

# Superficial Vein Thrombosis (SVT): A Therapeutics Review

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## ABSTRACT

The lower limbs are frequently involved sites of the superficial vein system, especially the saphenous veins, concerning varicosities. Lower-limb SVT has the same risk factors as DVT; it can spread into the deep veins and may result in pulmonary embolism. Symptom relief and prevention of venous thromboembolism (VTE) concerning the thrombotic burden are the treatment aims. Surgery, compression hosiery, non-steroidal anti-inflammatory drugs, unfractionated heparin, and low molecular weight heparins were included in randomized clinical trials of less severe forms of lower-limb SVT not involving the saphenofemoral junction (SFJ) with inconclusive results. Fondaparinux 2.5 mg once daily for 6 weeks is more effective than placebo in reducing the risk of the composite of death from any cause and symptomatic VTE (0.9% versus 5.9%) in the largest randomized clinical trial on 3004 patients with lower-limb SVT not involving the SFJ. Another study of Rivaroxaban 10 mg oral was found non-inferior to 2.5 mg subcutaneous fondaparinux once a day for 45 days for treatment of superficial-vein thrombosis.

**Key words:** Fondaparinux, Rivaroxaban, Heparin, Surgery, NSAIDs, Elastic stocking

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## INTRODUCTION

Small thrombus SVT less than 4-5 cm in length has been minor, benign, and self-limiting, requiring only symptom relief, whereas thrombus SVT greater than 4-5 cm in length requires treatment to avoid the extension risk [1]. Patients with the most frequent locations of SVT, i.e., the long and short saphenous veins included in randomized clinical trials, because of the higher risk of extension into the deep vein system through the saphenofemoral junction (SFJ) [2,3]. SVT of a long saphenous vein with the thrombus head within 3 cm of the SFJ is considered to be equivalent to a DVT about its high risk of progression (10-70%) and hence traditionally excluded from interventional studies [4]. The best therapeutic plan to manage SVT within less than 3 cm or to more than 3 cm from the SFJ remains unclear. A CALISTO analysis of Fondaparinux in SVT interpreted that, in 1500 patients, the risk of subsequent DVT or PE was same whether symptomatic extension progressed to less than 3 cm or more than 3 cm from the SFJ 9.3% and 8.9%, respectively, with the same use of medical assets in both groups. Thus, the authors concluded that patients with SVT extension are at significant risk for thrombotic complications [5]. A STEFLUX analysis has concluded that, after LMWH treatment has closed in patients with SVT of near about 5 cm of the lower limbs, the composite of SVT and VTE extension or recurrence was observed with the absence of

varicose veins. Higher risk patients were excluded from the STEFLUX analysis and CALISTO trial, such as cancer, bleeding conditions, thrombus within 3 cm of the SFJ, in the CALISTO trial patients with recent DVT/PE or SVT were excluded. Optimal treatment approaches for these patient populations have yet to be determined [6,7].

Treatment options from includes non-steroidal anti-inflammatory drugs to surgery, vitamin K antagonists, vasotonin, heparan sulfate, oxerutins, sulodexide, and oxyphenbutazone are the oral, enzymes are intravenous, desmin is intramuscular, and anticoagulants such as unfractionated heparin, LMWH, and Fondaparinux are parenteral treatment. For this review, only the roles of surgery, NSAIDs, graduated compression elastic stockings, and anticoagulants will be considered [8].

## Surgery

Surgery helps in inhibiting thrombus progression and thereby reducing the PE incidence and is one option for treatment of isolated SVT of lower-limb. In the case of varicose veins, a local thrombectomy has been proposed, especially when the SVT is very painful, as well as stripping or sclerotherapy, but the optimal timing and benefit of these procedures about SVT onset are unclear [9,10].

Surgical treatment of SVT of the lower limb related randomized controlled trial has concluded that heparin followed by oral anticoagulants is efficient than surgical treatment in preventing PE and DVT in SVT of the great saphenous vein in the thigh. (SFJ ligation alone or with vein stripping with or without perforating vein ligation).

Surgical treatment is associated with 2% risk of PE and extension into the deep venous system in 3.4% of cases. By recent guidelines and data, surgery should not be considered for lower-limb SVT and suggest only medical therapy [11-13].

### Elastic stocking and NSAIDs

NSAIDs with elastic stockings have traditionally and empirically been used for symptomatic management of inflammation of SVT clinical symptoms. The duration of these treatments is variable, usually between 7 days and 14 days, although no data are available on the optimal degree of compression required or the duration of use for elastic stockings [14].

Use of analgesics, thrombus regression improves the quality of life in 80 patients with isolated SVT of the lower-limb of at least 5 cm, no therapeutic benefit of compression stockings (23–32 mmHg at the ankle) for 3 weeks versus no compression on pain resolution, concluded in a randomized controlled trial. Patients received NSAIDs with LMWH allowed in the study. The role of elastic stockings is therefore uncertain, and current guidelines do not mention elastic stockings for lower-limb SVT although they are routinely prescribed, unless contraindicated [12,13-15].

Oral tenoxicam for one to two weeks was found benefits with lower rates in SVT extension and/or recurrence than placebo, and there was no benefits of NSAIDs with reductions in VTE rates concluded in STENOX study. The guidelines of the British Committee for Standards in Haematology recommend that NSAIDs should be offered for 8-12 days unless contraindicated, to those patients with SVT at low risk for complications (grade 1A); those with thrombus less than 4-5 cm in length and without additional risk factors, such as cancer, previous SVT/VTE, or an absence of varicose veins, although no clear definition of such low-risk SVT is provided [1,13].

### Anticoagulants

The guidelines of the British Committee for Standards in Haematology recommend that confirmed SVTs within 3 cm of the SFJ, should be considered for therapeutic anticoagulation (2B), although the optimal duration is uncertain [13].

Two studies compared different LMWH regimens head-to-head, suggested that 30-day intermediate doses or therapeutic doses of LMWH were associated with a trend for lower VTE event rates than shorter courses of intermediate doses or lower doses of LMWH, with no increases in major bleeding [16-18].

A synthetic heparin derivative, the pentasaccharide fondaparinux, was evaluated for SVT treatment in the double-blind, randomized, placebo-controlled CALISTO study [18]. A preventive dose of Fondaparinux (2.5 mg once daily) for 6 weeks was more efficient than placebo, with a significant decrease in the symptomatic events and composite endpoint of death from any cause, follow-up period was 77 days. This study was carried out in 3004 patients with SVT of the long saphenous vein of at least 5 cm. (0.9% in the fondaparinux group versus 5.9%

in the placebo group). Based on this study, the American College of Chest Physicians (ACCP) guidelines suggest prophylactic-dose Fondaparinux over prophylactic dose LMWH for lower-limb SVT (grade 2C) [12].

The guidelines of the British Committee for Standards in Haematology recommend prophylactic doses of LMWH for 30 days (currently an unlicensed indication) or Fondaparinux 2.5 mg once daily for 30-45 days in patients with SVT and risk factors for extension, recurrence, or progression (grade 1B) [13,19]. One published study of phase 3b trial interpreted that Rivaroxaban 10 mg oral was non-inferior to 2.5 mg subcutaneous fondaparinux once a day for 45 days for treatment of superficial-vein thrombosis in terms of symptomatic deep-vein thrombosis, and was not associated with more major bleeding. Therefore, rivaroxaban could offer patients with symptomatic superficial-vein thrombosis a less expensive oral treatment option instead of a more expensive subcutaneous injection.

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