OBJECTIVE:

To provide a diagnostic algorithm for 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 incidence of PE has increased significantly since the advent of computed tomography angiography (CTPA) due to its widespread availability and diagnostic sensitivity. The majority of PE originate in the proximal deep veins of the leg, despite the fact that only 25-50% of patients with PE have clinically-evident DVT. Active malignancy, surgery (especially orthopedic), immobilization >8 hours, and estrogen use/pregnancy are transient provoking factors. Approximately 50% of first-time PE are 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 of PE may be suggestive, 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). In cases with low to moderate clinical 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. 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.
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 result is considered less than patient age multiplied by 10 (for example, in a 76 year old, a negative result is less than 760 ug/L). For patients under the age of 50, a D-dimer value less than 500 ug/L remains the cutoff for a negative result.

In patients with low clinical probability of PE, and in the absence of D-dimer testing, the diagnosis of PE can be safely excluded if NONE of the following are present: age >50, prior VTE, surgery or trauma past 4 weeks, current exogenous estrogen use, hemoptysis, heart rate >100, oxygen saturation <94%, or unilateral leg swelling (PERC criteria).

With a high 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 result. Therefore, when the pre-test probability is high, one should go directly to CTPA to establish the diagnosis.

**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>
</tbody>
</table>

*Total Score: Low Risk: 0 to 1.5; Moderate Risk: 2 to 5.5; High Risk: ≥ 6
**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 or moribund.
- Features on echocardiography suggestive of massive PE include RV overload 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 moderate 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.

In patients with renal failure or an allergy to contrast dye (in whom a CTPA is felt to be contraindicated), it is reasonable to start with lower extremity compression ultrasound (CUS) looking for evidence of DVT. A positive result will mandate the same treatment as for PE; therefore, no further investigations for PE are required. Since up to 30% of patients with PE may not have a positive CUS, a negative CUS does not rule out PE. Therefore, a ventilation-perfusion (V/Q) scan should be obtained in this instance.

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 CTPA 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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*Please note that the information contained herein is not to be interpreted as an alternative to medical advice from your doctor or other professional healthcare provider. If you have any specific questions about any medical matter, you should consult your doctor or other professional healthcare providers, and as such you should never delay seeking medical advice, disregard medical advice or discontinue medical treatment because of the information contained herein.*