., DVT was diagnosed in 36.4% of cases when the affected vein was a varicose vein, and in 8.3% when the affected vein was not a varicose vein. However, although the absolute difference in frequencies was relevant, it was not significant (p = 0.097), which may be explained, according to the authors, by the extension mechanism of ST into the DVS through the perforating veins, which are more developed and more frequently insufficient in patients with varicose veins. Presence of thrombophilia changes occurred in 14.9% of patients in the group with varicose veins, and in 50% in the group without varicose veins.\textsuperscript{25} On the other hand, Bounamaux et al., in a retrospective survey (6-year period), in which plethysmography associated with continuous-wave Doppler ultrasound and DS were used as diagnostic methods for DVT, accounted for 551 confirmed cases of ST, and 31 of them (5.6%) had simultaneous DVT when ST was diagnosed, and in 26 of these DVT was proximal (4.7%). In this sample, the only variable that had statistical relevance (p < 0.02) for simultaneous occurrence of DVT and ST was previous immobilization.\textsuperscript{35} In an original study, out of 60 patients with ST, 13 (21.7%) had associated DVT.\textsuperscript{34}

**Pulmonary embolism**

The association between ST and episodes of pulmonary embolism (PE), whether or not symptomatic, has also been reported by many authors, and its frequency ranged from 3 to 33%.\textsuperscript{4,5,13,25} On the other hand, Weert et al., in a retrospective cohort study, showed that, over a 6-month period, occurrence of ST was not a predictive factor for PE occurrence (odds ratio = 1.0; 95%CI: 0.07-15.0).\textsuperscript{29} However, in a retrospective series, Blumemberg et al. demonstrated that thrombosis diagnosed by DS progressed to the DVS in 8.6% of cases, and in 10% of these there was PE, investigated using scintigraphy.\textsuperscript{4} Verlato et al., in a prospective study, found high frequency of PE using scintigraphy (33.3%) in patients who had ST as the only embolicigen source.\textsuperscript{5} Thrombus proximity with the DVS (especially represented by arches) and the concomitant impairment of these junctions (saphenofemoral and/or saphenopopliteal) did not show significant correlation with occurrence of PE in other series.\textsuperscript{1,3,5} In a retrospective survey, Lutter et al. observed indications
that being older than 60 years of age, history of DVT, prolonged rest, bilateral ST, male gender, and presence of infections were more frequently associated with DVT or PE. In the original study we performed, there was a 28.3% frequency of PE associated with ST, and the simultaneous presence of DVT was not a determinant for its occurrence (p = 0.36).

Diagnosis

Until the late 1980's, ST was considered as a benign disease, self-limited, with low morbidity and low potential for complications, and its treatment was symptomatic. However, more recent publications showing high frequencies of PTE associated with ST have changed that focus, with subsequent changes in diagnostic and therapeutic approaches.

Diagnosis should be performed carefully, with detailed clinical history, paying special attention to possible risk factors and occurrence of previous thromboembolic events: history of weight loss (neoplasms), smoking, infection (Lemierre's syndrome), among others.

Risk factors are the same for DVT, i.e., clinical or surgical conditions related to Virchow's triad, which may occur alone or combined, enhancing the potential, facilitating and/or triggering development of ST. The following are some examples:

- Endothelium lesion: intravenous injections, venous catheterization, trauma, infections;
- Flow changes: varicose veins, immobilization.
- Coagulation changes: neoplasms, pregnancy, thrombophilia, infection.

Physical examination should explore topographic diagnosis accurately (Figure 2), determining the affected venous trunk and its extension/concomitance for the DVS, which can determine change in therapeutic approach. Some authors support the systematic use of DS in patients with lower limb edema, in cases with previous history of ST, since ST has a high predictive value for DVT, especially in the 6 subsequent months after its first episode. Another advantage of DS is the possibility of establishing a differential diagnosis with other pathologies, such as lymphangitis.

