Prospective Evaluation of a Screening Protocol to Exclude Deep Vein Thrombosis on the Basis of a Combination of Quantitative D-Dimer Testing and Pretest Clinical Probability Score

Takashi Yamaki, MD, Motohiro Nozaki, MD, Hiroyuki Sakurai, MD, Masaki Takeuchi, MD, Kazutaka Soejima, MD, Taro Kono, MD

BACKGROUND: Clinical signs and symptoms such as swelling, pain, and redness are unreliable markers of deep vein thrombosis (DVT). Because of this venous duplex scanning (VDS) has been heavily used in DVT detection. The purpose of this study was to determine if a combination of D-dimer testing and pretest clinical score could reduce the use of VDS in symptomatic patients with suspected DVT.

STUDY DESIGN: One hundred seventy-four consecutive patients with suspected DVT were prospectively evaluated using pretest clinical probability (PCP) score and D-dimer testing before VDS. After calculating clinical probability scores developed by Wells and associates, patients were divided into low risk ($\leq$ 0 points), moderate risk (1 to 2 points), and high risk ($\geq$3 points) PCP.

RESULTS: One hundred fifty-eight patients were enrolled. The prevalence of DVT in this study was 37%. Thirty-eight patients (24%) were classified as low risk, 64 (41%) as moderate risk, and 56 (35%) as high risk PCP. DVT was identified in only one patient (2.6%) with low risk PCP. In contrast, DVT was found in 22 (34%) with moderate risk, and 35 (63%) with high risk PCP. In the high and moderate risk PCP groups, positive scan patients had a markedly higher value of D-dimer assay than negative scan patients ($p = 0.0001$ and $p = 0.0057$, respectively). In the low risk PCP patients, D-dimer testing provided 100% sensitivity, 46% specificity, 4.8% positive predictive value, and 100% negative predictive value in the diagnosis of DVT. Similarly, in the moderate risk PCP, the D-dimer testing showed 100% sensitivity, 45% specificity, 49% positive predictive value, and 100% negative predictive value. In the high risk group, D-dimer testing achieved 100% sensitivity, 57% specificity, 80% positive predictive value, and 100% negative predictive value in the diagnosis of DVT. These results suggested that 36 of 158 patients who had a non-high PCP (low and moderate PCP) and a normal D-dimer concentration were considered to have no additional investigation, so VDS could have been reduced by 23% (36/158).

CONCLUSIONS: A combination of D-dimer testing and clinical probability score may be effective in avoiding unnecessary VDS in suspected symptomatic DVT in the low and moderate PCP patients. The need for VDS could be reduced by 23% despite a relatively high prevalence of DVT. (J Am Coll Surg 2005;201:701–709. © 2005 by the American College of Surgeons)

Currently, more than 600,000 cases of pulmonary embolism occur with an estimated annual incidence of 23 to 69 per 100,000 population in the US alone.[1-3] Because pulmonary embolism is potentially life threatening, and 80% of cases arise from lower extremity veins,[4] diagnosis and treatment of deep vein thrombosis (DVT) is of primary importance. Although it is well recognized that the risk of DVT increases in patients with specific diseases,[5-7] clinical signs and symptoms such as swelling, pain, and redness are unreliable markers of DVT. So attempts have been made to improve the discriminating power in clinical assessment.[8-10] But this method cannot be used alone in clinical decision making.

Competing Interests Declared: None.

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From the Department of Plastic and Reconstructive Surgery, Tokyo Women's Medical University, Tokyo, Japan.

Correspondence address: Takashi Yamaki, MD, Department of Plastic and Reconstructive Surgery, Tokyo Women's Medical University, 8-1, Kawadacho, Shinjuku-ku, Tokyo, 162-8666, Japan.

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Abbreviations and Acronyms

DVT = deep vein thrombosis
EIA = enzyme immunoassay
NPV = negative predictive value
PCP = pretest clinical probability
PPV = positive predictive value
VDS = venous duplex scanning

The validated approach to patients with suspected DVT includes contrast venography, which had been regarded as the "gold standard" in detecting the presence and distribution of DVT. Recently, however, venous duplex scanning (VDS) has largely replaced contrast venography as the initial diagnostic test for DVT, with high sensitivity and specificity.[11] VDS has been shown to be a reliable and accurate means of identifying lower extremity venous thromboembolism, using B-mode and color flow Doppler imaging.[12-15] So, VDS has been heavily used in DVT detection, because it is noninvasive, and neither iodinated contrast media nor ionizing radiation are used; both are time consuming and expensive today.

D-dimer is a fragment specific to the degradation of fibrin, and is considered to indicate endogenous fibrinolysis in the presence of IV thrombosis.[16] Several studies have shown that a new rapid enzyme immunoassay (EIA) or ELISA are useful tests for suspected DVT with high sensitivity, moderate specificity, and high negative predictive value (NPV), so D-dimer assay plays an adjunct role in excluding the diagnosis of DVT.[17-19] The purpose of this study was to determine if a combination of quantitative D-dimer assay and pretest clinical score could be a valid approach for reducing the use of VDS in symptomatic patients with suspected DVT.

METHODS

Patients

Between June 2003 and January 2004, 174 consecutive patients with suspected DVT were prospectively evaluated in the Department of Plastic and Reconstructive Surgery, Tokyo Women's Medical University Hospital. Both inpatients and outpatients were included in the study. Exclusion criteria from the study included previously diagnosed DVT; features of chronic DVT on duplex scan results; symptoms lasting 1 month; therapeutic dose anticoagulation instituted for more than 48 hours before examination; or clinically suspected or confirmed pulmonary embolism with duplex ultrasonography scanning being performed to exclude thrombosis in the absence of lower limbs.

Clinical probability score

The pretest clinical probability (PCP) for DVT was assessed by junior residents using a questionnaire developed by Wells and associates[9] (Table 1). One point was added for each positive finding and two points were subtracted from the total points if an alternative diagnosis as likely as or more likely than DVT was found. After calculating clinical probability scores, patients were divided into low risk ($\leq$ 0 points), moderate risk (1 to 2 points), and high risk ($\geq$ 3 points) groups.

D-dimer assay

After calculating the PCP score of each patient, blood samples were collected in the clinical laboratory department, and D-dimer testing was performed by examiners who were not aware of the PCP scores. Plasma levels of D-dimer were measured by a commercially available EIA kit (D-dimer test, F; Kokusai-Shiyaku, Kobe, Ja-

Table 1. Pretest Clinical Probability Score

Criteria	Score
Active cancer (treatment ongoing) or within previous 6 mo or palliative	+1
Paralysis, paresis, or recent plaster immobilization of the lower extremity	+1
Recently bedridden for more than 3 days or major operation within 4 wk	+1
Localized tenderness along the distribution of the deep venous system	+1
Entire leg swollen	+1
Calf swelling by > 3 cm when compared with the asymptomatic leg (measured below tibial tuberosity)	+1
Pitting edema	+1
Collateral superficial veins (nonvaricose)	+1
Alternative diagnosis as likely as or more likely than DVT	−2

The examiner assesses each factor, and the score is calculated as the sum in each patient. One point is given for every positive finding, and 2 points are subtracted if an alternative diagnosis as likely as DVT is found. Low risk ($\leq$ 0 points); moderate risk (1–2 points); high risk ($\geq$ 3 points).
DVT, deep vein thrombosis.