Thrombosis in the Emergency Department

Use of a Clinical Diagnosis Model to Safely Avoid the Need for Urgent Radiological Investigation

David R. Anderson, MD; Philip S. Wells, MD; Ian Stiell, MD; Bruce MacLeod, MD; Martin Simms, MD; Lisa Gray, BScN; K. Sue Robinson, MD; John Bormanis, MD; Michael Mitchell, MD; Bernard Lewandowski, MD; Gordon Flowerdew, DSc

Context: The management of patients presenting to hospital emergency departments with suspected deep vein thrombosis (DVT) is problematic because urgent diagnostic imaging capability is sometimes unavailable. Experienced physicians using clinical skills alone can classify patients with suspected DVT into low-, moderate-, and high-probability categories.

Objectives: To determine the accuracy of an explicit clinical model for the diagnosis of DVT when applied by emergency department physicians and to assess the safety and feasibility of a management strategy based on the clinical pretest probability for patients presenting to the emergency department with suspected DVT outside of regular hospital staff work hours.

Methods: A prospective cohort study was performed in the emergency departments of 2 tertiary care institutions involving 344 patients with suspected DVT. Patient conditions were evaluated by an emergency department physician who determined the pretest probability for DVT to be low, moderate, or high using an explicit clinical model. Patients for whom DVT was considered a low pretest probability were discharged from the emergency department and returned the following day for venous compression ultrasound imaging of the affected leg. Patients for whom DVT was considered a moderate pretest probability received a single, weight-adjusted dose of subcutaneous unfractionated heparin sodium (between 12,500 and 20,000 U), were discharged from the emergency department, and returned the next morning to undergo ultrasonography. Patients for whom DVT was considered a high pretest probability were admitted to the hospital, administered intravenous unfractionated heparin, and ultrasonography was arranged within 24 hours. Patients with positive ultrasonographic findings were diagnosed with DVT, except for those with low pretest probability for whom confirmatory venography was performed. Patients with DVT excluded in the initial evaluation period did not receive anticoagulant therapy. All patients were followed up for 90 days to monitor development of thromboembolic or bleeding complications.

Results: Twenty-four (49.0% [95% confidence interval (CI), 34.5%-63.6%]) of 49 patients in the high-probability category, 15 (14.3% [95% CI, 8.3%-22.4%]) of 105 in the moderate-, and 6 (3.2% [95% CI, 1.2%-6.7%]) of 190 in the low-probability category were confirmed to have DVT. Overall, 45 (13.1%) of 344 patients were confirmed to have DVT. No patient developed pulmonary embolism or major bleeding complications within 48 hours of initial evaluation in the emergency department. Of the 301 patients who had DVT excluded during the initial evaluation period, only 2 (0.7% [95% CI, 0.1%-2.3%]) developed venous thromboembolic complications (calf vein thromboses in both) in the 3-month follow-up period.

Conclusions: Using an explicit clinical model, emergency department physicians can accurately classify patients with suspected DVT into high-, moderate-, and low-probability groups. A management plan based on probability for DVT that avoids the need for urgent diagnostic imaging is safe and feasible in the emergency department setting.

Arch Intern Med. 1999;159:477-482

PATIENTS WITH suspected deep vein thrombosis (DVT) frequently present to hospital emergency departments. Since symptoms and signs of DVT are nonspecific and found in a wide variety of nonthrombotic disorders, timely diagnostic testing must be performed to correctly identify patients with this condition. Compression ultrasound venous imaging is the most accurate noninvasive test for the diagnosis of DVT.

Difficult management decisions may arise when patients present to emergency departments with suspected DVT outside of regular hospital staff work hours because diagnostic imaging capability is usually not immediately available. The emergency department physician is then left with the dilemma of either trying to arrange for urgent
PATIENTS AND METHODS

A prospective cohort study was performed involving patients presenting with suspected acute DVT to the emergency departments of the QE II Health Sciences Centre, Halifax, Nova Scotia, and the Ottawa Civic Hospital, Ottawa, Ontario, between July 1994 and September 1996. Approval of the Research Review Committees was obtained at both institutions and informed consent was obtained from all participating patients.