DS plays a major role in diagnosing ST, since it provides a direct visualization of the thrombus inside
the superficial venous system and its proximity relationship with the DVS (Figure 3), as well as extension or simultaneous impairment of the DVS.\textsuperscript{40} For these reasons, its routine use is supported by several authors.\textsuperscript{3,24,28,39,40} Patients with clinical and ultrasound diagnosis of ST have an easily visible and non-compressible echogenic thrombus at DS.\textsuperscript{40}

![Figure 3 - Duplex scan of superficial thrombophlebitis, showing image of partial thrombus in the great saphenous vein and in the common femoral vein: A) mode B: hyperechogenic image of thrombus in the great saphenous vein going into the common femoral vein; B) power Doppler image showing partial flow around the thrombus in blue](image)

DS is particularly useful in the differential diagnosis of cellulitis, erythema nodosum, panniculitis and lymphangitis, accurately assessing whether there is DVS impairment and its extension.\textsuperscript{40} In addition, it has the advantage of being an innocuous and noninvasive method, opposed to phlebography, which has complications such as contrast allergy, exposure to radiation and propagation of thrombosis;\textsuperscript{40} no reference was found as to use of phlebography in ST diagnosis.

**Treatment**

Similarly to the diagnostic approach, treatment of ST has not been established due to lack of controlled clinical trials and to a number of uncertainties as to its natural history, which generates a range of therapeutic options. The treatment depends on its etiology, extension, symptom severity, and association with other thromboembolic phenomena, such as DVT and/or PE.\textsuperscript{2-4} The possibility of a coexistence of these and other systemic disorders interferes with the assessment and influences therapeutic conduct, which may be clinical, surgical or combined.

**Clinical treatment**

Similarly to other venous thrombotic diseases, treatment of ST should include measures that reduce
stasis and increase venous flow velocity. Among these measures, walking and rest in the Trendelenburg position are the most common and most widely accepted. During walking, there is activation of calf and plantar pumps, favoring increase in flow velocity and possibly a higher activity of the fibrinolytic system. Rest in the Trendelenburg position also favors venous return due to gravitational drainage, which can increase fibrinolytic activity.

Elastic compression, despite being widespread, is not consensual. Andreozzi et al. support the use of medium to high compression elastic band in the acute stage of the disease, interposing gauze with zinc oxide between the skin and the band, which seems to reduce the flogistic process; elastic stockings represent the form of maintenance treatment. De Palma indicates the use of elastic stockings associated with aspirin in cases of varicose vein with thrombophlebitis, as long as this impairment is away from saphenous trunks, and patients are advised to maintain their daily activities. In a prospective, randomized and controlled study comparing varied treatment forms of ST (elastic stockings, surgery, heparin and oral anticoagulation), elastic stockings were the therapeutic option that had the lowest cost, but it was associated with higher frequency of thrombus extension and higher social cost due to time of work leave and/or inactivity. In addition, compression with elastic stockings in acute ST stage may worsen local pain, and theoretically cause embolization of a more friable thrombus segment from the vein affected by ST.

Existence of flogistic signs and symptoms in ST suggests indication of anti-inflammatory drugs (systemic or topical); however, there is no evidence of their efficacy. Application of wet heat, such as warm compresses and thermal bags, seems to have an anti-inflammatory action and is commonly used. Becherucci et al., in a controlled series of 120 patients with thrombophlebitis associated with drug infusion, compared the efficacy of three different treatments:

- Group 1: diclofenac gel;
- Group 2: oral diclofenac 75 mg twice a day;
- Group 3: placebo.

Symptomatic relief in 48 hours of treatment was better in groups 1 and 2 in relation to placebo. However, in this study, the outcome was relief of symptoms, which is subjective. DS should have been used to assess thrombus extension and other more objective parameters.

In another prospective and randomized series, which included 68 patients with spontaneous ST or related to drug infusion, piroxicam gel was compared to a placebo and there was no significant difference between both groups. This result corroborated an experimental study conducted at our institution, showing no benefits in use of anti-inflammatory ointments or heparinoids in the course of local pathological process, seen at optical microscopy.

According to recommendations of the American College of Chest Physicians (ACCP), patients with ST secondary to drug infusion can benefit from use of diclofenac gel (degree 1B) or oral diclofenac (degree 2B), and there is no mention to spontaneous ST or associated with varicose veins. However, the series used to support this proposal are small and have outcomes based on subjective parameters.

