Comparison of four strategies for diagnosing deep vein thrombosis: a cost-effectiveness analysis

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Four strategies for diagnosing deep vein thrombosis in patients who are suspected of having this disorder. The following strategies were considered: Serial ultrasound: perform an ultrasound examination on day 1. If positive, treat; if negative, repeat the ultrasound examination on day 7. Do not treat unless the second examination is positive. Serial ultrasound with D-dimer (the assay considered in this study was enzyme-linked immunosorbent (ELISA); a whole blood agglutination assay was considered in sensitivity analysis): perform an ultrasound examination on day 1. If positive, treat; if negative, measure plasma D-dimer. Repeat the ultrasound examination only if the D-dimer result is abnormal (greater than 500 micro g/L). Treat according to the ultrasound result. Risk-based serial ultrasound: perform an ultrasound examination on day 1 in all patients. In patients with an intermediate clinical probability of deep vein thrombosis, repeat the ultrasound examination if the first test is negative, and treat according to the second result. In patients with a low clinical probability of deep vein thrombosis, do not treat if the day-1 result is negative; perform phlebography if the day-1 result is positive. In patients with a high clinical probability, treat if the day-1 result shows deep vein thrombosis; otherwise perform phlebography. For the latter two situations, treat based on the results of phlebography. D-dimer with risk-based single ultrasound: measure D-dimer level. If less than or equal to 500 micro g/L, do not treat; if greater than 500 micro g/L, perform an ultrasound examination. If positive treat; if negative and the patient has a low-to-intermediate clinical probability, do not treat; if negative and the patient has a high clinical probability, perform phlebography and treat accordingly.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-effectiveness analysis; cost-utility analysis.

Study population
The study population was a hypothetical cohort of patients who were suspected of having deep vein thrombosis.

Setting
Hospital. The economic analysis was carried out in Switzerland.

Dates to which data relate
Epidemiological and clinical probabilities were obtained from the published literature between 1960 and 1999. The price year appears to have been 1996.

Source of effectiveness data
The evidence for the effectiveness outcomes were based on a review of the literature and assumptions made by the authors or expert opinion.
Modelling
A decision analytic model was used to estimate the costs and effects associated with each diagnostic strategy, incorporating the clinical probabilities obtained from the literature.

Outcomes assessed in the review
The epidemiological and clinical probabilities obtained from the literature were as follows: prevalence of deep vein thrombosis, prevalence of deep vein thrombosis by clinical probability (low, intermediate, and high), sensitivity and specificity of the diagnostic tests, probability of being treated as an outpatient, mortality from treated deep vein thrombosis, mortality and morbidity (major haemorrhage) and permanent sequelae from major haemorrhage associated with anticoagulant treatment, coefficient to adjust quality-of-life for disabling sequelae, and mortality associated with phlebography.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
A total of 11 studies were included in the review. One of the studies was a meta-analysis of diagnostic performance of ultrasonography for symptomatic proximal deep vein thrombosis.

Methods of combining primary studies
The narrative method was used.

Investigation of differences between primary studies
Not reported.

Results of the review
The baseline values (95% CIs or ranges used in sensitivity analysis) for the epidemiological and clinical probabilities obtained from the literature were as follows:

- Prevalence of deep vein thrombosis, 24% (16-30%);
- Prevalence of deep vein thrombosis by clinical probability (low, 2% (3-6%); intermediate, 19% (17-30%); and high (96% (75-100%));
- Sensitivity and specificity of lower limb venous ultrasound, 97% (90-100%) and 98% (90-100%), respectively;
sensitivity and specificity of D-dimer (ELISA), 98% (95-99%) and 41% (37-45%), respectively;
sensitivity and specificity of D-dimer (whole blood agglutination assay, which was only considered in the sensitivity analysis), 86% and 75%, respectively;
probability of being treated as outpatient, 50% (30-80%);
mortality from treated deep vein thrombosis, 0.25% (0.1-1%);
mortality and morbidity (major haemorrhage) and permanent sequelae from major haemorrhage associated with anticoagulant treatment, 0.2% (0.1-0.4%), 0.8% (0.6-1.2%), and 8% (5-20%), respectively;
coefficient to adjust quality-of-life for disabling sequelae, 50% (20-80%); and
mortality associated with phlebography, 0.01 (0.005-0.05).

Methods used to derive estimates of effectiveness
Assumptions made by the authors or expert opinion.

Estimates of effectiveness and key assumptions
Mortality from untreated deep vein thrombosis was assumed to be 2.5% (1.5-7.5%). Sensitivity and specificity of phlebography were assigned to be 99% (90-100%) and 99% (90-100%), respectively. In the diagnostic strategies that used serial ultrasonography, the performance of the repeat ultrasound examination was considered identical to that of the first examination.

