D-dimer testing reduced the need for ultrasonographic imaging in outpatients with suspected deep venous thrombosis

Wells PS, Anderson DR, Rodger M, et al. **Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis.** N Engl J Med. 2003;349:1227-35.

QUESTION

In outpatients with suspected deep venous thrombosis (DVT), does the use of D-dimer testing safely reduce the need for venous ultrasonographic imaging (VUI) and rule out DVT on the day of presentation?

DESIGN

Randomized (allocation concealed*), blinded (ultrasonographers, technicians who measured D-dimer levels, and outcome assessors),* controlled trial with 3-month follow-up.

SETTING

Thrombosis units and emergency departments of 5 academic health centers in Canada.

PATIENTS

1096 outpatients (mean age 58 y, 58% women) who had suspected lower-extremity DVT. Exclusion criteria included refusal or inability to consent, geographic inaccessibility, symptom resolution for > 72 hours, suspected pulmonary embolism, life expectancy < 3 months, use of therapeutic anticoagulation for > 48 hours, pregnancy, and age < 18 years. 1082 patients (99%) completed follow-up and were included in the analysis.

INTERVENTION

Patients were stratified by the application of a clinical model as "likely" or "unlikely" to have DVT and allocated to D-dimer testing (n = 566) or VUI alone (n = 530). Patients in the D-dimer group received VUI if they were "likely" to have DVT or if they were "unlikely" to have DVT but the D-dimer test result was positive. Patients who were "unlikely" to have DVT and whose D-dimer test result was negative did not receive VUI. Patients in the VUI-alone group who were "likely" to have DVT received VUI 1 week later if the first test result was negative.

MAIN OUTCOME MEASURE

Development of proximal DVT or pulmonary embolism in patients in whom DVT had initially been ruled out.

MAIN RESULTS

The overall prevalence of DVT or pulmonary embolism was 15.7% during follow-up. The groups did not differ for rate of proximal DVT or pulmonary embolism in patients in whom DVT had initially been ruled out (Table). The mean number of ultrasonographic tests per patient was lower in the D-dimer group than in the VUI-alone group (0.78 vs 1.34, P = 0.008).

CONCLUSION

In outpatients with suspected deep venous thrombosis (DVT), the use of D-dimer testing reduced the need for venous ultrasonographic imaging and ruled out DVT in patients judged clinically unlikely to have DVT without compromising safety.

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*See Glossary.

D-dimer testing plus venous ultrasonographic imaging (VUI) vs VUI alone in suspected deep venous thrombosis (DVT) at 3 months†

Outcome	D-dimer + VUI	VUI alone	Difference between groups (95% CI)
Development of DVT or pulmonary embolism in patients in whom DVT had been initially ruled out	0.42%	1.35%	–0.93% (–2.2 to 0.2)‡

†CI defined in Glossary.
‡Not significant.

COMMENTARY

Previous cohort studies have shown the usefulness of D-dimer testing along with an assessment of the clinical probability of disease to exclude a diagnosis of DVT (1, 2). In this study, however, Wells and colleagues report the first randomized trial testing a diagnostic strategy incorporating D-dimer testing and convincingly show the value of this approach.

Whereas the study was powered to show that the rate of DVT during follow-up would be < 0.8% higher in the D-dimer group than in the VUI group, the rate was actually 0.9% lower in the D-dimer group than in the VUI group, thus showing that the 2 approaches are equivalent in safety. Furthermore, fewer extremity ultrasonographic tests were done in the D-dimer group than in the VUI group. This implies that use of D-dimer testing may be cost-saving, although this observation needs formal testing.

The authors used either of 2 assays: SimpliRED, a qualitative red-cell agglutination assay, or IL-Test, an automated quantitative assay. In previous work, Kovacs and colleagues reported negative predictive values of 96% for SimpliRED and 97% for IL-Test (3). Such high negative predictive values will not be seen in situations where the prevalence of thrombosis is higher.

This trial supports the use of D-dimer testing, after clinical assessment of the probability of thrombosis, in excluding DVT in outpatients. Results cannot be extrapolated to inpatients or to patients suspected of having pulmonary embolism.

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