

H. van Weert, MD, PhD,  
G. Dolan, MD, I. Wichers,  
MD, C. de Vries, MD,  
G. ter Riet, MD, PhD,  
and H. Buller, MD

Department of General  
Practice, Academic Medical  
Centre/University of  
Amsterdam (HvW, GD, CdV);  
Department of Vascular  
Medicine, Academic Medical  
Centre/University of  
Amsterdam (IW, HB); Horten-  
Zentrum, University of Zürich,  
Zürich, Switzerland (GtR)

# Spontaneous superficial venous thrombophlebitis: Does it increase risk for thromboembolism?

A historic follow-up study in primary care

## Practice recommendations

- Spontaneous superficial venous thrombophlebitis (SVTP) confers a 10-fold risk of developing DVT within 6 months compared with controls.
- Absolute risk of DVT following SVTP, however, is just 2.7%, and watchful waiting is probably a reasonable approach in primary care.
- Swelling of a leg within 6 months after a superficial thrombophlebitis should prompt diagnostic testing for DVT.

## Abstract

**Objectives** To determine the risk of arterial and venous complications after a spontaneous superficial venous thrombophlebitis (SVTP) in the leg in a general practice population.

**Study design** Retrospective cohort study (LOE: 2b [CEBM]). Exposure consisted of the diagnosis of SVTP of the lower limbs on an index date. The exposed cohort was compared with an (unexposed) cohort of practice-, age-, and sex-matched controls without SVTP.

**Population** Patients with spontaneous SVTP in the leg were identified through diagnostic coding in the medical

registers of 40,013 patients, enlisted with 5 health centers in Amsterdam, the Netherlands.

**Outcomes** Primary outcomes were deep venous thrombosis (DVT), pulmonary embolism (PE), acute coronary events, or ischemic stroke over a 6-month follow-up period. Odds ratios (OR) were used to quantify the associations between SVTP and outcome events.

**Results** No statistically significant odds ratios were found for PE, coronary events or stroke. DVT was the only primary outcome to show a significant relationship. DVT occurred in 2.7% of all SVTP patients as compared with 0.2% in the controls (OR=10.2; 95% confidence interval [CI], 2.0–51.6). When controlling for prior history of DVT, the OR decreased to 7.1 and the confidence interval crossed 1.0 (95% CI, 0.9–65.6).

**Discussion** Spontaneous SVTP in the leg is a risk factor for DVT, but is less predictive in patients with prior DVT. Although effective treatments for the prevention of DVT are available, the absolute risk is too low to advocate prophylaxis in a general practice population. More research on prophylaxis is needed to stratify these patients at risk.

## CORRESPONDENCE

Dr. H. van Weert, Department of General Practice, Academic Medical Centre/University of Amsterdam, PO Box 22660, 1100 DD Amsterdam, The Netherlands. E-mail: h.c.vanweert@amc.uva.nl

**T**he association between spontaneous superficial venous thrombophlebitis (SVTP) and subsequent venous or arterial thromboembolic events has been studied among referred populations, but not in the primary care setting. The aim of this study was to determine this association when primary care patients experience SVTP of the leg.

We found that, although the risk of developing a deep venous thrombosis (DVT) following SVTP is real, the absolute risk is quite low. Prospective studies are needed to identify those who are at greater risk. Until they can be identified, watchful waiting with SVTP seems the best strategy in general practice, because of the sequelae of the various treatment regimens and the relative lack of benefit for primary care patients in preventing DVT.

## ■ Background Treatment of SVTP

Spontaneous venous superficial thrombophlebitis of the leg veins is generally considered to be a benign condition. Not much is known about its natural course and prognosis,<sup>1</sup> except that it is usually expected to resolve spontaneously with 2 weeks.

The practice guideline of the Dutch College of General Practitioners does not recommend any specific treatment, but a recently published guideline of the American College of Chest Physicians advocates the use of an intermediate dosage of unfractionated heparin or low molecular-weight heparin for at least 4 weeks—they based this conclusion, however, on an unclear risk/benefit ratio.<sup>2,3</sup>

Consequently, family physicians treat thrombophlebitis with any number of means, ranging from watchful waiting, analgesics, ambulant compression stockings, anticoagulants, and referral for surgical intervention.

