EM CASES SUMMARY

Episode 113 Pulmonary Embolism Challenges in Diagnosis Part 1

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The diagnosis of PE is a tricky one. It is hardly gratifying when we find an incidental subsegmental filling defect in a 90-year-old patient with multiple comorbidities but missing a larger clot in an otherwise young and healthy patient can be devastating. The problem is, with such a wide variability in presentation and without clear diagnostic directives from the literature, it can be hard to tease apart those who are sick from those who don't have the disease at all.

What we really want are decision aids that maximize diagnostic accuracy while minimizing over-testing and patient harm resulting from over-testing, over-diagnosis and anticoagulant complications.

Pulmonary embolism challenges in diagnosis: What's all the fuss really about anyways?

PEs kill. But not as much as we might think.

In the 1990's The Prospective Investigation of Pulmonary Embolism Diagnosis study found a case fatality rate of 15% at 3 months [1], but only 10% of these deaths were directly attributable to PE [2]. Newer data from the EMPEROR Registry in 2011 found that the mortality rate directly attributed to PE was 1%, while the all-cause 30-day mortality rate was 5.4%, and mortality from hemorrhage was 0.2% [3]. Interestingly, most patients who died (85%) succumbed untreated while waiting for diagnostic confirmation. It appears from this data that most patients with PE die of comorbidities which might have placed the patient at risk for PE, such as malignancy or die while waiting for diagnostic confirmation. Much of this decreased mortality may be related to the increase in diagnosis of subsegmental PEs in the past two decades. Comparison of pooled data from uncontrolled outcome studies shows no increase in PE recurrence or death rates for patients diagnosed with isolated subsegmental PEs who were not anticoagulated compared to those who were anticoagulated [4].

What about the bleeding risk in treated pulmonary embolism?

The typical patient being worked up for PE is low risk for the diagnosis and low at low risk for bleeding complications. In the same 2018 metaanalysis looking at outcomes of subsegmental PEs, 8% of those anticoagulated had a significant bleeding complication [4]. The risk for a major bleed for all comers diagnosed with PE is around 3-5% in the first 3 months of treatment. Most of these will occur in the first week. It is important to weigh the likelihood of PE against the risk of bleeding prior to starting anticoagulation on speculation in the ED. The HAS-BLED score can help here. On the other hand, one or two doses of anticoagulant medication portends a negligible risk for major bleeding complications; ED patients with a high pretest probability for PE who have no absolute contraindications to anticoagulation, should be anticoagulated prior to diagnostic confirmation, as 85% of PE mortality in ED patients occured in untreated patients waiting for diagnostic confirmation in the EMPEROR Registry.

Pitfalls in the diagnosis of pulmonary embolism

Failure to consider the diagnosis in patients with comorbidities. A missed PE is rarely a failure of diagnostic strategy; it's more often a failure to consider the diagnosis to begin with. A PE is easy to miss in those with co-morbidities (e.g. CHF, pneumonia) – premature closure in patients with a clear reason for their shortness of breath or who are going to be admitted for other reasons is one source of missed diagnosis.

Overestimating the risk of PE. While we might think we see a lot of patients that are high risk for PE, the vast majority of patients who we are considering for PE diagnosis are in fact, low risk according to Well's Criteria. We order many needless CTPAs, with their inherent problems of overdiagnosis and radiation risk, for fear of a PE in low risk and negligible risk patients. Remember that placing PE in the top three considerations in your differential diagnosis of a patient who presents with chest pain or shortness of breath does not necessarily mean they are at high risk for PE. Even experienced clinicians have been shown to overestimate the risk of PE in low risk patients.

Misinterpretation of vital signs. One source of over-testing is misinterpreting the contribution of heart rate to the pretest probability. While tachycardia is one of the points in the Well's score, tachycardia in the absence of any other features of pulmonary embolism should not trigger the work-up. Conversely, a normal heart rate does not rule out PE. An important nuance is that a triage tachycardia that normalizes by the time the patient is assessed by the ED physician, according to a recent study, should be considered tachycardia when using the Wells score. In this study, in patients with an abnormal pulse rate, respiratory rate, shock index, or pulse oximetry at triage that subsequently normalized, the prevalence of PE was 18, 14, 19, and 33%, respectively [5].

