Pulmonary Embolism (PE): Diagnosis

Thrombosis Canada
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Objective:

To provide a diagnostic approach to patients with suspected acute pulmonary embolism (PE).

Background:

Venous thromboembolism (VTE), which comprises deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common disease, affecting approximately 1-2 in 1,000 adults per year. The majority of PE originates in the proximal deep veins of the leg, despite the observation that only 25-50% of patients with PE have clinically evident DVT at the time of PE diagnosis. While active malignancy, surgery (especially orthopedic), hospitalization, air travel >8 hours, hormone use, and pregnancy are common transient provoking factors, approximately 50% of first-time PEs are idiopathic.

Signs and symptoms of PE are not specific and are common to many other conditions. It may include complaints of sudden onset dyspnea, pleuritic chest pain, hemoptysis, and syncope. Signs of PE may include tachypnea, tachycardia, hypoxemia, hypotension, and features of right ventricular dysfunction (distended jugular veins). There may be accompanying signs and symptoms of DVT including swelling, redness, and pain in the leg.

Clinical presentation is highly variable, ranging from minor symptoms to cardiac arrest. Five to 10% of symptomatic PEs are fatal within the first hour of symptoms onset. After diagnosis, risk stratification is based on 1) hemodynamic stability (cardiac arrest, shock, systolic blood pressure [SBP] <90 mmHg); 2) right ventricular dilatation on CTPA/echocardiography, positive troponin, and elevated brain natriuretic peptide (BNP); 3) clinical and social assessment (kidney or liver impairment, need for oxygen, need IV pain killer, bleeding risk). This risk stratification will guide patients' orientation (ICU, hospitalization, ambulatory treatment).

Early diagnosis and treatment of PE reduces morbidity and mortality.

Diagnosis:

The advent of widely available computed tomography pulmonary angiography (CTPA) led to an explosion in the number of examinations performed in search of PE, with a twofold consequence: 1) the number of unnecessary CTPAs has increased, requiring rationalization, and; 2) the number of PEs diagnosed has increased without a significant reduction in overall PE mortality, raising the question of the clinical relevance of these previously undiagnosed PEs and the issue of overdiagnosis.

In order to rationalize imaging use, a 3-step approach is proposed.

1. **Assess the pretest clinical probability (PTP)** using a validated clinical prediction rule such as the Wells' score (**Table 1**), the Geneva score, or using empiric evaluation (see **Figure 1**). In patients with a low empiric pretest probability of PE and **all** clinical criteria of the Pulmonary Embolism Rule-out Criteria (PERC, **Table 2**), no further testing is required, not even D-dimer measurement.
2. **D-dimer measurement, using a sensitive assay.** Given the high sensitivity (greater than 90%) of D-dimer assays resulting in a high negative predictive value, a negative D-dimer rules out PE among patients with a low or moderate (or 'unlikely') PTP. Using a sensitive D-dimer assay, the age-adjusted threshold for positivity is >500 mcg/l for patients less than 50 years old and >"age x10" for patients 50 years of age or older.
3. **Proceed with imaging in patients with a positive D-dimer or high PTP** (or 'likely'). Imaging studies include multidetector CTPA and ventilation-perfusion scans.

Multidetector CTPA is widely available in Canada and is highly sensitive and specific. Nevertheless, if the PTP is high and CTPA is negative, further diagnostics may include a bilateral leg ultrasound or a ventilation-perfusion scan, which excludes the disease if negative, and indicates the need for treatment if a proximal DVT is diagnosed. Limitations of CTPA include radiation exposure (that might increase breast cancer rates in young women), risk of contrast nephropathy, and detection of small filling defects of uncertain clinical significance (subsegmental PE) or even false positive diagnoses.

