The cost-effectiveness of diagnostic strategies in patients with suspected pulmonary embolism

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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
Diagnostic strategy (and anticoagulant treatment in case of diagnosis of pulmonary embolism) recommended by the Dutch consensus meeting in 1992 consisting of ventilation-perfusion (VQ) scan followed by ultrasound of lower extremity, followed by lung angiography. Comparison strategies also may include a D-dimer test (marker of clot breakdown) and a clinical decision rule.

Type of intervention
Diagnosis; treatment.

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

Study population
Patients with an average age of 56.4 years (SD 17.6) with suspected pulmonary embolism (PE).

Setting
Hospital. The study was carried out in Amsterdam, the Netherlands.

Dates to which data relate
The data for the effectiveness analysis were collected mainly between June 1991 and April 1994. The resource use data were collected mainly during 1992. The date of the prices used in the final analysis were not explicitly reported.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken retrospectively and not on the same patient sample as that used in the effectiveness analysis.

Study sample
A total of 444 patients suspected of having PE were included in the study. 8.8% of the original 487 patients were excluded from the analysis.
A prospective case series study design was employed. The study was carried out in 2 centres and the duration of follow-up was 6 months after first test.

**Analysis of effectiveness**
The primary health outcomes used in the analysis were the sensitivity and specificity of the tests, the rate of bleeding complications and recurrence of PE during treatment with oral anticoagulant, and the mortality rate.

**Effectiveness results**
The ventilation-perfusion scan had a sensitivity of 0.68 and a specificity of 0.44. The deep leg vein ultrasonography had 0.29 sensitivity and 0.96 specificity. The D-dimer test at a cut off of 300, 500 and 700 had sensitivities of 1.0, 0.89, 0.75 and specificities of 0.12, 0.29, 0.44, respectively. The clinical decision rule with cut off points of 0.075, 0.192, 0.358 and 0.592 had sensitivities of 1.00, 0.78, 0.44, 0.11, and specificities of 0.22, 0.67, 0.83 and 1.00, respectively. From 38 patients treated with anticoagulant therapy, two died of a recurrence of PE within 6 months (5.3%). The total of PE recurrences represented 13.25% of the patients finally treated. Nine patients had a major bleeding episode in 709 patient months of treatment, and one of these patients died.

**Modelling**
A decision tree was used to estimate the costs and benefits of various combinations of tests.

**Measure of benefits used in the economic analysis**
The benefits accruing from the intervention were measured in terms of additional 6-month survival with respect to the recommended strategy, and incremental quality adjusted life years (QALYs). A sensitivity analysis was used to deal with the high degree of uncertainty and variety of possible outcomes involved in the implementation of strategies. The authors reported that the average quality of life “was set at the descriptive scores of the EuroQol questionnaire 3 months after the PE”. Score values were then normalised to the 0-1 scale “using median values of the Dutch public”. The benefits were discounted at 5%.

**Direct costs**
Costs were not discounted. Quantities were analysed separately from prices. The costs measured were operating costs, cost of complications, and overhead and capital costs. The boundary adopted was the hospital. The estimate of quantities and unit costs were mainly based on actual data from one institution's files (of the two centres included in the study), based on the hospital cost accounting system of its 1992 costs. Some costs were based on authors' assumptions and were taken from the literature. The prices used for the final report were not explicitly dated. Both average and incremental total costs were reported.

**Statistical analysis of costs**
Average costs were reported, but statistical analysis was not reported.

**Indirect Costs**
Not done.

**Currency**
Dutch Guilders (Dfl).

**Sensitivity analysis**
The variables used in the sensitivity analysis were the rate of mortality for untreated patients, mortality of recurrent PE
treated cases, cost of bleeding complications, cost of recurrent PE, days necessary for diagnosis and rate of bleeding complications. A one-way simple sensitivity analysis was performed.

Estimated benefits used in the economic analysis
The expected additional survival at 6 months for the 12 dominant intervention strategies, with respect to the 1992 Dutch consensus recommendations ranged from 0.0003 to 0.0040 years. Estimated QALYs of 9.2 per patient were calculated based on previous publications and conversion to median Dutch values, and an arbitrary reduction of 25% for comorbidities.

Cost results
The costs were not discounted. The additional costs in Dfl of the 12 strategies, with respect to the strategy recommended by the 1992 Dutch consensus panel, ranged from -59 to -280.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio per additional survivor (with respect to a previous strategy with lower clinical benefit) was used to synthesize costs and benefits. The incremental cost per additional survivor for the top 3 strategies were Dfl45,243, Dfl13,125 and Dfl37,214. The maximum incremental cost per QALY gained was Dfl48,365. The sensitivity analysis showed that the cost effectiveness of the strategies studied in terms of clinical benefit and cost was little affected by the specificity and sensitivity confidence intervals and was not affected by the changes in the rate (frequency) of major bleeding during treatment.

Authors' conclusions
The authors concluded that the best results in terms of survival were obtained with a strategy that uses less invasive tests before angiography, and that "leads to considerable savings as compared with the consensus strategy". This strategy involved performing sequentially a ventilation-perfusion scan, a clinical decision rule with cut off point of 0.75, a D-dimer test with cut off point of 300, a pulmonary angiography and leg ultrasonography. The authors added "This strategy will have to prove its value and usefulness in clinical practice in a subsequent prospective validation phase".

CRD COMMENTARY - Selection of comparators
The reason for the choice of comparator was clear. The comparator was defined as the 12 dominant diagnostic strategies using a clinical decision rule, D dimer test (with various cut-off points) and leg ultrasound plus angiogram, for patients with a clinically suspected pulmonary embolism (PE). This included oral anticoagulant treatment with an average of three tablets per day of 1 mg of acenocoumarol, for a maximum of 6 months. You as user of this database, should consider whether this is a widely used health technology in your own setting.

Validity of estimate of measure of benefit
The estimate of measure of benefit has important potential biases arising from the study design, as the authors recognized in the conclusions. Nonetheless, the data have not been used selectively to prove a particular point.

Validity of estimate of costs
No important cost items were omitted.

Other issues
The authors’ conclusions were justified. The issue of generalisability was not addressed. Appropriate comparisons were made with the onlyther study known by the authors to have been carried out. The results of that previous work were in favour of the Dutch consensus panel strategy. However, the authors pointed out that the first study was not based on prospectively collected patient data and neither detailed cost calculations nor quality of life data were included. The
authors pointed in particular to the validation needed for the sensitivity and specificity parameter values used in the model corresponding to the clinical decision rule.

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