# CONSENSUS

## Superficial vein thrombosis: a consensus statement

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*Under the auspices of the International Union of Angiology (IUA), the International Union of Phlebology (IUP), the Central European Vascular Forum (CEVF) and Vasculab.*

*Dedicated to the memory of Jecu Avram*

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Superficial vein thrombosis (SVT) is a relatively frequent disease, but its exact incidence is difficult to determine as it has never been properly investigated.[1, 2] It is estimated to be higher than the incidence of deep venous thrombosis (DVT) which is approximately 1.6 per 1000 per year.[2, 3] In many cases SVT is a mild condition, which resolves spontaneously, thus the patient does not seek medical help. Its true incidence will depend on the age of the population, the severity of the problem (mostly treated at the general practitioner level) and the threshold at which the patient seeks help. In a systematic review it was found that in patients with a diagnosis of SVT, 6-44% of cases are associated with DVT, 20-33% with asymptomatic pulmonary embolism (PE) and 2-13% with symptomatic PE.[4] The incidence of venous thrombosis, both superficial and/or deep in cancer patients with central venous catheters inserted perioperatively, is high, 45/68 (66.3%).[5] However, anticoagulant therapy generally is not used to treat SVT that occurs in association with an intravenous (i.v.) infusion (*i.e.* infusion thrombophlebitis).[6]

### Definition

SVT is a well recognized clinical entity characterized by a painful, warm, erythematous, tender, palpable cord-like structure along the course of a superficial vein, usually involving the lower extremities, but potentially affecting any superficial vein in the body.[7] With the increasing use of intravenous catheters and injections (*e.g.* drug abusers), upper extremity SVT remains a growing problem.

SVT is an acute disease where thrombus formation is connected with an inflammatory response of the venous wall. This may be caused by mechanical, chemical, biological and very rarely infectious factors. The most common form is a primary thrombosis in a varicose vein (VV) with a secondary sterile inflammation of the vein wall (varicophlebitis).[8] Non varicose NV-SVT is a group of miscellaneous disorders, where thrombosis is the dominating feature in some conditions, while inflammation dominates in other cases. It is not easy to distinguish the degree of thrombosis and inflammation, at the beginning of the disease but duplex ultrasound (U/S) may help in the diagnosis. Due to a marked inflammatory reaction of the venous wall the thrombus firmly adheres to it making the risk of pulmonary embolism (PE) smaller than in DVT. However, the inflammation does not protect from PE as shown by Partsch in 1979 and Verlato in 1999 with similar incidence of PE, around 30%.[9, 10] An important inflammatory activation is also described in DVT.[11-13] The term superficial thrombophlebitis should be discouraged because inflammation and infection is not the primary pathology. It should be called superficial vein thrombosis in order to avoid the unnecessary administration of antibiotics and the misconception that SVT is benign.

## SVT and venous thromboembolism

Some physicians consider SVT an integral part of venous thromboembolism (VTE), together with DVT and PE. The extent of thrombus seen in the superficial vein during U/S is often, much greater than clinically presumed. The thrombus often continues into the deep venous system via the sapheno-femoral (SFJ) or sapheno-popliteal junctions (SPJ) and/or through perforating veins. An U/S is essential for a complete evaluation. In a population-based case-control the Multiple Environmental and Genetic Assessment of risk factors for venous thrombosis (MEGA) study, they found that a history of clinical SVT was associated with a 6.3-fold increased risk of DVT and a 3.9-fold increased risk of PE.[14] Predisposing risk factors for SVT and VTE are similar and include: VVs, immobilization, trauma, post-operative conditions, pregnancy, the puerperium, active malignancies, auto-immune diseases, use of oral contraceptives or hormonal replacement therapy, advanced age, obesity, and a history of previous VTE.[15-24] Laparoscopy is also a risk factor.[25]

A SVT could be a marker of hypercoagulability.[26, 27] The presence of inherited thrombophilia in both SVT and VTE again suggest a similar pathophysiology. These include factor V Leiden, the prothrombin 20210A mutation and deficiencies of the natural anticoagulant proteins C, S and antithrombin III and factor XII.[21, 27-31] High levels of factor VIII is also a risk factor for SVT.[32] In patients where SVT occurred in normal non-varicose veins coagulation inhibitor deficiencies (proteins C, S and antithrombin III) were 6.45% in the absence of thrombus extension and 62.5% in patients with extension of the thrombus to the deep veins.[33] In patients with SVT associated with VVs, the presence of natural anticoagulant deficiencies was less evident. However, their prevalence was considerably higher in those with SVT extension to deep veins (36.3%) than in non-extension (6.06%). An underlying hypercoagulable state should be investigated when the diagnosis of migratory SVT is considered.[29]

A SVT in itself is a risk factor for DVT and PE development and also for VTE recurrence.[32] Several studies have confirmed an association between SVT and VTE.[34-38] A SVT located in the main saphenous trunk seems to have the strongest association with VTE.[1, 39, 40] In a group of 263 patients with SVT, 30 of them (11.4%) developed DVT.[36] Among the 125 patients with above knee great saphenous vein (GSV) SVT, 16.8% developed DVT, the majority developing by extension through the SFJ (85.7%), while the remainder extended via a thigh perforating vein. Among the 138 patients with SVT isolated to the below knee GSV or SSV or varicose tributaries, only 4.3% developed DVT.

