Strategies incorporating spiral CT for the diagnosis of acute pulmonary embolism: 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
Seven strategies for the diagnosis of pulmonary embolism (PE) were considered in the study. All the strategies were obtained from different combinations of the following diagnostic techniques: ventilation-perfusion (V/Q) scans, duplex ultrasound of the legs (US), spiral computed tomography (CT), and conventional pulmonary angiography. For each strategy, the choice of the next stage was based on the outcome of the test performed previously. The following strategies were considered:

- V/Q scan with or without (+/-) US +/- angiography (considered to be the traditional strategy);
- V/Q scan +/- CT;
- V/Q scan +/- US +/- CT;
- CT alone;
- CT +/- US;
- CT +/- US +/- angiography; and
- CT +/- angiography.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with suspected acute PE. The specific inclusion and exclusion criteria were not reported.

Setting
The setting was an institution. The economic study was carried out at the McGill University, Montreal, Canada.

Dates to which data relate
The effectiveness evidence and resource use data were derived from studies published between 1960 and 1998. The price year was 1996.
Source of effectiveness data
The effectiveness data were derived from a review of published studies.

Modelling
A decision tree model was used to simulate both the costs and the outcomes (survival and complications) of a hypothetical cohort of 1,000 patients with suspected acute PE, for a period of 3 months. The treatment for PE comprised 10 days of unfractionated heparin therapy in the hospital, and 3 months of oral warfarin treatment on an outpatient basis. The structure of the decision tree was derived from published approaches to the disease. There were two substantial differences from previous models. First, the exclusion of leg venography as an alternative diagnostic technique. Second, the elimination of leg US for patients with normal V/Q scan findings.

Outcomes assessed in the review
The outcomes assessed in the review that were used as inputs in the decision model were:

- the prevalence rate of PE;
- the probability of normal, low, intermediate, or high V/Q scan findings given the presence or absence of PE;
- the sensitivity and specificity of spiral CT;
- the sensitivity and specificity of pulmonary angiography;
- the sensitivity and specificity of leg US;
- the probabilities of death within 3 months due to several causes (untreated PE, treated PE, no PE, anticoagulation, angiography, and spiral CT); and
- the probabilities of haemorrhagic complications in patients receiving both contrast material (rise in creatinine or need for short-term haemodialysis) and anticoagulants (haemorrhagic cerebrovascular accident or other major bleeding).

Study designs and other criteria for inclusion in the review
Many primary studies were characterised by a prospective design and some were blinded (comparison of angiography and spiral CT). The data concerning the prevalence of PE and V/Q scan findings were mainly obtained from the Prospective Investigation of Pulmonary Embolism Diagnosis study (see Other Publications of Related Interest).

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 stated.

Number of primary studies included
The effectiveness evidence was obtained from thirty-four published studies.

Methods of combining primary studies
Some estimates were derived from single studies, while other outcomes were obtained from the combination of primary studies. However, the method used to pool the studies was not reported.

**Investigation of differences between primary studies**

Not reported.

**Results of the review**

The prevalence rate of PE was 28.4% (range: 15 - 50).

Given the presence of PE, the probability was 2.0% for normal V/Q scan findings, 15.9% for low V/Q scan findings, 41.2% for intermediate V/Q scan findings, and 40.9% for high V/Q scan findings. The corresponding probabilities given the absence of PE were 19.4% (normal), 40.3% (low), 38.0% (intermediate), and 2.3% (high).

The sensitivity of spiral CT for PE was 88.6% (range: 63 - 95) and the specificity was 92.5% (range: 78 - 97).

The sensitivity of pulmonary angiography for PE was 96% (range: 90 - 100) and the specificity was 97% (range: 90 - 100).

The sensitivity of leg US for deep vein thrombosis was 82.4% (range: 50 - 90) and the specificity was 98% (range: 86 - 100).

The probability of detecting deep vein thrombosis by leg US given suspected PE was 38.5% (range: 39 - 49).

The probability of death within 3 months was:

- 31% (range: 25.2 - 50) due to untreated PE,
- 6.5% (range: 4.5 - 7.6) due to treated PE,
- 3% (range: 0 - 6) due to no PE,
- 0.49% (range: 0 - 1) for anticoagulation,
- 0.5% (range: 0 - 1) for angiography, and
- 0.0006% (range: 0 - 0.001) for spiral CT.