PATIENT POPULATION

Patients presenting or referred to the emergency departments outside of regular hospital staff work hours with symptoms of swelling and/or pain in the lower extremity and for whom the emergency department physician could not clinically exclude the presence of acute DVT were potentially eligible for the study. Exclusion criteria were (1) symptoms or signs suggestive of acute pulmonary embolism; (2) previous DVT or pulmonary embolism documented by objective testing; (3) current use of oral anticoagulant therapy; (4) history of bleeding diathesis or other contraindication to the use of anticoagulant therapy; (5) younger than 18 years; (6) pregnancy; (7) life expectancy less than 3 months; (8) geographic inaccessibility to follow-up testing; or (9) refusal to give informed consent.

INTERVENTION

The simplified clinical model used in the study (Table 1) was derived using logistic regression analysis of data collected in a previous study that validated our original clinical criteria for the diagnosis of DVT. The clinical model is a 9-point scale in which 1 point is scored for specific signs and risk factors for DVT and 2 points are deducted if an alternative diagnosis is present that is at least as likely as DVT to account for a patient's symptoms. For patients with scores of 3 or higher, DVT was considered a high probability; for patients with scores of 1 and 2, DVT was considered a moderate probability, and for those with a score of 0 or less, DVT was considered low probability. Emergency department physicians at both institutions received a 1-hour educational session regarding the application of the clinical model before starting this study.

Eligible patients were evaluated by an emergency department physician who classified pretest probability for DVT into low-, moderate-, and high-probability categories using the clinical model. No diagnostic imaging for DVT was done in the emergency department. Patient management was dependent on the assigned pretest probability for DVT (Figure 1). Patients classified into the low-probability category were discharged from the emergency department without receiving anticoagulant therapy and returned within 24 hours to the radiology department to undergo venous compression ultrasound imaging. If no abnormalities were noted on compression ultrasound, DVT was excluded. However, if patients in the low-probability group had abnormal compression ultrasound results, contrast venography was performed. Patients with abnormal venogram results or those with abnormal results on compression ultrasound in whom venography could not be performed were treated for DVT.

Patients for whom the probability of DVT was moderate received a single, weight-adjusted dose of subcutaneous unfractionated heparin sodium and were discharged from the emergency department with instructions to return within 12 hours to undergo compression ultrasound imaging. The dose of subcutaneous unfractionated heparin sodium was adjusted as follows: (1) patients weighing less than 50 kg received 12,500 U; (2) those weighing 50 to 60 kg, 15,000 U; (3) those from 60 to 80 kg, 17,500 U; and (4) those weighing more than 80 kg, 20,000 U. Patients with abnormal compression ultrasound findings were treated for DVT. Patients with no abnormalities seen on compression ultrasound imaging returned 1 week later for a follow-up ultrasound test. If, again, no abnormalities were seen on compression ultrasound imaging, DVT was excluded. If the follow-up ultrasound results were abnormal, the patient was treated for an acute DVT.

Patients for whom DVT was a high probability were admitted to the hospital to receive treatment with intravenous unfractionated heparin and undergo compression ultrasound imaging within 24 hours. Patients with abnormalities seen on compression ultrasound imaging were continued on heparin therapy, and those with no abnormalities underwent contrast venography testing. If the venogram showed no abnormalities, anticoagulant therapy was discontinued, whereas patients with abnormal venogram results continued heparin therapy.

RESULTS

STUDY POPULATION

Over the 2-year recruitment period, 447 patients presented to the emergency departments outside of regular hospital staff working hours with suspected DVT. Eighty-seven patients had 1 or more of the exclusion criteria and were ineligible for the study for the following reasons:
Prior to discharge from the emergency department, all patients were given an information sheet outlining the symptoms of pulmonary embolism and worsening DVT and were asked to return immediately for evaluation if any of these developed. Patients were seen routinely in a follow-up clinic or contacted by telephone 1 week and 3 months after their initial evaluation.

Ultrasound testing was performed using a high-resolution, electronically focused linear array transducer (either 5- or 7.5-MHz probes). The entire proximal deep venous system between the proximal common femoral vein and the trifurcation of the popliteal vein in the calf was evaluated for compressibility at 1-cm intervals. Duplex color Doppler imaging was performed as an adjunct. Ultrasonography results were considered abnormal if a vein or venous segment was not fully compressible. The calf veins were deliberately not examined. Contrast venography was performed using the method of Rabinov and Paulin. Deep vein thrombosis was diagnosed by the presence of a constant intraluminal filling defect present in at least 2 projections.