Assuming low risk for PE in patients with no apparent risk factors. While risk factor assessment is important in assessing pretest probability, up to 50% of PEs are diagnosed in patients with no apparent risk factors [6].

Pearls in decision making on whether or not to work up a patient for pulmonary embolism

Take your time taking a history

Few will miss the woman on OCP who traveled in a trans-Atlantic plane a week ago who comes in dyspneic, coughing up blood with a swollen leg and a history of cancer. For the less clear cut patients there are some pearls to consider when taking a history.

Is it true exertional dyspnea? Where we need to drill down when it comes to assessing symptoms is whether the patient is experiencing true exertional dyspnea or not. Many patients will admit to feeling short of breath if you ask them "have you felt short of breath at all?", but this will inevitably label patients with dyspnea who do not in fact have dyspnea. You are more likely to identify true dyspnea if you ask the patient "how is your breathing" and "give me an example of when you feel breathless". If the patient says that when they walk their dog they need to stop every few steps to catch their breath, this is more likely to be true exertional dyspnea than the patient tells you that they sometimes feel the need to take one or two deeper breaths while watching television.

Fatigue is an overlooked symptom of pulmonary embolism. A common symptom in PE is fatigue, which while non-specific, should raise an eyebrow in the dyspneic patient who tells you that they developed unusual fatigue that coincides with their dyspnea.

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How should risk factors contribute to the pretest probability of pulmonary embolism?

While there is an ever-growing long list of risk factors for PE the important risk factors to consider in assessing pretest probability include personal and family history of venous thromboembolism, recent immobilization, active cancer and exogenous estrogen use. These are the risk factors that should be considered in your assessment of pretest probability for PE. Nonetheless, it is important to realize that up to 50% of PEs are diagnosed in patients with no apparent risk factors [6].

Up to 50% of pulmonary embolisms are diagnosed in patients with no apparent risk factors.

Which patients who present to the ED with syncope or COPD exacerbation require a CTPA to rule out pulmonary embolism?

The PESIT trial [7]
Although this study that showed a startling 17% PE prevalence in patients admitted to hospital with syncope, there are some important points to consider:

- This trial was conducted on those already admitted to hospital. The results are not generalizable to the ED population.
- A subsequent international study showed a <1% prevalence of PE in those who presented to EDs with syncope [8].
- A Canadian study showed a 1.4% prevalence of PE in those admitted with syncope [9].

A reasonable approach therefore would be to assess your syncope patients for PE the way you would any other patient in the ED.

Is COPD the only thing making my patient short of breath?
While one of the sources of missed PE is not considering the diagnosis in patients with respiratory comorbidities, and PE should be considered in patients presenting with unexplained COPD exacerbations, not every COPD patient requires a CTPA in the ED. A 2017 systematic review and meta-analysis showed a PE prevalence of 16% in patients with unexplained acute COPD exacerbations [10]. However, they only included a single ED study which had a PE prevalence of only 3%, and the clinical significance of these PEs were unclear – one third of the PEs were subsegmental. This is a tricky patient population. On the one hand they have poor respiratory reserve at baseline. A second hit from a PE will not be well tolerated. On the other hand, they are at higher risk of catastrophic bleeding given their comorbidities and frailty. So where does this leave us with regards to ordering CTPAs on patients with COPD exacerbations in the ED? Make sure the story fits. If the typical clinical features of COPD exacerbation are missing, or the patient has some features of PE, a workup for PE should be considered. Patients with typical COPD exacerbations with wheeze who have an identifiable infectious source on chest x-ray are unlikely to require a CTPA to rule out PE.

Suggested diagnostic decision tool algorithm for pulmonary embolism.

There are a number of decision rules that are used as objective aids in the work up of PE. **Wells** and **PERC** (Pulmonary Embolism Rule out Criteria) are the two most commonly utilized tools in North American EDs. It is important to understand how the prevalence of PE in your population impacts decision making. Simply put, the prevalence of a disease can be considered the pre-test probability of the patient ruling in for that disease. The maximum suggested prevalence for PE in order to use the PERC rule is 7%. In other words, if there is a high prevalence of PE in your population, PERC may not be applicable.

