Noninvasive diagnosis of deep venous thrombosis

Authors' objectives
To review noninvasive methods for the diagnosis of first and recurrent deep venous thrombosis (DVT) and to provide evidence-based recommendations for the diagnosis of DVT in symptomatic, asymptomatic and pregnant patients.

Searching
MEDLINE was searched up to January 1997; the search terms were provided. Additional literature was identified by searching the authors' personal files and the bibliographies of reviews and original studies.

Study selection
Study designs of evaluations included in the review
The review included prospective cohort studies for diagnostic accuracy and randomised controlled trials (RCTs) for management, if they satisfied the predefined methodological criteria.

Specific interventions included in the review
Noninvasive diagnostic tests for DVT were eligible for inclusion. Impedance plethysmography and venous ultrasonography (Duplex, B-mode or Colour Doppler) were the main focus of the review. Clinical assessment, fibrinogen leg scanning and D-dimer blood tests were considered as adjuncts.

Reference standard test against which the new test was compared
Diagnostic accuracy studies were required to use venography as the reference standard in all patients. For management studies, long-term follow-up served as the 'reference standard'.

Participants included in the review
Studies of symptomatic (in- and out-patient), asymptomatic (post-operative orthopaedic patients) and pregnant patients with first suspected or recurrent DVT were eligible for inclusion.

Outcomes assessed in the review
No inclusion criteria relating to outcomes were specified. For diagnostic accuracy studies, the outcomes assessed were: sensitivity for proximal DVT, isolated distal DVT, and all DVT; specificity for all DVT; positive predictive value for proximal DVT and all DVT; negative predictive value for proximal DVT, isolated DVT and all DVT. For management studies, the outcome assessed was the safety of withholding anticoagulation on the basis of negative test results, as defined by the incidence of venous thromboembolism during 6 months' follow-up. This was often supplemented by venographic determination of the positive predictive value of an abnormal test result at presentation.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The validity of the diagnostic accuracy studies was assessed using the following methodological criteria: all patients must have had venography (the 'gold' standard); the new test and venography must have been evaluated independently (blinded); consecutive patients must have been studied; and the study must have been prospective, including at least 50 evaluable patients.

The validity of the management studies was assessed using the following methodological criteria: the study must have been prospective with consecutively enrolled patients; all patients who had anticoagulation withheld on the basis of negative results of serial diagnostic tests must have had complete follow-up; objective testing during follow-up must
have been used to evaluate suspected venous thromboembolism; and at least 50 patients must have been studied.

The strength of the evidence was graded as level 1 or 2 depending on the study sample size. Level 1 evidence was precise (95% confidence intervals of plus or minus 5%, or statistically-significant differences for studies comparing diagnostic tests). The authors do not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.

Data extraction
The data were primarily extracted by one of the authors. A random sample of 10% of the included studies was independently abstracted by a second author to assess the reliability; 94% agreement was reached.

Methods of synthesis
How were the studies combined?
For studies of a first DVT, a random-effects model was used to combine the data from the individual studies. The weighted means were calculated using weights that were the inverse of the combined within-study and between-study variance. Studies examining recurrent DVT or DVT during pregnancy were summarised narratively, with recommendations graded from A to C based on the quality and quantity of evidence available.

How were differences between studies investigated?
The homogeneity of the study findings was assessed using the chi-squared statistic. This compared the equality of study-specific proportions that were derived using a fixed-effect model, weighted according to the inverse of within-study variance. An associated P-value of 0.05 or less was taken as statistically-significant evidence of heterogeneity.

Results of the review
A total of 43 studies appear to have been included in the review. There were 18 and 16 accuracy studies of venous ultrasonography for the diagnosis of a first DVT in symptomatic and asymptomatic patients, respectively; 7 management studies of impedance plethysmography for the diagnosis of a first suspected DVT in symptomatic patients; and 3 studies of venous ultrasonography.

Venous ultrasonography is the most accurate noninvasive test for the diagnosis of a first symptomatic proximal DVT. Neither ultrasonography nor impedance plethysmography is accurate in asymptomatic post-operative patients. Venous ultrasonography is less accurate for symptomatic isolated distal DVT than for proximal. In this patient group, clinical assessment and D-dimer testing are complementary to venous ultrasonography and impedance plethysmography.

Withholding anticoagulant therapy in symptomatic patients who have normal results in serial testing with either modality is safe.

The diagnosis of recurrent DVT requires evidence of new thrombus formation, such as new compressible venous segment on venous ultrasonography, conversion of a normal impedance plethysmography result to abnormal, or presence of an intraluminal filling defect on venography.

Suspected DVT in pregnant patients can usually be managed with serial venous ultrasonography or impedance plethysmography.

Authors' conclusions
The accuracy and utility of noninvasive tests for the diagnosis of DVT vary with the indication for testing. Symptomatic patients can usually be managed with noninvasive testing, venous ultrasonography being the optimum method available. However, if the findings of noninvasive tests are equivocal, or are discordant with clinical assessment, venography should be considered.

CRD commentary
This was a relatively poor-quality review. The research question was clearly defined and explicit inclusion criteria were used, but the review process and, in particular, the data analysis were weak. The literature search was limited to only one database, which may well have resulted in some retrieval bias, and there appears to have been no attempt to address the issue of publication bias. The validity assessment was appropriate and was used to select studies on the basis of quality, and some details of the primary studies were presented. However, the review methodology was poorly described, leaving open the possibility of biases introduced by the review process. The statistical pooling used was inappropriate; although heterogeneity testing was used and reported, weighted means for sensitivity, specificity and predictive values were presented regardless of heterogeneity, and no attempt was made to investigate sources of heterogeneity. The narrative element of the review was somewhat confused and could certainly have been more clearly presented.

In addition to the inappropriate approach to statistical pooling, the authors’ conclusions regarding the relative diagnostic accuracy of the different noninvasive tests appear to have been drawn from indirect comparisons alone. Given the reservations outlined, the authors’ conclusions should be viewed with extreme caution.

Implications of the review for practice and research
Practice: The authors present detailed practice guidelines for each category of patient studied.
Research: The authors did not present any implications for research.

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Other publications of related interest
These additional published commentaries may also be of interest. McNutt RA. Review: noninvasive tests are only useful for symptomatic deep vein thrombosis. ACP J Club 1998;129:46. McNutt RA. Review: noninvasive tests are useful only for symptomatic deep vein thrombosis. Evid Based Med 1998;3:158.

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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.