A Better Approach to the Diagnosis of PE

A simple diagnostic algorithm is all that’s needed to safely and effectively reduce reliance on CT pulmonary angiography to diagnose pulmonary embolism.

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PRACTICE CHANGER
Do not order CT pulmonary angiography when evaluating patients for suspected pulmonary embolism (PE) unless: (1) the patient has a d-dimer concentration $\geq$ 1000 ng/mL; or (2) the patient has a d-dimer concentration $\geq$ 500 ng/mL, PLUS (a) clinical signs of deep vein thrombosis or (b) hemoptysis or (c) pulmonary embolism is the most likely diagnosis.

STRENGTH OF RECOMMENDATION
A: Based on a prospective, multicenter, cohort study of 3616 patients with clinically suspected PE.

Penny E, a 48-year-old woman with a history of asthma, presents with wheezing and respiratory distress. There are no clinical signs of deep vein thrombosis or hemoptysis. PE is not your most likely diagnosis, but it is included in the differential, so you order a d-dimer concentration. It returns at 700 ng/mL. Should you order CT pulmonary angiography (CTPA) to evaluate for PE?

PE is the third most common type of cardiovascular disease after coronary artery disease and stroke, with an estimated incidence in the United States of 1-2/1000 individuals and a 30-day mortality rate between 10% and 30%. Improved adherence to a clinical decision support system has been shown to significantly decrease the number of diagnostic tests performed and the number of diagnostic failures.

A diagnostic algorithm that includes the Wells criteria and a d-dimer concentration can exclude PE without CTPA in 20% to 30% of patients. However, due to the complexity of the algorithm and insufficient time in busy emergency departments, adherence to recommended diagnostic strategies is variable.

Further, it is common for a d-dimer test to be obtained before clinical assessment by a provider. A fixed cutoff d-dimer concentration of 500 ng/mL is commonly used, despite an absolute reduction of 11.6% in the need for CTPA using an age-adjusted d-dimer concentration threshold (age $\times$ 10 ng/mL for patients older than 50).

Three items of the original Wells criteria—clinical signs of deep vein thrombosis, hemoptysis, and whether PE is the most likely diagnosis—are the most predictive for PE. The development of a more efficient algorithm based on these 3 items that uses differential d-dimer concentration thresholds could retain sensitivity and decrease unnecessary CTPA. Decreasing CTPA would avoid contrast-induced nephropathy and decrease cancers associated with radiation exposure.

Significant cost savings could also be achieved, as the estimated cost of one CTPA is $648, while a d-dimer concentration is estimated to cost $14.

STUDY SUMMARY
Simplified algorithm diagnoses PE with fewer CTPAs

The YEARS study was a prospective cohort study conducted in 12 hospitals in the Netherlands that included 3616 patients with clinically suspected PE. A total of 151 patients met exclusion criteria (life expectancy < 3 months, ongoing anticoagulation treatment, pregnancy, and contraindication to CTPA). Investigators managed the remaining 3465 study patients according to the YEARS algorithm, which calls for obtaining a d-dimer concentration in all patients...
and assessing for the 3 items in the YEARS clinical decision rule: clinical signs of deep vein thrombosis; hemoptysis; and whether PE was the most likely diagnosis.

PE was considered excluded if a patient had a d-dimer concentration < 1000 ng/mL and no positive YEARS items or if the patient had a d-dimer concentration < 500 ng/mL and 1 or more YEARS items. The primary outcome was venous thromboembolism (VTE) events at 3 months’ follow-up once PE was excluded. The secondary outcome was the number of required CTPAs using the YEARS decision rule compared with the number that would have been required if the Wells diagnostic algorithm had been implemented.

Of the 1743 patients who had none of the 3 YEARS items, 1320 had a d-dimer concentration below the 1000-ng/mL threshold. Of the 423 who had a d-dimer ≥ 1000 ng/mL, 55 had PE confirmed by CTPA. In the 1722 patients who had at least 1 YEARS item, 1391 had a d-dimer concentration ≥ 500 ng/mL threshold; 401 of them had PE confirmed by CTPA.

Eighteen of the 2964 patients who had PE ruled out by the YEARS algorithm at baseline were found to have symptomatic VTE during the follow-up period (0.61%), with 6 patients (0.20%) sustaining a fatal PE. The 3-month incidence of VTE in patients who did not have CTPA was 0.43%, which is similar to the 0.34% reported in a previous meta-analysis of the Wells rule algorithm. Overall, fatal PE occurred in 0.3% of patients in the YEARS cohort vs 0.6% in a meta-analysis of studies using standard algorithms.

Using an intention-to-diagnose analysis, 1611 (46%) patients did not have a CTPA indicated by the YEARS algorithm compared with 1174 (34%) using the Wells algorithm, for an absolute difference of 13% and estimated cost savings of $283,176 in this sample. The per-protocol analysis also had a decrease of CTPA examinations in favor of the YEARS algorithm, ruling out 1651 (48%) patients—a decrease of 14% and an estimated savings of $309,096.

**CAVEATS**

**No adjusting D-dimer for age**

The YEARS criteria do not consider an age-adjusted d-dimer threshold, which has been shown to further decrease CTPA use. This does not preclude the use of the YEARS criteria; applying age-adjusted d-dimer thresholds would have led to an absolute reduction of 8.7% in CTPA.

**CHALLENGES TO IMPLEMENTATION**

None to speak of

We see no challenges to the implementation of this recommendation.

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**REFERENCES**