










Safety of a D-dimer based strategy and repeated ultrasonography did not differ in DVT and normal proximal vein ultrasonography

Kearon C, Ginsberg JS, Douketis J, *et al.* A randomized trial of diagnostic strategies after normal proximal vein ultrasonography for suspected deep venous thrombosis: D-dimer testing compared with repeated ultrasonography. *Ann Intern Med* 2005;142:490-6.

Clinical impact ratings IM/Ambulatory care ★★★★★☆ Emergency medicine ★★★★★☆ Haematology ★★★★★☆

Q In patients with suspected deep venous thrombosis (DVT) and negative results on proximal vein ultrasonography, how does a D-dimer-based management strategy that minimises additional assessments compare with routine repeated ultrasonography?

METHODS

-  **Design:** randomised controlled trial.
-  **Allocation:** concealed.*
-  **Blinding:** blinded (outcome assessors).*
-  **Follow up period:** 6 months.
-  **Setting:** thrombosis services of 4 university hospitals in Hamilton, Ontario, Canada.
-  **Patients:** 810 patients (mean age 59.5 y, 62% women) with a suspected first episode of DVT and negative results on proximal vein ultrasonography who were referred by primary care and hospital-based physicians to a thrombosis outpatient service. Exclusion criteria included life expectancy <6 months, contraindication to venography, use of full dose heparin for >48 hours, use of long term warfarin therapy, symptoms of pulmonary embolism, and pregnancy.
-  **Intervention:** erythrocyte agglutination D-dimer testing with no further testing after a negative result and venography after a positive result (D-dimer strategy, n=408); or routine repeated ultrasonography at 1 week (repeated ultrasonography, n=402). Patients in the D-dimer strategy group who had DVT shown on venography were treated with anticoagulants for ≥3 months. Patients in the repeated ultrasonography group only received anticoagulant therapy if the second ultrasound was abnormal.
-  **Outcomes:** initial diagnosis and treatment of symptomatic DVT; and safety (assessed by rate of symptomatic venous thromboembolism in patients without DVT on initial testing at 6 mo).
-  **Patient follow up:** 96%.

*See glossary.

MAIN RESULTS

4.7% of patients in the D-dimer strategy group and 0.7% of patients in the repeated ultrasonography group received a diagnosis of DVT at initial testing and treatment (p<0.001). In patients without DVT on initial testing, groups did not differ for the rate of DVT at 6 months (table).

CONCLUSION

In patients with suspected deep venous thrombosis and negative results on proximal vein ultrasonography, the safety of a D-dimer based management strategy that minimises additional assessments did not differ from that of routine repeated ultrasonography.

Commentary

Kearon *et al* report on a new strategy to refute the diagnosis of symptomatic DVT efficiently in a single visit. This study did not use a pre-test probability score for clinical decision making, but included this information descriptively. Relatively few patients in the D-dimer strategy group were in the moderate (30%) or high (5%) pre-test probability groups.

Posthoc analysis by pre-test probability score shows events rates of 4.5% (estimated 95% CI 0.24 to 25%) among high probability patients and 2.4% (estimated CI 0.63 to 7.5%) among moderate probability patients. Interestingly, half of these patients had events following a single negative compression ultrasound and a negative D-dimer, a strategy that has been validated previously.^{1,2} As can be appreciated by the wide CIs, limited conclusions can be reached by analysing subgroups in a study not designed for such analysis. As summarised by Hulley *et al*,³ this study is useful to the extent that it yields valid inferences, first about events that happened in the study sample ("internal validity"), and then about generalising results to patients outside the study ("external validity"). This well designed and executed trial possesses internal validity; the conclusion that it is safe to withhold anticoagulation based on the interventions tested is valid for the population studied. Clinicians can always ask whether the patient whom they are evaluating was represented in the population studied, and hence whether or not the results provide information applicable to the evaluation of their patient ("external validity"). When confronted with a patient with known pre-test probability that is moderate or high, clinicians should apply the conclusions of this study with great caution. A prospective study testing this strategy on such patients is needed.

Scott M Stevens, MD,
C Gregory Elliott, MD
LDS Hospital and University of Utah School of Medicine
Salt Lake City, Utah, USA

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- 3 Hulley SB, Newman TB, Cummings SR. In: Hulley SB, Cummings SR, editors. *Designing clinical research*. Baltimore: Williams and Wilkins, 1998:1-11.

For correspondence: Dr C Kearon, McMaster University and the Henderson Research Centre, Hamilton, Ontario, Canada

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D-dimer strategy v repeated US in suspected DVT with negative results on proximal vein US and no DVT on initial testing*

Outcome at 6 months	D-dimer	Repeated US	RRI (95% CI)	NNH
Symptomatic DVT	2.1%	1.3%	64% (-43 to 372)	Not significant

*DVT = deep venous thrombosis; US = ultrasonography. Other abbreviations defined in glossary; RRI, NNH, and CI calculated from data in article.