In a prospective study of 60 consecutive patients with SVT, 13 (21.7%) had a concomitant DVT (confirmed by U/S) and 17 patients (28.3%) also had a PE (confirmed by pulmonary inhalation and perfusion scintigraphy).[41] In this study individuals without VVs had a nine fold greater chance of suffering DVT than those with them (OR 9.09; 95% CI: 1.75-50.00). Thus the presence of VVs reduced the risk of SVT patients having DVT. In the recent French national multicentre Prospective Observational Superficial Thrombophlebitis (POST) study among 844 consecutive patients with symptomatic SVT, 5 cm long on U/S, 210 (24.9%) also had a DVT or symptomatic PE.[15] Among 600 patients without DVT or PE at inclusion, 58 (10.2%) developed VTE complications at 3 months. A symptomatic PE occurred in 3 (0.5%) of the patients, symptomatic DVT in 15 (2.8%), symptomatic extension of SVT in 18 (3.3%), and symptomatic recurrence of SVT in 10 (1.9%) of the patients, despite the fact that 540 patients received anticoagulants. The most frequent treatment in the POST study was low molecular weight heparin (LMWH) for a median of 11 days at a therapeutic dose in 63% of the patients treated. Risk factors for VTE complications at three months were male sex, history of DVT or PE, previous cancer, and absence of VVs.

The true incidence of DVT involvement in clinically isolated SVT is not kown.[42] Published figures vary from 7 to 57%. In a study of 2646 lower limb venous U/S scans they found that 36 (9.3%) of patients had combined DVT and SVT.[43] The association with PE is up to 33%.[15, 44] In another study PE was present in 21/64 (34%) of SVT patients.[9] However, only one of them was clinically symptomatic. Similarly, in a consecutive series of 21 patients with SVT, 7 had findings compatible with a high probability of PE (33.3%; 95% CI 14.6 to 57. 0), although clinical symptoms of PE were present only in one patient.[10] No association was found between the presence of thrombosis at the SFJ and the risk for PE. The results

of these studies underline the fact that the majority of authors recommend treating SVT in the same way as DVT, especially if the thrombus is within 2-3 cm from the junctions. [44]

## Classification

A SVT occurs in two different forms, with varicose veins (V-SVT) and without varicose veins (NV-SVT). The SVT classification appears in Table I. An alternative SVT classification according to the pathophysiology is: primary SVT (the inflammation affects only the venous wall and surrounding tissues) and secondary SVT (the inflammation of the venous wall is associated with other chronic inflammatory process or systemic disease in the body: Büerger's disease, Behçet's disease, other vasculitic or chronic rheumatic syndromes with autoimmune etiology (*e.g.* antiphospholipid syndrome, systemic lupus erythematosus) and malignancy.[45-49]

Primary SVT of the legs is by far the most common form of SVT.[2] In 60-80% of such cases, SVT is localized in the greater saphenous vein (GSV), in 10-20% in the small saphenous vein (SSV) and in 10-20% in other veins of the legs, occurring bilaterally in 5-10% of the cases.[2] SVT in the upper limbs is much rarer than in the lower limbs, occurring especially in patients with i.v. catheters, Büerger's disease [45] or other secondary SVT causes. Mondor's disease is SVT of the thoracoepigastric veins, penis or groin.[50] In the majority of cases, no triggering factor is found. It follows a benign course and resolves spontaneously over 2 to 4 weeks. Henke described spontaneous arteriovenous fistulae after SVT.[51] Several risk factors and mechanisms contribute to the etiopathogenesis and clinical pathophysiology of SVT (Table II).

## Forms of SVT

### *Superficial vein thrombosis associated with varicose veins (V-SVT). This includes the previously used term varicophlebitis*

In contrast to SVT of a healthy vein, V-SVT is a mild condition in the majority of cases pro-

TABLE II.—*Risk factors and etiopathogenic mechanisms involved in SVT.*

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|---|
| **Slowing of the blood flow** |
| Varicose veins |
| Prolonged bed rest (immobilization) for several reasons (operation, trauma, serious infection, heart failure, chronic obstructive pulmonary disease, etc.) |
| **Coagulation disorders** |
| Thrombophilia – Factor V Leiden mutation, protein C or S deficiency, AT III deficiency, prothrombin G20210A mutation, etc |
| Cancer |
| Pregnancy |
| Oral contraceptives |
| Anti-phospholipid syndrome. |
| **Damage of the venous wall** |
| Intravenous injections |
| Intravenous catheters |
| Trauma |
| Varicose veins and chronic venous insufficiency (CVI) |
| Side effect of endovenous treatment of varicose veins |
| **Other risk factors and diseases** |
| Age (over 60 yrs) |
| Obesity |
| Other chronic inflammatory autoimmune diseases |
| Büerger's, Behçet's, Mondor's disease |

