Combination of D-dimer testing and pretest clinical probability score

Original Article

Title of the article:

Prospective evaluation of a screening protocol to exclude the deep vein thrombosis on the basis of a combination of quantitative D-dimer testing and pretest clinical probability score

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Brief title:
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ABSTRACT

BACKGROUND: The clinical signs and symptoms such as swelling, pain, and redness are unreliable markers of deep vein thrombosis (DVT). As a consequence, 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 (≤ 0 points), moderate risk (1–2 points), and high risk (≥ 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 1 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 significantly higher value of D–dimer assay than negative scan patients (p=0.0001 and =0.0057, respectively). In the low risk PCP patients, D–dimer testing provided 100% sensitivity, 46% specificity, 4.8% positive predictive value (PPV), and 100% negative predictive value (NPV) in the diagnosis of DVT. Similarly, in the moderate risk PCP, the D–dimer testing showed 100% sensitivity, 45% specificity, 49% PPV and 100% NPV. In the high risk group, D–dimer testing achieved 100% sensitivity, 57% specificity, 80% PPV, and 100% NPV in the diagnosis of DVT. These results suggested that 36 of 158 patients who have a non–high PCP (low and moderate PCP) and a normal D–dimer concentration considered to have no further investigation, and thus VDS could have been reduced by 23% (36/158).

CONCLUSIONS: A combination of D–dimer testing and clinical probability score may be effective in terms of 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.

Key words: deep vein thrombosis, D–dimer assay, clinical provability score, venous duplex scans
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INTRODUCTION

Currently, more than 600,000 cases of pulmonary embolism (PE) occur with an estimated annual incidence of 23–69 per 100,000 population in the United States alone.\textsuperscript{1,2,3} Since PE is potentially life-threatening, and 80% of cases arise from lower extremity veins,\textsuperscript{4} diagnosis and treatment of deep vein thrombosis (DVT) is of primary importance. Whilst it is well recognized that the risk of DVT increases in patients with specific diseases,\textsuperscript{5,7} clinical signs and symptoms such as swelling, pain, and redness are unreliable markers of DVT. Therefore, attempts have been made to improve the discriminating power in clinical assessment.\textsuperscript{5-10} However, this method cannot be used alone in clinical decision making.

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.\textsuperscript{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.\textsuperscript{12-15} As a consequence, VDS has been heavily used in DVT detection, because it is noninvasive, and neither iodinated contrast media nor ionizing radiation are used, which are both 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 intravenous thrombosis.\textsuperscript{16} Several studies have shown that a new rapid enzyme immunoassay (EIA) or enzyme-linked immunosorbent assay (ELISA) is a useful test for suspected DVT with high sensitivity, moderate specificity, and high negative predictive value, and thus, D–dimer assay plays an adjunct to exclude the diagnosis of DVT.\textsuperscript{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.

MATERIALS AND 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: (1) previously diagnosed DVT; (2) features of chronic DVT on duplex scan results; (3) symptoms lasting 1 month; (4) therapeutic dose anticoagulation instituted for greater than 48 hours before examination; or (5) clinically suspected or confirmed pulmonary embolism with duplex ultrasound scanning being performed to exclude thrombosis in the absence of lower limbs.

Clinical probability score

The pre–test clinical probability (PCP) for DVT was assessed by junior residents using a questionnaire developed by Wells and associates (Table I).\textsuperscript{9} One point was added for each positive finding and 2 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 (≤ 0 points), moderate risk (1–2 points), and high risk (≥3 points) groups.

D–dimer assay

After calculating the PCP score of each patient, blood samples were collected at the clinical laboratory department, and D–dimer testing was performed by the examiners who were not aware of the pretest clinical probability scores. The plasma levels of D–dimer were measured by a commercially available enzyme immunoassay (EIA) kit (D–dimer test–F; Kokusai–Shiyaku, Kobe,
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Japan). The results were expressed as μg/mL. Briefly, D–dimers are bound to murine anti–human D–dimer monoclonal antibodies fixed on the surface of the test tube. After incubation and washing, an excess of polyclonal rabbit anti–D–dimer coupled with peroxydase was added to the test tubes and bound to the fixed D–dimer–anti–D–dimer complex. After washing the excess enzyme conjugated antibody, the amount of D–dimer fixed to the tube was quantified by adding a substrate that converts to a colored substance using peroxydase. The recommended cut–off value of 0.5μg/mL was used.