The use of **ventilation/perfusion (V/Q) scan** is a valid alternative. V/Q lung scanning has high sensitivity and specificity in patients with a normal chest X-ray and who do not have significant lung disease. V/Q scanning should be considered in patients with renal insufficiency, contrast allergy, in young patients with a normal chest X-ray, and in pregnant women. If the V/Q scan is normal, further testing is not required. When the V/Q scan is neither normal nor high probability for PE (i.e., diagnostic for PE), serial compression ultrasounds (CUS) of the legs should be performed. The SPECT V/Q scan uses a binary interpretation (either negative or positive for PE).

Both imaging tests are safe to use during pregnancy (see **Clinical Guide** **Pregnancy: Diagnosis of PE and DVT**), particularly in terms of teratogenicity for the fetus. It is widely acknowledged that the risks of not performing imaging tests outweigh the risks associated with their use.

Besides the age-adjusted D-dimer, two others diagnostic algorithms have been proposed to increase the efficiency of the D-dimer test and increase the proportion of patients in whom PE can be ruled out without imaging:

- The YEARS algorithm uses 3 criteria from the Wells' score, namely signs of DVT, hemoptysis, and whether PE is the most likely diagnosis. PTP is low if none of the criteria are present, and in those patients, the positivity threshold for D-dimer is 1000 mcg/l. If one criterion or more is present, PTP is high and the threshold for D-dimer is 500 mcg/l.
- The PeGeD algorithm uses the Wells' score to assess PTP. The D-dimer threshold for positivity is set at 1000 mcg/l in patients with a low PTP and at 500 mcg/l in patients with moderate PTP. Patients with high PTP should proceed to imaging directly without D-dimer testing.

Note that although both algorithms were prospectively validated, an independent confirmatory prospective validation study is lacking.

In patients with hypotension who are too unstable to undergo imaging or if imaging is not immediately available, an urgent echocardiogram should be obtained to look for evidence of right heart strain, or embolus in the right ventricle (RV) or main pulmonary arteries. If present, and in the absence of an alternative diagnosis, treatment for PE should be initiated. However, RV dysfunction alone is not sufficient to confirm PE diagnosis. If feasible, confirmatory evidence of VTE should be sought with further imaging (CTPA or V/Q once stabilized, or lower extremity CUS). If a hypotensive patient does not have echocardiographic features of RV dysfunction, it is unlikely that hemodynamic instability is due to high-risk PE (although this does not exclude smaller PE).