On the other hand, anticoagulants, either in prophylactic or therapeutic doses, are the class of drugs that seem to have the highest number of benefits for the patient, since they act on the core of the disease physiopathology – clot formation and propagation. They can be used as the only therapeutic option or as an adjuvant in surgical treatment. In addition to the obvious thrombotic effect, anticoagulants, especially heparins, have anti-inflammatory activities that enhance the potential of their benefits.
Although some characteristics of the disease behavior, such as its occurrence in a non-varicose venous territory or the thrombus proximity relationship with the DVS, are suggestive of a non-benign course followed by PTE, there is still no evidence of this hypothesis. Ascer et al., in a prospective study, suggested that anticoagulant therapy could prevent recurrence and pulmonary embolism; therefore, it is the ideal treatment for ST, especially when it reached the saphenofemoral junction (SFJ). Most series on anticoagulant treatment of ST with heparin use unfractioned heparin (UFH) or low-molecular-weight heparin (LMWH) as an initial choice of drug for the treatment.

Heparin dose (UFH or LMWH) is also controversial; some series compared different heparin doses between themselves and to others with alternative therapeutic modalities, such as anti-inflammatory drugs. There seems to be a trend of favorable response when higher heparin doses are used (when compared with prophylactic doses). In a multi-center and randomized study, 117 patients were divided into three groups: I) nadroparin calcium – fixed prophylactic dose; II) nadroparin calcium – weight-corrected dose; and III) naproxen (AINH). By the end of 6 days, symptomatic relief was significantly higher in groups I and II than in the group using anti-inflammatory (p < 0.001). There was no difference in efficacy between the two groups using nadroparin. In another series with a similar design, comparing enoxaparin sodium with anti-inflammatory and placebo, there was no significant difference as to DVT incidence between both groups after 12 days of treatment. However, the incidence of symptomatic venous thromboembolism was significantly higher in groups using enoxaparin (p < 0.001), and this protection was maintained until the first 3 months of treatment.

High UFH doses were compared to prophylactic doses in a randomized series of 60 patients diagnosed with GSV proximal ST. There was significant difference in favor of high heparin doses regarding occurrence of symptomatic and asymptomatic thromboembolic events by the end of a 6-month follow-up. In a prospective, double-blind and randomized study, 436 patients with ST were divided into four groups:

- Group 1: enoxaparin 40 mg day + elastic stockings;
- Group 2: enoxaparin 1.5 mg/kg/day + elastic stockings;
- Group 3: oral tenoxicam 20 mg/day + elastic stockings;
- Group 4 (control): only elastic stockings (control).

There was no significant difference between groups (homogeneous sample). The treatment was
prescribed for 10 days and the patients were followed for 3 months (clinical and ultrasound assessment). Over the first 12 days, the patients using enoxaparin (groups 1 and 2) or tenoxicam (group 3) had significant reduction in disease progression (thrombus extension) compared with those who exclusively used elastic stockings, and there was no difference between both enoxaparin groups. When enoxaparin and tenoxicam were compared, there was a favorable trend (nonsignificant) in terms of benefits for the enoxaparin. In terms of thromboembolic events, there was no trend of a favorable result in the three groups that had drug treatment, with no significant difference between them when compared with the control group. By the end of the study period (3 months), that trend disappeared (Table 2), suggesting evidence of a rebound effect or of an unknown trait of ST natural history. It was not possible to reach a conclusion as to the best therapeutic option for this disease in this study.\(^{53}\)