TABLE I.—*SVT classification according to localization, risk factors and etiology.*

| | | | | |
|---|---|---|---|---|
| SVT | V-SVT | Localization: GSV, SSV or collateral varicose veins | Risk factors: Endothelial or haemodynamic alterations | Etiology: Trauma, Iatrogenic (EVLA, RFA, USGFS), infections |
| | NV-SVT | Localization: Any superficial vein | Risk factors: Alterations of coagulative status | Etiology examples: SVT during pregnancy; Oral contraceptive; Pre or para-neoplastic |
| | | | Risk factors: Endothelial alterations | Etiology examples: VASCULITIDES; Bürger, Behçet, Mondor |
| | Others (on varicose or healthy veins) | Localization: Lower or upper limbs | Etiology: Post-traumatic; Burn; IATROGENIC (iv catheters, hemodialysis); Septic | |

vided it is not saphenous. The great saphenous vein by its connection to the deep veins (including perforating veins) increases the risk of DVT. V-SVT occurs in 10 to 20% of patients suffering from VVs.[52] It is one of the complications in the course of CVI of lower limbs. The V-SVT is the most common form of SVT, about 10 times more frequent than the NV-SVT, preferentially affecting older people with long standing VVs.[16] In a prospective study of 100 patients with SVT, 88 of them had VVs and only in 12 patients the SVT appeared on a healthy non-varicose vein.[53] Slowing of the blood flow in a dilated VV is the most important factor of the V*irchow's triad* which contributes to the SVT.

The role of venous wall damage in V-SVT is probably less important than slowing of blood flow. However, altered conditions of blood flow resulting from valve dysfunction in dilated VVs modulate the endothelial function as well as the soluble and cellular components of blood.[54, 55] The V-SVT may also appear when local venous hypertension and venous reflux progress to a degree which results in the breakdown of the mechanisms compensating a pre-existing form of thrombophilia.[33] A SVT arising in VVs is probably because of slowing of blood flow and/or wall damage, independently of other factors. Furthermore, natural inhibitor deficiencies may have a significant effect in the possible progression into the deep venous system and an eventual PE. Evidently, a hypercoagulable state leads to thrombus formation at a site of severely altered flow conditions. Passive or active venous hypertension may lead to a hypoxic injury of the endothelium, leukocyte accumulation and finally blood coagulation.[56] Varicose vein thrombi are rich in red cells and relatively poor in fibrin.[16] More solid thrombi may stretch further than what would be expected from the size of the area of inflammation. Propagation to the deep veins often depends on the location and extent of SVT. In a retrospective study of 114 patients with SVT the incidence of a concomitant DVT was 15.6% when SVT affected the GSV or SSV, but only 5.2% when the side branches were involved.[57] With VVs as a single risk factor, the frequency of a concomitant DVT was 6% while VVs combined with further risk factors showed a DVT frequency of 15.4%.

Endothermal heat induced thrombosis (EHIT) is a more recent iatrogenic entity. In a literature review, the incidence of DVT after EVLA ranges between 0% and 7.7%.[58, 59] All patients who undergo EVLA and foam sclerotherapy should have routine U/S screening to evaluate for successful ablation of the treated vein segment as well as to evaluate for thrombus propagation.[60]

### *Superficial vein thrombosis without varicose veins i.e. non varicose SVT (NV-SVT)*

The NV-SVT is a group of disorders (Table III), where inflammation is the dominating feature in some conditions, while thrombosis dominates in other cases. The SVT without associated VVs typically shows a small thrombus and a minor inflammation in the surrounding tissues. Histology reveals a thickened intima with myocyte and fibroblast proliferation and abundant media fibrosis with a large number of capillaries.[16]

Very little information is available about the occurrence of NV-SVT in the general population, however, SVT is frequently observed in Behçet's disease. Among 2319 patients diagnosed with Behçet's disease SVT was present in 53.3% and DVT in 29,8%.[46] The NV-SVT is associated with erythema nodosum-like lesions and often precedes serious visceral involvement in Behçet's disease.[61] *Thrombophlebitis migrans* (the inflammation of the venous wall travels proximally and distally on a superficial vein) and *thrombophlebitis saltans* [8] (the inflammation "jumps" from one vein to another vein) are specific forms of SVT often seen in patients with Büerger's disease.

