

# Review: a low clinical probability plus a normal D-dimer test result excludes a diagnosis of deep venous thrombosis

Fancher TL, White RH, Kravitz RL. Combined use of rapid D-dimer testing and estimation of clinical probability in the diagnosis of deep vein thrombosis: systematic review. *BMJ* 2004;**329**:821.

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

## Q In patients with suspected deep venous thrombosis (DVT), is a combination of rapid D-dimer testing with estimation of clinical probability accurate for excluding a diagnosis of DVT?

### METHODS



**Data sources:** Medline (1993–2003), Database of Abstracts and Reviews, and bibliographies of relevant articles.



**Study selection and assessment:** prospective studies (published in English) that used a rapid D-dimer assay on at least a subgroup of consecutive outpatients with features of DVT; estimated the risk of DVT using a validated clinical probability tool that categorised patients as having low, intermediate, or high risk of DVT; evaluated outpatient data separately if inpatients were included; evaluated DVT data separately if patients with pulmonary embolism were included; had 100% patient follow up at ≥3 months; documented DVT using ultrasonography, venography, or impedance plethysmography; and presented sufficient data for calculation of sensitivity and specificity of the D-dimer assay and prevalence of venous thrombosis stratified by clinical probability level. Study quality was assessed based on the recommendations of the Cochrane Methods Group on Systematic Reviews of Screening and Diagnostic tests.



**Outcome:** incidence of objectively confirmed symptomatic DVT and pulmonary embolism among patients with a normal D-dimer test result, stratified by the level of clinical probability.

### MAIN RESULTS

6 studies each of diagnostic accuracy (n = 2199) and 6 studies of diagnostic management (n = 3232) met the selection criteria. Meta-analysis was done using a random effects logistic meta-regression model. The table contains pooled incidence rates of venous thrombosis among patients with a normal D-dimer test result, stratified by level of clinical probability. Pooled sensitivity for the

For correspondence: Dr T L Fancher, Division of General Medicine, University of California at Davis, Sacramento, California, USA. Tonya. Fancher@ucdmc.ucdavis.edu

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Rapid D-dimer testing combined with estimation of clinical probability for excluding a diagnosis of DVT\*

D-dimer test result	Estimated clinical probability	3 month cumulative incidence of DVT (95% CI)
Normal on the SimpliRED D-dimer test	Low	0.5% (0.07 to 1.1)
	Moderate	3.5% (1.4 to 6.9)
	High	21.4% (8.5 to 38)
Normal on the highly sensitive D-dimer tests	Low or moderate	0.4% (0.04 to 1.1)
	High	6.4% (1.7 to 15)

\*DVT = deep venous thrombosis; CI defined in glossary.

simpliRED D-dimer assay was 88% (95% CI 82 to 92) and specificity was 77% (CI 65 to 86) resulting in a negative likelihood ratio of 0.16. The pooled sensitivity for the highly sensitive D-dimer assays was 98% (95% CI 96 to 99) and specificity 46% (CI 28 to 67) resulting in a negative likelihood ratio of 0.05.

### CONCLUSIONS

In patients with suspected deep venous thrombosis (DVT), a low clinical probability plus a normal result on the SimpliRED D-dimer test excludes a diagnosis of acute DVT. Furthermore, a normal result on the highly sensitive D-dimer test is effective for ruling out DVT in patients with a low to moderate clinical probability of DVT.

A modified version of this abstract appears in *Evidence-Based Nursing*.

### Commentary

The meta-analysis by Fancher *et al* provides strong evidence that plasma D-dimer measurement combined with clinical probability assessment may rule out DVT in selected outpatients and thus spare them unnecessary venous compression ultrasonography. However, it also highlights that differences exist among D-dimer assays.

The SimpliRED D-dimer assay has a sensitivity of 88% and a negative result rules out a DVT safely only in patients with a low clinical probability, while highly sensitive ELISA assays can be safely used for that purpose in patients with a low or moderate clinical probability. So which test should we select? The ELISA assays are quantitative and observer independent, but they require a dedicated analyser. The SimpliRED assay does not require any equipment and could theoretically be used as a bedside test. However, this observation is debatable considering its poor interobserver agreement.<sup>1</sup> The higher specificity (true-negative rate) of the SimpliRED assay should result in the exclusion of DVT in a higher proportion of patients compared with the ELISA assays. However, this potential advantage may be offset by the necessary restriction of its use to patients with a low clinical probability. Published studies have not settled this issue because the number of patients who must be submitted to a D-dimer test to rule out 1 DVT depends not only on the test's specificity but also on the prevalence of DVT in the studied population, which is highly variable.

Finally, the number of patients evaluated by an ELISA assay in outcome studies (ie, studies in which patients with a negative D-dimer assay and a low to intermediate clinical probability of DVT are not treated and are followed up for ≥3 mo) is still limited. Therefore, further studies would be welcome. In conclusion, D-dimer testing is a useful tool for ruling out DVT in outpatients, and ELISA assays should probably be preferred because they are observer-independent and can be used in patients with a low or intermediate clinical probability.

Arnaud Perrier, MD  
Geneva University Hospital  
Geneva, Switzerland

1 Perzanowski C, Eiger G. Limited interobserver agreement in the SimpliRED D-dimer assay [letter]. *J Thromb Haemost* 2003;**1**:849–50.