OUTCOME MEASUREMENTS

A priori, the primary outcome cluster in this study was defined as the development of 1 of the following within 48 hours of evaluation in the emergency department: (1) symptomatic pulmonary embolism confirmed by ventilation perfusion V/Q lung scanning or pulmonary angiography or (2) major bleeding following the institution of anticoagulant therapy for patients who were confirmed not to have DVT. Bleeding complications were classified using previously described criteria.

The secondary outcome was the development of objectively documented proximal DVT or pulmonary embolism in a 3-month follow-up period in patients for whom the diagnosis of DVT was originally considered excluded. Proximal DVT was diagnosed using either ultrasonography or contrast venography as described above. The assessment of patients with suspected DVT or pulmonary embolism was standardized to avoid bias. Patients with suspected DVT underwent ultrasonography of the proximal venous system as previously described. Those whose ultrasonic results showed no abnormalities underwent a follow-up ultrasound examination 1 week later. Patients with abnormal ultrasound results were treated for DVT. For those with negative results DVT was excluded. If ultrasonography was unavailable or if patients had persistent severe calf pain despite normal ultrasound results, contrast venography was performed.

Patients with suspected pulmonary embolism were initially investigated using V/Q lung scanning. Normal V/Q scan results excluded pulmonary embolism and a high probability scan confirmed the diagnosis. Patients with non–high-probability lung scans underwent compression ultrasound imaging and an abnormal result confirmed the presence of pulmonary embolism. Patients with normal compression ultrasound results were referred for pulmonary angiography where the presence of pulmonary embolism was defined using previously described criteria. The results of compression ultrasonograms, venograms, V/Q lung scans, and pulmonary angiograms from all suspected symptomatic thromboembolic events as well as all bleeding episodes and deaths were reviewed by a panel unaware of the pretest probability categorization of the emergency department physicians.

PROJECTED SAMPLE SIZE AND STATISTICAL ANALYSIS

Prior to initiating the study, we estimated the primary event rate would be 1.5% (pulmonary embolism or major bleeding). We planned to include a sufficient number of patients to ensure that the upper bounds of the 95% confidence interval (CI) of this estimate was less than 2.5%.

This resulted in a projected sample size of 350 patients. After an interim analysis revealed our primary event rate was less than estimated, we decreased our target sample size to 330 patients.

The rate of symptomatic pulmonary embolism or major bleeding that developed within 48 hours after enrollment in the study was determined along with the associated 95% CI. The proportion of patients in each of the low-, moderate-, and high-probability categories who actually had DVT and the associated 95% CIs of these rates were determined. In addition, the proportion of patients for whom the diagnosis of DVT was originally excluded and who subsequently developed either DVT or pulmonary embolism in the 3-month follow-up period was determined along with the associated 95% CI. The CIs were derived using exact binomial probabilities.

58 patients had previously objectively documented DVT or pulmonary embolism; 7 were geographically inaccessible for follow-up testing; 5 had concomitant symptoms of pulmonary embolism; 4 were pregnant; 3 required long-term anticoagulants, and 10 had other reasons. Thus, 360 patients met the eligibility criteria. Of these, 9 refused consent and 4 patients for whom pretest probability was moderate were not enrolled because ultrasonography could not be performed within 12 hours of presentation to the emergency department. A total of 347 patients were entered in the trial, of whom 3 patients were lost to follow-up, leaving 344 evaluable patients (Figure 2). The average age of these patients was 53.8 years, and 154 patients (44.7%) were women (Table 2). The mean duration of symptoms prior to presentation in the emergency department was 6.7 days. Of the 344 evaluable patients, 49 (14.2%) were categorized at high, 105 (30.5%) moderate, and 190 (55.2%) low pretest probability for DVT.

PATIENT OUTCOMES

One hundred eighty-five (97.4%) of the patients for whom pretest probability was low had no abnormalities on ultrasound imaging. The remaining 5 patients for whom probability for DVT was low had normal ultrasound findings; DVT was confirmed by venography in 3 of these patients and venography was not performed in the other 2. All 5 patients were treated for proximal DVT. One patient in the low-probability category, who developed worsening symptoms of calf pain, underwent an unscheduled ultrasound examination 1 week following his initial presentation, which again showed no abnormalities. This patient subsequently had contrast venography per-
formed and calf DVT was diagnosed for which the patient was treated.

