Pulmonary Emboli Manifestations and Prediction Rules

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ABSTRACT

Pulmonary thrombus emboli (PTE) have a wide clinical spectrum, from asymptomatic small PTE to life-threatening one, which may cause cardiogenic shock. It is classified as acute/chronic and massive/sub massive. PTE risk factors and relative causes to elevate its mortality are present in this review article. At last, we have a brief recommendation for treatment. There are several diagnosing test such as D-dimer, echocardiography, electrocardiography, brain natriuretic peptide, laboratory tests, chest X-ray, ultrasound, and pulmonary angiography which are different in specificity and sensitivity. Finally, in the diagnostic approach, we explain relative studies to Wells rule, Geneva rule, pulmonary embolism (PE) severity index, and PE rule out criteria.

Keywords: Pulmonary emboli, prediction rules, pulmonary embolism rule-out criteria

INTRODUCTION

Pulmonary thrombus emboli (PTE) defined as an obstruction of the pulmonary artery or one of its branches by thrombosis which is originated elsewhere in the body. PTE can classify as acute and chronic. In the chronic form, patients experience dyspnea over a period of years. In the other classification, PTE defines as massive or sub massive. Patients with massive PTE have systolic blood pressure <90 mmHg or a fall in systolic blood pressure of more than 40 mmHg from baseline in more than 15 min. Generally, when hypotension accompanied by an elevated central venous pressure which cannot be explained by acute myocardial infarction, tension pneumothorax, pericardial tamponade, or a new arrhythmia, massive PTE propounded.¹,² Saddle PTE defines when PTE lodge at the bifurcation of the main pulmonary artery. Usually, they are sub massive.³ Most PTE originate from lower limbs and travel to lungs. Larger thrombi cause hemodynamic compromise while smaller ones continue traveling distally and produce pleuritic chest pain. Risk factors for venous thrombus emboli are present in Table 1.

MORTALITY RATE IN PTE

Study shows right ventricle (RV) dysfunction is associated with recurrent PTE and increases in mortality rate.⁴,⁵ RV dysfunction can be predicted by elevated brain natriuretic peptide (BNP) level.⁶ Researchers showed that serum BNP levels >90 pg/mL were associated with cardiopulmonary resuscitation, mechanical ventilation, vasopressor therapy, thrombolysis, and embolectomy.⁷ Deep vein thrombosis, elevated serum troponin, and RV thrombosis are related to increasing mortality.⁸,⁹

DIAGNOSTIC TESTS

Symptoms and signs in patients with acute pulmonary embolism without preexisting cardiopulmonary disease classified in Table 2. As you see, most of the PTE manifestations are unspecific. Major diagnostic test to evaluate patients with PTE, includes:

Laboratory test, which is not specific, includes leukocytosis, an increased erythrocyte sedimentation rate, and an
Elevated serum lactate dehydrogenase or aspartate aminotransferase serum glutamic oxalocetic transaminase with a normal serum bilirubin.

Arterial blood gas (ABG) measurement indicates the hypoxia, hypocapnea, and respiratory alkalosis. When saturation $O_2 < 95\%$ is reported in pulse oximetry, patient is at risk of respiratory failure, cardiogenic shock, and death.

BNP elevation is seen in PTE patients, which is insensitive and nonspecific.$^{13}$ Patients with PTE who do not have preexisting cardiovascular disease reveals electrocardiogram abnormalities. RV dysfunction is associated with T-wave inversion in precordial leads.$^{16}$

Chest radiography abnormalities such as atelectasis, plural effusion, and pulmonary parenchymal abnormalities are common between PTE patients but they are not specific.$^{17}$

Lower limbs venous ultrasound sometimes performed during PTE diagnosing.

The use of magnetic resonance angiography for diagnosing is limited due to respiratory and cardiac motion artifact and suboptimal resolution.$^{19}$

Echocardiography includes increased RV size, decreased RV function, and tricuspid regurgitation. In massive PTE, echocardiography is more useful.$^{20,21}$

In acute PTE, vascular occlusion bands perfusion but ventilation continues. Hence, alveolar dead space fraction increases.$^{22}$

Pulmonary angiography is gold standard test for diagnosing PTE. For pulmonary artery branch’s evaluation, a contrast material injects into the femoral artery.

D-dimer is a degradation product of cross-linked fibrin detected in serum using a variety of different assays:$^{18}$

- Enzyme-linked immunesorbent assay (ELISA) (results in >8 h)
- Quantitative rapid ELISA (results in 30 min)
• Semi-quantitative rapid ELISA (results in 10 min)
• Qualitative rapid ELISA (results in 10 min)
• Quantitative latex agglutination assay (results in 10-15 min)
• Semi-quantitative latex agglutination assay (results in 5 min)
• Erythrocyte agglutination assay (results in 2 min).

Some researches indicate that shortening of activated partial thromboplastin time (aPTT) and low international normalized ratio might increase the risk of thromboembolism. Antiphospholipid antibody prolonged aPTT, which paradoxically increases propensity to thrombosis.

**DIAGNOSTIC APPROACHES**

The best validate and most widely used, clinical decision rules are the Wells rule which is based on physician judgment. It is important to know that its criteria are objective and cannot be standardized (Table 3). Geneva score based on objective variables and requires ABG (Table 4). The revised Geneva score is a simple score according to clinical variables and independent from physician’s implicit judgment (Table 5).

A study compares revised Geneva score with Wells score and suggests that the performance of the revised Geneva score is equivalent to that of the Wells rule. Patients by the combination of a low or intermediate clinical probability by the revised Geneva score and a normal D-dimer level can exclude PTE. In a study which evaluates medical records of 242 patients suspected for PTE, who underwent computed tomography (CT) scan of the lung, it reveals revised Geneva score had an acceptable predictive accuracy in low and intermediate-probability groups. High probability patients were a small number of cases, and there is no conclusion for them.

