

# An unexpectedly high rate of pulmonary embolism in patients with superficial thrombophlebitis of the thigh

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**Purpose:** The rate of objectively proven pulmonary embolism in patients with thrombophlebitis of the greater saphenous vein was studied.

**Methods:** Consecutive ambulant patients with thrombophlebitis of the greater saphenous vein, involving the above-knee segment, underwent a complete venous echo color Doppler examination of the lower limbs, perfusion lung scanning, and chest radiography. A high probability of pulmonary embolism was defined as the presence of two or more large segmental defects, one large and two or more moderate perfusion defects, or four or more moderate perfusion defects, with no corresponding abnormality found by means of chest radiography.

**Results:** Of the 21 patients included in the study, findings compatible with a high probability of pulmonary embolism were detected in seven patients (33.3%; 95% CI, 14.6 to 57.0), although clinical symptoms of pulmonary embolism were present only in one patient. No association was found between the presence of thrombosis at the saphenofemoral junction and the risk for pulmonary embolism.

**Conclusion:** The rate of pulmonary embolism in patients with thrombophlebitis of the greater saphenous vein is unexpectedly high. This risk is similarly high in patients with thrombosis at the saphenofemoral junction and in patients without thrombosis at the saphenofemoral junction. Our results are consistent with those of other recent investigations and suggest that superficial thrombophlebitis of the thigh is not as benign a disease entity as previously described. (*J Vasc Surg* 1999;30:1113-5.)

Thrombophlebitis of the superficial veins (SVT) of the leg is usually regarded as a mild and uncomplicated disease. Although this is generally true in the case of acute thrombosis of the branches of the saphenous vein, the natural history of SVT involving the main trunk may not be as benign. The association of SVT with deep venous thrombosis (DVT) has been reported to range from 17% to 40%.<sup>1,2</sup> In a recent study, the progression of the thrombotic process from the greater saphenous vein into the

deep venous system has been reported in 8.6% of the cases, of which 10% embolized to the lungs, whereas no clinical symptoms of pulmonary embolism (PE) occurred when SVT did not involve the deep venous system.<sup>3</sup> The true frequency of PE is likely to have been underestimated in this study, because only patients in whom clinical manifestations suggestive of this complication developed underwent objective testing.<sup>3</sup> It is well known that, in patients with DVT, scintigraphic findings compatible with PE are found in approximately 50% of cases, although the most of these emboli are clinically silent.<sup>4-6</sup>

To assess the true rate of PE arising as a complication of SVT, we performed perfusional lung scanning and chest radiography in a consecutive series of patients with SVT of the greater saphenous vein of the thigh.

## METHODS

Consecutive ambulant outpatients, in whom there was the clinical suspicion of acute SVT of the greater saphenous vein involving the above-knee segment,

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Table I. Study patient characteristics

| Features  | PE<br>(N = 7)    | Non-PE<br>(N = 14) |
|---|------------------|--------------------|
| Age (years; mean, range)                                | 64<br>(60 to 78) | 60<br>(22 to 84)   |
| Sex (men:women)   | 3:4              | 8:6                |
| PDD (days; mean, range)                                 | 7 (2 to 9)       | 8 (2 to 10)        |
| Risk factors for venous thrombosis                      |                  |                    |
| Varicose veins  | 5                | 12                 |
| Previous SVT  | 2                | 4                  |
| Recent (within 3 months) surgery                        | 1                | 0                  |
| Recent (within 3 months) trauma                         | 0                | 1                  |
| Prolonged (> 7 days) immobilization                     | 0                | 1                  |
| Cancer  | 0                | 1                  |
| Ongoing prophylactic heparin                            | 2                | 3                  |
| Involvement of the SFJ                                  | 2                | 5                  |
| Mean distance of the thrombus head<br>from the SFJ (cm) | 10.5             | 9.0                |

PE, Pulmonary embolism; PDD, patient-doctor delay (interval between the onset of symptoms and the examination); SVT, superficial vein thrombosis; SFJ, saphenofemoral junction.

who were referred to the Unit Care of Angiology of the University Hospital of Padua from October 1997 to May 1998 were eligible for the study. Eligible patients had an extensive noninvasive study with venous echo color Doppler (Acuson XP 128 and Hewlett Packard Sonos 5500) of both legs, including the superficial vein system, the posterior tibial and peroneal veins, the popliteal, femoral and iliac veins, and the inferior cava vein. Patients in whom the clinical suspicion was not confirmed were excluded from the investigation, as were patients with involvement of the deep venous system, patients with signs of venous thrombosis in other peripheral body districts or a history of earlier venous thromboembolism, pregnant patients, and those patients who refused to give their informed consent. The involvement of the saphenofemoral junction was defined as the presence of a thrombosis involving the greater saphenous vein to a point less than 3 cm from the common femoral vein.

