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Updated 2/13/09
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Pulmonary Embolism: Diagnosis with Computed Tomographic Angiography (Teacher's Guide)

(50 minutes)

I. Objectives

- Learn how to assess the pretest probability of a patient having a pulmonary embolism.
- Understand when a D-dimer is useful in ruling out pulmonary embolism.
- Know when to order and how to apply the results of a multidetector row computed tomographic angiogram (CTA).

II. Case

A 63-year old woman with stage II non-small cell lung cancer calls 911 for acute shortness of breath (SOB). At baseline, she has mild SOB controlled by her inhalers. She is also taking hormone replacement therapy. On the day of admission, she develops a sudden increase in SOB and new pleuritic chest pain. She does not improve with nebulizer treatment on the way to the hospital. In the ER, her pulse is 115, RR = 36, temp = 100.1°F and O₂ sat = 88% on room air. On exam, her lungs are clear, and her extremities are normal. A chest x-ray (CXR) shows mild right-sided atelectasis. An ABG shows pH = 7.48, PCO₂ = 32 mm Hg and PO₂ = 50 mm Hg on room air.

What is this patient's pretest probability for having a pulmonary embolism?

Ask team members what their "gut feeling" is for this patient's pretest probability of having a PE.

Ask someone to calculate the patient's Revised Geneva Score.^{3(Table 2)} Review the clinical probability of PE in the low, intermediate and high risk categories.³

Note that although the score is "intermediate," there are certain features of the patient's presentation that suggest that she actually has a high pretest probability for having a PE.

Note that the Revised Geneva Score does not include data from ABG, EKG or CXR that may be used to refine your assessment. It also does not include information on some hypercoagulable states, such as pregnancy or antiphospholipid antibody syndrome.

Emphasize that clinical judgment can and should sometimes override clinical prediction rules. (In fact, studies have shown that a clinician's assessment is as good as these clinical prediction rules, and that rules are most useful when the clinician is relatively inexperienced.)

The ER physician orders a D-dimer, which comes back negative. Does this patient require any further work-up?

A negative D-dimer does not rule out PE in a high-risk patient. Further work-up is mandated.

You decide to order a chest CTA on this patient. If the CTA does not show a pulmonary embolism, what are the chances that this is a false-negative, and that the patient really does have a PE? What further work-up, if any, is required?

Discuss the methods and results of the NEJM article, "Multidetector Row Computed Tomography in Suspected Pulmonary Embolism." (Recommend writing out the algorithms outlined in the summary of the key article on a board.)¹

In both key articles, the false-negative rate of CTA was 1-2%. Further work-up with a Doppler ultrasound of the lower extremities or a pulmonary angiogram improves the diagnostic yield by about only 1%.^{1,2}

If the CTA confirms a pulmonary embolism, what are the chances that the patient truly has a pulmonary embolism? (I.e., what is the positive predictive value?)

The NEJM study does not provide you with the information to calculate the positive predictive value of a CTA that shows a PE, since none of those patients had the gold standard, conventional pulmonary angiography. The false positive rate of CTA for pulmonary embolism is unknown.

How accurate is ventilation-perfusion (V/Q) scanning compared to CTA? Would a V/Q scan be an appropriate test in this patient?

A normal V/Q scan effectively rules out PE, with a false-negative rate <1%, and a high probability V/Q scan virtually rules in PE. However, most scan results (54% in the Anderson article) are nondiagnostic.²

Review the methods and results of key article #2, asking learners to refer to the diagnostic algorithms in figure 1. The bottom line is that CTA appears to have a higher sensitivity than V/Q scanning in detecting PE. However, it is not clear if the additional diagnoses of PE detected by CTA are clinically important and warrant anticoagulation.

Given the patient's underlying lung disease (COPD and cancer), a V/Q scan is unlikely to be normal, and a low to intermediate probability result would require further testing. Thus, it is best to proceed to a multidetector row CTA. The other benefit of CTA is that it can sometimes detect alternative causes of the patient's symptoms (e.g., progressive cancer, pneumonia).

III. Questions for Further Discussion

If the CT shows an isolated, subsegmental pulmonary embolism, what would be the appropriate management?

Isolated, subsegmental PE on CTA has a positive predictive value of only 25% for a true PE diagnosis.² Although in the Anderson study, these patients were started on anticoagulation, most clinicians would consider this finding inconclusive and order further testing.

