Meta-analysis of plethysmography and rheography in the diagnosis of deep vein thrombosis

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CRD summary
This well-conducted and clearly reported review concluded that although plethysmography and rheography techniques have diagnostic value, their accuracy is insufficient for them to be used as stand-alone tests for deep venous thrombosis. These conclusions are likely to be reliable.

Authors' objectives
To review the accuracy of plethysmography and rheography in the diagnosis of clinically suspected deep vein thrombosis (DVT).

Searching
MEDLINE, EMBASE, CINAHL, Web of Science, the Cochrane Database of Systematic Reviews, the Cochrane Controlled Trials Register, DARE, HTA, BIOSIS Previews and ACP Journal Club were searched from inception to April 2004; the search terms were not reported. The bibliographies of included studies were screened to identify further studies, and manufacturers were contacted for unpublished studies. Studies published in languages other than English, French, Spanish or Italian were excluded. The authors of studies published as abstracts or letters were contacted for further information.

Study selection
Study designs of evaluations included in the review
Diagnostic cohort studies were eligible for inclusion. Case-control studies and studies that included less than 10 patients were excluded.

Specific interventions included in the review
Studies of plethysmography or rheography were eligible for inclusion. The specific tests evaluated in the review were impedance plethysmography, strain gauge plethysmography, air plethysmography, light reflex rheography and phleborheography.

Reference standard test against which the new test was compared
Studies that used contrast venography or ultrasound as the reference standard were eligible for inclusion.

Participants included in the review
Studies of patients with clinically suspected DVT were eligible for inclusion. Studies of patients with suspected pulmonary embolism were excluded, as were studies that included asymptomatic or mixed cohorts of symptomatic and asymptomatic patients. Studies were conducted in primary care, in-patient, out-patient and mixed settings.

Outcomes assessed in the review
It appears that studies had to report sufficient data to extract a 2x2 table of test performance, although this was not explicit (several studies were excluded because it was not possible to extract data). Sensitivity and specificity were the main measures of test performance reported.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed studies for inclusion. Any disagreements were resolved by discussion.

Assessment of study quality
Two reviewers independently assessed whether studies fulfilled the following three criteria: application of the reference standard independent of the index test; interpretation of the index test blind to the results of the reference
standard; interpretation of the reference standard blind to the results of the index test.

**Data extraction**
Two reviewers independently extracted the data using a standardised form. Any disagreements were resolved through discussion. Data were extracted on the number of true-positive, false-positive, true-negative and false-negative results, separately for proximal, distal and all DVT. Sensitivity (all DVT combined and for proximal and distal DVT) and specificity were calculated for each study. Where studies contained zero cells, 0.5 was added to every value for that study. If studies provided insufficient data, study authors were contacted for further information.

**Methods of synthesis**

How were the studies combined?
The pooled sensitivity (proximal DVT, distal DVT and all DVT) and specificity were calculated using a random-effects model. Data were combined separately for each diagnostic test.

How were differences between studies investigated?
Heterogeneity was assessed using the chi-squared statistic. A random-effects meta-regression was used to evaluate study level covariates associated with test performance for those tests evaluated by more than 10 studies. If a significant covariate was identified (p<0.1) then the meta-analysis was repeated, stratified by the covariate. The covariates investigated using meta-regression were: age, gender, DVT prevalence, setting, consecutive recruitment, prospective study, reference standard, method of interpretation of the results (automatic versus manual) and quality criteria.

**Results of the review**
Seventy-eight articles reporting 82 patient cohorts were included (the number of patients was unclear).

Impedance plethysmography (42 cohorts, data reported separately for distal and proximal DVT in 28 cohorts).

The pooled sensitivity was 75% (95% confidence interval, CI: 73, 77) for all DVT, 88% (95% CI: 86, 90) for proximal DVT and 28% (95% CI: 24, 33) for distal DVT. The pooled specificity was 90% (95% CI: 89, 91). There was evidence of statistical heterogeneity in all accuracy measures (p<0.001). Setting of recruitment (p=0.098) and blind reporting of the reference standard (p=0.056) were associated with variations in sensitivity. Proportion of males in the cohort (p=0.01), DVT prevalence (p=0.043), setting for recruitment (p=0.09), consecutive recruitment (p=0.017) and prospective study (p=0.046) were associated with variations in specificity.

Strain gauge plethysmography (20 cohorts, data reported separately for distal and proximal DVT in 10 cohorts).

The pooled sensitivity was 83% (95% CI: 81, 85) for all DVT, 90% (95% CI: 88, 92) for proximal DVT and 56% (95% CI: 50, 63) for distal DVT. The pooled specificity was 81% (95% CI: 79, 82). There was evidence of statistical heterogeneity in all accuracy measures (p<0.001), except for sensitivity for distal DVT (p=0.033). Setting of recruitment (p<0.001) and proportion of males (p=0.0005) were associated with variations in sensitivity; no variables were associated with variation in specificity.

Air plethysmography (4 cohorts, data reported separately for distal and proximal DVT in 2 cohorts).

The pooled sensitivity was 85% (95% CI: 79, 90) for all DVT, 98% (95% CI: 93, 100) for proximal DVT and 39% (95% CI: 22, 58) for distal DVT. The pooled specificity was 91% (95% CI: 81, 95). There was evidence of statistical heterogeneity in the overall sensitivity and specificity (p<0.02), but not in separate estimates of sensitivity for proximal and distal DVT (p>0.18).

Light reflex rheography (9 cohorts, data reported separately for distal and proximal DVT in 4 cohorts).

The pooled sensitivity was 91% (95% CI: 87, 94) for all DVT, 94% (95% CI: 88, 98) for proximal DVT and 92% (95% CI: 74, 99) for distal DVT. The pooled specificity was 71% (95% CI: 66, 75). There was evidence of statistical...
heterogeneity in the overall sensitivity and specificity (p<0.001), but not in separate estimates of sensitivity for proximal and distal DVT (p>0.17).

Phleborheography (7 cohorts, data reported separately for distal and proximal DVT in 4 cohorts).

The pooled sensitivity was 86% (95% CI: 83, 89) for all DVT, 92% (95% CI: 88, 94) for proximal DVT and 58% (95% CI: 48, 68) for distal DVT. The pooled specificity was 93% (95% CI: 91, 95). There was evidence of statistical heterogeneity (p<0.001).

Authors' conclusions
Plethysmography and rheography add diagnostic value but have insufficient accuracy to act as stand-alone tests in DVT diagnosis. Further research is required.

CRD commentary
This was a well-conducted and clearly reported review. The review question was clear and supported by defined inclusion criteria. Extensive literature searches were undertaken and these included steps to identify unpublished studies. The review was limited to studies published in a limited number of languages, so language bias might be a problem. The review methods involved appropriate steps to minimise bias, and a reasonable quality assessment was conducted.

The methods used to pool the studies were appropriate, but it would have been helpful had further details of individual study results been reported: receiver operating curve plots, which provided an overview of individual study results, were provided for two of the tests investigated but it would have been helpful if these had also been given for the other tests investigated, especially given the substantial heterogeneity between the studies. Potential sources of heterogeneity were investigated and factors influencing the results were identified. The authors' conclusions are supported by the data presented.

Implications of the review for practice and research
Practice: The authors stated that neither plethysmography nor rheography have an adequate diagnostic performance to be used as the sole method of diagnosing DVT.

Research: The authors stated that an evaluation of the role of these tests in combination with other tests or standardised clinical assessment is required.

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