TABLE III.—*Causes of NV-SVT.*

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| Tumors (especially malignant neoplasia) |
| Systemic vasculitis – Büerger's, Beçhet's, Mondor's disease, polyarteritis nodosa, Horton Giant cell and Takayasu arteritis. |
| Collagenoses: Systemic lupus erythematosus,. |
| Thrombophilia - Inherited: (Factor V Leiden, prothrombin gene mutation, antithrombin deficiency, protein C and/or protein S deficiency, elevated levels of other procoagulants proteins VII, IX, XI etc) |
| Acquired: (surgery, immobilisation, advanced age, pregnancy, contraceptive, hormonal replacement therapy etc) |
| Hematologic diseases: Hypochromic anaemia, secondary polycythemia, leukemia, Hodgkin's lymphoma, thrombocytosis, cryoglobulinemia and cryoagglutinemia, nocturnal paroxysmal hemoglobinuria |
| Infections including: viral, dental foci, urogenital infections, tuberculosis, oral or genital afthae. |
| Iatrogenic conditions: Chemotherapy, radiotherapy, hemodialysis access. |

The SVT in Büerger's disease (thrombangeitis obliterans) is part of the diagnostic criteria for an inflammatory arterial occlusive disease involving mainly medium and small sized arteries.[61] In a group of 22 of these patients SVT was present in 8 (36.4%).[62]

The prevalence of thrombophilia in NV-SVT is 50%, while in V-SVT it is only 15%.[53] In a prospective analysis of 42 patients with NV-SVT, investigation for risk factors revealed a neoplasm in 2 (4.8%), a non neoplasmic systemic disease in 4 (9.5%) and a thrombophilic condition in 20 (48%).[63] The most frequent thrombophilia was the heterozygous mutation of coagulation factor V Leiden. A routine thrombophilia evaluation is rarely performed. However, screening for thrombophilia is advisable especially for patients with unexplained SVT in normal veins (after accurate exclusion of an occult cancer) and/or those with thrombus progression despite appropriate anticoagulation.[33]

In a retrospective analysis of 140 consecutive patients at a surgery department over a period of nine years an association between SVT and malignancy was found in 18 (12.9%);[64] breast cancer in 7, colon and haematological cancer in 4, skin cancer in 3 and one patient each for oesophageal, prostatic, kidney and neck cancer. The SVT preceded the diagnosis of malignancy in only two patients (1.4%).

Screening for malignancy in a SVT patient is performed if symptoms and/or objective signs suggest the presence of a possible neoplasia. Tests include full blood count, prostatic specific antigen (PSA), chest X – ray, mammography, gastroscopy, colonoscopy etc.

*Recommendation 1:*

*In every patient with spontaneous NV-SVT or recurrent V-SVT investigate extensively for SVT risk factors, especially cancer and thrombophilia.*

## Diagnosis

The diagnosis is primarily clinical, based on the presence of erythema and tenderness in the distribution of the superficial veins, with the thrombosis identified as a palpable cord.[17, 65] The presentation of SVT is usually obvious, especially in patients with V-SVT. The VV becomes inflamed containing a palpable thrombus.[38] The vein feels tender and hard, and the skin over it becomes inflamed (warm and red), due to a perivenous inflammatory reaction. Often there is some edema of the surrounding tissue, but without generalized edema of the limb. The extent may be limited to 1-2 cm or cover the whole leg. When the SVT is extensive severe pain is present. The recovery process includes slow resorption of the thrombus with resolution of the inflammation. After some weeks the skin and the veins may return to normal. The affected part of the vein is reduced to a fibrous cord, but usually undergoes recanalization after a few months. However, sometimes the veins remain occluded and there may be a hard area of scarring and the skin over this area may be permanently hyperpigmented. In a patient without VVs the NV-SVT presents as a red, warm painful cord along the course of a non-varicose superficial vein. The appearance of unilateral limb edema signalizes the possibility of thrombus extension from the superficial to the deep venous system.

However, a GSV thrombosis can occur in both V-SVT and NV-SVT patients. This distinction is often difficult especially if the GSV is in its normal anatomical position in its own fascial compartment in the thigh.[66] Patients present with a painful, reddened and tender inner thigh and the affected leg may be edematous. An acute GSV thrombosis is detected by U/S with a characteristic increased cross-sectional diameter, homogenous echolucent intraluminal material, and lack of compressibility.[59] Occasionally there is a characteristic perivenous halo indicating the edema.

The clinical diagnosis of SVT is usually straight forward as symptoms and signs are overt (Table IV). Extensive color flow U/S is mandatory for the precise evaluation of SVT.[36] The U/S evaluates the length of the thrombosis in the superficial vein and also the extension of thrombus into the deep venous system through perforating veins or the SFJ and/or SPJ. Bilateral compression U/S may also reveal the presence of an associated DVT in the contralateral limb. In a series of 106 patients with SVT the SVT was bilateral in 9 cases.[67] The GSV was affected in 60 cases, the SSV in 22 cases, both saphenous veins in 6 cases

TABLE IV.—*SVT: Symptoms and signs.*

1. CLINICAL PRESENTATION
   - Pain, erythema, tenderness, and induration corresponding to one or more superficial veins (often dilated varicose veins) with variable edema over the inflamed vein.
   - Palpable, painful "cords"
   - Local infection (at the foot, malleolar ulcerations) only if the SVT is septic
   - Venous trauma, even minimal trauma
   - Erythema along veins
   - Recurrent, migratory SVT secondary to neoplasmic disorders (Trousseau's sign)
   - Fever, leucocytosis (if the SVT is extensive or septic)
2. LOCALIZATION
   - Great saphenous vein and its branches
   - Short saphenous vein
   - Other veins on lower or upper limbs
3. COURSE
   - Inflammatory reaction lasting 2 to 3 weeks
   - Vein recanalization in 6 to 8 weeks (if it occurs)
   - Normally there is no edema unless the SVT is acute
   - Limb edema may indicate association with DVT
   - Post-inflammatory hyper-pigmentation may last several months

and a non-collateral saphenous vein in 17 cases. In 38 cases, a DVT added to the SVT, either separately in 19 cases, 9 of which in controlateral or by proximity extension from an arch in 7 cases or from a more distal perforating vein in 8 cases.