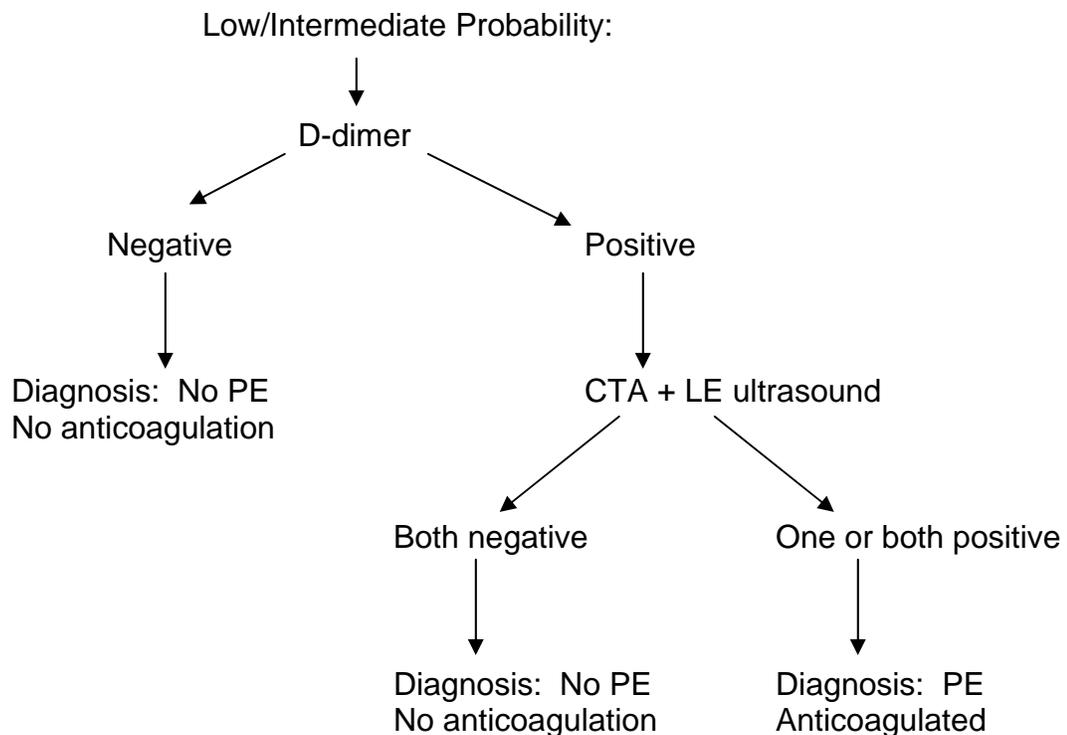
IV. Teacher's Guide to Key Articles

1. Perrier A, *et al.* Multidetector-row computed tomography in suspected pulmonary embolism. *NEJM* 2005; 352: 1760-8. [FULL TEXT](#) [PDF](#)

Methods

- Multicenter trial of 4- to 16-slice multidetector-row CTA in 756 consecutive ER patients with suspected pulmonary embolism.
- Patients stratified into low, intermediate and high pretest probabilities based upon the Geneva score.

Algorithm for low to intermediate risk patients:



All patients were followed up for 3 months for interval development of thromboembolic event.

False-negative CTA defined as a negative CTA with a positive LE ultrasound or subsequent diagnosis of thromboembolic event within the next 3 months.

Results

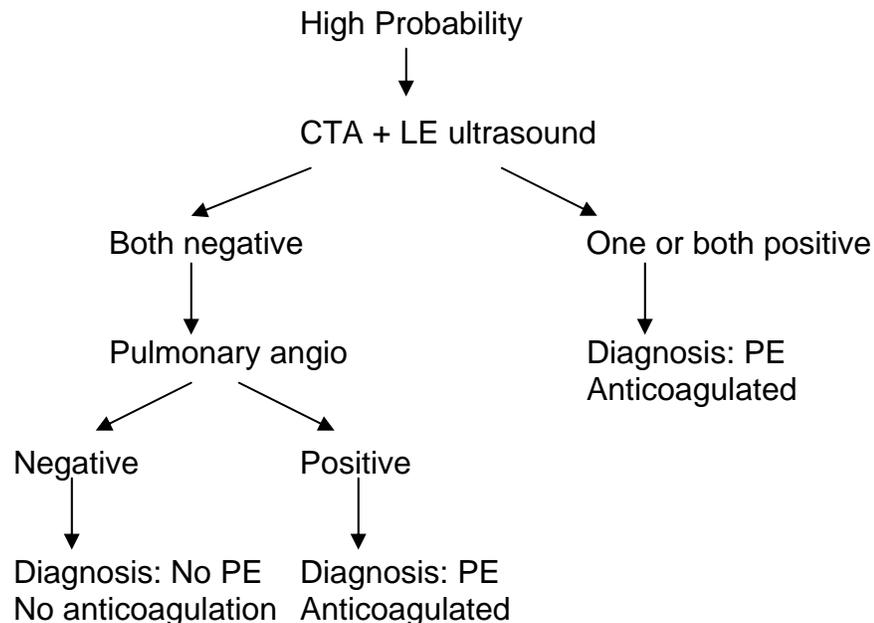
Performance of D-dimer in low-intermediate risk patients:

- One-third of patients had a negative D-dimer and were ruled out for PE on the basis of this test alone.
- None of the patients with a negative D-dimer was subsequently diagnosed with a thromboembolic event (false-negative rate = 0%).

