

A Useful Diagnostic Strategy for Suspected Pulmonary Embolism

Perrier A, Roy PM, Aujesky D, et al. Diagnosing pulmonary embolism in outpatients with clinical assessment, D-Dimer measurement, venous ultrasound, and helical computed tomography: a multicenter management study. *Am J Med* 2004;116:291–9.

Study Overview

Objective. To evaluate a diagnostic strategy for outpatients presenting to the emergency department (ED) with symptoms suggestive of pulmonary embolism (PE).

Design. Prospective cohort study.

Setting and participants. Patients presenting with unexplained new or worsening dyspnea or chest pain were recruited from EDs at 3 European medical centers. Patients were excluded if they took anticoagulation therapy for reasons other than thromboembolism, could not undergo computed tomography (CT) scanning with intravenous contrast, had a creatinine clearance below 30 mL/min, could not provide consent, were pregnant, could not be followed after discharge, were suspected of having a massive PE with shock, or did not undergo the testing specified by the algorithm.

Intervention. Enrolled patients were managed using a diagnostic algorithm to establish or exclude the diagnosis of PE. Clinical probability of PE was assigned using a published prediction rule [1], which clinicians could override. In the first step of the algorithm, PE was considered excluded without further testing if the plasma D-dimer level (rapid ELISA [enzyme-linked immunosorbent assay], Vidas DD, BioMérieux, Marcy l'Etoile, France) was less than 500 µg/L. When the D-dimer was ≥ 500 µg/L, compression ultrasound of the lower extremities was performed, and patients with deep vein thrombosis were treated for thromboembolism. Remaining patients had helical contrast CT performed. Patients with negative CT scans and low or intermediate clinical probability of PE were diagnosed as not having PE. Patients who had high clinical probability of PE but had negative CT scans at this point underwent pulmonary angiography and were treated if PE was detected.

Main outcome measures. Proportion of patients assigned a diagnosis at the various stages of the algorithm and proportion of patients diagnosed as not having PE who developed clinically evident thromboembolism within 3 months.

Main results. Of 1290 patients screened, 965 were included.

The prevalence of PE was similar in patients who were included (23%) and excluded (21%). By sequentially following the algorithm, diagnoses were assigned as follows: 280 (29%) patients had PE excluded after a negative D-dimer measurement, 92 (9.5%) patients had thromboembolism diagnosed after a positive ultrasound, and 574 (59%) additional patients had diagnoses made after CT scan. 124 (13%) patients had PE detected by CT scan, and 450 (47%) patients had PE excluded by having a low or intermediate clinical suspicion for PE and a negative CT scan. Eight patients with high clinical suspicion and negative CT scans underwent pulmonary angiography, which diagnosed PE in 2 patients. Eleven patients with inconclusive findings on CT underwent subsequent testing (ie, lung scintigraphy or angiography), and 4 were determined to have PE. Among the 685 patients for whom PE was excluded by this algorithm and who did not receive anticoagulation for another reason (eg, atrial fibrillation), 7 had clinically evident venous thromboembolism in the subsequent 3 months (1.0% [95% confidence interval {CI}, 0.5%–2.1%]). All of these patients had a positive D-dimer measurement, negative ultrasound and CT scan, and low or intermediate clinical suspicion for PE (thromboembolism occurred in 1.7% of patients [95% CI, 0.8%–3.5%] in the group with these characteristics).

Conclusion. This noninvasive diagnostic strategy provided a diagnosis for 98% of outpatients with suspected PE with a low short-term rate of clinically evident thromboembolism.

Commentary

PE has always presented a formidable diagnostic challenge. Many diagnostic strategies have been investigated [2]. Normal results on pulmonary angiography or lung scintigraphy can effectively rule out PE, but angiography is invasive, and scintigraphy frequently fails to establish a firm diagnosis. CT scanning has emerged as a useful modality in the diagnosis of PE, but it is expensive and there is a small risk involved in the administration of intravenous contrast. A variety of D-dimer tests have been examined as a means of excluding thromboembolism, but most data regarding these tests pertain to individuals with low clinical suspicion of PE [2].

This study by Perrier et al is important for several rea-

sons. It demonstrates that in a large group of patients, the D-dimer ELISA assay that was used did an excellent job of excluding PE in all clinical risk groups and eliminated the need for additional testing in 29% of patients. The authors also showed that by using ultrasound as the next step, 39% of the total population could be given a diagnosis without requiring CT. When clinical risk assessment (which included room air arterial blood gas determination) and CT were combined with these methods, almost all patients received a diagnosis. The study was done at several centers using a variety of CT techniques, thereby adding to the generalizability of these findings.

Clinicians who wish to apply this algorithm should keep several important facts in mind. First, a highly sensitive D-dimer ELISA test was used. Other D-dimer assays may not be as reliable at excluding PE. Second, all patients with negative CT scans already had normal lower extremity ultrasound findings. The use of CT alone to exclude PE in patients with a low to moderate clinical suspicion of PE and positive D-dimer tests may not be as reliable. Last, patients in this study with a low to moderate clinical suspicion for PE, a positive D-dimer, and negative ultrasound and CT tests had a short-term thromboembolism risk of 1.7% (95% CI,

0.8%–3.5%). Future advances in CT technique may further improve PE diagnosis, but at present, a small number of patients with this combination of test results still may have undiagnosed PE.

Applications for Clinical Practice

For patients presenting to the ED with symptoms suggestive of PE, a diagnostic algorithm that uses clinical risk assessment and D-dimer ELISA followed by lower extremity ultrasound and CT scanning when necessary can provide an accurate diagnosis for almost all patients and avoid the need for CT scanning in 39% of patients.

—Review by Stephen D. Persell, MD, MPH

References

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2. Kruip MJ, Leclercq MG, van der Heul C, et al. Diagnostic strategies for excluding pulmonary embolism in clinical outcome studies. A systematic review. *Ann Intern Med* 2003; 138:941–51.

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