Venous duplex scans

All venous duplex studies were performed by one experienced physician (T.Y.) who was blinded to the results of PCP and D–dimer testing. A color duplex scanner (LOGIQ 500MD: GE Medical Systems, Milwaukee, WI, USA) with a 5–10 MHz transducer was used. Initially, each patient was placed supine in a reverse Trendelenburg position at 15°. Venous duplex scanning began at the distal segment of the external iliac vein and the common femoral vein, and moved to the femoral vein at the adductor canal. The deep femoral vein, and the anterior and posterior tibial veins were also recorded. Afterwards, the patient was placed in a prone position with the knee flexed at 30°, and the residual popliteal, peroneal, gastrocnemius and soleal veins were evaluated. The diagnosis of DVT was based on both noncompressibility of the vein on B–mode, and no spontaneous flow on color Doppler imaging. If there was no intraluminal defect with a full venous compressibility, and a normal flow, the examination was considered as negative. Thrombosis was considered as proximal if thrombus was detected in the deep veins in the pelvis, the thigh, and popliteal region with or without calf vein thrombosis. Thrombosis was considered as distal if thrombus was detected only in the calf veins.

Screening Protocol

All patients had an initial VDS at presentation after calculating PCP and examining D–dimer assay. Patients with moderate or high PCP and a normal D–dimer assay had a single VDS at presentation. Serial VDS was not routinely performed to confirm initial negative results in patients who have a normal D–dimer test because this procedure has been described as costly and inefficient. Patients who have an elevated D–dimer assay and initial negative scan had a VDS repeated after 1 week.

Statistical analysis

All data were analyzed using StatView for Windows (Version 5.0, SAS Institute Inc., Cary, NC). The unpaired t test was used to evaluate differences between means for continuous data, and a chi–square test was used to evaluate differences between proportions. The analysis of variance (ANOVA) was used for comparison of D–dimer assay means among high, moderate, and low PCP groups. Continuous data were expressed as mean ± standard deviation (SD). Statistical significance was defined as p < 0.05.

RESULTS

Of the 174 consecutive patients evaluated, 16 patients were excluded according to the criteria previously described. Thus 158 patients were eligible for this study. The study group included 88 (56%) inpatients and 70 (44%) outpatients. The mean age of the patients was 59 (range 19–91) years. There were 106 (67%) women and 52 (33%) men. Of the 158 patients, 58 (37%) were found to have DVT.

Table II shows the distribution of the patients with low, moderate, and high risk PCP according to the calculated clinical probability score. Of 158 patients, a total of 38 patients (24%) were classified as low, 64 (41%) as moderate, and 56 (35%) as high risk PCP. In the low risk PCP, DVT was identified in only 1 patient (3%). In contrast, DVT was found in 22 (34%) in moderate, and 35 (63%) in high risk PCP patients. The results of D–dimer assay showed a statistically higher mean value in the high risk PCP compared to the low risk PCP patients (7.83 ± 9.85 vs. 0.81 ± 0.73, respectively, p=0.024). But there was no statistically significant difference in
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the mean D–dimer assay values between moderate and low risk PCP patients (2.21 ± 3.31 vs. 0.81 ± 0.73, respectively, \( p=0.664 \)). Similarly, no statistically significant difference was found in the value of D–dimer testing between high and moderate risk PCP patients (7.83 ± 9.85 vs. 2.21 ± 3.31, respectively, \( p=0.621 \)).

Table III shows the results of the D–dimer assay between positive and negative scan patients. In the high risk PCP, positive scan patients had a significantly higher mean value of D–dimer assay than negative scan patients (11.98±10.46 vs. 0.91±0.75, respectively, \( p=0.0001 \)). Similarly, in the moderate risk PCP, there was a statistically significant difference in the value of D–dimer assay between positive and negative scan patients (4.37±4.91 vs. 1.14±0.89, respectively, \( p=0.0057 \)).