<table>
<thead>
<tr>
<th>Table 2 - Prevalence of thromboembolic events between days 1 and 12 and between days 1 and 97 in a retrospective series (STENOX GROUP, 2003)(^{53})</th>
<th>Enoxaparin 40 mg</th>
<th>Enoxaparin 1.5 mg/kg</th>
<th>Tenoxicam 40 mg</th>
<th>Elastic stockings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VTE (D1-D12)</strong></td>
<td>(n = 112)</td>
<td>(n = 106)</td>
<td>(n = 99)</td>
<td>(n = 112)</td>
</tr>
<tr>
<td>PE</td>
<td>0</td>
<td>0</td>
<td>1 (1.0%)</td>
<td>0</td>
</tr>
<tr>
<td>DVT</td>
<td>1 (0.9%)</td>
<td>1 (0.9%)</td>
<td>1 (1.0%)</td>
<td>4 (3.5%)</td>
</tr>
<tr>
<td>ST (non-episode or thrombus extension)</td>
<td>9 (8.1%)</td>
<td>6 (5.6%)</td>
<td>13 (13.0%)</td>
<td>33 (29.4%)</td>
</tr>
<tr>
<td>p</td>
<td>0.37</td>
<td>0.37</td>
<td>0.69</td>
<td></td>
</tr>
<tr>
<td><strong>VTE (D1-D97)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PE</td>
<td>2 (1.8%)</td>
<td>0</td>
<td>1 (1.0%)</td>
<td>0</td>
</tr>
<tr>
<td>DVT</td>
<td>5 (4.3%)</td>
<td>4 (3.7%)</td>
<td>3 (3.0%)</td>
<td>5 (4.4%)</td>
</tr>
<tr>
<td>ST (non-episode or thrombus extension)</td>
<td>16 (14.5%)</td>
<td>16 (15.0%)</td>
<td>15 (15.0%)</td>
<td>37 (33.0%)</td>
</tr>
<tr>
<td>p</td>
<td>0.76</td>
<td>&gt; 0.99</td>
<td>&gt; 0.99</td>
<td></td>
</tr>
</tbody>
</table>

\(^{D1-D12} = \text{from treatment day 1 to 12; } D1-D-97 = \text{from follow-up day 1 to 97; } DVT = \text{deep venous thrombosis; PE = pulmonary embolism; ST = superficial thrombophlebitis; VTE = venous thromboembolism.}\)

Heparin can also be found in gel for topical use; however, despite supported by some authors,\(^{54-57}\) its safety and efficacy have not been properly confirmed. Görski et al. proposed application of micronized and encapsulated gel heparin – in the form of slow-release spray (Lipohep Forte Spraygel) – for symptomatic relief in ST.\(^{55}\) However, there was no conclusion as to prophylaxis of thromboembolic complications, since this was not the objective of the study.

With regard to the antivitamin K oral anticoagulant, only one prospective and randomized study compared it to other therapeutic modalities (elastic stockings, UFH, LMWH, surgery), and found no significant difference as to complications (thrombus extension, DVT). However, it represented a therapeutic option of high social cost compared with the others as a consequence of work leave.\(^{42}\)

**Surgical treatment**

Surgical treatment is also controversial. The possible advantages of surgery are faster symptomatic relief and shorter hospital stay, which could reduce costs.\(^{58}\) On the other hand, its disadvantage is not preventing thromboembolic complications, since for cases of simple ligation of saphenous trunks, it could not prevent the thrombus passage through the perforating veins, besides not minimizing the hypercoagulability condition that might be present. Surgical treatment options include arch ligation, saphenous vein stripping and removal of thrombosed pathways, and its
indications will depend on thrombus location within the superficial venous system (its proximity relationship with the DVS), existence of favorable technical and clinical condition.

Surgical treatment is more indicated for ST affecting varicose veins. In cases of thrombophilia and neoplasms – and, therefore, with higher thromboemboligenic risk – treatment with anticoagulants is the best alternative.

Surgical treatment basically has three objectives:

- Avoiding thrombosis extension from the superficial to the deep venous system;
- Treating superficial venous insufficiency, likely to be the cause of ST;
- Preventing recurrences.

The surgical techniques that can be used are crossectomy at the SFJ level or saphenopopliteal junction and ligation of perforating veins to avoid thrombus extension for the DVS and removal of segments with thrombus. The main complication of this treatment is postoperative hematoma, more frequent than in elective varicose vein surgery, due to the inflammatory component and to adherence to adjacent tissues.

