Evaluating the use of a negative D-dimer and low Wells score in excluding deep venous thrombosis in outpatients presenting to a large London teaching Hospital

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Purpose

The aim of this retrospective audit is to investigate the relationship of the Wells score and D-Dimer in excluding lower limb DVT in an outpatient setting and to construct a model to identify which patient group needs to proceed to imaging and in which group a DVT can be reliably ruled out with no imaging. An additional aim of the audit was to identify any risk factors for DVT which are not part of the Wells score.

Deep Venous Thrombosis (DVT) is a common cause of mortality and morbidity with an estimated incidence of 67 per 100000 general populations per year (1). Accurate diagnosis of DVT is necessary because untreated DVT can result in thromboembolic disease and misdiagnosis is associated with bleeding due to the treatment with anticoagulants (2).

Diagnosis of DVT is made by varying combinations of clinical history, examination, probability score, blood test for D-Dimer and Ultrasonography.

CUS (Compression Ultrasonography) is still the initial approach in the diagnosis of DVT in many centres (3, 4). It is a reliable and accurate diagnostic test to confirm or rule out DVT but since only 17% to 24% of suspected patients have a DVT, it is not appropriate and cost-effective to request this investigation in all patients (5, 6).

Numerous studies demonstrate that a combination of Wells score, D-dimer and CUS, might be a reliable means of excluding suspected DVT and guiding treatment decisions (7). It has been proved in recent investigations that D-dimer measurement has a high negative predictive value in ruling out DVT and is highly sensitive but not specific (8, 9). A combination of pre-test probability with a D-dimer test has been proved to be effective (10, 11).

The clinical probability score using patients' clinical signs and symptoms as described by Wells et al. is the most widely used. It consists of 9 parameters, as described in table 1. Wells scoring system categorizes patients into 3 groups according to their probable risk for DVT: low (score 0), medium (score of 1 or 2), or high (score 3) (12).

In a recently introduced version of the Wells rule, patients with a Wells score of 1 or less and a negative D-dimer test were defined to be at very low risk for DVT (13).
<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active cancer</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 more than 3 cm when compared with the asymptomatic leg</td>
<td>1</td>
</tr>
<tr>
<td>Pitting oedema (greater in the symptomatic leg)</td>
<td>1</td>
</tr>
<tr>
<td>Collateral superficial veins (nonvaricose)</td>
<td>1</td>
</tr>
<tr>
<td>Alternative diagnosis as likely or more possible than that of deep venous thrombosis</td>
<td>-2</td>
</tr>
</tbody>
</table>

**Table 1:** Wells clinical probability scoring test
Methods and Materials

Patients: We performed a retrospective audit of patients who had presented to our fast response team (FRT) with clinical symptoms of lower limb DVT. The FRT is a nurse led outpatient clinic where patients with suspected DVT are referred by GPs, A&E and outpatients. All patients have a clinical history, D-dimer and Wells score as well as CUS results documented in a database.

The initial audit period was March 2009 to March 2010 and a re-audit on our implemented changes and new patient management algorithm was performed from September 2011 to February 2012. Patients had a clinical history and examination, D-dimer and CUS performed as appropriate. Patients with no D-dimer result were excluded from our audit. A total of 816 patients were evaluated. Out of these, 526 patients were referred between March 2009 and March 2010 and 290 patients from September 2011 to February 2012.

Procedure: All patients who had a D-dimer assay and CUS were eligible for the study. The Biopool Auto-Dimer quantitative immuno-turbidometric micro-particle latex assay (Diagnostica Stago, UK) was used for D-dimer level estimation. A D-dimer result below 230ng/mL was considered to be negative.

During our re-audit the D-dimer assay was changed from Biopool AutoDimer to Innovance D-Dimer (Sysmex UK, Milton Keynes, UK), and a D-dimer value of below 0.50mg/L FEU (fibrin equivalent units) was considered negative.

All D-Dimer assays were performed on a Sysmex CS2100i automated coagulation analyser (Sysmex UK, Milton Keynes, UK).

Patients who had a negative D-dimer result were then classified into 3 groups with pre-test clinical probability score according to Wells et al.: low (score 0), medium (score of 1 or 2), or high (score 3) (12).

Doppler US results of patients with a negative D-dimer test and low Wells score were assessed. See figure 1 for the initial diagnostic algorithm for the FRT. The standard US technique for evaluating above knee DVT included a combination of compression B-mode US and Doppler study evaluating flow augmentation with respiration and calf compression.

Results
526 patients (225 male, 301 female) were included in the initial audit, of which 510 (96.9%) patients had both D-dimer and US results available. 265 (51.9%) out of these 510 patients had a negative D-dimer result. Among patients with negative D-dimer, 143 (53.9%) had low, 88 (33.2%) moderate, 19 (7.1%) high and 15 (5.6%) no result for Wells score.

Out of 143 patients with a negative D-Dimer and low Wells score, 7 patients were found to have a DVT on CUS. On further analysis of these seven patients, they were all found to have risk factors for DVT. Some of these risk factors are not part of the Wells score (12), i.e. long haul flight, OCP, previous DVT and pregnancy.

No patient with a negative D-Dimer, low Wells score and no risk factor had a DVT on CUS. Based on these results we introduced a new diagnostic algorithm for all patients presenting to the FRT for outpatient assessment for DVT. See Figure 2. This included the assessment of risk factors as well as the Wells score.

Following this audit A CUS was omitted in any patient with a negative D-Dimer, no Wells score and no risk factor.

