

Measurement of the clinical and cost-effectiveness of non-invasive diagnostic testing strategies for deep vein thrombosis

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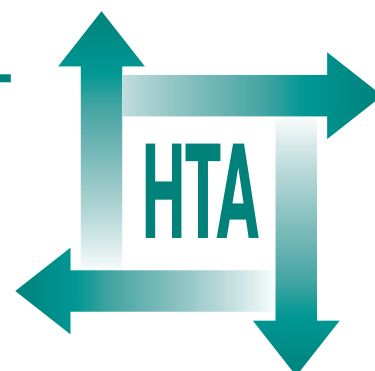
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Executive summary

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Executive summary

Background

A wide range of diagnostic tests may be useful in diagnosing deep vein thrombosis (DVT), including clinical assessment, D-dimer, plethysmography, rheography, ultrasound, computed tomographic (CT) scanning, magnetic resonance imaging (MRI) and venography. These may be used in isolation or combined as an algorithm.

Objectives

The objectives of the study were:

- To estimate the diagnostic accuracy of non-invasive tests for proximal DVT and isolated calf DVT, in patients with clinically suspected DVT or high-risk asymptomatic patients, and identify factors associated with variation in diagnostic performance.
- To identify practical diagnostic algorithms for DVT, and estimate the diagnostic accuracy, clinical effectiveness and cost-effectiveness of each.

Methods

Data sources

Diagnostic test data and diagnostic algorithms were sought from electronic searches of MEDLINE, EMBASE, CINAHL, Web of Science, Cochrane Database of Systematic Reviews, Cochrane Controlled Trials Register, Database of Reviews of Effectiveness, NHS Economic Evaluations Database, Health Technology Assessment database, BIOSIS and the ACP Journal Club, 1966–2004. Additional diagnostic test data were sought from the bibliographies of articles included in the review and contact with manufacturers of assays and instruments.

A postal survey of hospitals in the UK was undertaken to describe current practice and availability of tests, and identify additional diagnostic algorithms.

Study selection

Diagnostic cohort studies published in English, French, Spanish or Italian that compared a non-invasive diagnostic test for DVT to an acceptable reference standard were included in the review.

Data extraction

Details of study setting, recruitment, exclusions, population characteristics, reference standard, operator and results were extracted. Quality was judged against validated criteria.

Data synthesis

Pooled estimates of sensitivity, specificity and likelihood ratios were obtained for each test using random effects meta-analysis (MetaDISC software). The effect of study-level covariates was explored using random effects metaregression. A decision-analytic model was used to combine estimates from the metaanalysis and estimate the diagnostic performance of each algorithm in a theoretical population of outpatients with suspected DVT. The net benefit of using each algorithm was estimated from a health service perspective, using cost–utility analysis, assuming thresholds of willingness to pay of £20,000 and £30,000 per quality-adjusted life-year (QALY). The model was analysed probabilistically and cost-effectiveness acceptability curves were generated to reflect uncertainty in estimated cost-effectiveness.

Results

Individual clinical features are of limited diagnostic value, with most likelihood ratios being close to 1. Wells clinical probability score stratifies proximal, but not distal, DVT into high-, intermediate- and low-risk categories. Unstructured clinical assessment by experienced clinicians may have similar performance to Wells score. In patients with clinically suspected DVT, D-dimer has 91% sensitivity and 55% specificity for DVT, although performance varies substantially between assays and populations. D-dimer specificity is dependent on pretest clinical probability, being higher in patients with a low clinical probability of DVT. Plethysmography and

rheography techniques have modest sensitivity for proximal DVT, poor sensitivity for distal DVT, and modest specificity. Ultrasound has 94% sensitivity for proximal DVT, 64% sensitivity for distal DVT and 94% specificity. Computed tomography scanning has 95% sensitivity for all DVT (proximal and distal combined) and 97% specificity. Magnetic resonance imaging has 92% sensitivity for all DVT and 95% specificity. The diagnostic performance of all tests is worse in asymptomatic patients.

The most cost-effective algorithm discharged patients with a low Wells score and negative D-dimer without further testing, and then used plethysmography alongside ultrasound, with venography in selected cases, to diagnose the remaining patients. However, the cost-effectiveness of this algorithm was dependent on assumptions of test independence being met and the ability to provide plethysmography at relatively low cost. Availability of plethysmography and venography is currently limited at most UK hospitals, so implementation would involve considerable reorganisation of services.

Two algorithms were identified that offered high net benefit and would be feasible in most hospitals without substantial reorganisation of services. Both involved using a combination of Wells score, D-dimer and above-knee ultrasound. For thresholds of willingness to pay of £10,000 or £20,000 per QALY the optimal strategy involved discharging patients with a low or intermediate Wells score and negative D-dimer, ultrasound for those with a high score or positive D-dimer, and repeat scanning for those with positive D-dimer and a high Wells score, but negative initial scan. For thresholds of £30,000 or more a similar strategy, but involving repeat ultrasound for all those with a negative initial scan, was optimal.

Conclusions

Implications for healthcare

Diagnostic algorithms based on a combination of Wells score, D-dimer and ultrasound (with repeat if negative) are feasible at most UK hospitals and are among the most cost-effective. Use of repeat scanning depends on the threshold for willingness to pay for health gain. Further diagnostic testing for patients with a low Wells score and negative D-dimer is unlikely to represent a cost-effective use of resources.

Recommendations for research

The recommendations for further research include the following:

- Evaluation of the costs and outcomes of using the optimal diagnostic algorithms in routine practice,
- The development and evaluation of algorithms appropriate for specific groups of patients with suspected DVT, such as intravenous drug abusers, pregnant patients and those with previous DVT,
- The evaluation of the role of plethysmography: interaction with other diagnostic tests, outcome of low-risk patients with negative plethysmography and measurement of the costs of providing plethysmography,
- Methodological research into the incorporation of meta-analytic data into decision-analytic modelling.

Publication

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NHS R&D HTA Programme

The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the 'National Knowledge Service' that is being developed to improve the evidence of clinical practice throughout the NHS.

The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA Programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, service-users groups and professional bodies such as Royal Colleges and NHS Trusts. Research suggestions are carefully considered by panels of independent experts (including service users) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or conducting a trial to produce new evidence where none currently exists.

Additionally, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme is able to commission bespoke reports, principally for NICE, but also for other policy customers, such as a National Clinical Director. TARs bring together evidence on key aspects of the use of specific technologies and usually have to be completed within a short time period.

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Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this monograph was commissioned by the HTA Programme as project number 02/03/01. The contractual start date was in April 2003. The draft report began editorial review in November 2004 and was accepted for publication in July 2005. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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