Of the patients classified with moderate pretest probability, 13 had abnormal compression ultrasound findings and were treated for DVT, and 92 (87.6%) had normal ultrasound findings on the day of initial presentation. One of these latter 92 patients had abnormal ultrasound findings in a test conducted 7 days later. Of the remaining 91 patients, 1, because of persistent severe calf pain, underwent contrast venography following the second ultrasound with no abnormal findings and was diagnosed and treated for calf DVT.

The diagnosis of DVT was given for 20 of 49 patients at high probability on the basis of the findings of the initial ultrasound examination. Four (13.8%) of the 29 patients with normal ultrasound imaging findings were confirmed by venography to have either calf and popliteal DVT (2 patients) or isolated calf vein thrombosis (2 patients). None of the other 25 patients at high probability developed complications of DVT or pulmonary embolism during the 3-month follow-up.

Overall, 49.0% (95% CI, 34.3%-63.6%) of the patients with high, 14.3% (95% CI, 8.3%-22.4%) of those with moderate, and 3.2% (95% CI, 1.2%-6.7%) of those patients with low pretest probability were confirmed to have DVT over the 3-month follow-up period. Overall, 45 (13.1%) of the 344 patients studied were confirmed to have DVT. None of the 344 evaluable patients developed pulmonary embolism or major bleeding within 48 hours of their evaluation in the emergency department (95% CI, 0%-0.9%).

Four of the patients who participated in the study died. Two patients in the high-probability category died subsequent to being given the diagnosis and treated for DVT. Two patients in the low-probability category died who were not considered to have DVT: one from complications of a stroke and the other from complications of lymphoma. These patients died 48 and 71 days following assessment in the emergency department.

We have demonstrated that emergency department physicians can classify patients with suspected DVT into high-, moderate-, and low- pretest probability groups using a simple explicit clinical model. Furthermore, we have shown that by following management algorithms based on clinical pretest probability, urgent diagnostic imaging for DVT in the emergency department can be safely avoided. The short-term safety of our approach was confirmed in that no patient developed pulmonary embolism or major bleeding within 48 hours of their evaluation in the emergency department (95% CI, 0%-0.9%).

This study confirmed the validity of a simplified 9-point clinical model for the diagnosis of DVT. A minimal period of instruction, this model was successfully used by emergency department physicians to categorize patients into high-, moderate-, and low-probability groups. The prevalence of DVT in the high-pretest probability category was lower than was observed in our other studies. This, in part, may reflect the lower prevalence of DVT in patients presenting to emergency departments compared with specialized thrombosis clinics. It may also reflect that emergency department physicians were cautious and that, when in doubt, they may have tended to assign a higher score, which resulted in the patient being admitted to the hospital for intravenous heparin therapy. Nevertheless, using our strategy, only 10% of the entire cohort of patients (those considered at high probability for DVT) were admitted to the
hospital through the emergency department, and 49% of these patients were confirmed to have DVT on subsequent diagnostic testing.

In only 4 of 34 patients scheduled to undergo venography because of discordance between the clinical pretest probability assessment and the ultrasonography results did the diagnosis made by compression ultrasound imaging prove to be incorrect. In each case, thrombi involving the calf and/or distal popliteal veins were diagnosed by venography in patients at high probability with normal ultrasound findings. Since the veins of the calf were deliberately not examined in this study because of the limited accuracy of ultrasonography in this region, these results should not be regarded as an indication of failure of ultrasonography.

The development of safe and feasible algorithms for the management of patients with suspected DVT that avoids the need for emergency diagnostic imaging has several practical advantages. First, for centers that do not have the capacity for routine diagnostic imaging, these algorithms provide an alternative to admitting patients to the hospital for empiric anticoagulation until diagnostic imaging can be performed. Second, these algorithms allow for the effective triage of patients in the emergency department and thus avoid unnecessary delays. Third, cost savings can be achieved by avoiding the callback of staff to perform urgent ultrasonography.