The discriminating power of D–dimer testing by PCP category is shown in Table IV. In the low risk PCP, D–dimer testing provided 100% sensitivity, 46% specificity, 5% positive predictive value (PPV), and 100% negative predictive value (NPV) in the diagnosis of DVT. Similarly, in the moderate risk PCP, the D–dimer testing showed 100% sensitivity, 45% specificity, 49% PPV and 100% NPV. In the high risk group, D–dimer testing achieved 100% sensitivity, 57% specificity, 80% PPV, and 100% NPV in the diagnosis of DVT.

The distribution of DVT in the moderate and high risk PCP is shown in Table VI. Proximal DVTs were found in 27 (77%) patients in the high risk PCP, whereas only 6 (27%) were found to have proximal DVTs in the moderate risk PCP \( (p=0.0002) \).

Repeated ultrasonic examinations were applied in 9 patients with high risk PCP who had an abnormal D–dimer testing and an initial negative VDS. After 1 week, all patients were found to have a negative VDS, and no further examinations were performed.

These results showed that 36 of 158 patients who have a non–high PCP (low and moderate PCP) and a normal D–dimer concentration considered to have no further investigation, and thus VDS could have been reduced by 23% (36/158).

**DISCUSSION**

The clinical symptoms of DVT may include leg swelling, pain, and erythema which result from outflow obstruction and venous wall inflammation.\(^{21}\) The clinical presentation of DVT, however, varies from minimal symptoms to massive features of DVT, and it is commonly believed that this variability is unreliable in predicting the diagnosis of DVT in patients with leg symptoms, leading to a large number of negative studies with VDS.

Several investigators have evaluated clinical parameters that might predict the diagnostic value of VDS. Nypaver and associates analyzed the factors predictive of a negative study, and found that the set of no neoplasia, symptom duration greater than 7 days, and difference in thigh circumference of less than 3 cm had a NPV of 96 to 97% among outpatients. This set of factors, however, gave a NPV of only 75% among inpatients.\(^{21}\) Criado and associates investigated the predictive value of clinical features and the use of ultrasonographic testing in the diagnosis of DVT, and concluded that a NPV of the absence of a calf circumference difference less than 2 cm and no history of trauma, operation, DVT, malignancy, or hypercoagulable state in the absence of acute DVT was 92% for inpatients and 97% for outpatients.\(^{22}\) The combination of various clinical factors increased the PPV but decreased the sensitivity, making them useless for the purpose of selecting patients at high risk of having DVT.\(^{14}\)

Wells and associates developed a clinical model for estimating pretest probability for DVT, and divided patients with suspected DVT into high, moderate, and low probability groups.\(^{9}\) Using this criteria, they found that patients in the high risk PCP group had a 75% chance of DVT compared with 17% and 3% chance in the moderate and low risk groups, respectively. They found that the difference in prevalence of DVT in the three categories was statistically significant, and concluded that combination of patients’ PCP with ultrasound results had the potential to simplify and improve the diagnostic process in patients with suspected DVT. Our present study agrees with most of the published study on pretest probability on DVT, however, the variability of sensitivity and NPV between the groups limits the usefulness of clinical probability score as a single pretest.
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The role of D–dimer assays in the diagnosis of patients with suspected DVT has been previously reported.\textsuperscript{16-19} There are several methods that are commercially available for measuring D–dimer concentrations. Latex agglutination assay is relatively inexpensive, and results are quickly available, but it has low sensitivity and specificity for DVT.\textsuperscript{18} Recent studies have shown that a rapid method on the basis of whole blood agglutination that could be performed at the bedside by a technologist is useful in excluding patients without DVT.\textsuperscript{23, 24} Wells et al. evaluated 214 patients with clinically suspected deep vein thrombosis using the SimpliRED D–dimer assay, which had a sensitivity of 93% for proximal deep vein thrombosis and a negative predictive value of 98%.\textsuperscript{26} Turkstra et al. also found similar accuracy when using the SimpliRED assay.\textsuperscript{27} But other investigators demonstrated that this method has relatively low sensitivity for DVT.\textsuperscript{28, 29} Despite the laboratory based and relatively time consuming examinations, EIA or ELISA–based techniques are widely used, with the highest sensitivity and NPV for DVT. D–dimer is a product of fibrin degradation by plasmin, and is generated in the presence of thrombus. The D–dimer testing, therefore, is expected to increase in relation to the extent of the thrombus process. Furthermore, D–dimer assays may be positive in patients with other conditions that could activate the coagulation and fibrinolytic cascade.\textsuperscript{30-32} Caution should be exercised when considering the use of this assay as the sole exclusionary pre–selection test for the evaluation of DVT.\textsuperscript{19,19} Indeed, our study demonstrated that the mean values of D–dimer assays in negative scan patients were greater than 0.5$\mu$g/mL. The high sensitivity D–dimer assay for DVT might be achieved at the expense of specificity, and this will cause a high frequency of false positive results, thereby reducing diagnostic utility.\textsuperscript{29}