A *post hoc* analysis of a prospective, multicentre, cohort study (POST) on 537 patients with SVT who had a planned compression U/S follow up at 8-15 days looked at the 3 month's outcomes.[68] They concluded that systematically planned compression US detected a few asymptomatic VTE complications but failed to identify patients at risk of VTE events during follow-up. Therefore the use of a follow-up compression US was neither efficient nor cost effective. The Erasmus study comparing compression U/S versus an extensive color flow U/S for diagnosis of DVT showed that there is no difference between the two methods.[69] However, it suggests that in centers where there is vascular expertise the extensive U/S should be preferred. Venography is not recommended because it may contribute to the onset of phlebitis.[19, 65, 70]

*Recommendation 2:*

*Clinical examination may underestimate the real extent of SVT and does not provide information on the status of the deep venous system. Therefore, it is mandatory to perform an extensive color duplex ultrasound scan of both the superficial and deep venous system.*

*Recommendation 3:*

*Duplex ultrasound should be performed both on the affected and contralateral limb.*

*Recommendation 4:*

*It is necessary to follow-up with duplex patients with SVT that is localized in the great or small saphenous vein less than 5 cm from the junctions. Also, although there are no data, duplex is indicated in clinical worsening despite appropriate treatment.*

## Treatment

As a general rule, when a specific treatment is not satisfactory a few options are available, either on their own or in combination. Treatment options are assessed in the light of data from the main studies reported in the literature.[42, 71-73] A new Cochrane analysis concluded that the existing studies do not demonstrate strong recommendations for any treatment.[74] Ongoing trials will add to our knowledge about the optimal treatment of SVT. Since SVT should not be considered a benign disease, management with topical and/or systemic anti-inflammatory drugs in combination with compression therapy alone may prove inadequate. As SVT is etiologically a heterogeneous group of disorders with a different degree of inflammation and thrombosis the main aetiological factor and contribution of different risk factors should also be considered before treatment decisions are taken.

Contrary to DVT, little is known about the most appropriate management of SVT. The aim of treatment is to prevent the extension of SVT in the superficial vein, to reduce the inflammation of the superficial vein and perivenous tissues as well as to prevent the extension of thrombus formation into the communicating veins and the deep venous system. There is no consensus on the optimal treatment of SVT in clinical practice. Several therapies have been proposed in the literature, including surgical therapy (ligation or stripping of the affected veins), elastic stocking, non-steroidal anti-inflammatory drugs (NSAIDs) which aim to reduce pain and inflammation, and different anticoagulant agents for prevention of DVT (Table V).[75-87]

TABLE V.—*Treatment of SVT.*

1. COMPRESSION. [16, 75, 76]
   – bandages
   – Stockings, bilaterally
2. NORMAL PHYSICAL ACTIVITY
   – Walking with compression, not bed rest.[72, 77, 78]
3. DRUGS
   – Anticoagulants - low molecular weight heparins (LMWH), [77, 79-81] unfractionated heparin (UFH), oral anticoagulants – vitamin K antagonists (VKA), fondaparinux.
   – Non-steroidal anti-inflammatory drugs (NSAIDs).[72, 73, 82, 83] However, the ACCP (American
   – College of Chest Physicians) Conference on Antithrombotic and Thrombolytic Therapy indicates that NSAIDs should not be used in addition to anticoagulation.
   – Topical anti-inflammatory treatment (gel, cream, spray)[73, 84-87]
   – Minor fibrinolytic drugs – in patients with varicose SVT
   – Antibiotics – only in patients with septic SVT
   – Corticosteroids – in patients with vasculitic and autoimmune syndromes
4. SURGERY.
   – Emergency SFJ or SPJ ligation with or without stripping and/or thrombectomy.[81,88] In iatrogenic SVT, following endovenous treatment aspiration of the thrombus is possible.
   – Elective treatment of CVI after recovery of acute SVT by ligation or thrombectomy.

The treatment of V-SVT and NV-SVT is the same in the acute stage of the disease. Once the acute stage of the disease is over, in the case of V-SVT, it is important to treat the VVs (by sclerotherapy and/or surgical methods) to prevent recurrent SVT. In case of NV-SVT it is mandatory to investigate and treat the underlying condition.

*Compression and mobilization*

The main treatment in all types of SVT is compression and mobilization.[75] Everyday experience shows that compression of the thrombosed vein relieves the symptoms and speeds up healing. There have been no randomized studies demonstrating the effectiveness of compression, although this approach is considered by all experts to be essential.

