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# Risk factors for presence and severity of pulmonary embolism in patients with deep venous thrombosis

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#### **ABSTRACT**

**Objective:** The Caprini model estimates patients' risk for venous thromboembolism by 30 different factors. Hemodynamically significant pulmonary embolism (PE), defined as high-risk (massive) or intermediate-risk (submassive) PE, has high morbidity and mortality rates. This study tests whether the Caprini model and deep venous thrombosis (DVT) characteristics correlate with the prevalence of PE and hemodynamically significant PE in patients with DVT.

**Methods:** A retrospective review of patients diagnosed with DVT between January 2013 and August 2014 in a tertiary care center was performed. Multivariable analysis was used to determine predictors of PE and hemodynamically significant PE.

**Results:** Of 838 consecutive patients with DVT, 217 (25.9%) had concomitant PE at presentation, of whom 135 had hemodynamically significant PE (101 submassive PE, 34 massive PE). The mean age was 65 years, and 51.0% were women. There was no significant relation between age or gender and the occurrence of PE or hemodynamically significant PE. Patients with PE were less likely to have undergone recent surgery (18.4% vs 30.3%; P = .001), to have sepsis (4.6% vs 11.8%; P = .002), and to have higher Caprini scores (6.1 vs 6.5; P = .047). Patients with DVT were less likely to have hemodynamically significant PE after recent surgery (13.3% vs 27.2%; P = .011) but more likely to have hemodynamically significant PE with proximal DVT (80.7% vs 64.2%). There was no association between Caprini score and hemodynamically significant PE (6.3 vs 5.7; P = .171).

**Conclusions:** The Caprini model has a poor association with PE or hemodynamically significant PE in patients with DVT. Among all patients with DVT, a concomitant diagnosis of PE or hemodynamically significant PE is less common in those with sepsis or undergoing recent surgery but more common in those with proximal DVT. (J Vasc Surg: Venous and Lym Dis 2017: 1-6.)

Venous thromboembolism (VTE) is a blood clotting condition that includes deep venous thrombosis (DVT) and pulmonary embolism (PE). Although VTE can be manifested as DVT or PE separately, they often occur concomitantly. About 40% of patients presenting with DVT also have PE, and conversely, about 70% of patients presenting with PE are diagnosed with DVT.<sup>1</sup> It is

believed that >90% of PE originates from DVT in the lower extremities.<sup>2</sup>

PE can be further subdivided into massive/high risk, submassive/intermediate risk, and low risk, depending on the presence of hemodynamic instability and evidence of cardiac ischemia or strain. This classification has implications on management and prognosis. Patients who are hemodynamically unstable at the time of PE presentation have a 3-month mortality rate of 60% vs 15% for hemodynamically stable patients. Even in patients with submassive PE who are normotensive, right ventricular dysfunction seems to have significant hemodynamic consequences. Depending on the study, mortality ranges from about 4% to 13% in patients with submassive PE vs 0% to 1% in patients with low-risk PE.5

The mainstay of VTE prevention is pharmacologic prophylaxis, depending on individual risk factors. The Caprini model is commonly used to risk stratify patients for the development of VTE and to determine the optimal dose of prophylaxis. However, whether certain risk factors may increase specifically the risk of PE or whether patients at higher risk of VTE based on the Caprini score are more likely to develop PE in association with DVT is unknown. This study attempts to identify predictors of

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the occurrence of PE and its severity in a large population of patients with diagnosed DVT. The identification of a subgroup of patients at high risk of PE could potentially allow better risk stratification and justify more aggressive VTE prophylaxis.

#### **METHODS**

Study design. This is a retrospective study that looked at consecutive adult patients (age ≥18 years) with newly diagnosed DVT at a tertiary care center from January 2013 through August 2014. The study protocol and waiver of informed consent were approved by the hospital's Institutional Review Board. All ultrasound examinations were reviewed for findings of DVT.

