Pulmonary Embolism (PE): Diagnosis

Thrombosis Canada
Thrombose Canada

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 diagnosis of PE has increased significantly since the advent of computed tomography pulmonary angiography (CTPA) with its widespread availability and enhanced sensitivity. 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, and hormone use/pregnancy are common transient provoking factors, approximately 50% of first-time PEs appear to be unprovoked.

Symptoms of PE may include 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. The ECG may show right ventricular strain ($S_1Q_3T_3$, right bundle branch block and T-inversion in leads V1-V4).

Up to 10% of symptomatic PEs are fatal within the first hour of symptom onset. Independent predictors of mortality within the first few days after diagnosis of PE include hypotension (systolic blood pressure [SBP] $\leq$90 mmHg), clinical right heart failure, right ventricular dilatation on CTPA/echocardiography, positive troponin, and elevated brain natriuretic peptide (BNP). Early diagnosis and treatment of PE reduces morbidity and mortality.

Diagnosis:

The constellation of symptoms and signs may be suggestive of PE but do not alone have the sensitivity or specificity to rule in or rule out the diagnosis. When the diagnosis of PE is considered, the clinical stability of the patient and associated pre-test probability will dictate the diagnostic approach (see **Figure 1**).

In patients without hypotension (SBP ≥90 mmHg), pre-test probability can be assessed by a validated clinical prediction rule such as the Well's score (see **Table 1**). In patients who are <50 years of age, with a low pretest probability of PE, further testing (such as d-dimer measurement or diagnostic imaging) is **not** necessary provided **all** clinical features/criteria in the Pulmonary Embolism Rule-out Criteria (PERC) are present (see **Table 2**).

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

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

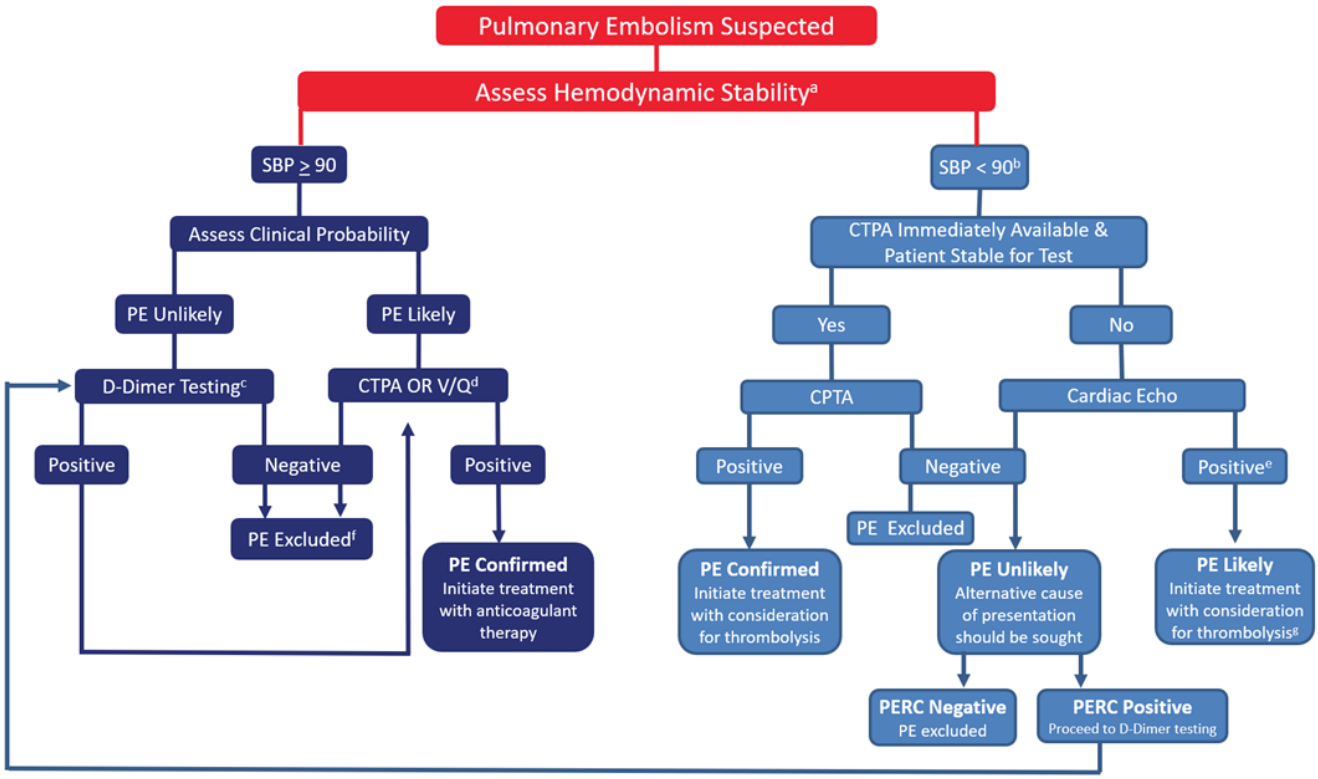
In cases with **PE unlikely pre-test probability**, a negative high sensitivity D-dimer result rules out the diagnosis of PE. However, a positive D-dimer test MUST be followed up with a definitive test to confirm/refute the diagnosis of PE.

