From the New England Society for Vascular Surgery

Characteristics of provoked deep venous thrombosis in a tertiary care center

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ABSTRACT

Objective: Provoked deep venous thrombosis (DVT) is precipitated by a specific event. This paper compares the characteristics of provoked DVT in patients with transient risk (TR) factors and patients with continuous risk (CR) factors.

Methods: A retrospective review of records of all consecutive patients diagnosed with DVT between January 2013 and August 2014 was performed. Patients with provoked DVT were included in the TR group if the provoking event resolved in 2 weeks and they did not have ongoing risk of thrombosis. Patients in the CR group had a provoked DVT with ongoing risk of thrombosis due to individual factors deemed to be ongoing risks of thrombosis, such as cancer, hypercoagulable disorder, and prolonged immobilization. Demographics, risk factors, association with pulmonary embolism (PE) and its severity, risk of recurrent venous thromboembolism (VTE), and mortality were compared between the two groups.

Results: A total of 838 patients were diagnosed with DVT, and 50.7% (425) were provoked. There were 127 (29.9%) patients with TR and 298 (70.1%) with CR. TR patients were younger (60.4 ± 16.3 vs 65.9 ± 16.0; $P = .001$). TR was more likely to be provoked by surgery (70.9% vs 55.4%; $P = .003$), whereas CR was more likely to be provoked by immobilization (21.5% vs 12.6%; $P = .032$). CR patients were affected by cancer (48.7%) and hypercoagulable disorders (4.4%). TR patients were more likely to have calf DVTs (36.2% vs 26.2%; $P = .047$). There was a trend toward lower association with PE on presentation in TR (17.3% vs 21.1%; $P = .072$), but that did not reach statistical significance. However, TR factors were more likely to be associated with low-risk PE compared with CR factors (30.2% vs 54.6%; $P = .040$). After mean follow-up of 7.2 months, CR had higher risk of recurrent VTE (14.0% vs 6.8%; $P = .045$) and mortality (23.5% vs 7.1%; $P < .0001$).

Conclusions: Provoked DVT with CR factors affects older patients and is associated with high recurrence of VTE and mortality compared with provoked DVT with TR factors. (J Vasc Surg: Venous and Lym Dis 2017;5:477-84.)

Venous thromboembolism (VTE) is a disease process that includes both deep venous thrombosis (DVT) and pulmonary embolism (PE). The incidence is estimated at 0.1% to 0.2% per year in developed countries,[1-8] with approximately two-thirds of these patients presenting with DVT alone.[1] DVTs are categorized on the basis of etiology as either provoked, for which there is a specific precipitating factor (such as surgery, travel, trauma, or immobilization) that precedes thrombosis, or unprovoked in the absence of such events. The mainstay of therapy for VTE is anticoagulation. The American College of Chest Physicians recommends 3 months of anticoagulation for provoked DVT and extended therapy beyond 3 months for unprovoked DVT.[9] Most experts recognize that isolated calf vein thrombosis associated with a transient, reversible risk factor can be treated for 4 to 6 weeks of anticoagulation.[10] Even though the nature of the provoking event and its duration, whether transient or not, are crucial in the determination of the length of anticoagulation, there have been no studies comparing provoked DVTs with transient risk (TR) factors with provoked DVTs in patients with continuous risk (CR) factors for thrombosis. This study provides that comparison based on a review of all provoked DVTs in a tertiary care center. It also introduces a contemporary definition of TR factor to identify the patients with the lowest risk of VTE recurrence.

METHODS

A retrospective review of the records of all consecutive patients diagnosed with DVT by ultrasound between January 2013 and August 2014 in a tertiary care center

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was performed. Each patient's electronic medical record was reviewed for demographics and comorbidities. The study was approved by the human investigation committee. There was no need for patient consent.