Performance of CTA in low-intermediate risk patients:

- 33% of patients ruled in for a PE based upon a positive CTA
- 0.6% of patients had a positive LE ultrasound with a negative CTA
- 1.7% of patients were diagnosed with a VTE within 3 months of follow-up.
- Overall false-negative rate for CTA = 2.3%

Algorithm for high-risk patients:



Results for high risk patients:

- 95% of patients ruled in for a PE based upon a positive CTA
- In patients with a negative CTA:
 - 1.2% of patients had a positive LE ultrasound
 - 0% of patients had a positive pulmonary angiogram
 - False-negative rate = 1.2%

Conclusions

- Overall, the sensitivity of multidetector row CTA for suspected PE was extremely high, with a false-negative rate of only 1.5%. This sensitivity is similar to pulmonary angiography.
- Routine lower extremity ultrasound added little to the diagnostic yield for PE
- Note that the false-positive rate and the specificity of multidetector row CTA is unknown, as none of the patients who had a positive CTA underwent pulmonary angiogram.

2. Anderson D, *et al.* Computed tomographic pulmonary angiography vs. ventilation-perfusion lung scanning in patients with suspected pulmonary emboli: a randomized controlled trial. *JAMA* 2007; 298: 2743-53. [PDF](#)

Methods

- Randomized patients with suspected PE to either CTA or V/Q scan
- Excluded patients who were clinically unlikely to have a PE (defined by Wells score < 4.5) *and* had a negative D-dimer
- Complicated diagnostic algorithm followed for each arm of the study, designed to minimize false-negatives (see Figure 1). For example, all patients with negative CTAs underwent lower extremity ultrasound, regardless of the presence or absence of DVT symptoms.
- Patients who had negative CTAs or V/Q scans by these algorithms followed without anticoagulation for three months.
- Primary outcome: Subsequent development of symptomatic PE or proximal DVT in patients whom PE had initially been excluded.

Results

- None of the 178 patients excluded because of a low Wells score and a negative D-dimer subsequently ruled in for a VTE (*i.e.*, sensitivity = 100%).
- Remaining 1417 patients were randomized to CTA or V/Q scan.
- In patients undergoing CTA:
 - 17.7% had a PE on CTA
 - False-negative rate = 1.8%
 - Positive ultrasound with a negative CTA in 1.4%
 - Subsequent PE diagnosed within 3 months in 0.4%
- In patients undergoing V/Q scan:
 - 54% of patients had nondiagnostic scans (low or intermediate probability)
 - 11.7% had a PE on V/Q scan
 - 2.5% of patients with a nondiagnostic V/Q scan had a positive LE U/S

- Subsequent VTE diagnosed within 3 months in 0.7% of patients in whom PE was initially excluded
- No statistically significant difference between CTA and V/Q scan in the primary outcome.
- No difference in overall mortality.
- Crossovers:
 - Although the protocol discouraged crossovers, 31 patients in the V/Q scanning group underwent CTA or pulmonary angiography, mostly because their physicians did not believe that PE had not been adequately excluded.
 - Of these patients, 29% ruled in for a PE on CTA or pulmonary angiography.

Conclusions

- Overall, no difference between CTA and V/Q scan in the primary outcome.
- However, PE was diagnosed more often on CTA (17.7%) than on V/Q scan (11.7%).
- Authors conclude that it is unclear if the increased PE diagnosis rate was due to a higher sensitivity of CTA (*i.e.*, more false negatives with V/Q scanning) or lower specificity of CTA (*i.e.*, more false positives with CTA).

Limitations

- Although both diagnostic algorithms resulted in very low rates of the primary outcome (0.4-1%), this study also illustrated the importance of clinical judgment in knowing when to deviate from protocol.
- Investigators defined patients with isolated subsegmental filling defects on CTA as being positive for PE, when the positive predictive value for subsegmental defects is only 25%. This may have led to overdiagnosis of PE in the patients receiving CTA. It is likely that the incremental thrombi detected on CTA may be clinically unimportant.
- Most of the patients in this study were outpatients.

V. Teacher's Guide to Reference Articles

3. **Le Gal G, et al. Prediction of pulmonary embolism in the emergency department: the Revised Geneva Score. *Ann Int Med* 2006; 144: 165-71.**
[PDF](#)

Methods

Derivation of Revised Geneva Score:

- Study of 965 patients admitted to the emergency department with suspected PE
- Physicians filled out a standardized data form with demographic characteristics, risk factors, signs and symptoms, ABG results, EKG, CXR and likelihood of an alternative diagnosis.
- Every patient underwent a standardized diagnostic algorithm to work up possible PE.
- Using this data, an 8-item score based upon H & P was derived to stratify patients into low, intermediate and high clinical probabilities. (See Table 2.)

Validation of Revised Geneva Score:

- The Revised Geneva Score was then applied to another 756 patients with suspected PE, who also underwent the standardized diagnostic work-up.

Results

- The overall prevalence of PE in this population was 23%
- Predictive value of the Revised Geneva Score in the derivation and validation sets:

<u>Score</u>	<u>Clinical Probability</u>	<u>Diagnosed with PE</u>
0-3	Low	9%
4-10	Intermediate	28%
> 11	High	73%

VI. Resources