Recruited patients underwent chest radiography and perfusion lung scanning within 3 hours after the diagnosis of isolated SVT of the thigh was made by means of duplex scanning. Six-view perfusion lung scans were performed with technetium-99m-macroaggregated albumin. In patients with clinical symptoms of PE, ventilation lung scanning was also scheduled. Routine ventilation lung scanning in asymptomatic patients was not allowed by the local institutional board. By means of the results of objective tests, patients were classified in three categories: those patients with normal or near normal lung scanning results, those patients with a high probability of PE,

and those patients with an intermediate (non-high) probability of PE. A high probability of PE was defined as the presence of two or more large segmental defects, one large and two or more moderate perfusion defects, or four or more moderate perfusion defects, with no corresponding abnormality found by means of chest radiography or ventilation. A lung scan was defined as normal or near normal in the absence of perfusion abnormalities or in the presence of non-segmental perfusion defects with corresponding abnormalities detected by means of chest radiography or ventilation. All the other situations were regarded as an intermediate probability of PE.

The rate of PE and its 95% confidence intervals (CI) in the cohort of patients with SVT and the differences between the demographic and clinical characteristics of patients with and without findings suggestive of PE were calculated with standard methods. The Fisher exact test was used for the categorical variables, and the Student *t* test was used for the continuous variables. *P* values lower than .05 were considered statistically significant.

The local institutional board approved the study protocol.

## RESULTS

Of the 25 eligible patients, three patients were excluded because of the extension of the thrombosis in the common femoral vein, and one patient was excluded because of pregnancy. Thus, 21 patients with SVT of the thigh were included in the study.

At the time of recruitment, clinical symptoms suggestive of PE were present in one patient. The results of perfusion lung scanning were normal or near normal in 14 patients (66.6%), whereas findings compatible with a high probability of PE were found in seven patients (33.3%; 95% CI, 14.6 to 57.0), including the symptomatic patient, by means of the combination of lung scanning with chest radiography.

The main demographic and clinical characteristics of study patients are shown in Table I; they are listed separately for those patients with the scintigraphic demonstration of PE and those patients without the scintigraphic demonstration of PE. As shown in the table, no significant differences were observed between the two cohorts for age, sex, patient-doctor delay (interval between the onset of symptoms and the ultrasound examination), distance of thrombosis from the common femoral vein, and the presence of risk factors for venous thrombosis. The involvement of the saphenofemoral junction was demonstrated in two of seven patients with PE

(28.6%), and in five of the 14 patients without PE (35.7%; non-significant difference).

## DISCUSSION

The rate of PE observed in our cohort of patients with SVT of the thigh that did not involve the deep venous system of the leg was unexpectedly high. In fact, of the 21 consecutive patients undergoing objective lung investigations, findings suggestive of PE were found in seven patients, although clinical symptoms suggestive of this complication were present only in one patient. PE was as likely to develop in patients free from thrombi at the saphenofemoral junction as in patients with thrombosis involving the junction. Because the deep vein systems of both legs at the time of investigation were free from thrombi and thrombotic disease was not detectable in any other body district, it is likely that thrombotic material dislodged directly from the superficial veins of the thigh into the pulmonary circulation. These results are consistent with those of other recent investigations,<sup>1-3</sup> and strongly suggest that SVT is not always as benign and self-limiting as described. Because, however, our investigation was confined to ambulant outpatients, our conclusions cannot be generalized to all patients with SVT.

Our diagnostic approach did not include routine ventilation lung scanning in asymptomatic patients. Our results might, therefore, have overestimated the rate of PE, as defined according to the criteria of the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) study.<sup>7</sup> However, a re-evaluation of objective findings from patients enrolled in the PIOPED study showed that the frequency of PE among patients with different scan categories was not significantly different with perfusion scanning alone or combined perfusion/ventilation studies.<sup>8</sup> Reliable information could indeed be obtained if interpretation of perfusion scans was classified as high, low, or near normal/normal, in combination with chest radi-

ography.<sup>8</sup> Surprisingly, we did not observe cases with intermediate probability of PE. This finding was likely caused by the low sample size.