## SVTP and deep vein thrombosis/ pulmonary embolism

Until the early 1990s, no relationship had been established between SVTP and

either DVT or pulmonary embolism (PE). Subsequently, no standard preventive measures were recommended.<sup>2</sup>

In the late 1990s, several reports were published about concomitant or subsequent DVT or pulmonary embolism PE.<sup>4-7</sup> In a prospective hospital-based study, DVT occurred in approximately 2% of the patients with SVTP during 3 months of follow-up.<sup>8</sup>

This perceived increased risk led to trials that showed a significant reduction within 12 days in the incidence of recurrent or extended SVTP among patients treated with nonsteroidal anti-inflammatory drugs (NSAIDs) or low-molecular-weight heparins, compared with those receiving placebo. Furthermore, the incidence of venous thromboembolism (VTE) after 10 days tended to be lower in the treatment groups compared with placebo, but this treatment effect tended to disappear after discontinuation of treatment.<sup>9</sup>

## The primary-care population

All studies published so far, however, have been conducted in a referred population of patients, which could lead to an unknown selection of patients with relatively cumbersome symptoms or diagnostic uncertainty.<sup>10</sup>

The primary objective of the present study was to determine the association between a history of SVTP and subsequent venous or arterial thromboembolic events in patients, presenting in a primary care setting with a spontaneous episode of SVTP of the leg. Given the emphasis of recent publications on pharmacotherapy with low-molecular-weight heparin and NSAIDs to prevent DVT after SVTP, we analyzed the prescription policy of family physicians, as this could influence the primary outcome: the occurrence of venous or arterial thromboembolic events.

## ■ Methods

In the Dutch health care system, all citizens are enlisted with a family physician of their choice. This family physician functions as a gate-keeper to secondary care,

## FAST TRACK

**Severe venous insufficiency, varicose veins, hypercoagulable state, male gender, older age, history of DVT predict complications of SVTP**

## FAST TRACK

## GI bleeding and renal failure increase by about 30% with the use of NSAIDs

evaluating all health related complaints and answering questions before referral is considered.

We carried out a historic 6-month follow-up study. The exposed cohort consisted of patients who had presented to their family physician with an uncomplicated and spontaneous SVTP. Nonexposed patients had no history of SVTP, but were matched for practice, age (within 1 year), and sex. For exposed and unexposed patients alike, the occurrence of all venous and arterial thromboembolic events were tallied over a follow-up period of 6 months using the electronic patient records of 5 health care centers. All centers participate in the registration network of the Academic Medical Centre–University of Amsterdam in Amsterdam, the Netherlands.

### The database

Family physicians electronically register all their enlisted patients and their medical problems. Medical problems are coded using the International Classification of Primary Care (ICPC). Furthermore, at each health care center all physician-patient contacts (including reason for encounter, diagnosis, and treatment/prescription) are recorded in an electronic medical database and available for further analysis.

The anonymous data are stored centrally at the Department of General Practice. The system has been in use since 1995 and gradually extended to include more health care centers in the hospital's catchment area. For this study, the data of all 40,013 enlisted patients of 34 family physicians in the period 1995 to 2002 were used.

### Identifying exposure

In the central electronic medical database, possible consultations concerning SVTP were identified using truncated keywords. After testing in another time period in the same database, successful truncated keywords were *t(h)romb\**, *phleb\** and *fleb\**. Afterwards, full con-

sultations were assessed to identify patients with SVTP from the initial potential cases. SVTP was diagnosed clinically according to the rules of the ICPC: "signs of inflammation along a superficial vein."<sup>11</sup>

As SVTP could be misdiagnosed, we scrutinized all consultations occurring within a month after the event for misclassified cases and excluded them. For each patient with thrombophlebitis, 2 nonexposed patients matched for center, age, and sex were randomly selected from the entire (nonexposed) enlisted population. The date of diagnosis of the thrombophlebitis was taken as index date.

The medical records of patients and controls were prospectively searched both electronically and manually by the same investigator for new thromboembolic events (DVT, PE, stroke, and myocardial infarction [MI]) during the 6 months following the index date. As all patients with any of these events were hospitalized, none of these diagnoses was made without adequate diagnostic procedures.

DVT was diagnosed when noncompressibility of the vein in the groin or fossa poplitea was observed with serial compression ultrasound (on day 1 or day 7). Problem lists contained information about the previous medical history.

### Statistics

We calculated the 6-month cumulative incidences of thromboembolic events and their 95% confidence intervals (CIs). Logistic regression was used to quantify the associations between SVTP and the 6-month cumulative incidences of DVT, PE, stroke, and MI, respectively. Odds ratios are adjusted for age and sex (matched design) and for a history of the particular outcome event at issue. Clustering by health center was accounted for by using robust variance estimation commands in Stata (version 8.2).

## Results

Initially, 206 patients with thrombophlebitis of the leg were identified.

Twenty patients were excluded as the thrombophlebitis was induced by an intravenous catheter. One 97-year-old male patient was excluded as 2 matched controls could not be found.

Thus, for this analysis, data were available for 185 patients with a spontaneous episode of thrombophlebitis of the lower limb and 370 age and sex-matched nonexposed patients. The mean age of the patients was 63.2 years (range, 20–96; standard deviation, 15.7), and 77% were female.

**TABLES 1 AND 2** show the distribution of the types of venous and arterial sequelae during the 6 months follow-up period in the 2 cohorts as well as the odds ratios (OR). DVT occurred in 2.7% of the SVTP patients as compared to 0.2% in the controls (OR=10.2; 95% CI, 2.0–51.6). Correction for DVT in the past decreased the OR to 7.1. ORs for PE (1.0), stroke (0.7), and MI (2.0) were smaller and had wider confidence intervals.

