CLINICAL STUDY

Insufficient Recanalization of Thrombotic Venous Occlusion—Risk for Postthrombotic Syndrome

Luka Jeraj, MD, Mateja Kaja Jezovnik, MD, PhD, and Pavel Poredos, PhD, MD

ABSTRACT

Purpose: To investigate the relationship between recanalization rate of occluded veins after deep venous thrombosis (DVT) and development of postthrombotic syndrome (PTS).

Materials and Methods: Patients treated for DVT of the lower limbs were evaluated 12–36 months after acute DVT. Of 100 patients, 34 developed PTS, defined as Villalta score of ≥ 5. Symptoms and signs of PTS were assessed, and ultrasound examination of the veins was performed, checking for residual thrombus and presence of reflux.

Results: Patients with PTS were older (64.0 y vs 55.5 y; $P = .007$) and more frequently experienced recurrent DVT (15% vs 3%; $P = .030$). Patients with PTS had a lower rate of recanalization. Patients with residual thrombus appeared to be at increased risk for PTS development compared with patients with total recanalization (odds ratio 6.0; 95% confidence interval, 1.7–21.9; $P = .006$). No difference in the presence of reflux was observed.

Conclusions: Incomplete or absent recanalization is associated with a higher incidence of PTS, probably as a consequence of deteriorated blood flow and increased venous pressure. This suggests early recanalization could improve the outcome of DVT treatment in selected patients.

ABBREVIATIONS

DVT = deep venous thrombosis, PTS = postthrombotic syndrome

Postthrombotic syndrome (PTS) is a frequent chronic complication of deep venous thrombosis (DVT), affecting 20%–50% of patients with DVT within months to years after acute DVT. This syndrome is characterized by a combination of symptoms and signs, including leg heaviness, pain, edema, cramps, venous ectasia, hyperpigmentation, and venous ulceration. PTS severely affects the quality of life and increases health-related costs of patients with DVT. Many risk factors for PTS have been identified, such as elevated body mass index, older age, preexisting venous insufficiency, more proximal thrombosis, recurrent DVT of the same leg, and subtherapeutic anticoagulation (1).

Treatment of DVT in the initial phase is based on anticoagulation, which prevents clot propagation. In selected cases, systemic or local thrombolysis is used (2). Thrombus evolution is a natural process, usually leading to recanalization of the affected veins (3). Although thrombus load is reduced by 50% in the first 3 months after acute DVT, some residual thrombus is still present 3 years after the diagnosis in half of the patients (4,5). Numerous studies have shown an increased incidence of recurrent DVT in patients with less efficient recanalization, seen as residual thrombosis (6,7). Data on the direct relationship between PTS and recanalization are scarce; however, they indicate an association between residual thrombosis and PTS (8). The aim of this study was to assess the prevalence of PTS in patients with a history of DVT and further evaluate its relationship to the recanalization rate of the affected veins.

MATERIALS AND METHODS

This study included patients with a diagnosis of acute DVT of the lower limbs who underwent treatment in a single

From the Department of Vascular Disease (L.J., P.P.), University Medical Centre Ljubljana, Zaloška cesta 7, Ljubljana 1000, Slovenia; and Center for Advanced Heart Failure (M.K.J.), University of Texas Health Science Center at Houston, Houston, Texas. Received January 5, 2017; final revision received and accepted March 21, 2017. **Address correspondence to** P.P.; E-mail: pavel.poredos@kclj.si

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outpatient clinic. Consecutive male and female patients with acute iliofemoral, femoropopliteal, or popliteal thrombosis with or without calf involvement were included. Patients were excluded if they had active cancer, symptomatic peripheral arterial disease, or chronic inflammatory disease or were unwilling to participate in the study. Only patients treated with anticoagulation and compression were included; patients treated with thrombolytic therapy were excluded. All patients signed a consent form before inclusion in the study. The study was approved by the National Medical Ethics Committee.

