Meta-analysis: outcomes in patients with suspected pulmonary embolism managed with computed tomographic pulmonary angiography

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CRD summary
The review assessed the safety of withholding anticoagulation therapy in patients with suspected pulmonary embolism and negative results on spiral computed tomographic pulmonary angiography (CTPA). The authors concluded that it appeared to be safe to withhold treatment following a negative CTPA result when lower-extremity imaging was performed concurrently. The conclusion appears appropriate based on the evidence presented.

Authors' objectives
To determine the safety and efficacy of withholding systemic anticoagulation following negative results on computed tomographic pulmonary angiography (CTPA) in patients with suspected pulmonary embolism (PE).

Searching
MEDLINE (from 1966 to 2004) and EMBASE (from 1974 to 2004) were searched for published reports in English and other languages; the search terms were given. Additional articles were sought in the reference lists of retrieved articles and the authors' personal files.

Study selection
Study designs of evaluations included in the review
Studies that used a consecutive sample, or a well-defined reason for a selected sample, with a minimum of 3 months' follow-up were eligible for inclusion.

Specific interventions included in the review
Studies that evaluated CTPA to diagnose suspected PE were eligible for inclusion. The method of CTPA varied across the included studies. In most studies CTPA was used as part of a diagnostic algorithm in combination with other tests, including pre-test probability, lung scintigraphy, lower-extremity compression ultrasonography and D-dimer testing.

Reference standard test against which the new test was compared
The review did not include any diagnostic accuracy studies that compared the performance of the index test with a reference standard of diagnosis.

Participants included in the review
Studies of adults with suspected PE who had negative or indeterminate CTPA results and in whom anticoagulation therapy was withheld, or there was a clearly reported reason for administering anticoagulation when venous thromboembolism (VTE) was excluded, were eligible for inclusion. Participants who received anticoagulation therapy were excluded from the final analysis. Reasons for administering anticoagulation therapy despite negative CTPA results included the detection of deep vein thrombosis on concomitant ultrasonography, chronic VTE, and cardiac arrhythmias or other cardiac abnormalities.

Outcomes assessed in the review
Studies that reported recurrent VTE events and fatal PE with a means of confirmation were eligible for inclusion. Where reported, objective imaging was used to confirm recurrent VTE events and fatal events were confirmed by autopsy or central adjudication.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.
Assessment of study quality
Each study was assessed for the following: description of the patients' characteristics; description of the inclusion and exclusion criteria; potential for selection bias; the length and completeness of follow-up; description of the patients lost to follow-up; reasons for incomplete follow-up; definition of outcome at study commencement; and the objectivity of outcome measures used. Two reviewers independently assessed the validity of each included study. Any disagreements were resolved by consensus.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data were extracted on the proportion of participants who obtained negative CTPA results and who then went on to experience a fatal or nonfatal PE.

Methods of synthesis
How were the studies combined?
The results from the individual studies were combined using the inverse variance method. A pooled rate with 95% confidence intervals (CI) was calculated separately for VTE events and fatal PE. Publication bias was investigated through visual assessment of funnel plots and statistically using the method proposed by Egger et al. (see Other Publications of Related Interest no.1). In addition, the sensitivity of the results to publication bias was assessed using the method of Duval and Tweedie (see Other Publications of Related Interest no.2).

How were differences between studies investigated?
Heterogeneity was investigated through visual assessment of Galbraith plots of study results. Sensitivity analyses were performed to investigate the influence of the following on the results obtained: study type (prospective versus retrospective), year of study, patient sample (consecutive versus selected), generation of computed tomography (CT) scanner, the thickness of CT cuts, caudocranial image acquisition, view box interpretation (view box versus no view box), and the prevalence of PE.

Results of the review
Twenty-three studies reporting on 4,657 participants (who were eligible for outcome assessment) were included in the analysis. Fifteen studies were prospective and eight were retrospective.

Three studies met nine quality indicators, 1 study met eight, 4 studies met seven, 5 studies met six, 4 studies met five, 5 studies met four and 1 study met three. The results for the quality ratings of the included studies are available on the Annals of Internal Medicine website (accessed 23/05/2005). See Web Address at end of abstract.

The 3-month rate of subsequent VTE after obtaining negative results on CTPA was 1.4% (95% CI: 1.1, 1.8) and the rate of fatal PE was 0.51% (95% CI: 0.33, 0.76). The results were not affected by any factors investigated in the sensitivity analyses (P>0.2 for all comparisons). In a separate analysis, no evidence of publication bias was found.

The cumulative rate of subsequent VTE among patients who had inconclusive CTPA results and who did not receive anticoagulation was 16.2%.

Authors' conclusions
It appeared to be safe to withhold anticoagulation treatment in patients with suspected PE following a negative CTPA result when imaging of the lower extremities was performed concurrently.

CRD commentary
The study addressed a clear research question and the inclusion criteria appeared appropriate. Several sources were searched for relevant studies and attempts were made to limit language bias. The methods used to select studies for inclusion and to abstract the data were not reported, thus the potential for reviewer error and bias could not be assessed.
Unpublished data were not sought, although the authors did not find any evidence of publication bias. The quality of the included studies was assessed systematically, in duplicate, and aspects of validity were appropriately discussed.

Adequate details of each of the included studies were given in the report, which highlighted clinical and methodological differences across the studies, suggesting that the decision to statistically combine the studies might not have been appropriate. However, the authors conducted sensitivity analyses to account for some of the differences. The authors’ conclusion regarding the fact that the role of CTPA without concomitant lower-extremity imaging remained undefined was justified, and the recommendations for practice were based on the evidence presented in the review. However, there were limitations in the reporting of the review process. Furthermore, the fact that some patients in the included studies were given anticoagulation therapy but were not included in the analysis suggests that further research is needed to establish in whom it is safe to withhold anticoagulation therapy.

**Implications of the review for practice and research**

**Practice:** The authors stated that withholding anticoagulation therapy appeared safe in patients with suspected PE who were managed with concurrent CTPA and imaging of the lower extremities (using either lower-extremity ultrasonography or CT venography).

**Research:** The authors stated that, ideally, a randomised controlled trial comparing CTPA with conventional pulmonary angiography (as the 'gold' standard), in which anticoagulation therapy is withheld in all patients with negative results and VTE events are well documented, is needed to provide clear guidance on the management of patients with suspected PE. However, the authors acknowledged that this would require more than 10,000 participants.

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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.