Variables. The demographics and clinical characteristics of the patients were extracted. Caprini risk factors according to the 2005 version<sup>7</sup> were noted, including history of inflammatory bowel disease, cancer, congestive heart failure, sepsis within the past month, hypercoagulable conditions, major surgery, elective major lower extremity arthroplasty, hip fracture, pelvis fracture, and leg fracture. The presence of metastatic cancer was also noted when present. The variable recent surgery was defined as both arthroplasty and other major surgery. Ultrasound characteristics of DVT were also abstracted: occlusive vs nonocclusive, laterality, proximal vs distal. DVT was categorized as proximal if the popliteal vein or more central veins were involved. In patients with bilateral DVT, characteristics of the more extensive DVT were used for the analysis of that particular patient. The presence of PE confirmed by imaging that the treating physician chose to obtain was noted. PE severity was classified massive (high risk) as characterized by a sustained period >15 minutes of hypotension <90 mm Hg; submassive, by blood pressure >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, by an absence of these features.<sup>3</sup> Also included were cases in which PE was highly suspected as documented by the treating physician without definitive imaging. Hemodynamically significant PE was defined as either intermediate- or high-risk PE.

Outcomes. The characteristics and risk factors of patients with DVT and PE were compared with those of patients without PE. Similarly, the characteristics of patients with hemodynamically significant PE were compared with those of patients with low-risk PE. Independent predictors of PE in the total population of patients with diagnosed DVT were subsequently identified. Predictors of hemodynamically significant PE in the population of patients with diagnosed PE were identified through a separate analysis.

#### **ARTICLE HIGHLIGHTS**

- Type of Research: Retrospective cohort study
- Take Home Message: Among 838 consecutive patients with deep venous thrombosis (DVT), 25.9% also had pulmonary embolism (PE) and 16.1% had hemodynamically significant PE. PE was more frequent among those with proximal DVT (80.7% vs 64.2%), but there was no association between Caprini score and hemodynamically significant PE (6.3 vs 5.7; P = .17).
- **Recommendation:** The authors suggest that patients with proximal DVT should have more aggressive anticoagulant therapy and evaluation for PE.

Statistical analysis. Sample descriptive data were expressed as means  $\pm$  standard deviation. Categorical variables were expressed as counts and percentages. Student t-test was used for unadjusted comparison of continuous variables between two groups. The  $\chi^2$  test was used for unadjusted comparison of dichotomous variables between two groups. P values < .05 were considered statistically significant. Multivariable regression analyses were done to adjust for relevant variables. Statistical analyses were performed using Stata 11 1C software (StataCorp LP, College Station, Tex).

#### **RESULTS**

Study population. There were 838 patients with DVT during the study period; 217 (25.9%) patients had a concomitant PE at presentation, and 135 patients had hemodynamically significant PE (101 intermediate-risk/ submassive PE and 34 high-risk/massive PE). The population was 50.9% female, and the mean age was  $65 \pm 17$  years. The mean Caprini score was  $6 \pm 3$  and had normal distribution in the study population (Fig. A). When divided into subpopulations of patients without PE and those with PE, the mean Caprini score was  $6.5 \pm 2.9$  and  $6.1 \pm 2.8$ , respectively (Fig. B and C). DVT most commonly affected both proximal and distal leg veins (38.2%), followed by proximal only (35.7%) and distal only (26.1%). The number of left- vs right-sided DVTs was roughly equal (50.4% vs 49.6%). Moreover, 39.3% of patients had cancer, 22.1% had history of VTE, 27.2% had recent major surgery, and 3.0% had recent major joint surgery (total with recent surgery, 30.2%; Table I).

Predictors of PE. In patients with vs without concomitant PE (Table II), there was no significant association with age or gender. Patients with PE were less likely to have undergone recent surgery (18.4% vs 30.3%; P=.001) and less likely to have sepsis (4.6% vs 11.8%; P=.002) but more likely to have inflammatory bowel disease (3.7% vs 0.6%; P=.001) and to have a body mass index >25 (74.7% vs 68.0%; P=.048). However, on multivariable analysis, only recent surgery (P=.001) and sepsis

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