In conclusion, our results, although obtained in a small series of patients, strongly suggest that findings suggestive of PE are to be expected in a surprisingly high number of patients with SVT. Future ample studies are warranted to better explore the risk for DVT, PE, or both in patients with superficial thrombophlebitis of the thigh and to evaluate definitively the benefit-to-risk ratio of proper anticoagulant therapies in this disease.

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outpatient therapy with subcutaneous low-molecular-weight heparin and warfarin. This recommendation warrants caution inasmuch as it requires careful patient selection and education, availability of home health care, and close follow-up for laboratory monitoring and to assess for potential complications. Patients who cannot be anticoagulated and patients who have VTE recurrence despite anticoagulation should be considered for vena caval interruption.

### Superficial Thrombophlebitis

Although thrombophlebitis of the superficial leg veins uncommonly evolves into a thromboembolic event, many patients with clinically suspected **superficial thrombophlebitis** have a synchronous DVT. Patients with clot in the greater saphenous vein that extends above the knee are at risk for progression to DVT via the saphenous-femoral junction and should be considered for anticoagulation. When DVT has been excluded, **superficial thrombophlebitis** should be treated symptomatically with nonsteroidal anti-inflammatory drugs, heat, and graded compression stockings (fitted to exert 30 to 40 mm Hg of pressure on the extremity). Increased ambulation and elevation of the extremity above the level of the heart while at rest help to decrease venous stasis. Routine anticoagulation is not indicated for **superficial thrombophlebitis**.

### Isolated Calf or Saphenous Vein Thrombosis

The optimal management strategy for thromboses of the saphenous, tibial or peroneal veins remains controversial. Previously, isolated calf vein thrombosis was thought to be a benign self-limiting condition that carried a low risk of embolization and did not warrant anticoagulation. Longitudinal studies subsequently found that approximately 25% of isolated calf vein thromboses propagate proximally, prompting many experts to recommend treatment with anticoagulation as for DVT.<sup>[7]</sup> Others argue that a reasonable alternative in an otherwise healthy, ambulatory patient with an isolated calf thrombus and no other indication for anticoagulation is to prescribe antiplatelet therapy with aspirin (325 mg/day of enteric-coated acetylsalicylic acid) and arrange for close follow-up with serial duplex ultrasound scans (at 3-7 days) to evaluate for clot propagation.

### Phlegmasia Cerulea Dolens (Painful Blue Leg)

Massive iliofemoral occlusion results in swelling of the entire leg with extensive vascular congestion and associated venous ischemia producing a painful, cyanotic extremity. There may be associated arterial spasm resulting in phlegmasia alba dolens (painful white leg or milk leg), which may mimic an acute arterial occlusion. Prompt consultation with a vascular surgeon should be obtained because these patients may require emergent thrombectomy. If timely consultation is not possible, early thrombolytic therapy may be a limb-salvaging procedure.

### Upper Extremity Venous Thromboses

DVT of the upper extremity is less common than in the lower extremity and is associated most often with central venous catheters, pacemakers, and malignancies. Upper extremity DVT can cause PE, and all patients with upper extremity DVT require definitive treatment.<sup>[8][9][10]</sup> Treatment should be individualized to the particular clinical scenario, and, if present, central venous catheters should be removed from the affected extremity. Anticoagulation usually is indicated, and thrombolysis should be considered to treat apparent phlegmasia cerulea dolens of the arm.

### Complications

Although the most feared complication of DVT is fatal PE, DVT also can cause or exacerbate chronic venous insufficiency, resulting in disabling pain and swelling, varicose veins, skin changes, and nonhealing ulcers.

## PULMONARY EMBOLISM

### Pathophysiology

PE results from a clot that formed hours, days, or weeks earlier in the deep veins that dislodges, travels through the venous system, traverses the right ventricle, and lodges in the pulmonary vasculature. During transit and after docking in the pulmonary vasculature, the embolism produces a highly variable set of sensations felt by the patient, and a wide range of physiologic perturbations observed by the physician. This variability contributes to the difficulty in diagnosing PE. No one knows exactly how many patients