Diagnosis of pulmonary embolism with CT pulmonary angiography: a systematic review


CRD summary
The authors concluded that there was insufficient evidence to determine the accuracy of computed tomographic (CT) pulmonary angiography for diagnosing pulmonary embolism (PE), but negative CT in combination with negative examination for deep vein thrombosis can exclude PE. This was a well-conducted and clearly reported review and the conclusions, though based on a small number of patients, are likely to be reliable.

Authors’ objectives
To assess the diagnostic accuracy of computed tomographic (CT) pulmonary angiography and the prognostic value of a negative result in the diagnosis of pulmonary embolism (PE).

Searching
MEDLINE and EMBASE were searched from inception to 2005; the search terms were reported. ACP Journal Club, the Cochrane Database of Systematic Reviews, DARE, MEDION, SIGLE and international published guidelines on the diagnosis of PE were also searched. No language restrictions were applied. In addition, the bibliographies of retrieved publications were checked for additional studies and experts in the field were contacted.

Study selection

Study designs of evaluations included in the review
Diagnostic accuracy studies, or prospective follow-up studies involving patient contact, which had a greater than 85% follow-up rate were eligible for inclusion.

Specific interventions included in the review
Studies that evaluated CT pulmonary angiography were eligible for inclusion. Studies that used electron beam CT scanners were excluded.

Reference standard test against which the new test was compared
The included diagnostic accuracy studies were required to apply an acceptable reference standard to all or a subgroup of participants. Acceptable reference standards were combinations of ventilation perfusion scanning, clinical diagnosis/follow-up and pulmonary angiography. Studies in which the CT scan result formed part of the reference standard were excluded.

Participants included in the review
The included studies were diagnostic accuracy studies of patients with suspected PE, or follow-up studies of patients with a negative CT result. The prevalence of PE ranged from 19 to 79% in the included diagnostic accuracy studies and from 10 to 35% in the follow-up studies. One study in patients with suspected massive PE and two studies in intensive care patients were excluded.

Outcomes assessed in the review
The included diagnostic accuracy studies were required to report the numbers of true-positive, false-positive, false-negative and true-negative results for PE. The included follow-up studies had to report sufficient data to calculate the numbers of participants who developed deep vein thrombosis (DVT) or PE during follow-up. The review reported sensitivity and specificity for diagnostic accuracy studies and false-negative rate for follow-up studies.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed all titles and abstracts identified through the database searches; all potentially relevant publications were retrieved in full. Two reviewers then assessed all potentially relevant papers, with any disagreements resolved by a third reviewer.
Assessment of study quality
Two reviewers independently assessed the methodological quality of the included studies using predetermined criteria; any discrepancies were resolved by a third reviewer. The quality assessment criteria addressed the recruitment process and characteristics of the included participants, the prevalence of PE, and details of the CT scan. For diagnostic accuracy studies, interpretation of the reference standard blind to the CT result and vice versa was also assessed. For follow-up studies, the outcomes assessed, consistency of assessment across patients, details of additional investigations (including method of determining cause of death where appropriate) and length of follow-up were also assessed.

Data extraction
Three reviewers independently extracted the study results. For diagnostic accuracy studies, the numbers of true positives, false positives, false negatives and true negatives were extracted and used to calculate the sensitivity and specificity. For follow-up studies, the numbers of false-negative CT scans were calculated; false negatives were defined as positive venous ultrasound or pulmonary angiogram, high probability ventilation-perfusion scan, or death caused by PE.

Methods of synthesis
How were the studies combined?
The results of the included studies were displayed in forest plots and pooled estimates were calculated using a random-effects model.

How were differences between studies investigated?
For diagnostic accuracy studies, the presence of a diagnostic threshold effect was assessed by calculating the Spearman correlation coefficient between sensitivity and specificity. The Breslow-Day test was used to examine heterogeneity in the results between studies. Subgroup analyses, based on participant characteristics and quality assessment scores, were used to investigate potential sources of heterogeneity.

Results of the review
Thirteen diagnostic accuracy studies (749 participants) and 11 follow-up studies (2,763 participants) were included.

Diagnostic accuracy (13 studies).
Twelve studies used pulmonary angiography as the reference standard; the thirteenth used a diagnostic algorithm. All but three studies used a single detector scanner. Twelve studies used more than one radiologist to interpret the CT scan; the other did not report numbers. Participant characteristics and quality assessment results varied widely. The sensitivity ranged from 53 to 100% and the specificity from 7% to 100%. The pooled estimates for sensitivity and specificity were 88.9% (95% confidence interval, CI: 82.0, 95.0) and 94.6% (95% CI: 91.3, 98.0), respectively, and there was significant between-study heterogeneity (p<0.005) which was not improved by any of the subgroup analyses. There was no evidence of a diagnostic threshold effect.

Prognostic value (11 follow-up studies).
The baseline characteristics of the participants and follow-up varied. Follow-up ranged from clinical examination at 6 weeks to 3 months to one telephone call at 6 months. Only four studies reported a uniform investigative process after negative CT. The false-negative rate was heterogeneous (p=0.000), ranging from 0.009 (95% CI: 0.002, 0.048) to 0.107 (95% CI: 0.085, 0.133), and heterogeneity was not reduced by either participant subgroup analyses or a sensitivity analysis in which studies with poor quality scores were removed. When false-negative rates were calculated for a combination of both negative CT angiography and negative investigation for DVT there was no evidence of significant between-study heterogeneity (p=0.382); the pooled estimate for the false-negative rate (5 studies) was 1.5% (95% CI: 1.0, 1.9).
Authors' conclusions
The reported diagnostic accuracy of CT angiography for PE varied between studies and there was little evidence on the performance of modern multislice CT. Follow-up studies showed that CT, in combination with investigation for DVT, could safely be used to exclude PE.

CRD commentary
The review addressed a valid research question and applied appropriate and clearly stated inclusion criteria. A thorough literature search, which included attempts to locate unpublished studies, was conducted and no language restrictions were applied; retrieval of the available data was therefore likely to have been good. Measures to reduce the potential for error and bias in the review process were reported. The methodological quality of the included studies was assessed and summarised in the text and in the authors' interpretation of their results, as well as being used in sensitivity analyses. The methods used to pool the results of the individual studies were broadly appropriate, though the generation of pooled estimates of sensitivity and specificity is of questionable value given the extent of between-study heterogeneity. The authors' conclusions follow from the data presented and are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that CT can safely be used in combination with investigation for DVT to rule out PE.

Research: The authors stated that high-quality, multicentre studies using multislice scanners are required to determine the true diagnostic accuracy of CT pulmonary angiography as currently used.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract
contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.