VIDAS D-dimer in combination with clinical pre-test probability to rule out pulmonary embolism: a systematic review of management outcome studies


CRD summary
This review assessed the combined negative VIDAS D-dimer result and a non-high pre-test probability to exclude pulmonary embolism. The authors concluded that this method can safely and effectively exclude pulmonary embolism in outpatients with a suspected event. This was a largely well-conducted review, although a lack of clarity regarding study quality limited the interpretation of reliability.

Authors' objectives
To assess efficacy and safety of combined negative VIDAS D-dimer result with a non-high pre-test probability using Wells or Geneva models to exclude pulmonary embolism.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and EBM Reviews were searched. Search dates spanned 1950 to 2008. Relevant journals and conference proceedings of International Society on Thrombosis and Haemostasis (2005 to 2007) were searched. Investigators and manufacturers were contacted and reference lists of included studies and reviews were scanned for other potentially relevant studies. There were no restrictions on language, publication type or year of publication.

Study selection
Studies of prospective consecutive patients with suspected pulmonary embolism diagnosed by pre-test probability and VIDAS D-dimer testing, and where anticoagulants or further testing were withheld when pulmonary embolism was excluded by these tests, were eligible for inclusion. Included studies had to have a minimum three-month follow-up. Studies that compared the intervention with a reference test were excluded. Primary outcomes of interest were pulmonary embolism-related death and sudden death that was possibly pulmonary embolism-related, and the rate of symptomatic venous thromboembolism (VTE) during the three-month follow-up. Symptomatic VTE was defined as a high probability V/Q (Ventilation/Perfusion) scan or computed tomography or pulmonary angiography with segmental intraluminal defects. Non-high pre-test probability was defined as unlikely using Wells' score or low/intermediate using Geneva score, Revised Geneva score or gestalt estimation. A negative D-dimer result was defined as less than 500ng/mL. Patients were largely emergency outpatients. Prevalence of pulmonary embolism was 20%.

Two independent reviewers selected studies for inclusion in the review. Discrepancies were resolved by discussion.

Assessment of study quality
Study quality assessment was carried out by two independent reviewers using the Newcastle-Ottawa Quality Assessment Scale. This covered selection and comparability of study groups and ascertainment of outcomes or exposure for cohort and case-control studies. The scale was adapted to include allocation concealment for assessment of randomised controlled trials (RCTs).

Discrepancies were resolved with the involvement of a third reviewer.

Data extraction
Data were extracted to enable the calculation of three-month thromboembolic risk, sensitivity, specificity, negative predictive value, negative likelihood ratio and 95% confidence intervals (CIs). Study authors were contacted for missing data where necessary.

Two reviewers independently extracted data. Disagreements were resolved with the involvement of a third reviewer.
Methods of synthesis
Studies were pooled in a statistical synthesis (method not reported). Heterogeneity was assessed using the $I^2$ statistic. Sensitivity analysis was performed by adding in patients lost to follow-up.

Results of the review
Seven studies were included in the review (n=8,371): one RCT (n=1,693) and six prospective cohort management studies (n=6,678). Sample size ranged from 331 to 3,306 patients. Study quality was reported to be similar across included studies (detailed results not provided). Heterogeneity was reported to be low.

Diagnostic safety:
Three-month thromboembolic risk in patients untreated after a combined negative VIDAS D-dimer with a low/intermediate or unlikely pre-test probability of pulmonary embolism was three out of 2,166 patients (0.14%, 95% CI 0.05 to 0.41%). Sensitivity analysis increased this risk to 0.64% (95% CI 0.38 to 1.08%).

Diagnostic accuracy:
Overall results for combined non-high pre-test probability and negative D-dimer were: sensitivity 99.7% (95% CI 99.0% to 99.9%); specificity 47.4% (95% CI 46.0% to 48.9%); negative predictive value 99.9% (95%CI 99.6% to 100%); and negative likelihood ratio 0.01 (95% CI 0.00 to 0.02).

Sensitivity results were high for all combinations using any pre-test probability model (range 98.7% to 100%). Specificity ranged from 40.8% (low/intermediate pre-test probability) to 57.4% (unlikely pre-test probability).

In an analysis of six studies, the number of patients needed to be tested by VIDAS D-dimer to rule out one pulmonary embolism with no further investigations was 2.8 (95% CI 2.7 to 2.9).

Authors' conclusions
A negative VIDAS D-dimer combined with a non-high pre-test probability (defined as unlikely by Wells' model or low/intermediate by Geneva model or clinical gestalt) can safely and effectively exclude pulmonary embolism in outpatients with a suspected event.

CRD commentary
The review question was clear and supported by inclusion criteria that appeared to be potentially reproducible. The search strategy included a number of sources to locate published and unpublished material. Adequate attempts were made to minimise language and publication biases. The review process was conducted with sufficient attempts to minimise reviewer error and bias. An appropriate quality assessment tool was applied to included studies, but the results were not fully presented. Study details were presented. A statistical synthesis seemed appropriate in light of the authors' claim of low level heterogeneity. This was a largely well-conducted review, although a lack of clarity regarding study quality limited the interpretation of the reliability of findings.

Implications of the review for practice and research
Practice: The authors stated that the VIDAS D-dimer test could be used in all patients with suspected pulmonary embolism, regardless of their clinical probability.

Research: The authors did not state any implications for research.

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Bibliographic details
Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.