The role of plasma D-dimer concentration in the exclusion of 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
Plasma D-dimer concentration in the exclusion of pulmonary embolism.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
Consecutive patients (both in- and outpatients) who underwent diagnostic work-up for clinically suspected pulmonary embolism.

Setting
The practice setting was two large teaching hospitals in Amsterdam, the Netherlands. The economic study was also carried out in the Netherlands.

Dates to which data relate
Data on the effectiveness of all other diagnostic tests considered and the costs of procedures and therapy were based on a study from 1993. The effectiveness of the D-dimer assay was derived from the authors' own study reported in this 1996 paper (dates were not given). Whilst the quantities of resource use were derived from the defined strategies, the price year was not stated.

Source of effectiveness data
The efficacy data associated with the D-dimer test were based on a single study.

Link between effectiveness and cost data
Costing was not based on the same sample as that used in the effectiveness study.

Study sample
The sample was selected as consecutive patients reporting with the suspected condition. Power calculations did not determine the sample size. 203 patients were initially included in the study and considered for the D-dimer assay test and angiography and/or lung scan. Of these, 24 patients were excluded, and 179 were evaluated.

Study design
Case series. D-dimer assays were evaluated without knowledge of the results of other diagnostic tests. This was a multi-centre study (two sites). Follow-up was for 6 months.

Analysis of effectiveness
The principle of analysis was not relevant. The primary health outcome was adequate exclusion of pulmonary embolism. D-dimer assays were evaluated without knowledge of the results of the other diagnostic tests (angiography and/or lung scan), which were used as reference tests.

Effectiveness results
Results varied according to the type of assay used. Pulmonary embolism was adequately excluded in between 8% and 18% of all patients, in 3% - 7% of inpatients and in 11% - 27% of outpatients.

Clinical conclusions
D-dimer assays should be used in excluding pulmonary embolism. The highest clinical utility lies in excluding outpatients, where it may be used as a screening test or following perfusion-ventilation lung scintigraphy. Only a sensitivity and negative predictive value approaching 100% should be accepted for this test.

Modelling
A decision analysis model was used to estimate the costs and benefits associated with different strategies, and roles for the D-dimer test, in the diagnostic management of patients with suspected pulmonary embolism. The model included the costs and outcomes associated with diagnostic and therapeutic procedures.

Measure of benefits used in the economic analysis
Deaths avoided, complications avoided and patients spared angiography were the outcome measures used in the economic analysis. A decision-analysis model was used to compare the different strategies. Health states were measured directly by clinicians.

Direct costs
The estimation of costs and quantities for the D-dimer assay was based on the authors' calculations and definition of strategies. The estimation of costs and quantities associated with other events was based on assumptions presented in a previous study from 1993. Costs relate to the perspective of the hospital. Total costs were estimated using a model. The price year was not stated.

Currency
European Currency Units (ECU).

Sensitivity analysis
One-way sensitivity analysis was performed. The tested parameters were the specificity and sensitivity of the D-dimer assay, prevalence of pulmonary embolism, risk of major haemorrhage, and sensitivity and specificity of pulmonary angiography.

Estimated benefits used in the economic analysis
The addition of D-dimer assay to diagnostic strategies resulted in a mortality rate of 0.97 (strategy 2), 1.04 (strategy 5) and 0.98 (strategy 6), whilst strategies 1 and 4 were associated with 0.87 and 0.94 values, respectively. Morbidity rates were 1.97, 2.19 and 2.14, respectively, for strategies 2, 5 and 6. The strategies not incorporating the D-dimer test had corresponding values of 2.17 (strategy 1) and 2.41 (strategy 4). The percentage of patients requiring pulmonary
angiography with strategies 2, 5, and 6 were, respectively, 44.4%, 54.4%, and 54.4%. The corresponding figures for strategies 1 and 4 were 61.8 and 72.2, respectively. Adverse effects were considered in the model, these were related to the complications of invasive diagnostic methods and complications of anticoagulation. Data for strategy 3 were not given. The ability of the D-dimer test to exclude pulmonary embolism was more effective in the outpatient subgroup, whereas it was virtually unable to exclude the condition in inpatients.

Cost results
The model estimated that strategies including D-dimer assay cost per patient: ECU1,131 (strategy 2), ECU1,133 (strategy 5), and ECU1,171 (strategy 6). This was compared to strategies without the D-dimer test which cost ECU1,265 (strategy 1) and ECU1,254 (strategy 4) per patient. Use of D-dimer assay in any strategy resulted in a 10% reduction in costs due mainly to a 25-28% reduction in the number of patients requiring angiography. Adverse effects were considered in the model. Data for strategy 3 were not given.

Synthesis of costs and benefits
A synthesis was not undertaken by the authors since the intervention (strategies involving the D-dimer test) was the dominant strategy. The sensitive parameters were specificity and sensitivity of the D-dimer test and the probability of haemorrhagic complications. Varying the specificity of the D-dimer test in the range 50 - 10% leads to decreased cost savings in the range 13 - 1%, mortality is unaffected. Varying the sensitivity of the test in the range 100 -90% leads to an increase in the mortality rate in the range 0.83 -1.25%. This is an increase of 0.085% with every 2% decrease in sensitivity. Cost savings were marginal as the angiography rate was not significantly changed. For every 1% increase in the risk of major haemorrhage, mortality was increased by 0.7%.

Authors' conclusions
D-dimer assays should be used in patients with clinically suspected pulmonary embolism, but this should be limited to outpatients where it appears to be cost-effective. The test is best performed after lung scintigraphy. Sensitivity for the test must be approaching 100% in order to guarantee safe practice in the adequate exclusion of pulmonary embolism.

CRD Commentary
The authors’ own effectiveness study was appropriate for estimating the predictive value of the intervention. Because sampling was based on consecutive patients in only two hospitals this study may lack some external validity. Sensitivity analysis on the cost-effectiveness model was thorough in terms of the variables associated with effectiveness and this may help generalisability. However, sensitivity analysis was not performed on any of the cost variables. There was no clear justification for the selection of the one study on which the cost-effectiveness assumptions were based. Adverse knock-on effects were apparently costed in the previous study and included in the model, thus ensuring a more comprehensive analysis.

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