In the re-audit, 290 patients (160 male, 130 female) were investigated. 290 (100%) patients had all results available. 94 (32.4%) out of these 290 patients had a negative D-dimer value. 43 (45.7%) had low, 45 (47.8%) moderate and 6 (6.3%) high Wells score.

Of the 43 patients with a negative D-Dimer and a low Wells score, 30 had risk factors for DVT. In keeping with the new algorithm these patients were all scanned. Thirteen patients with a negative D-Dimer, low Wells score and no risk factors were not scanned according to protocol. The results of this study are summarised in Table 2.

Combining both audits, of 816 patients, no patient with a negative D-Dimer, low Wells score with no clinical risk factors had a DVT on US (Negative predictive value 100%).

In our re-audit study 30 patients with a negative D-dimer and low Wells score also had other risk factors including: 11 patients with previous DVT in the same leg, 6 with a history of recent long haul flight, 3 with Factor V Leiden, 5 with longstanding history of smoking and 4 patients using OCP. Only 3 out of 30 patients with a negative D-dimer, low Wells score and no risk factors proceeded for US among whom 2 were obese and 1 had a past history of Baker cyst and these scans were requested for clinical reasons.

Table 3 shows a list of the clinical risk factors.
Fig. 1: Old Suspected DVT Algorithm
Fig. 2: New FRT Diagnostic Algorithm for outpatient assessment of DVT
<table>
<thead>
<tr>
<th>Test Number</th>
<th>I</th>
<th>II</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time period</strong></td>
<td>March 2009-March 2010</td>
<td>September 2011-February 2012</td>
</tr>
<tr>
<td><strong>Total number of patients</strong></td>
<td>526</td>
<td>290</td>
</tr>
<tr>
<td><strong>Number of eligible patients</strong></td>
<td>510 (96.9%)</td>
<td>290 (100%)</td>
</tr>
<tr>
<td><strong>Negative D-dimer</strong></td>
<td>265 (51.9%)</td>
<td>94 (32.4%)</td>
</tr>
<tr>
<td><strong>Low Wells score</strong></td>
<td>143 (53.9%)</td>
<td>43 (45.7%)</td>
</tr>
<tr>
<td><strong>Moderate Wells score</strong></td>
<td>88 (33.2%)</td>
<td>45 (47.8%)</td>
</tr>
<tr>
<td><strong>High Wells score</strong></td>
<td>19 (7.1%)</td>
<td>6 (6.3%)</td>
</tr>
<tr>
<td><strong>No result for Wells score</strong></td>
<td>15 (5.6%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>DVT positive patients</strong></td>
<td>7 (2.6%)</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

**Table 2:** Comparison of results for both studies
### Identified risk factors

- Active Cancer
- Previous venous Thromboembolism
- Family history of venous Thromboembolism
- Hospital admission/ surgery within past 12 weeks
- Pregnancy
- High BMI (BMI > 30 kg/m²)
- Intravenous drug use
- Recent journey of more than 31/2 hours
- Thrombophilia
- Age > 60 years
- OCP/ HRT

**Table 3: Identified risk factors**
Conclusion

In our outpatients with suspected lower limb DVT, a combination of no clinical risk factors, negative D-dimer and low Wells score can reliably exclude an above knee DVT and there is no need for US imaging in these patients. We recommend that outpatients with a clinical risk factor for DVT or a moderate or high Wells score should be imaged. A D-dimer can be omitted in these patients thus saving further money for the Health Service. Also any patients with a positive D-dimer should be imaged. The Wells score needs to be revised to include additional risk factors.

It has been well described that incorporating D-Dimer testing in a diagnostic strategy involving pre-test probability and Ultrasonography simplifies the diagnosis of DVT in outpatient setting without compromising safety (14).

Wells et al. previously described that only 3% of patients with low clinical probability had DVT (12). Some authors have suggested that low or moderate Wells score and a normal D-dimer concentration is a safe strategy to rule out deep venous thrombosis and to withhold anticoagulation (15); based on our results we do not agree. In our audits, we found that some patients with a negative D-dimer and low Wells score did have a DVT but all these had risk factors (Table 3).

There was a reduction in the percentage of patients with a negative D-dimer in the re-audit, 51.9% to 32.4%; note should be made that the D-dimer assay used was different in the two audits and the new threshold may have been set lower. Nevertheless, both showed similar results when assessing negative D-dimer, low clinical probability and no risk factors in accurately excluding DVT. There was also a reduction in patients with a low Wells score in the re-audit, 53.9% to 45.7% and an increase in a moderate probability score from 33.2% to 47.8%. This could be explained by better record keeping and nursing vigilance when assessing these patients.

In our re-audit we avoided CUS in 13 (13.8%) patients based on our new algorithm. This was a smaller number than predicted from our first audit probably due to an improved D-Dimer sensitivity of our new assay and more vigilant clinical assessment in the knowledge that some patients would not get an ultrasound.

We are aware of the NICE guidelines (16) which does not include risk factors and has a two stage Wells score as apposed to our 3 stage score. The patient on the OCP who had a DVT in the second audit was scanned because of her OCP risk factor. She would not have been scanned if the NICE guidelines were followed and therefore the DVT would not have been picked up as she would have been assessed as an unlikely DVT. We feel that our FRT diagnostic algorithm allows us to better identify at risk outpatients, however
it does mean that more patients are scanned. This approach can be used in other centres in the NHS with prior validation of the D-Dimer assay locally.

References


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Personal Information