**Table 3: Wells score**

| Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins) | 3 |
| An alternative diagnosis is less likely than PE | 3 |
| Heart rate>100 | 1.5 |
| Immobilization or surgery in the previous 4 weeks | 1.5 |
| Previous DVT/PE | 1.5 |
| Hemoptysis | 1 |
| Malignancy (on treatment, treated in the last 6 months or palliative) | 1 |

**Clinical probability**

- Low <2
- Intermediate 2-6
- High >6

PE: Pulmonary embolism, DVT: Deep-vein thrombosis

**Table 4: Geneva pulmonary embolism prognostic index**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Original PESI score</th>
<th>Simplified PESI score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active cancer</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Systolic blood pressure&lt;100 mmHg</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Concomitant deep venous thrombosis at diagnosis</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>History of venous thromboembolism</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hypoxia (arterial PaO2&lt;60 mmHg)</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

**Geneva risk categories**

- Low risk 2 or fewer points
- High risk 3 or more points

**Table 5: The revised Geneva score**

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Original PESI score</th>
<th>Simplified PESI score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age&gt;65 years</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Previous DVT or PE</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Surgery (under general anesthesia) or fracture (of the lower limbs) within 1 month</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Active malignant condition (solid or hematologic malignant condition, currently active or considered cured 1 year)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral lower-limb pain</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Clinical signs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate 75-94 beats/min</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Heart rate&gt;95 beats/min</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Pain on lower-limb deep venous palpation and unilateral edema</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

**Clinical probability**

- Low 0-3
- Intermediate 4-10
- High >11

PE: Pulmonary embolism, DVT: Deep-vein thrombosis

**Table 6: Pulmonary embolism severity index (low risk=Class I and II)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points</th>
<th>30-day mortality risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age&gt;80 years</td>
<td>1 point/year</td>
<td>1</td>
</tr>
<tr>
<td>Male gender</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>30</td>
<td>1</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Heart rate&gt;110/min</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>Systolic blood pressure&lt;100 mmHg</td>
<td>30</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory rate&gt;30/min</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Body temperature&lt;36°</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Disorientation, lethargy, stupor or coma</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Oxygen saturation&lt;90% (pulse oxymetry)</td>
<td>20</td>
<td>1</td>
</tr>
</tbody>
</table>

**Risk category**

- Class I <65 0
- Class II 66-85 1.0
- Class III 86-105 3.1
- Class IV >125 24.4

Patients with 0 score of simplified PESI are considered low risk. PESI: Pulmonary embolism severity index
The pulmonary embolism severity index (PESI) score uses 11 weighted clinical parameters (Table 6). Patients are categorized by their scores into five classes of increasing risk of death. There are many variables to be considered, each with its own weight. Hence, it is difficult to apply PESI in a busy clinical environment.

In a study involves 15531 patients with pulmonary embolism (PE) evaluated to compare the prognostic performance of the original and simplified PESI (sPESI). The proportions of patients classified as a low versus higher risk between the original and sPESI and estimated 30-day mortality within each risk group is compared. Finally, it becomes clear that the original PESI classified a higher proportion of patients as low-risk and had a greater separator power than the spESI. Both PESI and spESI have similar accuracy while spESI is easier to use.

A systematic review and meta-analysis designed to evaluate the diagnostic performance of PE rule-out criteria (PERC) in deferring the need for D-dimer testing to rule out PE. It suggests high sensitivity and low but acceptable specificity of the PERC to rule out PE in patients with low pretest probability (Table 7).

**TREATMENT STRATEGIES**

In acute PTE, if hypoxemia exists, supplement oxygen, intubation, and mechanical ventilation should be administered. Remember patients with coexistent RV failure are prone to hypotension following intubation. In acute PTE and hypotension, hemodynamic support should be instituted. If intra venous fluids do not improve the patient’s blood pressure and hemodynamic status, then intravenous vasopressor therapy such as norepinephrine, dopamine, or epinephrine may be effective. According to risk of bleeding and the degree of clinical suspicion for acute PTE, decide about initiating of empiric anti-coagulant during resuscitation and diagnosing evaluation. If diagnostic evaluation confirmed acute PE anti-coagulant therapy and thrombolytic therapy are initiated. A pooled analysis of three anticoagulation trials indicate if the aPTT was not therapeutic within the first 24 h after initiation of heparin, the risk of recurrent PE was 25%. Catheter or surgical embolectomies are useful for patients who fail thrombolysis or have contraindications to thrombolysis.

**CONCLUSION**

After these changes have happened to pulmonary emboli diagnosing rules, it is important to know, clinician decision is the most useful and determining tool for diagnosing. For example, if we obey Wells rule, this pattern can be appropriate:

“With a patient who is suspected to have PE, Wells criteria should be applied. Patients categorized as PE unlikely, undergo D-dimer testing with a quantitative rapid ELISA assay or a semi quantitative latex agglutination assay. If the D-dimer level is <500 ng/mL or negative, the diagnosis of PE can be excluded.

CT-pulmonary angiogram (PA) applied for the patients classified as PE likely and patients classified as PE unlikely who have a D-dimer level >500 ng/mL. A negative CT-PA rules out the diagnosis of PE.”

Remember PE is a rare but recognizable concern in the pediatric population. Pediatric multicenter studies are required to evaluate risk factors, signs, and symptoms of PE to develop pediatric-specific clinical decision rules to provide reliable means of determining pretest probability of PE.

**REFERENCES**