The use of D–dimer testing combined with PCP has been established as an adjunct to the VDS by many.\textsuperscript{23-25, 28, 29, 31, 32} Combination of these methods has the ability to make the diagnosis of DVT more convenient and economical. When considering proximal DVT, this combination provided a sensitivity and NPV of 100%.\textsuperscript{29} Similarly, this combination had a sensitivity of 82% and NPV of 97% for isolated calf vein thrombosis, which showed no significant decrease compared to proximal DVT.\textsuperscript{29} In the present study, quantitative EIA D–dimer assay showed a significant increase as the clinical risk progressed. Furthermore, there was a significant difference between the mean level of D–dimer of patients with and without DVT among the moderate and the high risk patients. The excellent sensitivity and NPV of 100% were maintained in each group at a cut–off level of 0.5$\mu$g/mL. To exclude DVT, the PCP and the D-dimer testing are recommended instead of using the D–dimer testing alone.

Several investigators propose that patients with a low PCP and a normal D–dimer concentration do not need further vascular investigations.\textsuperscript{23, 29, 33} This approach will reduce the need for VDS. And the use of D–dimer testing also reduces the need for repeated VDS without thromboembolic complications in patients who are likely to have DVT and establishes a definitive diagnosis on the day of presentation in a larger proportion of the patients.\textsuperscript{34} Anderson et al. showed that observed NPV of D–dimer using SimpliRed assay was 100% in the low probability patients, 94.1% in moderate probability patients, and 86.7% in high probability patients.\textsuperscript{25} He concluded that D–dimer assay may be a potentially useful adjunctive test to exclude the diagnosis of DVT in patients at low pretest clinical probability. Furthermore, Schutgens et al. showed that DVT could be also excluded in patients with normal D–dimer concentration and a low and moderate PCP.\textsuperscript{35} He used latex agglutination D–dimer assay to fulfill the strategy because the sensitivity of the SimpliRED D–dimer assay was only 85%.\textsuperscript{33} In this present study, EIA D–dimer has the highest sensitivity and NPV for DVT,\textsuperscript{17-19} and 36 (23%) patients who have a normal D–dimer assay and a low and moderate PCP could be safely excluded from subsequent VDS in this regard. For exclusion of DVT in patients with a non–high PCP and a normal D–dimer concentration, we recommend the use of D–dimer assay with the sensitivity and the NPV of nearly 100%.

With D–dimer testing and PCP, the discriminating power of its components is important. The specificity and PPV for the combined procedure were poor especially in low and moderate PCP. It might be assumed that additional D–dimer testing will have little impact on the patient’s treatment especially in case of a low PCP. However, Aschwanden et al. showed that the impact of both components in the algorithm is equivalent and that neglecting to perform the D–dimer testing would have led to an unacceptably high number of false–negative pretest results.\textsuperscript{35}

The overall prevalence of DVT in our study was 37% which was relative high compared
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with recent studies. In our institute, the prevalence of DVT has been greater than 30% for several years. We have been trying to rule out even small isolated calf vein thrombi as well as proximal vein thrombosis because missed diagnosis directly reflects the low sensitivity of VDS in the diagnosis of DVT, leading to the large volume of negative VDS studies. When comparing the prevalence of DVT, our study showed that the proportion of the moderate PCP is higher than previous studies. In this study, 73% of the patients who have an elevated D–dimer assay and a moderate PCP have calf vein thrombosis without proximal vein involvement, and much care should be taken in the evaluation of these patients.

