Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review

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CRD summary
This generally well-conducted review concluded that methodological limitations, large between-study differences and small sample sizes limited the evidence on tests for diagnosing clinically suspected upper extremity deep vein thrombosis. These cautious conclusions reflect the limitations of the available evidence.

Authors’ objectives
To assess the accuracy of diagnostic tools for the diagnosis of clinically suspected upper extremity deep vein thrombosis and to determine whether any of these tests (alone or in combination) can be used as triage tests or as a replacement for venography.

Searching
MEDLINE and EMBASE were searched to June 2009 without language restrictions; search terms were reported. Bibliographies of included studies and reviews were screened for additional articles.

Study selection
Studies that assessed the accuracy of a diagnostic test (including clinical assessment, D-dimer, or imaging tests) for upper extremity deep vein thrombosis were eligible for inclusion. Studies were required to verify index test results using an independent reference standard and to report sufficient data to populate 2x2 contingency tables (numbers of true positive, false negative, false positive, and true negative test results). Case reports were excluded.

Included studies evaluated clinical signs and symptoms, a clinical score, D-dimer, Doppler ultrasonography, compression ultrasonography, time of flight magnetic resonance imaging (MRI), contrast-enhanced MRI, light reflection rheography, phleboreography, impedance plethysmography, and strain gauge plethysmography. Studies were conducted in in-patient, outpatient and mixed settings. Mean participant age ranged from 30 to 61 years (where reported). Venography was used as the reference standard in most studies.

Two reviewers independently assessed studies for inclusion and disagreements were resolved by discussion, or consultation with a third reviewer.

Assessment of study quality
Two reviewers independently assessed the methodological quality of studies using the QUADAS (Quality Assessment of Diagnostic Accuracy Studies) tool; disagreements were resolved by discussion or consultation with a third reviewer.

Data extraction
Data were extracted on the numbers of true positive, false negative, false positive, and true negative test results. Sensitivity and specificity, with 95% confidence intervals (CIs), were calculated. Numbers of indeterminate test results and withdrawals were also extracted (where reported).

Two reviewers independently extracted data using a standardised form.

Methods of synthesis
A bivariate random-effects model was used to calculate joint estimates of sensitivity and specificity, with 95% confidence intervals, for any test evaluated by three or more studies. Where only two studies assessed a test, a fixed-effect model was used.

Bivariate analyses with co-variates were planned to explore the effects on accuracy estimates of different test types, and
Results of the review

Seventeen studies (n=793 patients) were included in the review. No study evaluated a combination of tests in a diagnostic strategy, or explicitly reported the evaluation of a test as a replacement for, or triage before, venography. The patient spectrum was considered representative in five studies; two additional studies reported consecutive recruitment. Ten studies were judged to have avoided differential verification bias; seven avoided partial verification bias. Only four studies explained uninterpretable results or withdrawals. Two studies fulfilled all quality criteria and were considered at low risk of bias.

The diagnostic accuracy summary estimates of sensitivity were 97% (95% CI 90 to 100) for compression ultrasonography (two studies), 84% (95% CI 72 to 97) for Doppler ultrasonography (three studies), 91% (95% CI 85 to 97) for Doppler ultrasonography with compression (six studies), and 85% (95% CI 72 to 99) for phleboreography (two studies). The corresponding summary estimates of specificity were 96% (95% CI 87 to 100) for compression ultrasonography, 94% (95% CI 86 to 100) for Doppler ultrasonography, 93% (95% CI 80 to 100) for Doppler ultrasonography with compression, and 87% (95% CI 71 to 100) for phleboreography.

The following test diagnostic accuracies were evaluated by one study each: clinical score (sensitivity 78%, 95% CI 67 to 88; specificity 64%, 95% CI 56 to 72), D-dimer (sensitivity 100%, 95% CI 78 to 100; specificity 14%, 95% CI 5 to 29), contrast-enhanced MRI (sensitivity 50%, 95% CI 12 to 88; specificity 80%, 95% CI 44 to 97), time of flight-MRI (sensitivity 71%, 95% CI 29 to 96; specificity 89%, 95% CI 52 to 100), rheography (sensitivity 92%, 95% CI 61 to 100; specificity 100%, 95% CI 66 to 100), impedance plethysmography (sensitivity 100%, 95% CI 78 to 100; specificity 28%, 95% CI 4 to 71), and strain gauge plethysmography (sensitivity 100%, 95% CI 79 to 100; specificity 83%, 95% CI 36 to 100).

Authors’ conclusions

Methodological limitations, large between-study differences and small sample sizes limited the evidence on tests for clinically suspected upper extremity deep vein thrombosis.

CRD commentary

The review addressed a clearly stated research question defined by appropriate inclusion criteria. A number of sources were searched for relevant studies and no language restrictions were applied. Measures were taken, throughout the review process, to minimise error and/or bias.

The methodological quality of included studies was assessed and included in the interpretation of results. Appropriate analytical methods were used.

The authors’ cautious conclusions reflect the limitations of the available evidence.

Implications of the review for practice and research

Practice: The authors stated that compression ultrasonography may be an acceptable alternative to venography and that the addition of (colour) Doppler does not seem to improve accuracy.

Research: The authors stated that adequately designed diagnostic accuracy or management studies are needed to clarify the sensitivity and specificity of these and all other tests and strategies, whilst demonstrating how performance may vary over different spectra of disease.

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