The PROPER trial out of France, where the prevalence of PE is low, showed that gestalt performed similarly to PERC in terms of 3-month PE rate, but PERC resulted in an 8% decrease in unnecessary CT scanning, and a 40-minute decrease in ED stay [11]. While studies have suggested that physician gestalt may be as accurate as these decision tools [11,12], there is an argument to be made that even seasoned docs should take the time to calculate these scores because even they can have a tendency to overestimate pretest probability at times.

An Algorithmic Approach
Once you have decided to test for PE, our experts suggest starting with Wells to get an idea of the pre-test probability.
1. If <2, use PERC
2. If 2-4, send D-dimer
3. If >4, consider a CTPA

Should The YEARS Algorithm supplant Wells?

The **YEARS score** is essentially a simplified Wells, and uses two different D-dimer thresholds to direct the work up of PE. Limitations of the YEARS study [13,14] include the physicians not being blinded to the initial D-dimer, and higher PE rates compared to other studies. Our experts believe that while promising, the YEARS algorithm requires further study.
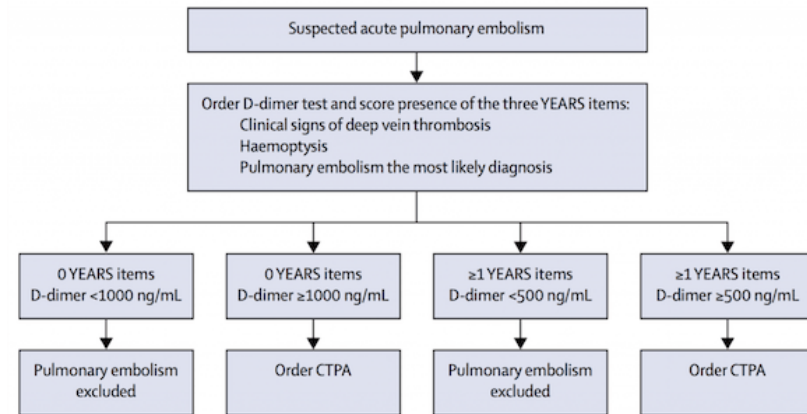
Age-Adjusted D-Dimer

D-dimer threshold = Age (>50) x 10

There are conflicting policy statements from different international societies, but the evidence is reasonably convincing for the use of age-adjusted D-dimer [15] and is recommended by our experts. ACEP suggests that using an age-adjusted approach may reduce the need for advanced imaging without significantly increasing missed cases of PE [16].

Utility of ancillary testing for the diagnosis of pulmonary embolism

CXR. While decades ago we depended more so on CXR and ECG to help in the diagnosis of PE, their utility has recently become less important. Nonetheless, findings on chest X-ray and ECG may aid in your decision making. The main role of a chest X-ray is to rule out alternative diagnoses. Beware of diagnosing pneumonia based on an infiltrate, as a pulmonary infarct from PE can look similar. The chest X-ray is often normal in PE. The classic findings are raised hemidiaphragm, pleural effusion, **Westermark's sign** and **Hampton's hump**. The latter are usually identified in retrospect after the diagnosis of PE has already been made.

ECG. Signs of PE on ECG include sinus tachycardia, RV strain pattern, incomplete RBBB, S1Q3T3, dominant R wave in V1, ST-segment elevation in V1 and aVR and low voltages.
The most specific ECG finding in PE is flipped T waves in anterior AND inferior leads. This finding is almost never found in ischemia-mediated disease. S1Q3T3 has a poor specificity for PE.

POCUS. In general, bedside ultrasound will not be your primary modality to diagnose PE. However, it can be helpful in the arrest or peri-arrest patient who are not safe to leave the ED to get a CTPA. Our experts do not recommend using POCUS to aid in disposition decisions. Even if sonographic signs of right heart strain are present, PE can still be managed as an outpatient if criteria for outpatient management are fulfilled.

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