In patients receiving contrast material, the probability was 1.3% (range: 1.2 - 5.2) for a rise in creatinine, and 0.29% (range: 0%-0.95%) for the need of short-term haemodialysis.

In patients receiving anticoagulants, the probability of haemorrhagic cerebrovascular accident was 0.36% (range: 0 - 0.71), and the probability of other major bleeding was 7.4% (range: 0 - 15.5).

**Measure of benefits used in the economic analysis**

The benefit measure used in the economic analysis was the survival in the cohort of 1,000 patients, at 3 months after the initial diagnosis of PE. The survival rate was obtained from the decision model. It was expressed as the number of patients still alive after 3 months of follow-up.

**Direct costs**

Discounting was not carried out due to the short time horizon of the analysis (3 months). The resource quantities and the unit costs were not reported separately. The cost/resource boundary reflected the perspective of the study.
The cost analysis included the costs related to both diagnostic tests and hospitalisation. The diagnostic test costs included the sum of technical, professional, and capital costs. The hospitalisation costs included were for the diagnosis of PE, acute renal failure with or without haemodialysis, gastrointestinal bleeding and haemorrhagic cerebrovascular accident. These reflected the length of hospitalisation, physician fees, nursing, pharmacy costs, and overhead costs. The costs of 3 months of anticoagulant therapy and follow-up were also included.

The item costs were estimated using actual data, which were derived from the Royal Hospital financial information services and from Quebec physician fee schedules. The expected cost per patient of each strategy was then calculated using modelling techniques. The resource use was measured using studies published from 1960 and 1998. The price year was 1996. For some cost items, the 1998 prices in US dollars were used and then converted into Canadian dollars.

**Statistical analysis of costs**

No statistical test of the difference between the costs was reported, although the costs were treated stochastically.

**Indirect Costs**

The indirect costs were not included.

**Currency**

Canadian dollars (Can $). The 1996 exchange rate from Can$ into US$ was Can$ 1 = US$ 0.68.

**Sensitivity analysis**

Sensitivity analyses were performed to investigate the uncertainty around some estimates used in the model. One-way sensitivity analyses were carried out on all the test properties, clinical events, and costs. Two-way sensitivity analyses were conducted to assess the impact of simultaneous variations in the sensitivity and specificity of spiral CT on estimated survival, and the impact of variations in the cost of spiral CT and V/Q scan on the average total cost.

**Estimated benefits used in the economic analysis**

The number of patients still alive after 3 months was: 958.2 for CT +/- US and for CT +/- US +/- angiography,

953.7 for V/Q scan +/- US +/- angiography,

953.4 for V/Q scan +/- US +/- CT and for CT +/- angiography,

952.8 for CT alone, and

952.7 for V/Q scan +/- CT.

**Cost results**

The costs of the diagnostic procedures amounted to Can$53 (range: 27 - 300) for compression US, Can$102 (range: 51 - 950) for V/Q scan, Can$203 (range: 102 - 339) for spiral CT, and Can$607 (range: 304 - 2,553) for pulmonary angiogram.

Among the hospitalisation causes,

PE (10.6 days) cost Can$3,519 (range: 1,760 - 7,798),

gastrointestinal bleeding (7.8 days) cost Can$2,875 (range: 1,438 - 8,625),

haemorrhagic cerebrovascular accident (3 months) cost Can$25,112 (range: 12,556 - 75,336),
contrast-induced acute renal failure (4 days) cost Can$1,614 (range: 807 - 4,842),
contrast-induced acute renal failure requiring haemodialysis (25.4 days) cost Can$12,294 (range: 6,147 - 36,882),
anticoagulation and follow-up (3 months) cost Can$207 (range: 104 - 621),
compression US cost US$184,
V/Q scan cost US$450,
spiral CT cost US$339,
pulmonary angiogram cost US$783, and
hospitalisation due to PE (5.4 days) cost US$7,798.
The cost per patient was:
Can$ 1,731 for CT +/- US,
Can$1,751 for CT +/- US +/- angiography,
Can$1,416 for V/Q scan +/- US +/- angiography,
Can$1,391 for V/Q scan +/- US +/- CT,
Can$1,513 for CT +/- angiography,
Can$1,472 for CT alone, and
Can$1,461 for V/Q scan +/- CT.