In some situations, the thrombus can extend proximally beyond the site where it is palpable or visible by inflammatory signs, enhancing the potential risk of thromboembolic complications. For some authors, SFJ involvement is an indication of surgical treatment.

A retrospective series assessed 221 patients, who were divided into four treatment groups:

- Local heat + systemic anti-inflammatory drugs;
- Anticoagulant therapy;
- Surgery + anticoagulation;
- Surgery.

Surgical treatment, (ligation + segment removal), in addition to bringing faster symptomatic relief, definitively treated the disease, since it eliminated the possibility of recurrences and reduced hospital stay and its cost, although such difference was not significant.

However, all cases of PE occurred in group A, whereas DVT was observed only in group D (Table 2).
This series only evaluated cases of ST in patients with varicose veins, which may be a bias, since the intrinsic morphological change in these venous trunks can account for occurrence of ST, differently from what occurs when the disease is present in patients without varicose disease, when a hypercoagulability condition can be the determining factor and is not being treated by surgery.

Many authors consider the SFJ involvement as an absolute indication for surgery.\textsuperscript{58,59,61} In a retrospective series, Lohr et al. assessed 43 cases of ST affecting the SFJ that were treated with saphenous vein stripping or SFJ ligation, and after a 4-month follow-up, there was no progression of the thrombus neither PE. The authors also assessed the costs for each type of therapeutic approach and found that, when the clinical treatment (anticoagulation) was chosen, the cost was US$ 7,967.62. When the surgical treatment was indicated, there was a reduction of nearly 40% (US$ 4,831.11) of the total cost, and the patients submitted to surgery returned faster to their everyday activities.\textsuperscript{58}

Low morbidity rate of the surgical procedure should also be considered. In cases of SFJ ligation, it can be performed under local anesthesia in most patients, reducing hospital stay and cost.\textsuperscript{61}

In a systematic review article on the treatment of supragenicular ST without DVS involvement, Sullivan et al. claimed that surgery (SFJ ligation + removal of phlebitic segments + interruption of perforating veins) produces better results when compared with anticoagulation in terms of thrombus extension, recovery time, bleeding, and symptomatic relief. However, it does not prevent thromboembolic complications and has higher morbidity rates.\textsuperscript{62}

In situations in which ST occurs in varicose veins, the benefits of surgery are clear, since it can repair possible causes, minimizing risk of recurrences. Nevertheless, when it occurs in non-varicose veins, this protective effect may not be present, justifying, to some authors, the option for the clinical treatment or its association with the surgical treatment, both before and after the surgery.\textsuperscript{3,5,27,28,61}

Few studies have prospectively evaluated the therapeutic approach to ST, comparing varied types of treatment. Belcaro et al. assessed 444 cases of ST in varicose veins that were randomized in six treatment groups and followed by a 6-month period\textsuperscript{12} (Table 4).
There was no difference as to DVT incidence between the groups of treatment (p > 0.05), but the incidence of thrombus extension was significantly higher in groups of elastic compression and simple ligation (p < 0.05). The most expensive treatment was that using LMWH, and the cheapest was with elastic compression, although it had the highest social cost (time and cost due to inactivity). On the other hand, it should be considered that, in this study, only patients with varicose veins were assessed. Anticoagulant dose and duration of anticoagulation were not mentioned, and the ultrasound performed during follow-up was not blinded, which is a favorable bias to the group submitted to surgery. In another prospective and consecutive series, whose objective was evaluating safety, efficacy and cost of clinical treatment using LMWH compared with surgery (saphenofemoral disconnection), there were no significant differences between both groups as to complications, ST recurrence and incidence of new episodes of DVT and PE.

**Conclusion**

Based on clinical history data, physical examination and DS, treatment of ST can be clinical, surgical or both. It is necessary to establish whether the episode occurs in varicose veins or in non-varicose veins; whether the event was preceded by a triggering factor; which level the thrombus is located within saphenous trunks; and which its proximity with the DVS is. These two latter are dependent on ultrasound findings.

