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JUST THE FACTS

Just the facts: testing patients with suspected pulmonary embolism

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Clinical scenario

A 60-year-old woman is brought to the emergency department by ambulance with a 1-day history of dyspnea, chest pain, and fever. She had myalgia and sore throat for 4 days prior. She denies hemoptysis and leg swelling. Her past medical history includes essential hypertension. She has no surgical history. There is no personal or family history of venous thromboembolic (VTE) disease. At triage, her temperature is 38 °C, heart rate of 120, blood pressure of 158/77, and oxygen saturation of 92% on room air. On examination, she is in mild respiratory distress with fine bibasilar crackles and normal heart sounds. Peripheral vascular exam is unremarkable. You are waiting for her COVID-19 test results. An electrocardiogram shows sinus tachycardia. Her chest X-ray is normal. She has positive Pulmonary Embolism Rule-out Criteria (PERC score) [1] based on her age, heart rate, and oxygen saturation, meaning you cannot use the PERC score to exclude pulmonary emobolism (PE).

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Key clinical questions

Is CT pulmonary angiography the next step?

In Canada, around half of the patients tested for PE in emergency departments can have PE excluded with D-dimer testing [2]. This is a safe approach, even when the patient is suspected of having COVID [3]. The disadvantages of ordering a CT pulmonary angiogram on everyone you test includes: longer emergency department stays, department overcrowding, blocking access to the CT scanner for other sicker patients and hospital transfer in some settings. In addition, reducing CT use avoids patients being wrongly diagnosed with PE (false positives occur in 1–17% of cases) [4].

There are four different pathways for using D-dimer to exclude PE (Fig. 1). These pathways are described here in order of increasing efficiency [5] and decreasing external validation for PE exclusion. Physicians should be familiar with and use one of these approaches to exclude PE without requesting pulmonary imaging.

Option 1: An 'unlikely' Wells score combined with D-dimer at the manufacturer-recommended cutoff

Developed in Canada, the Wells score is the most widely used pre-test probability score (Table 1). A total of ≤ 4 points on the Wells score is termed 'PE unlikely'. A Wells score of ≤ 4 combined with a D-dimer below the recommended manufacturer cutoff (usually < 500 ng/ml, which equates 0.5 µg/mL reported with some assays) excludes the diagnosis of PE with high sensitivity [6]. In a recent multicentre Canadian study, 48% of all emergency patients tested for PE had a Wells score ≤ 4 and a D-dimer < 500 ng/ml [2].