Risk factors. Only patients with a provoked DVT were included in this study and were divided into two groups. The first group included the patients with a TR factor if the provoking event was transient and the patient did not have a CR factor for thrombosis. The second group included patients with a CR factor if the provoking event was not transient or if the patient had other significant factors that contributed to venous thrombosis. In this study, a TR factor is defined as a risk factor that resolves within a period of 2 weeks. The provoking risk factors were trauma; recent surgery or procedure; travel, in which the patient was seated for a continuous period of >4 hours; and immobilization, in which the patient was confined to bed for >72 consecutive hours, especially in the setting of hospitalization. A risk factor was considered a provoking event if the patient developed a DVT within a month (30 days) of the event. Some patients had more than one provoking factor. The types of surgery were divided by specialty and included orthopedic, neurologic, cardiothoracic, vascular, and general/transplant surgery. Urology, plastic surgery, ear-nose-throat surgery, and obstetrics and gynecology had a low number of DVTs and were grouped together as "other." Some patients developed DVT after procedures performed with deep sedation, such as percutaneous angiography and gastrointestinal endoscopy, and those were referred to as "procedures." DVT occurrence coinciding with initiation of oral contraceptive pills (OCPs) in women was also considered a provoked DVT. Women who developed a DVT after initiation of OCPs were in the TR group if the OCPs were discontinued. Placement of a central venous femoral line was considered a precipitating factor if the patient developed an ipsilateral lower extremity DVT while the catheter was in situ or within a month of removal of the line. Immobilization was considered a reversible risk factor if it lasted <2 weeks. Patients in the CR group had a continued increased risk of thrombosis even after resolution of the provoking event sometimes. This group included patients with provoked DVTs who additionally had cancer, hypercoagulable disorder, immobilization for >14 days, and paralysis. For instance, a patient who underwent colectomy for colon cancer and developed a postoperative DVT would be in the CR group because of the diagnosis of cancer. Patients who had history of recurrent VTE or unprovoked VTE were also considered to be in the CR group. Pregnant women with DVT were considered to be in the CR group because of the increased risk of thrombosis for several months and even in the early postpartum period.[11] Caprini scores were calculated.[12] Chronic conditions, such as congestive heart failure, varicose veins, and obesity, are not considered provoking events, and because they have low association with VTE (1 point on the Caprini score), they were not analyzed separately.

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center retrospective cohort study
- **Take Home Message:** Provoked deep venous thrombosis (DVT) with continuous risk factors was associated with higher recurrence of venous thromboembolism and mortality in 298 patients compared with outcome in 127 patients with provoked DVT with transient risk factors.
- **Recommendation:** The data suggest that provoked DVT with transient risk factors has lower recurrence and mortality than provoked DVT with continuous risk factors.

DVT characteristics. The characteristics of the thrombus on ultrasound and any association with PE were recorded. DVTs were divided by anatomic location into proximal if the popliteal vein or more central veins were affected and distal if only calf veins were affected. Extensive DVTs had thrombus in the proximal and distal segments. DVT was defined as occlusive if there was evidence of total occlusion of the vein with no flow at any level by ultrasound.

The severity of the PE was classified as low risk, intermediate risk, and high risk, depending on whether there were associated hemodynamic changes or other relevant markers. PE severity was classified as massive (high risk) if there was a sustained period >15 minutes of hypotension (systolic blood pressure <90 mm Hg), submassive (intermediate risk) if the systolic blood pressure was >90 mm Hg but accompanied by right ventricular dysfunction (dilation or elevated brain natriuretic peptide >90 pg/mL or N-terminal pro-brain natriuretic peptide >500 pg/mL) or myocardial necrosis (elevated troponin I >0.4 ng/mL or troponin T >0.1 ng/mL), and low risk if there was absence of these features.[13] Hemodynamically significant PE (HS PE) was defined as intermediate- or high-risk PE.

Treatment and outcomes. Treatment modalities including anticoagulation, inferior vena cava (IVC) filter placement, and catheter-directed thrombolysis were abstracted. Some patients received more than one treatment modality. Patients were considered to be managed by serial ultrasound if they had repeated ultrasound within a month of initial diagnosis. Any repeated ultrasound examination of any patient was reviewed, and thrombus burden was compared with the initial ultrasound. Patients with no evidence of DVT on