As expected, few patients received specific treatment (**TABLE 3**). If treatment was given, NSAIDs were most commonly prescribed. Occasionally compression stockings were advised.

## ■ Discussion

This study reveals that in the absence of prior DVT, primary care patients with spontaneous SVTP of the leg have a 10-fold increased risk of developing DVT during the subsequent 6 months when compared with an age- and sex-matched group without SVTP. The absolute risk of DVT, however, is just 2.7%. The associations between SVTP and other primary outcomes (coronary syndromes, stroke, and PE) were not statistically significant.

### Strengths of this study

The strengths of this study are that, as far as we know, this is the first study in general practice on arterial and venous events after a SVTP. With our search strategy within our patient registry, the

**TABLE 1**

### 6-mo incidence of thromboembolic events in patients with and without SVTP

OUTCOME	SVTP (N=185)	NO SVTP (N=370)
Deep venous thrombosis	5 (2.7%)	1 (0.2%)
Pulmonary embolism	1 (0.5%)	2 (0.5%)
Stroke	2 (0.5%)	2 (0.2%)
Myocardial infarction	1 (0.5%)	1 (0.2%)

**TABLE 2**

### Association between SVTP and cumulative 6-mo occurrence of major thromboembolic events

OUTCOME	OR (95% CI)	ADJUSTED OR* (95% CI)
Deep venous thrombosis	10.3 (2.0–51.6)	7.1 (0.9–65.6)
Pulmonary embolism	1.0 (0.07–15.0)	NE
Stroke	0.7 (0.04–10.3)	NE
Acute myocardial infarction	2.0 (0.1–45.0)	NE

OR, odds ratio; CI, confidence interval; NE, not estimable.

\*ORs were adjusted for age and sex (matched design). The adjusted OR is adjusted for a history of the particular outcome event at issue.

Within practice clustering was accounted for by using robust variance estimation commands in Stata (version 8.2).

identification of cases (patients with SVTP) is quite complete. The incidence of DVT in our patients is comparable with the incidence observed in previous studies in a referred population.<sup>8</sup> We were able to identify an almost perfectly matching control group.

### Limitations

Weaknesses are that we identified SVTP retrospectively, so no objective assessment of the diagnosis was undertaken. Family physicians diagnose this condition clinically.

It is possible that we had some misclassifications, but we scrutinized the files for alternative diagnoses. It cannot be excluded, however, that family physicians changed their diagnosis when it

TABLE 3

## Treatment of thrombophlebitis

TREATMENT	N (%)
NSAIDs	15 (8)
Compression stockings	7 (4)
Heparinoid cream	4 (2)
Acenocoumarol	2 (1)
NSAIDs and compression stockings	3 (2)
No treatment registered	154 (83)
NSAIDs, nonsteroidal anti-inflammatory drugs.	

proved wrong without writing that down. In that case, misclassification would lead to underestimation of the associations found.

A small proportion (13%) of the patients received an active pharmacological treatment. As NSAIDs could prevent DVT following SVTP, the finding of a 7- to 10-fold increased risk probably is a slight underestimation of the risk without active treatment.

Our study was not meant to detect concomitant DVT. Although DVT occurs simultaneously with SVTP quite frequently, patients with a concomitant DVT were excluded as they all will be referred for objective testing and consecutive treatment.<sup>12</sup>

Factors known to predict complications in patients with SVTP are severe venous insufficiency, varicose veins, male gender, older age, hypercoagulable state, and a history of DVT.<sup>10,13</sup> We controlled for age and gender and adjusted for a history of DVT, but were not able to identify the other predictive factors because of the retrospective identification of cases in our study. Especially venous insufficiency and varicose veins will not be recorded by family physicians, unless it causes medical problems. Inclusion of these risk factors would probably have led to information bias, as general practitioners

would be inclined to register these conditions when SVTP or DVT occurs.

## Treatment of SVTP

Treatment with low-molecular-weight heparin or NSAIDs during the 10 days following SVTP decreases the risk of developing a DVT with about 15% and 9% respectively.<sup>9</sup> To prevent 1 case of DVT in this group of patients, a family physician would have to treat 247 patients with low-molecular-weight heparin (absolute risk=2.7%) or 412 patients with an NSAID.

Although low-molecular-weight heparin therapy does have a low risk of major bleeding complications, treatment with NSAIDs has clear risks. The frequency of both gastrointestinal bleeding as well as renal failure increases by about 30% with the use of NSAIDs.<sup>14-16</sup> Moreover, this strategy appears not to be cost effective in preventing DVT. At this time, watchful waiting is probably the best strategy. Swelling of a leg following SVTP must raise the suspicion of a DVT and needs prompt further investigation.

## CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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## FAST TRACK

## Watchful waiting is the best strategy for SVTP



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