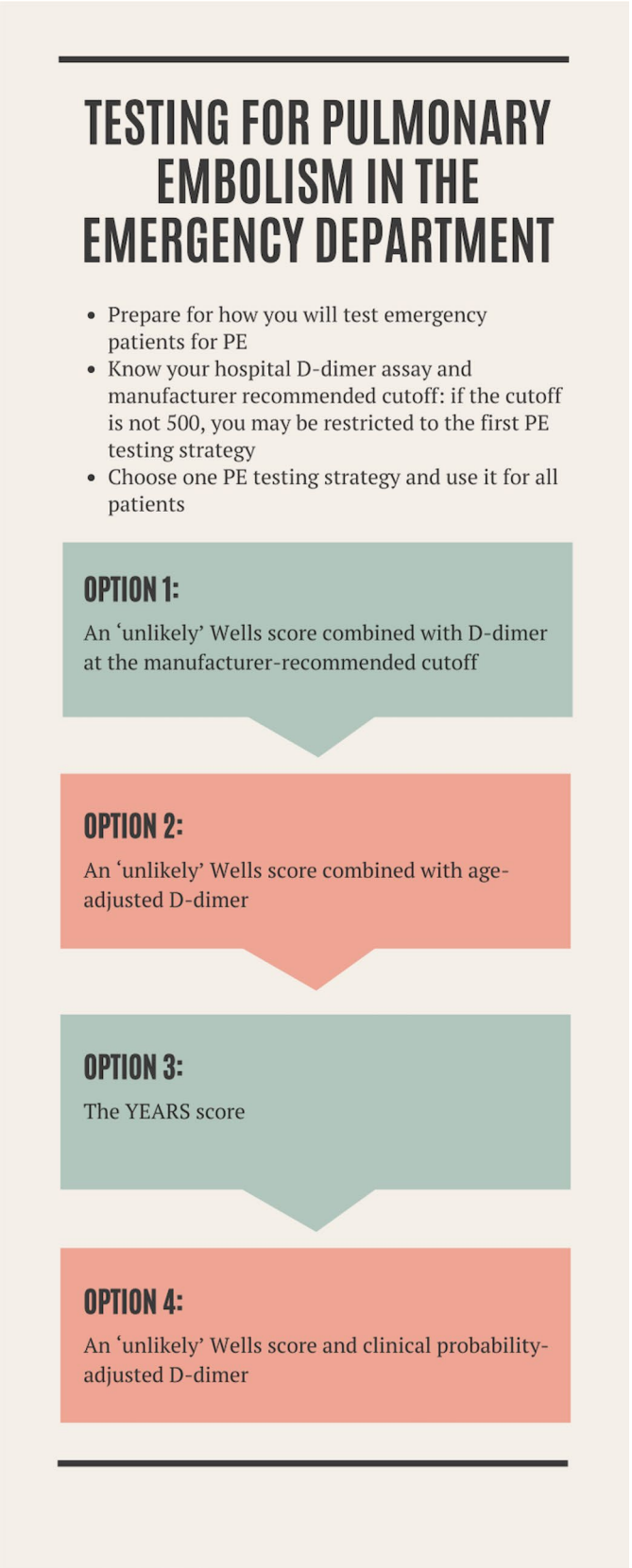

Fig. 1 How to exclude pulmonary embolism without CT scan

Table 1 The two-level Wells score

	Points
Score	
Clinical signs and symptoms of DVT	3.0
PE is the most likely diagnosis	3.0
Heart rate greater > 100	1.5
Previous PE or DVT	1.5
Surgery or bedbound 3 + days in past 4 weeks	1.0
Hemoptysis	1.0
Cancer	1.0
Clinical probability	
Unlikely	≤ 4
Likely	> 4

Table 2 The YEARS score

Items	D-dimer interpretation
Clinical signs of deep vein thrombosis Hemoptysis Pulmonary embolism is the most likely diagnosis	If any items present, use D-dimer < 500 ng/ml to exclude PE If no items are present, use D-dimer < 1000 ng/ml to exclude PE

Option 2: An 'unlikely' Wells score combined with an age-adjusted D-dimer

Emergency physicians can exclude PE in patients who have a Wells score of ≤ 4 using negative age-adjusted D-dimer. Physicians may increase the D-dimer threshold between positive and negative from 500 ng/ml to (10 × patient's age) ng/ml, for patients over the age of 50 and Wells score ≤ 4 [7]. Age-adjusted D-dimer has been prospectively validated in one European study, where only 1/1421 patients with negative age-adjusted D-dimer was diagnosed with venous thrombosis over the following 3 months [8]. Some D-dimer assays (such as HemosIL D-dimer) have a different recommended cutoff in which case this adjustment cannot be applied. Studies have used (age × 5) ng/ml when the D-dimer assay manufacturer-recommended cutoff is close to 250 ng/ml (such as HemosIL D-dimer) [9].

Option 3: The YEARS score

The YEARS score includes D-dimer testing for every patient. The YEARS score can be remembered more easily than the Wells score with only three items [10]. When there are no YEARS items, use a D-dimer threshold of 1000 ng/ml to exclude PE. When there are one or more YEARS items, use a D-dimer threshold of 500 ng/ml. One European study has externally validated a form of the YEARS score, (modified with age-adjust D-dimer in the patients with no YEARS items), where 1/648 patients negative for PE were diagnosed with venous thrombosis over the following 3 months [11]. Some D-dimer assays (such as the HemosIL D-dimer) have a different recommended cutoff and have never been studied use with the YEARS score (Table 2).

Option 4: An 'unlikely' Wells score and clinical probability-adjusted D-dimer

Clinical probability-adjusted D-dimer excludes PE with a D-dimer threshold of twice the manufacturer-recommended cutoff (1000 ng/ml for most assays) in patients with a Wells score ≤ 4 [2]. This was validated in Canadian emergency departments where 0/1325 patients with negative clinical probability-adjusted D-dimer were diagnosed with venous thrombosis within the following 3 months. Unlike age-adjusted and YEARS, there has been no external validation study assessing this approach.

Clinical pearls

Become an expert in the Wells score when you use it. Be sure to document the Wells score (or YEARS score if you are using it) every time you use D-dimer. Choose one of these four strategies and use that strategy for every patient you test for PE. Cherry picking the strategy according to your patient (e.g., using age-adjusted for older patients and YEARS for younger patients) will expose you to a greater risk of missing PE than if you simply choose one strategy and stick to it. Tell your patient that their 'blood clot test' (D-dimer) was negative so they know you have tested for PE.

Case resolution

You decide to use age-adjusted D-dimer because the patient's Wells score is 1.5 (tachycardia), which places her in the 'PE unlikely' category. Her D-dimer result is 580 ng/ml (normal is < 500 ng/ml) and you tell the patient that her PE testing is negative. You manage her as a case of community-acquired pneumonia. Next day, her nasopharyngeal swab result is positive for COVID-19.

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Declarations

Conflict of interest The authors have no competing interests.

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