Synthesis of costs and benefits
The costs and the benefits were combined by performing an incremental cost-effectiveness analysis. Four strategies (CT +/- US +/- angiography, CT +/- angiography, CT alone, and V/Q scan +/- CT) were excluded because they were dominated (less or equally effective and more expensive). The incremental costs per additional life saved of V/Q scan +/- angiography (considered the traditional strategy) over V/Q scan +/- US +/- CT were Can$83,333. The incremental costs per additional life saved of CT +/- US (the innovative diagnostic procedure) over V/Q scan +/- US +/- CT were Can$70,833. The CT +/- US strategy was the most cost-effective diagnostic strategy. In fact, as mentioned in the paper, CT +/- US extendedly dominated VG +/- V/Q +/- angiography. This means that V/Q +/- US +/- angiography would not be considered on this basis of cost-effectiveness (assuming divisibility of programmes and constant return to scale). Therefore, CT +/- US should be compared with V/Q +/- US +/- CT.

Overall, the results were robust to variations of several parameters in the sensitivity analyses. In particular, the specificity and cost of spiral CT for acute PE had a great impact on the analysis. This resulted in a reduction of the cost-effectiveness of all strategies including CT, and improved the economic efficiency of the other procedures. The cost of leg US also affected the analysis results. When leg US exceeded 48% of the cost of spiral CT, the two least expensive strategies became V/Q scan +/- spiral CT and spiral CT alone.

Authors’ conclusions
The authors concluded that “clinicians who are faced with the challenge of diagnosing acute pulmonary embolism (PE) can safely use spiral computed tomography (CT) instead of pulmonary angiography after nondiagnostic ventilation-perfusion (V/Q) scans and negative ultrasound (US) findings of the lower extremities. This approach is associated with equivalent survival and, in our health-care centre, reduced cost relative to the traditional approach”. "When spiral CT is the initial diagnostic test, followed by leg US, expected survival improves, but costs are also considerably higher. These
findings were robust to variations in the assumed sensitivity and specificity of spiral CT.”

**CRD COMMENTARY - Selection of comparators**
The reason for the selection of the comparators was clear. V/Q scan possibly followed by pulmonary angiography was considered the ‘gold standard’ for the diagnosis of patients with acute PE. You should consider whether it represents a common approach in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness measures were obtained from a review of the literature, and some estimates were combined. However, the search methods, and the criteria used to ensure the validity of the primary studies, were not reported. Further, the authors did not consider the impact of differences between the primary studies when combining the effectiveness measures.

**Validity of estimate of measure of benefit**
Survival at 3 months was used as a benefit measure in the economic analysis and was modelled. The 3-month survival estimates were similar for all seven strategies considered. Therefore, it would have been interesting to have adopted a different benefit measure, reflecting the patient preferences, since some of the diagnostic techniques adopted were based on invasive procedures. Also, lives saved, when used as a benefit measure, can be misleading in that it does not indicate the time period, which in this case was 3 months. Life-years gained would be more appropriate.

**Validity of estimate of costs**
It appears that all the categories of costs relevant to the perspective adopted were included in the analysis. The cost estimates used in the model were derived from Canadian and US data, and appropriate currency conversions were performed. Two specific problems were related to this procedure. First, the authors did not state whether a single price year was used, since US dollars referred to 1998 and Canadian dollars to 1996 (although a 1996 exchange rate was used). Second, the comparison of the two different sources used for the cost estimates (Medicare for the US and mainly a single institution in Canada) could have been problematic, due to the strong differences in the Canadian and US reimbursement systems. As the authors pointed out, the US Medicare costs used charges and not actual costs, which reflect the true resources consumed. In addition, the unit costs and the resource quantities were not reported separately, thus reducing transparency and generalisability.

**Other issues**
The study results were consistent with the findings from other published studies. The issue of the generalisability of the study to other settings was not specifically addressed. However, extensive sensitivity analyses were conducted over all model parameters, thereby enhancing the external validity of the analysis. The results were not reported selectively, except for the resource quantities and the unit costs. The authors' conclusions were in keeping with the population studied.

**Implications of the study**
The study implies that spiral CT can safely replace invasive pulmonary angiography in the diagnosis of acute PE. Further research should focus on improvements in the estimation of spiral CT properties.

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Other publications of related interest

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