When a high-sensitive d-dimer assay is used, age-adjusted D-dimer levels can increase the specificity of D-dimer testing without sacrificing sensitivity. In patients over the age of 50, a D-dimer result is considered negative if it is less than the patient age multiplied by 10 (for example, in a 76-year-old, a negative result is less than 760 µg/L). For patients under the age of 50, a D-dimer value less than 500 µg/L remains the cutoff for a negative result.

With a high **PE pre-test probability (Well's score ≥ 4.5)**, there is no role for ordering a D-dimer, as the clinical likelihood of PE remains unacceptably high among those with a negative D-dimer result. Therefore, when the Wells score is 4.5 or greater, one should go directly to imaging to establish the diagnosis.

Multidetector CTPA is widely available in Canada and is sufficiently sensitive and specific to exclude the diagnosis of PE when it is negative and to confirm it when positive. Limitations of CTPA include radiation exposure (that may increase breast cancer rates in young women), risk of contrast nephropathy, and detection of small filling defects of uncertain clinical significance. **Ventilation-perfusion (V/Q) lung scanning** has high sensitivity and specificity in patients with a normal chest X-ray 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.

Figure 1: Suggested Diagnostic Algorithm for Suspected Pulmonary Embolism



[a] For the hemodynamically unstable who is high risk for bleeding with thrombolysis, consideration should be made for clot removal (surgery or interventional radiology)

[b] Consideration for thrombolysis without diagnostic test confirmation should be made if the patient has a high clinical suspicion of PE and is very unstable

[c] Excluding a diagnosis of PE with a PE unlikely pre-test probability requires the use of a *highly sensitive* D-dimer assay. The use of age-specific or pre-test probability specific D-dimer cut-off values, if available, appears to improve the specificity of D-dimer testing.

[d] V/Q is the preferred test in patients with a contrast allergy or severe renal dysfunction and young patients with a normal chest X-ray and should be considered in pregnancy. If the perfusion scan is normal, further testing is not required. When the V/Q scan is neither normal nor high probability for PE (diagnostic for PE), serial compression ultrasounds (CUS) of the legs should be undertaken.

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

[f] 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

[g] If patient condition stabilizes, consideration should be given to performing CTPA to confirm the diagnosis

In patients with hypotension who are too unstable to undergo CTPA or if CTPA is not immediately available, an urgent echocardiogram should be obtained to look for evidence of right heart overload 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 does not prove PE (ie. baseline pulmonary hypertension); therefore, if feasible, confirmatory evidence of VTE should be sought with further imaging (CTPA, V/Q or lower extremity compression ultrasounds [CUS]). If a hypotensive patient does not have echocardiographic features of RV dysfunction, it is unlikely that hemodynamic instability is due to massive PE (although this does not exclude smaller PE).

For patients with COVID, the incidence of thrombosis is low for non-hospitalized individuals. Data collected prior to widespread vaccination and infection, suggested the incidence of VTE increases with severity of disease. These studies demonstrate venous thrombosis rates as high as 7.9% on the medical wards and 40-57% in the intensive care units. Arterial thrombosis incidence is also increased in those with COVID (cerebral, myocardial, mesenteric, limb) with studies quoting rates of 0.9-5.6%. Since COVID causes an increase in d-dimer in the absence of VTE, it is not typically a useful diagnostic test for COVID positive patients with suspected VTE.

Most patients with pulmonary embolism can be safely managed at home provided they are not hypotensive or oxygen requiring, their pain is well managed, they have adequate social supports, they have financial access to anticoagulation treatment, and are not considered to be at high bleeding risk. Typically, these patients would be seen in follow up within a week of diagnosis to ensure clinical improvement and anticoagulant tolerability. Various risk stratification algorithms exist including the PESI, sPESI and Heista scores. However, their clinical utility for determining requirement for admission is limited, especially since outcomes were measured at 30 days. Isolated abnormalities in laboratory markers (troponin, BNP) should **not** be used to determine if a patient is suitable for home treatment, and these markers should not be routinely measured in patients with VTE.

Other Relevant Thrombosis Canada Clinical Guides:

- Cancer and Thrombosis
- COVID-19: Primary Thromboprophylaxis in Hospitalized Patients
- Deep Vein Thrombosis (DVT): Diagnosis

- Pregnancy: Diagnosis of DVT and PE
- Pulmonary Embolism: Treatment

References:

Becattini C, et al. Acute pulmonary embolism: mortality prediction by the 2014 European Society of Cardiology risk stratification model. ERJ 2016; 48: 780-786.

Eddy M, et al. External validation of the YEARS diagnostic algorithm for suspected pulmonary embolism. J Thromb Haemostas 2020;(12):3289-3295.

Jenner WJ, et al. Incidence of thrombotic complications in COVID-19. J Thromb Thrombolysis 2021;52:999-1006.

Kearon C, et al. Diagnosis of pulmonary embolism with D-dimer adjusted to clinical probability. N Engl J Med 2019;381(22):2125-2134.

Konstantinides SV, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): The task force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology. Eur Heart J 2020;41(4):543-603.

Lim W, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism. Blood Adv 2018;2(22):3226-3256.

Singh B, et al. Pulmonary embolism rule-out criteria (PERC) in pulmonary embolism revisited: a systematic review and meta-analysis. Emerg Med J 2013;30(9):701-706.

Date of version: 06August2023