The results of this study suggest that using management algorithms based on pretest probability for patients presenting to the emergency department with suspected DVT is safe and feasible. However, there were several limitations to our algorithms that could potentially be improved. First, the management of the high-probability subgroup was suboptimal in that more than 50% of these patients were confirmed not to have DVT on radiographic imaging and were thus unnecessarily admitted to the hospital. Second, owing to the short half-life of unfractionated heparin, patients in the moderate-probability group had to return for ultrasound imaging within 12 hours of their evaluation in the emergency department. Management of high- and moderate-probability patients may be improved by substituting low-molecular-weight heparin for unfractionated heparin in the respective algorithms. Two studies have demonstrated that subcutaneously administered low-molecular-weight heparin is safe and effective for the outpatient treatment of DVT. Owing to its longer half-life, low-molecular-weight heparin preparations may be administered once daily for the treatment of DVT. Therefore, the use of low-molecular-weight heparin would reduce the need to empirically admit patients at high clinical suspicion for DVT to the hospital. Such patients would then have up to 24 hours before diagnostic ultrasonographic imaging would need to be arranged. Patients subsequently confirmed to have DVT could potentially be entered into an outpatient DVT treatment program, reducing the cost of managing this condition.

---

**Table 2. Demographic and Clinical Characteristics of Patients Based on the Confirmation of a Diagnosis of DVT**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>With DVT</th>
<th>Without DVT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>45</td>
<td>299</td>
<td>344</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>57.1</td>
<td>53.4</td>
<td>53.8</td>
</tr>
<tr>
<td>Sex, No. M/F</td>
<td>20/25</td>
<td>134/165</td>
<td>154/190</td>
</tr>
<tr>
<td>Mean duration of symptoms, d</td>
<td>5.7</td>
<td>6.9</td>
<td>6.7</td>
</tr>
<tr>
<td>No. (%) of patients with</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>5 (11.1)</td>
<td>12 (4.0)</td>
<td>17 (4.9)</td>
</tr>
<tr>
<td>Recent surgery</td>
<td>6 (13.3)</td>
<td>11 (3.7)</td>
<td>17 (4.9)</td>
</tr>
<tr>
<td>Immobilization</td>
<td>14 (31.1)</td>
<td>36 (12.0)</td>
<td>50 (14.5)</td>
</tr>
</tbody>
</table>

*DVT indicates deep vein thrombosis.*
Finally, the D-dimer test has been assessed as a surrogate marker for DVT. Several D-dimer assays have been demonstrated to be highly sensitive but nonspecific for the diagnosis of DVT. The high negative predictive value of D-dimer may be useful in reducing the need for diagnostic testing, especially in patients at low clinical probability presenting to the emergency department with suspected DVT. However, the safety of this approach requires confirmation in large prospective clinical trials in the emergency department.

Accepted for publication June 10, 1998.

From the Departments of Medicine (Drs Anderson and Robinson and Ms Gray), Emergency Medicine (Dr MacLeod), Radiology (Drs Simms and Mitchell), and Community Health and Epidemiology (Drs Anderson and Flowerdew), the QE II Health Sciences Centre and Dalhousie University, Halifax, Nova Scotia; and the Departments of Medicine (Drs Wells and Bormanis), Emergency Medicine (Dr Stiell), and Radiology (Dr Lewandowski), Ottawa Civic Hospital and University of Ottawa, Ottawa, Ontario.

This study was supported by grants from the Nova Scotia Heart and Stroke Foundation, Halifax (Dr Anderson), and Physician Services Incorporated of Ontario, Toronto (Dr Wells, grant No. 94-3). Drs Anderson and Wells are Research Scholars of the Canadian Heart and Stroke Foundation. Dr Stiell is a Career Scientist of the Medical Research Council of Canada.

Presented in part at the XVIIth Congress of the International Society of Thrombosis and Haemostasis in Florence, Italy, June 8, 1997, and at the 38th meeting of the American Society of Hematology in Orlando, Fla, December 7, 1996.

The authors would like to acknowledge the support of the emergency department physicians and ultrasound technologists at the QE II Health Sciences Centre, Halifax, Nova Scotia, and the Ottawa Civic Hospital, Ottawa, Ontario, along with the efforts of Kathy Clement, BScN, Sue Pleasance, BScN, Erica Burton, BSc, and Ms Linda Woodbury for her secretarial assistance.

Corresponding author: David R. Anderson, MD, Room 432, Bethune Building, QE II Health Sciences Centre, 1278 Tower Rd, Halifax, Nova Scotia, Canada B3H 2Y9.