Literature data suggest that, in case the event occurs in non-varicose veins and with no apparent triggering factor, it is only necessary to search for other changes, such as neoplasms or thrombophilias. It is necessary to maintain the patient anticoagulated for a variable period of time, depending on disease extension. In case the thrombosis is restricted to the superficial venous system, i.e., until its arches, the treatment is maintained for at least 3 months. In case the thrombus invades the lumen of deep veins (diving thrombus), the treatment should be maintained for 6 months. In situations of recurrence and with no involvement of the DVS, anticoagulation should be restarted for a variable period, depending on extension of the process. If there is concomitant DVT, the anticoagulant treatment is imposed, and duration will depend on DVT level and existence of a triggering factor (thrombophilia, neoplasm).

<table>
<thead>
<tr>
<th>Group Description</th>
<th>Sample size</th>
<th>DVT Incidence</th>
<th>Thrombus Extension</th>
<th>Cost of Treatment (US$)</th>
<th>Social Cost (US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I) EC</td>
<td>78</td>
<td>06</td>
<td>32</td>
<td>480</td>
<td>571</td>
</tr>
<tr>
<td>II) EC SFI ligation</td>
<td>78</td>
<td>02</td>
<td>11</td>
<td>1180</td>
<td>221</td>
</tr>
<tr>
<td>III) EC + saphenous vein stripping + ligation of perforating veins + removal of segments</td>
<td>70</td>
<td>02</td>
<td>0</td>
<td>1280</td>
<td>238</td>
</tr>
<tr>
<td>IV) EC + UFH (prophylactic dose)</td>
<td>71</td>
<td>0</td>
<td>4</td>
<td>980</td>
<td>184</td>
</tr>
<tr>
<td>V) EC + LMWH (prophylactic dose)</td>
<td>76</td>
<td>0</td>
<td>4</td>
<td>3720</td>
<td>228</td>
</tr>
<tr>
<td>VI) EC + AVK</td>
<td>71</td>
<td>0</td>
<td>5</td>
<td>660</td>
<td>321</td>
</tr>
</tbody>
</table>

* Lost work days and/or costs due to inactivity.

AVK = antivitamin; DVT = deep venous thrombosis; EC = elastic compression; LMWH = low molecular weight heparin; UFH = unfractioned heparin.
In case the event occurs in varicose veins, diagnostic assessment using DS will be a determinant when choosing the conduct, and the surgery can be performed first, after a brief period of therapeutic anticoagulation, in case there is no concomitant DVT or PE.

In case of segment impairment in isolated and distal leg veins, anticoagulation may not be necessary initially, focusing on local cares and a new assessment 7 days later, or if there is worsening in clinical status. In case there is proximal extension of the thrombus or major symptomatology in the affected limb, UFH or LMWH in therapeutic doses should be used, in addition to local cares. If there is evolution to DVT and/or PE and/or maintenance or worsening of inflammatory symptoms, UFH or LMWH in therapeutic doses should also be used with period reassessments (Figures 4 and 5).

**Figure 4** - Graphic representation of diagnostic approach in cases of superficial thrombophlebitis

**Figure 5** - Graphic representation of therapeutic approach in cases of superficial thrombophlebitis according to type of affected vein
A systematic review on the treatment of lower limb ST concluded that AINH and LMWH seem to be the best therapeutic options, significantly reducing ST extension and recurrence when compared with placebo.\textsuperscript{64} However, further studies are needed to safely establish the best therapeutic scheme.\textsuperscript{64}

The actual benefit of each therapeutic method or their association remains unclear. Future studies on the treatment of ST are needed to establish the best option. Prospective, multi-center and randomized studies using a sample population that is large enough to obtain statistical power should collect data regarding natural history of this disease, such as frequency of complications associated with each therapeutic approach (clinical or surgical), presence of varicose veins, thrombus extension in the superficial venous system, thrombus propagation inside the DVS, frequency of associated concomitant DVT (non-contiguous), frequency of PE, frequency of associated venous insufficiency, recurrence rate, and screening for associated hypercoagulability factors.\textsuperscript{10,42,61-63} Based on the knowledge of these characteristics and on evidence, it will be possible to choose the best treatment option for each patient.

References


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