This study provides a new diagnostic strategy for patients with suspected DVT as demonstrated in Fig 1. All the patients are stratified into non–high (low or moderate) risk, and high risk group according to PCP method, and undergo D–dimer testing. Patients who have a non–high PCP and a normal D–dimer concentration need no further investigation. Patients with a high PCP and a normal D–dimer concentration undergo a single VDS at presentation. Patients with an abnormal D–dimer concentration and an initial negative scan result have repeated VDS after 1 week because these patients have possible high prevalence of DVT. And VDS is still necessary for these patients because the distribution and the extent of thrombus affect the treatment strategy for acute DVT. Our previous study revealed that the lower extremity venous segments show different proportions of occlusion, partial recanalization, and total recanalization after acute DVT, and the oral anticoagulant therapy should be indicated for ≤ 3 months in patients with isolated calf vein thrombosis, 3–6 months in those with isolated popliteal vein thrombosis, and ≥ 6 months in those with isolated common femoral, femoral, and multisegment DVT.  

A duplex scan is estimated to cost $67 (¥7000) per procedure and D–dimer assay approximately cost $12 (¥1300) per test. With this strategy, 23% of referrals who were found to have low or moderate risk patients with negative D–dimer results would proceed to D-dimer testing. The average charge per patients associated with this strategy was $63 (¥6710). The use of the combined pretest procedure will result in a substantial reduction of costs. But it might be assumed that the saving potential will change in populations where the incidence of DVT is much lower. In this cost estimation, however, further related direct and indirect costs (time to refer patients for a diagnostic study, loss of productivity with a patient having to spend time for additional test, etc.) were not considered.  

At the moment, all venous duplex studies were performed by a single experienced physician (T.Y.) including “off–hours” emergency venous duplex scanning, several investigators developed protocols for evaluation of the patients suspected of having DVT in the emergency department (ED). Langan III el developed the algorithm for treatment of patients with suspected DVT seen after 9 pm, and found that the ED physician could give the patient low molecular weight heparin, and the venous duplex evaluation could be put off until the next routine working hours if the referring physician suspected that a patient had a DVT during “off–hours”, and the patient had no contraindications for anticoagulation. He concluded that after–hours VDSs could be reduced by 89% without causing patients’ morbidity or mortality. Anderson el. found that ED physicians could accurately stratify patients suspected DVT into high, moderate, and low PCP, and that SimpliRED D–dimer assay could be a potentially useful adjunctive test to exclude the diagnosis of DVT in patients with low PCP.  

In conclusion, a combination of D–dimer testing and clinical probability score provides an effective means in terms of avoiding a large number of unnecessary VDS in suspected symptomatic DVT in the low and moderate PCP for DVT. The need for VDS could be reduced by 23% despite a relatively high prevalence of DVT, and this proposed protocol may be very helpful to the hospitals with busy vascular related physicians.
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REFERENCES

Combination of D-dimer testing and pretest clinical probability score


Combination of D-dimer testing and pretest clinical probability score

<table>
<thead>
<tr>
<th>Factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active cancer (treatment ongoing) or within previous 6 months or palliative</td>
<td>+1</td>
</tr>
<tr>
<td>Paralysis, paresis, or recent plaster immobilization of the lower extremity</td>
<td>+1</td>
</tr>
<tr>
<td>Recently bedridden for more than 3 days or major surgery within 4 weeks</td>
<td>+1</td>
</tr>
<tr>
<td>Localized tenderness along the distribution of the deep venous system</td>
<td>+1</td>
</tr>
<tr>
<td>Entire leg swollen</td>
<td>+1</td>
</tr>
<tr>
<td>Calf swelling by &gt; 3cm when compared with the asymptomatic leg (measured below tibial tuberosity)</td>
<td>+1</td>
</tr>
<tr>
<td>Pitting edema</td>
<td>+1</td>
</tr>
<tr>
<td>Collateral superficial veins (nonvaricose)</td>
<td>+1</td>
</tr>
<tr>
<td>Alternative diagnosis as likely as or more likely than DVT</td>
<td>–2</td>
</tr>
</tbody>
</table>

- Low risk (≤ 0 points)
- Moderate risk (1-2 points)
- High risk (≥3 points)

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.

