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

Background:
Venous thromboembolism (VTE) is a common disease, affecting approximately 1-2 in 1,000 adults per year. Approximately one third of first VTE presentations are due to PE while the remainder is due to deep vein thrombosis (DVT). The diagnosis of PE has increased significantly since the advent of computed tomography pulmonary angiography (CTPA) due to its widespread availability and diagnostic accuracy. 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), immobilization >8 hours, and estrogen use/pregnancy are transient provoking factors, approximately 50% of first-time PE appear to be unprovoked.

Symptoms of PE may include sudden onset dyspnea, pleuritic chest pain and syncope. Signs of PE may include tachypnea, tachycardia, hypoxemia, hypotension, and features of right ventricular dysfunction (distended jugular veins). The ECG may show right ventricular strain (S1Q3T3, right bundle branch block and T-inversion in leads V1-V4).

Up to 10% of symptomatic PEs are fatal within the first hour of symptoms. Independent predictors of mortality within the first few days after diagnosis of PE include hypotension (systolic blood pressure ≤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 of PE:
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 their pre-test probability will dictate the diagnostic approach (see Figure 1).

In patients without hypotension (SBP ≥90 mmHg), pre-test probability should be assessed by experienced clinician ‘gestalt’ or a validated clinical prediction rule (see Table 1).
### TABLE 1: WELLS SCORE* FOR PE

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>POINTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical symptoms and signs of DVT</td>
<td>3</td>
</tr>
<tr>
<td>Previous DVT or PE</td>
<td>1.5</td>
</tr>
<tr>
<td>Immobilization for &gt;3 days or surgery within 4 weeks</td>
<td>1.5</td>
</tr>
<tr>
<td>Heart rate &gt;100 beats/minute</td>
<td>1.5</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1</td>
</tr>
<tr>
<td>Malignancy</td>
<td>1</td>
</tr>
<tr>
<td>No alternative diagnosis more likely than PE</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total score</strong>*</td>
<td><strong>4.5</strong></td>
</tr>
</tbody>
</table>

*Total Score: PE unlikely <4.5; PE likely >4.5

In cases with **PE unlikely pre-test probability**, a negative 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.

Depending on the assay in use at your institution, age adjusted D-dimer levels can increase the specificity of D-dimer testing without sacrificing sensitivity. In patients over the age of 50, a negative D-dimer result is considered less than 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 **PE likely pre-test probability**, there is no role for ordering a D-dimer, as the clinical likelihood of a PE remains unacceptably high among those with a negative D-dimer result. Therefore, when the pre-test probability is high (PE likely), 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 substantial radiation (that may increase breast cancer rates in young women), risk of contrast nephropathy, and detection of small filling defects, the clinical significance of which is uncertain. **Ventilation-perfusion (V/Q) lung scanning**, especially modern techniques such as SPECT V/Q, 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 and in young patients with a normal chest X-ray.
**FIGURE 1: SUGGESTED DIAGNOSTIC ALGORITHM FOR SUSPECTED PULMONARY EMBOLISM**

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

** Features on echocardiography suggestive of massive PE include severe RV dysfunction and RV/pulmonary artery thrombus

*** If patient condition stabilizes, consideration for CTPA should be given to confirm diagnosis

**** 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 D-dimer cut-off values, if available, appears to improve the specificity of D-dimer testing.

***** 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.

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 RV or 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; therefore, if feasible, confirmatory evidence of VTE should be sought with further imaging (CTPA, V/Q or CUS). If a hypotensive patient does not have echocardiographic features of RV dysfunction, it is unlikely that their hemodynamic instability is due to massive PE (although this does not exclude smaller PE).

**OTHER RELEVANT THROMBOSIS CANADA CLINICAL GUIDES:**
- Apixaban (Eliquis®)
- Cancer and Thrombosis
- Dabigatran (Pradaxa®)
• Deep Vein Thrombosis (DVT): Diagnosis
• Deep Vein Thrombosis (DVT): Treatment
• Pregnancy: Venous Thromboembolism Treatment
• Pulmonary Embolism (PE): Treatment
• Rivaroxaban (Xarelto®)
• Unfractionated Heparin and Low-molecular-weight Heparin
• Vena Cava Filter
• Venous Thromboembolism: Duration of Treatment
• Warfarin

REFERENCES:


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