Fixed compression bandages used as the only treatment improved duplex findings in 81.1% of patients, no change on U/S was found in 13.2% while 3.8% of the patients developed new DVT and 1.9% showed thrombus extension in the superficial system.[76] According to Blatter *et al.* this is the only study checking the outcome of SVT without any additional drug therapy. Adhesive short stretch bandages have been used.[16] There are data on compression stockings plus medication from the Decousus group [17] but nothing else with different material.

In patients with a limited SVT in a varicose collateral vein, local treatment and mobilization with elastic compression will be sufficient.[73] For compression treatment bandages or graduated elastic compression stockings (GEC) [77] are used. Bandages are used initially for 10 days, especially on the thigh, as they allow moulding to the local anatomy.

In V-SVT the following advice can be given:

An anti-inflammatory or heparin-containing ointment applied to the inflamed vein section, covered with gauze. This is frequently used although not supported by scientific evidence.[74]

An eccentric reinforcement of compression by means of foam rubber strips, silicone or rolls of cellulose, cotton or gauze.

A compression bandage with short stretch or non-elastic material, preferably cohesive or adhesive to prevent slippage, above or below the knee.

The compression bandage should exceed the proximal limits of the thrombosed section by at least 10 cm.[75]

If a 20-30 mmHg GEC stocking is already applied to the lower leg, it is practical to slip a foam rubber cushion underneath the stocking ensuring it is longer and wider than the inflamed vein section. In order to increase pressure an additional knee high stocking or a compression bandage can be applied. Regular walking supports the effectiveness of compression on the lower extremity. The patient must walk regularly throughout the day and avoid prolonged periods of being seated or standing. Confinement to bed would favour progression of the thrombus in both the superficial and the deep venous system and is therefore strictly contraindicated. Some authors judge the progression to the deep system as the prime complication.[75]

*Medical treatment*

The treatment of choice is anticoagulation. NSAIDs (apart from aspirin) may be given, preferably locally or even systemically.[6] They reduce pain and perivenous inflammation. However, there is no evidence that they reduce the incidence of VTE. Different studies included a NSAIDs group [1, 78-80] and compared NSAIDs with

placebo and two with LMWH.[79, 80] NSAIDs significantly reduced the risk of SVT extension and/or recurrence by 67% compared with placebo.[80] However, there were no differences in the incidence of VTE or in the resolution of local symptoms and signs. Interestingly, no major bleeding episodes were recorded in any NSAIDs or placebo groups. Other analgesics should be considered also. Anticoagulant therapy is recommended in patients with extensive SVT. LWMH, UFH, VKA or fondaparinux can be used in prophylactic or therapeutic doses. Treatment options regarding dose and duration differ in individual hospitals and medical care centres.

In a study in 60 patients comparing unmonitored high doses of UFH (12500 IU for one week followed by 10000 IU) *vs.* low (prophylactic) doses of UFH (5000 IU) for four weeks, they concluded that the first regimen was more effective in preventing VTE complications and equally safe.[81] This was in 2002 before the wider use of LMWHs. If UFH is anticipated the VKA should be overlapped for a minimum of 5 days and should be continued until the recommended INR has been therapeutic.

Different studies included a LMWH as a treatment option in patients with SVT.[42] The rationale of treating SVT with LMWH is the neutralization and inhibition of thrombin generation and the prevention of PE and extension and thrombus recurrence. There is limited experience on patients with protein C deficiency with recurrent episodes of SVT and DVT (including iliofemoral, massive mesenteric, renal vein and cavernus sinus thrombosis and PE).[82] The thrombotic problems of these patients were controlled satisfactorily by long-term (three years) administration of LMWH alone or in combination with low dose VKA. No osteoporotic symptoms have been observed.

Both prophylactic and therapeutic LMWH and the NSAID tenoxicam given for 8 to 12 days were associated with a significantly lower incidence of SVT extension and/or recurrence, compared with placebo.[80] Although the differences were not statistically significant, the incidence of VTE may have been lower both with prophylactic and therapeutic LMWH shortly after treatment but not at the end of three month follow-up period. No episodes of major bleeding or heparin-induced thrombocytopenia were observed in any treatment group.

A multicenter, prospective, controlled, double-blind clinical trial compared two regiments of LMWH.[83] In this study 164 consecutive patients with acute SVT of the GSV were randomized to receive either fixed prophylactic or body-weight adjusted therapeutic doses of nadroparin s.c. once daily for 1 month. On the prophylactic dose 7/81 patients (8.6%; 95% CI 3.5-17.0) developed SVT progression or VTE complications *vs.* 6/83 (7.2%; 95% CI 2.8-15.1) on the therapeutic dose. They concluded that over a 3-month follow-up period, therapeutic doses of LMWH for 1 month in patients with SVT do not improve the results obtained by prophylactic doses, administered for the same period.

The Belgian Society on Thrombosis and Haemostasis and the Belgian Working Group of Angiology have good experience and good therapeutic results with 10 days of LMWH in full therapeutic dose followed by 20 days of LMWH in half-therapeutic dose.[84]

According to the guidelines of the previous (8th) American College of Chest Physicians (ACCP), SVT should be treated in the following modes.[85, 86] The level of evidence has been graded from 1A, the best, down to 2C.