Table 1: Wells Score* for PE

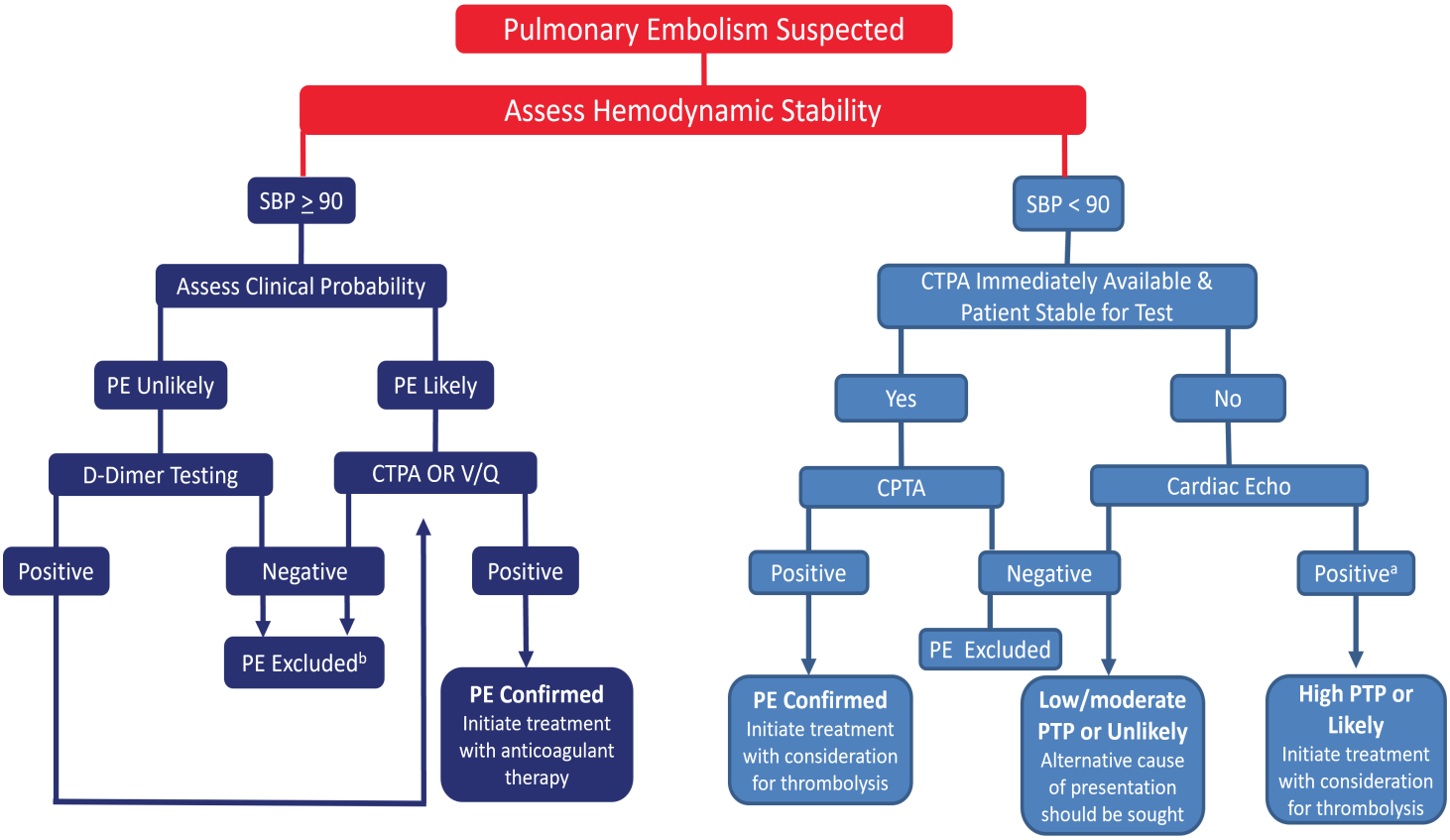
VARIABLE	POINTS
Clinical symptoms and signs of DVT	3
Previous DVT or PE	1.5
Immobilization for >3 days or surgery within 4 weeks	1.5
Heart rate >100 beats/minute	1.5
Hemoptysis	1
Malignancy	1
No alternative diagnosis more likely than PE	3
TOTAL SCORE*	

*Total Score: PE unlikely <4.5; PE likely >4.5; low PTP <2 / moderate PTP 2-6 / high PTP >6

Table 2: PE Rule-out Criteria (PERC) for patients with low pretest probability for PE

CLINICAL CHARACTERISTIC	MEETS CRITERIA	DOES NOT MEET CRITERIA
Age <50	0	1
Initial heart rate <100 beats/min	0	1
Initial SaO2 >94% on room air	0	1
No unilateral leg swelling	0	1
No hemoptysis	0	1
No surgery or trauma ≤4 weeks	0	1
No history of VTE	0	1
No estrogen use	0	1

Figure 1: Suggested Diagnostic Algorithm for Suspected Pulmonary Embolism



[a]Features on echocardiography suggestive of high-risk PE include severe right ventricle (RV) dysfunction, RV>LV size, septal shift and RV/main pulmonary artery embolus

[b]Where clinical suspicion for PE remains high with a negative initial CTPA, additional testing with V/Q scan and/or proximal ultrasound of the lower extremities may be considered.

Special considerations:

Timing of diagnostic testing:

Testing should be undertaken as quickly as possible. However, if there will be a significant delay (greater than 4 hours), patients with a moderate/high or likely pre-test probability of PE should receive a rapidly acting anticoagulant (e.g. low-molecular-weight heparin or a direct oral anticoagulant) until testing is performed, unless they are at high risk of bleeding or have a contraindication to anticoagulant therapy.

Other Relevant Thrombosis Canada Clinical Guides:

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