There were 100 patients with a mean age of 58.9 years (± 11.2) included; 57% were men. The location of DVT was iliofemoral in 23%, femoropopliteal in 44%, and popliteal (with or without calf involvement) in 33%. DVT was unprovoked in 59% and provoked in 41%. A concurrent pulmonary embolism was present in 10% of patients; 7% had a recurrent DVT. Of patients, 61% had been treated with rivaroxaban, and 39% received warfarin together with dalteparin for the first 5–7 days, after which dalteparin was discontinued. Median time of anticoagulation was 6 months. Most patients in both groups were using compression therapy daily at least 6 months after DVT diagnosis (95%), either compression stockings (78%) or compression bandages (22%).

All patients were followed until the check-up performed in the period between 12 and 36 months after the acute episode of DVT. At that time, signs and symptoms of PTS were assessed by a single investigator (L.J.), and the Villalta score was calculated for each patient (9). A Villalta score $\geq$ 5 was considered to be PTS positive, whereas a Villalta score $<$ 5 was considered to be PTS negative.

Deep veins of the lower limbs were assessed with ultrasound using a 10-MHz probe (ProSound Ultra 7; Hitachi Aloka Medical, Ltd, Mitaka, Japan). Recanalization status was defined as complete recanalization if the vein was totally compressible to no more than 2 mm, partial recanalization if the vein was partially compressible, or absent recanalization if the vein was occluded and incompressible. The competence of the vein valve function was checked and was defined as incompetent if a reversal flow (reflux) was $>$ 0.5 second.

Statistical Analysis

Patients were divided into 2 groups based on development of PTS. Continuous variables with normal distribution, as determined by the Kolmogorov-Smirnov test, were expressed as means and standard deviations. Variables without normal distribution were expressed as median and interquartile range. Differences between groups in normally distributed variables were analyzed using a *t* test for unpaired data, and a Mann-Whitney *U* test was used for the others. Categorical variables were expressed as percentages; χ^2 test was used to test differences between the groups. Variables with significant or near-significant values were analyzed using univariate logistic regression. A *P* value $<$ .05 was considered significant. All statistical analyses were performed with IBM SPSS Statistics for Windows Version 23.0 (IBM Corp, Armonk, New York).

Table 1. Demographic Characteristics of Patients and Type of Acute DVT

Characteristic	PTS-Positive* (n = 34)	PTS-Negative (n = 66)	*P*
Age, y†	64.0 (58–71)	55.5 (49–67)	.007‡
Sex			
Male	15 (44%)	42 (64%)	.062
Female	19 (56%)	24 (36%)	
BMI, kg/m^2†	28.6 (25.6–33.9)	28.7 (24.6–30.9)	.421
Hypertension	16 (47%)	21 (32%)	.135
Hyperlipidemia	12 (35%)	26 (39%)	.689
Smoker	7 (21%)	12 (18%)	.771
Venous segment affected			
Iliofemoral	9 (26%)	14 (21%)	.593
Femoropopliteal	16 (47%)	28 (42%)	
Popliteal with/ without calf	9 (26%)	24 (36%)	
Concurrent pulmonary embolism	4 (12%)	6 (9%)	.673
Type of DVT			
Unprovoked	21 (62%)	38 (58%)	.687
Provoked	13 (38%)	28 (42%)	
Recurrent DVT	5 (15%)	2 (3%)	.030‡

BMI = body mass index; DVT = deep venous thrombosis; PTS = postthrombotic syndrome.
*PTS-positive patients are patients with Villalta score $\geq$ 5.
†Median (interquartile range), Mann-Whitney *U* test.
‡Statistically significant.

RESULTS

Patients were assessed for the presence of PTS 12–36 months after acute DVT (median 23 months). Of 100 patients, 34 developed PTS. These patients were older and more frequently had a recurrent DVT (Table 1). Most patients with PTS had a mild form (Villalta score = 5–9), whereas 15% developed a moderate form, and 3% developed a severe form.

Compared with patients without PTS, patients who developed PTS had a lower percentage of completely recanalized veins (9% vs 38%) and a higher percentage of both no recanalization (24% vs 6%) and partial recanalization (68% vs 56%). However, there was no statistically significant difference in the presence of reflux between the groups (Table 2). In the logistic regression analysis, residual thrombus in the vein showed an odds ratio of 6.0 for PTS development compared with complete recanalization (Table 3).

DISCUSSION

The main finding of this study is an association between vein recanalization in the chronic phase of DVT and the