1. For patients with extensive SVT, prophylactic or intermediate doses of LMWH (Grade 2B) or intermediate doses of UFH (Grade 2B) for at least 4 weeks is suggested. As an alternative to 4 weeks of LMWH or UFH, VKA (target INR 2.5, range 2.0 to 3.0) is recommended. The VKA should be overlapped with 5 days of heparin and then continue with VKA for 4 weeks (Grade 2C). Medical treatment with anticoagulants over surgical treatment is recommended (Grade 1B). It is likely that less extensive SVT, where the affected venous segment is short in length or further from the SFJ, does not require treatment with anticoagulants. It is reasonable to use topical or oral NSAIDs for symptoms control in such cases.

2. For patients with symptomatic infusion SVT as a complication of intravenous infusion, oral diclofenac or another NSAID (Grade 2B), topical diclofenac gel (Grade 2B), or heparin gel (Grade 2B) until resolution of symptoms or for up to 2 weeks is suggested. The use of systemic anticoagulation is not recommended (Grade 1C). There is no indication for using antiplatelet drugs (*e.g.* aspirin), as this class of drugs has

not been shown to be effective in treating venous thrombosis, as opposed to arterial atherothrombosis.[6]

Treatment with a LMWH or with an oral NSAID should be evaluated further in the treatment of SVT.[4] Different dosage schemes and duration of treatment should be compared. The Cochrane Database Review evaluated 24 studies involving 2469 patients with SVT of the legs, but the methodological quality of most of the trials was poor.[74] Treatment included LMWH, NSAIDs and surgery. Both LMWH and NSAIDs significantly reduced the incidence of SVT extension or recurrence by about 70% compared to placebo and both seemed to have a similar efficacy and safety. Overall, topical treatments improved local symptoms. However, no data were provided on the effects of these treatments on VTE incidence. They concluded that while the available data are too limited to make clear recommendations, an intermediate dose of LMWH for at least a month might be advised.[4, 74]

The CALISTO is a multicentre randomized, double-blind trial on 3002 patients assigned to receive either fondaparinux s.c. 2.5 mg o.d. or placebo for 45 days.[87] The primary efficacy outcome was a composite of death from any cause or symptomatic VTE, extension to the SFJ or recurrence of SVT at day 47. The main safety outcome was major bleeding. Patients were followed until day 77. The primary efficacy outcome occurred in 0.9% (13/1502) patients in the fondaparinux and 5.9% (88/1500) patients in the placebo group (RRR with fondaparinux, 85%; 95% CI, 74 to 92; P<0.001). The incidence of each component of the primary efficacy outcome was significantly reduced in the fondaparinux compared with the placebo group, except for the outcome of death which was 0.1% in both groups. The rate of VTE was 85% lower with fondaparinux vs placebo (0.2% *vs.* 1.3%; 95% CI 50 to 95; P<0.001). Similar risk reductions were observed at day 77. It should be noted that only one DVT (out of 118) was detected in patients with SVT not in the GSV (0.8%). A total of 88 patients would need to be treated to prevent one instance of PE or DVT. Major bleeding occurred in one patient in each group. The incidence of serious adverse events was 0.7% with fondaparinux and 1.1% with placebo. They concluded that 2.5 mg of fondaparinux o.d. for 45 days was effective in the treatment of patients with acute, symptomatic SVT. This a grade B recommendation based on level 2 evidence.[86]

In a subsequent cost-effectiveness analysis, fondaparinux for 45 days did not appear to be cost-effective when used in all patients with isolated SVT of the legs.[88] They suggested that better value for money could be obtained in a subgroup of patients with a higher incidence of VTE after SVT and that shorter durations of treatment should be evaluated in future clinical studies. It should be considered that this economic analysis has been carried out based on the cost of fondaparinx in the USA which is signifially higher than in Europe. In addition CALISTO is the only study involving such a large population, which has shown clear efficacy in the treatment of SVT, without the need for laboratory monitoring. In the current ACCP, for extensive SVT, they suggest prophylactic-dose fondaparinux or LMWH over no anticoagulation (Grade 2B), and also suggest fondaparinux over LMWH (Grade 2C).[6]

The cost of therapy should also be considered.[89] By extrapolation of data from DVT studies perhaps the new oral direct factor Xa inhibitors (apixaban, rivaroxaban) [90, 91] and thrombin inhibitors (dabigatran)[91] have better risk profiles than UFH, LMWH and VKA, and the favorable risk-to-benefit ratio associated with them could lead to an extension of indications for anticoagulant therapy. The fact that these new drugs are administered orally may be attractive to patients. But the comparative effectiveness and cost-effectiveness of fondaparinux and these new oral agents for the treatment of SVT is awaited. In addition, regarding the generic LMWHs and newer anticoagulants, monitoring assays are not being developed and there is no antidote to reverse bleeding.[92] Also there are concerns about reproducibility, product variation, and quality. Therefore, though they may appear to be effective for qualified indications, their safety remains a concern. Though these new drugs could be another option, there are no data as yet for recommended dosages or duration of treatment on patients with SVT. Until such data are available, it would seem premature to recommend that the oral Xa and IIa inhibitors be used routinely in the treatment of SVT.