Measure of benefits used in the economic analysis
The measures of benefit used were quality-adjusted 3-month survival and lives saved per 1,000 patients (50-year-old patient with a life expectancy of 29 years). The false-negative and false-positive rates were also calculated. Strategies were considered to be equivalent clinically if the difference in 3-month survival was less than 0.5 per 1,000 patients.

Direct costs
Costs were not reported to have been discounted, despite a 29-year life expectancy considered for a hypothetical 50-year-old patient (perhaps because the time frame of the cost analysis was less than a year). Hospitalisation days were reported separately. Cost items were reported separately. The cost analysis covered the costs of diagnostic tests, anticoagulant treatment (including initial treatment as inpatient, initial treatment as outpatient, 3-month anticoagulant treatment, and major haemorrhage). The perspective adopted in the cost analysis appears to have been that of the health care system. Cost data were obtained from the database of the study hospital, a 1,300-bed urban facility. The appropriate literature was reviewed to ensure that US and Canadian costs were included in the range of costs studied in the sensitivity analysis. The price year was 1996. Indirect costs were not included.

Currency
US dollars ($). The conversion rate from Swiss currency to US dollars for 1996 was not reported.

Sensitivity analysis
A series of one-way and two-way sensitivity analyses was performed on all parameters of the model. Threshold values for the influential parameters were reported.

Estimated benefits used in the economic analysis
Quality-adjusted 3-month survival was 99.879% for serial ultrasound, 99.878% for serial ultrasound with D-dimer,
99.877% for risk-based serial ultrasound, 99.865% for D-dimer with risk-based single ultrasound, and 99.4% for the
'no treatment' strategy.

The corresponding values in terms of lives saved per 1,000 patients were: serial ultrasound, 4.8; serial ultrasound with D-
dimer, 4.8; risk-based serial ultrasound, 4.8; and D-dimer with risk-based single ultrasound, 4.6 when compared with
the 'no treatment' strategy. False-negative rates (%) were 0.02 for serial ultrasound, 0.03 for serial ultrasound with D-
dimer, 0.04 for risk-based serial ultrasound, and 0.85 for D-dimer with risk-based single ultrasound. The corresponding
values in terms of false-positive rates (%) were: serial ultrasound, 3.0; serial ultrasound with D-dimer, 2.4; risk-based
serial ultrasound, 2.0; and D-dimer with risk-based single ultrasound, 0.9.

Cost results
The cost per patient was $1,482 for serial ultrasound, $1,425 for serial ultrasound with D-dimer, $1,402 for risk-based
serial ultrasound, and $1,200 for D-dimer with risk-based single ultrasound.

Synthesis of costs and benefits
The cost per additional QALY compared to the no treatment strategy was $10,716 for serial ultrasound, $10,281 for
serial ultrasound with D-dimer, $10,909 for risk-based serial ultrasound, and $8,897 for D-dimer with risk-based single ultrasound. Based on the 0.2 per 1,000 patients difference in lives saved with the different strategies, the incremental
costs of the serial ultrasound strategies compared with a single ultrasound ranged from $61,616 to $95,080 per QALY
 gained.

Authors' conclusions
Combining clinical probability and D-dimer with a single ultrasound in the diagnostic workup of patients with possible
deep vein thrombosis is highly cost-effective, allowing a reduction in costs and resource use without any substantial
increase in mortality. Serial ultrasonography is less cost-effective.

CRD COMMENTARY - Selection of comparators
The 'no treatment' strategy was explicitly regarded as the comparator. This was appropriate and allowed the active value
of the various strategies to be evaluated.

Validity of estimate of measure of benefit
The effectiveness estimates were handled credibly within the modelling and the sources used (one being a meta-
analysis) and should have high validity. However, more details could have been provided concerning the design of the
search strategies used to identify the primary studies, criteria used to ensure the validity of primary studies, and
differences between studies. These limitations were, however, mitigated in the sensitivity analyses.

Validity of benefits was modelled using a decision analytic model, which appears to have been appropriate.

Validity of costs
Positive aspects of the cost analysis which will have enhanced its validity were as follows: some details of methods of
cost estimation were given; it appears that all important cost elements were included in the cost analysis; the price year
and the perspective adopted in the cost analysis were specified; and sensitivity analysis was performed on costs.
However, it is not entirely clear whether the cost data were based on true costs or charges; the conversion rate was not
reported; and the effects of alternative procedures on indirect costs were not addressed, although their relevance would
need to be assessed over the long term. Note: correspondence with the authors has indicated that the cost data were
based on true costs.
Other issues
The authors' conclusion appears to be justified given the extensive sensitivity analysis performed. The issue of generalisability to other settings or countries appears to have been addressed (it seems that the range of values considered in the sensitivity analysis was broad enough to address the issue of generalisability). Some comparisons were also made with other studies. It was reported that the efficacy of anticoagulant treatment in preventing post-thrombotic syndrome is not well established; therefore this complication was not considered.

Implications of the study
The cost-effectiveness findings support the combination of clinical probability and D-dimer with a single ultrasound in the diagnosis of DVT.

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