**Table I.**
Combination of D-dimer testing and pretest clinical probability score

<table>
<thead>
<tr>
<th>Pretest clinical probability</th>
<th>n (%)</th>
<th>Frequency of DVT (%)</th>
<th>D–dimer (μg/mL)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td>56 (35.4)</td>
<td>35 (62.5)</td>
<td>7.83 ± 9.85</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>64 (40.5)</td>
<td>22 (34.4)</td>
<td>2.21 ± 3.31</td>
</tr>
<tr>
<td>Low risk</td>
<td>38 (24.1)</td>
<td>1 (2.6)</td>
<td>0.81 ± 0.73</td>
</tr>
<tr>
<td>Total</td>
<td>158 (100)</td>
<td>58 (36.7)</td>
<td></td>
</tr>
</tbody>
</table>

Values expressed as mean ± SD.

* The analysis of variance (ANOVA) for multiple comparison.

High risk versus Low risk, $p = 0.024$

Table II.
Combination of D-dimer testing and pretest clinical probability score

<table>
<thead>
<tr>
<th>D-dimer (µg/mL)</th>
<th>VDS</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Positive</td>
<td>Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>value</td>
<td>n</td>
<td>value</td>
<td>p–value*</td>
</tr>
<tr>
<td>High PCP</td>
<td>35</td>
<td>11.98±10.46</td>
<td>21</td>
<td>0.91±0.75</td>
<td>0.0001</td>
</tr>
<tr>
<td>Moderate PCP</td>
<td>22</td>
<td>4.37±4.91</td>
<td>42</td>
<td>1.14±0.89</td>
<td>0.0057</td>
</tr>
<tr>
<td>Low PCP</td>
<td>1</td>
<td>2.73</td>
<td>37</td>
<td>0.76±0.66</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

Values expressed as mean ± SD.

*The unpaired t test

PCP: pretest clinical probability

Table III.
Combination of D-dimer testing and pretest clinical probability score

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>High PCP</td>
<td>35/35 (100%)</td>
<td>12/21 (57%)</td>
<td>35/44 (80%)</td>
<td>12/12 (100%)</td>
</tr>
<tr>
<td>Moderate PCP</td>
<td>22/22 (100%)</td>
<td>19/42 (45%)</td>
<td>22/45 (49%)</td>
<td>19/19 (100%)</td>
</tr>
<tr>
<td>Low PCP</td>
<td>1/1 (100%)</td>
<td>17/37 (46%)</td>
<td>1/21 (5%)</td>
<td>17/17 (100%)</td>
</tr>
</tbody>
</table>

PCP: pretest clinical probability

High PCP group; true positive (D-dimer positive / DVT present; n = 35), true negative (D-dimer negative / DVT absent; n = 12), false positive (D-dimer positive / DVT absent; n = 9), false negative (D-dimer negative / DVT present; n = 0)

Moderate PCP group; true positive (D-dimer positive / DVT present; n = 22), true negative (D-dimer negative / DVT absent; n = 19), false positive (D-dimer positive / DVT absent; n = 23), false negative (D-dimer negative / DVT present; n = 0)

Low PCP group; true positive (D-dimer positive / DVT present; n = 1), true negative (D-dimer negative / DVT absent; n = 17), false positive (D-dimer positive / DVT absent; n = 20), false negative (D-dimer negative / DVT present; n = 0)

D-dimer positive; value of D-dimer assay $\geq 0.5 \mu g/mL$

D-dimer negative; value of D-dimer assay $< 0.5 \mu g/mL$

Table IV.
Combination of D-dimer testing and pretest clinical probability score

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Proximal DVT (%)</th>
<th>Distal DVT (%)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>High PCP</td>
<td>35</td>
<td>27 (77)</td>
<td>8 (23)</td>
<td></td>
</tr>
<tr>
<td>Moderate PCP</td>
<td>22</td>
<td>6 (27)</td>
<td>16 (73)</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

*Pearson’s chi-square test

PCP: pretest clinical probability

Table V.
Fig 1.
Combination of D-dimer testing and pretest clinical probability score

Legends

Table I. Pretest clinical probability score
Table II. Prevalence of DVT by pretest clinical probability risk classification
Table III. Results of D–dimer assay between positive and negative scan patients
Table IV. The discriminating power of D–dimer testing by PCP category
Table V. The distribution of DVT in the moderate and high risk PCP

Fig.1 Proposed strategy for patients with suspected DVT.

DVT: deep vein thrombosis
Non-high clinical score: low or moderate clinical score