*Topical treatment*

A significant improvement in local symptoms was observed with diclofenac gel,[78, 93] essaven gel (that contains aescin, heparin and essential phospholipids),[94, 95] when compared with placebo. Only one study evaluated two different NSAI gels, diclofenac gel and erofenac gel, and showed a comparable efficacy profile.[96] None of these studies that evaluated topical treatment, reported data on VTE or SVT extension and/or recurrence. Two studies randomized patients to topical treatment with heparin-spray gel or LMWH.[97, 98] A non-significant decrease in DVT was found with LMWH, while local symptoms were similarly relieved by both treatments after three weeks.

*Surgery*

The current ACCP recommends medical treatment with anticoagulants over surgical treatment.[6]

According to the guidelines of the American Venous Forum, patients with SVT should be treated with heparin or LMWH with or without oral anticoagulation therapy or superficial venous ligation.[99] Excision of the involved vein is recommended for symptoms that persist over two weeks despite treatment or for recurrent SVT within the same venous segment. If there is progressive proximal extension with involvement of the SFJ or the cephalic-subclavian junction, ligation and resection of the vein at the junction could be considered. Alternatively, full dose of anticoagulation can be attempted.[100] Following the acute phase, in patients with CVI and SVT different surgical procedures are used, most frequently stripping and/or ligation.[101] Stripping has the advantage, of treating both the complication and its cause.[102-104] In a recent document on VVs and CVI from the Society of Vascular Surgery and the American Venous Forum surgical therapy is still a controversial issue and further studies are fundamental.[105]

In a series of 43 patients who underwent ligation of the SFJ with and without local common femoral vein thrombectomy and stripping of the GSV, only two patients were found with postoperative contralateral DVT, one of whom had a PE.[106] They recommend that thrombus within 3 cm of the SFJ is an indication for surgical intervention. When comparing the surgical ligation with the systemic anticoagulation treatment it should be considered that the surgical options do not address the hypercoagulable state of these patients or the contralateral leg and in addition, may create injury to the endothelium at the SFJ. Therefore, the surgical treatment seems to be less appealing, at least on a theoretical basis.[65] Zaraca describes two types of SVT which require different treatment.[107] In type 1, the thrombus does not reach the pre-ostial valve and simple SFJ ligation after its opening is necessary. In type 2, the thrombus goes beyond the pre-ostial valve, thrombectomy, SFJ ligation and postoperative anticoagulation are mandatory.

Tributary thrombosis in patients with VVs are due to VVs. These patients usually do not have thrombophilia. Therefore foam sclerotherapy under U/S guidance is likely to be safe. Saphenous thrombosis without VVs deserves further investigation.

*Minor fibrinolytic drugs (Heparan-sulphate)*

At the completion of the anticoagulant treatment, a treatment with minor fibrinolytics such as heparan-sulphate, oral sulodexide or mesoglycan could be considered for secondary prevention.[108, 109] One study on 30 STV patents evaluating oral heparan-sulphate *vs.* oral sulodexide for two weeks, suggested that both treatments were able to reduce signs and symptoms to a similar degree.[110] The efficacy of three doses/route of administration of desmin has been assessed in one trial.[111] A better control of local symptoms was obtained with higher doses of desmin (s.c. or i.m.) without increase in the risk of adverse events. However, desmin is no longer available.

## Conclusions

In general, medical treatment for acute SVT is superior for minimizing complications and preventing subsequent DVT or PE development, as opposed to surgical treatment with ligation of the GSV vein at the SFJ or ligation and stripping, which provides pain relief.[112] Surgical ligation for acute SVT has not found much support in the literature for its routine use. Surgical treat-

ment for underlying CVI is usually performed electively in V-SVT patients. Investigation and treatment of the underlying cause is mandatory in NV-SVT patients.

*Recommendation 5:*

*All patients with SVT should be treated with compression therapy*

*Recommendation 6:*

*Immediate mobilization with elastic compression is mandatory.*
*Patients should not be confined to bed.*

*Recommendation 7:*

*Patients with SVT, with an inflamed and thrombosed superficial vein longer than 5 cm on duplex ultrasound should have LMWH at intermediate or therapeutic dose for 4 weeks. The dosage and duration of anticoagulation depends on concomitant diseases and other risk factors for VTE.*

*Recommendation 8:*

*In patients with extended SVT (>10 cm) with additional risk factors for VTE s.c. fondaparinux in prophylactic dose should be considered for 6 weeks.*

*Recommendation 9:*

*Routine surgical ligation of the SFJ or the SPJ to prevent SVT extension into the deep veins is not advised. However, following SVT treatment, since V-SVT could recur and it is a sign of advanced CVI, appropriate treatment of varicose veins could prevent further problems.*

This consensus document was based on a consenus proposal from the Central European Vascular Forum published in Acta Phlebologica.[113]

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