Safety of ruling out acute pulmonary embolism by normal computed tomography pulmonary angiography in patients with an indication for computed tomography: systematic review and meta-analysis

Mos IC, Klok FA, Kroft LJ, De Roos A, Dekkers OM, Huisman MV

CRD summary
This review found that a normal computed tomography pulmonary angiography result alone can safely exclude pulmonary embolism in patients at moderate or high risk of disease; there was no need for additional ultrasonography to exclude venous thromboembolism in these patients. The conclusions were supported by the data presented and are likely to be reliable.

Authors' objectives
To determine the safety of ruling out pulmonary embolism by computed tomography (CT) pulmonary angiography in patients with a “likely” or “high” clinical probability of pulmonary embolism or an elevated D-dimer concentration.

Searching
MEDLINE, EMBASE, Web of Science and the Cochrane Library were searched for studies published between 1990 and September 2008. Search terms were reported. References of included studies were screened. No language restrictions were applied.

Study selection
Prospective studies that evaluated computed tomography (CT) pulmonary angiography in consecutive increased risk patients, identified through a diagnostic strategy based on a clinical decision rule and D-dimer test without additional imaging tests prior to CT pulmonary angiography, were eligible for inclusion. Studies that assessed the additional value of compression ultrasonography performed after a negative CT pulmonary angiography test for excluding venous thromboembolism were also eligible. Eligible studies were required to report predefined endpoints, have a clear description of inclusion and exclusion criteria, and have clinical follow-up of greater than one month.

The primary outcome was the negative predictive value of CT pulmonary angiography and the safety of withholding anticoagulant therapy on the basis of a normal CT pulmonary angiography result. Endpoints for safety were the incidence of confirmed adverse thrombotic events subsequent to a normal CT pulmonary angiography result, including all occurrences of venous thromboembolism (both pulmonary embolism and deep vein thrombosis), and mortality attributable to pulmonary embolism.

The mean age of included patients ranged from 50 to 60 years; the proportion of males ranged from 35 to 46%. Most included patients were outpatients. Different clinical decision rules were used to identify patients with an increased risk of pulmonary embolism (the Geneva Score, revised Geneva Score, the Wells rule and the Hyers criteria). All studies also used D-dimer, although the assay varied across studies. Some studies used single-detector CT; others used multi-detector row CT modalities.

Two reviewers independently assessed studies for inclusion. Disagreements were resolved through referral to a third reviewer.

Assessment of study quality
Study quality was assessed according to the following criteria: patient enrolment, outcome assessment, duration of follow-up, loss to follow-up, and funding source.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Data were extracted on the number of events and used to calculate the proportion of patients experiencing each event. The negative predictive value (the proportion of patients with a negative CT pulmonary angiography result who did not experience an adverse thrombotic event) was calculated. Data to calculate the sensitivity of CT pulmonary angiography alone, and CT pulmonary angiography combined with ultrasound, were also extracted. Patients who received anticoagulants for reasons other than thromboembolism were excluded from the analysis, as were patients who were lost to follow-up.

Two reviewers independently extracted data.

Methods of synthesis
The proportion of patients experiencing each adverse event, the negative predictive value, and sensitivity were pooled using fixed-effect and random effects models. Heterogeneity was assessed using the $I^2$ statistic. Studies with CT pulmonary angiography alone, and those with additional compression ultrasonography following a negative CT pulmonary angiography test, were pooled separately.

Results of the review
Six studies were included in the review (n=6947 patients). Three studies assessed computed tomography (CT) pulmonary angiography alone; three studies assessed CT pulmonary angiography with additional compression ultrasonography following a negative CT pulmonary angiography test. Two studies randomised patients to different testing strategies. Only the arms relating to CT pulmonary angiography testing were included in the review. Duration of follow-up was three months in all studies. Loss to follow-up ranged from 0 to 1.3%. Outcome assessment was either blinded or performed by an independent adjudication committee.

The proportion of inconclusive CT pulmonary angiography results was 1.8% (range 0.9 to 4.6). The incidence of pulmonary embolism as determined by a positive CT pulmonary angiography result was 28% (range 18 to 36).

The incidence of confirmed venous thromboembolism following a negative CT pulmonary angiography scan was 1.2% (95% CI 0.8 to 1.8; three studies); the incidence of fatal pulmonary embolism was 0.6% (95% CI 0.4 to 1.1).

The incidence of confirmed venous thromboembolism was almost identical after a negative CT pulmonary angiography scan followed by a negative ultrasonography results (1.1%, 95% CI 0.6 to 2.0; three studies), as was the incidence of fatal pulmonary embolism (0.5%, 95% CI 0.2 to 1.1). Results were similar using a random-effects model.

The sensitivity of CT pulmonary angiography alone for detecting pulmonary embolism was 97.3% (95% CI 96.1 to 98.2). The sensitivity of CT pulmonary angiography combined with ultrasound was almost identical at 97.4% (95% CI 95.1 to 98.6). There was no evidence of statistical heterogeneity.

Authors’ conclusions
A normal computed tomography pulmonary angiography result alone could safely exclude pulmonary embolism in all patients in whom CT pulmonary angiography is required to rule out this disease. There was no need for additional ultrasonography to exclude venous thromboembolism in these patients.

CRD commentary
The review addressed a focused question, supported by clearly defined inclusion criteria. The literature search was adequate, but restriction to published studies meant that relevant studies may have been missed. Appropriate steps were taken to minimise bias and errors when selecting studies and extracting data, but it was unclear whether such steps were also taken when assessing quality.

Some relevant criteria were used to assess study quality; the results of the quality assessment were reported. Appropriate methods were used to pool data. The results were clearly presented using forest plots and tables.

The conclusions were supported by the data and are likely to be reliable.
Implications of the review for practice and research

**Practice:** The authors stated that a normal CT pulmonary angiography result alone can safely exclude pulmonary embolism in patients at moderate or high risk of disease. There is no need for additional ultrasonography to rule out venous thromboembolism in these patients.

**Research:** The authors did not state any implications for research.

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