Pulmonary Embolism: Risk stratification

Hisham Selim
Combat MI 2014
National Heart Institute
March 2014

Goals

- Understand the Basic context of pulmonary emboli
- Knowing some common risk factors
- Be aware of the clinical features of PE and have a basic understanding of various diagnostic test
- Attempt to dispel a few “myths” about pulmonary emboli
Introduction

- Pulmonary embolism (PE) is a relatively common cardiovascular emergency. By occluding the pulmonary arterial bed it may lead to acute life-threatening but potentially reversible right ventricular failure.

- PE is a difficult diagnosis that may be missed because of non-specific clinical presentation.


Introduction

• However, early diagnosis is fundamental, since immediate treatment is highly effective.

Perspective – scope of the problem

• The diagnosis of pulmonary embolism is confounded by a clinical presentation that may be subtle, atypical, or obscured by another coexisting disease.

• Highest incidence in hospitalized patients

• Autopsy reports suggest it is commonly “missed” diagnosed

Perspective

• Presentation is often “atypical”

• Signs and symptoms are frequently vague and nonspecific and rarely “classic”

• Untreated mortality rate of 20% - 30%, declines to 5% with timely intervention
So What Do We Do ???

- Confusing for Emergency Physician

  Do we under diagnose/over diagnose?

  Why don’t we have a standardized method of work up after all these years?

Pathophysiology

Rudolph Virchow, 1858

Triad:

- Hypercoagulability
- Stasis to flow
- Vessel injury
The definition of high-risk (European classification) or massive (North American classification) PE is usually straightforward and relies on the presence of clinically overt RV failure which results in haemodynamic compromise. This condition, which is encountered in 5% of all cases.

Suspicion should be high if ANY risk factors or symptoms/signs are present

>70% of patients who die of PE are not suspected of having it

Only ~35% of patients suspected of having PE actually have it

Pre-test probability is very important for making clinical (diagnostic) judgments

PE testing is less reliable in older persons than in younger persons

Age is a major risk factor, particularly with underlying predisposing conditions

Advanced risk stratification: clinical scores

The **Pulmonary Embolism Severity Index (PESI)** is the most extensively validated prognostic clinical score to date. Its major strength lies in excluding (ruling out) an adverse outcome as indicated by the high negative predictive value (NPV) of the lowest PESI classes I and II.
### Clinical Probability calculation

**Wells Score**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical signs &amp; symptoms of DVT [minimum of leg swelling &amp; pain with palpation of the deep veins]</td>
<td>3</td>
</tr>
<tr>
<td>Other diagnosis less likely than PE</td>
<td>3</td>
</tr>
<tr>
<td>Heart rate &gt; 100</td>
<td>1.5</td>
</tr>
<tr>
<td>Immobilization or surgery in previous 4 weeks</td>
<td>1.5</td>
</tr>
<tr>
<td>Previous DVT /PE</td>
<td>1.5</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1.0</td>
</tr>
<tr>
<td>Malignancy [on treatment, treated in the last 6 months]</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>PE likely</strong> → score &gt; 4</td>
<td></td>
</tr>
<tr>
<td><strong>PE unlikely</strong> → Score ≤ 4</td>
<td></td>
</tr>
</tbody>
</table>
Clinical Probability calculation

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Points value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Age</td>
<td></td>
</tr>
<tr>
<td>60–70 years</td>
<td>+1</td>
</tr>
<tr>
<td>≥80 years</td>
<td>+2</td>
</tr>
<tr>
<td>2. Previous DVT or PE</td>
<td>+2</td>
</tr>
<tr>
<td>3. Recent surgery (&lt;4 weeks ago)</td>
<td>+3</td>
</tr>
<tr>
<td>4. Heart rate &gt;100/minute</td>
<td>+1</td>
</tr>
<tr>
<td>5. PaCO₂:</td>
<td></td>
</tr>
<tr>
<td>&lt; 35 mmHg</td>
<td>+2</td>
</tr>
<tr>
<td>35–39 mmHg</td>
<td>+1</td>
</tr>
<tr>
<td>6. PaO₂:</td>
<td></td>
</tr>
<tr>
<td>&lt; 49 mmHg</td>
<td>+4</td>
</tr>
<tr>
<td>49–59 mmHg</td>
<td>+3</td>
</tr>
<tr>
<td>60–71 mmHg</td>
<td>+2</td>
</tr>
<tr>
<td>72–82 mmHg</td>
<td>+1</td>
</tr>
<tr>
<td>7. Chest X-Ray</td>
<td></td>
</tr>
<tr>
<td>Beach Area Infarct</td>
<td>+1</td>
</tr>
<tr>
<td>Elevation of hemidiaphragm</td>
<td>+1</td>
</tr>
</tbody>
</table>

Total Score < 5 ➞ low probability of PE

5–8 ➞ moderate probability of PE

> 8 ➞ high probability of PE

Evaluation Scheme Based on Clinical Probability

[Diagram showing decision tree for diagnostic approach]

Figure 2. Diagnostic Approach to an Outpatient with a Low Clinical Probability of Pulmonary Embolism, Using a D-Dimer Assay as the Initial Diagnostic Assay. If ventilation-perfusion scanning or CT scanning is performed, the subsequent diagnostic steps should be determined according to the clinical probability of embolism.
Clinical Presentation

• **The Classic Triad: (Hemoptysis, Dyspnea, Pleuritic Pain)**
  - Not very common!
  - Occurs in less than 20% of patients with documented PE

• **Three Clinical Presentations**
  - Pulmonary Infarction
  - Submassive Embolism
  - Massive Embolism
Mythology of PE

• **Myth**
  
  – “Patients with pulmonary embolism are short of breath and have chest pain!”

• **Reality:**
  
  You can forget about making the diagnosis on clinical grounds, but wait…don’t plan on completely ruling it out either!

Clinical Features

**Symptoms in Patients with Angio Proven PTE**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>84</td>
</tr>
<tr>
<td>Chest Pain, pleuritic</td>
<td>74</td>
</tr>
<tr>
<td>Anxiety</td>
<td>59</td>
</tr>
<tr>
<td>Cough</td>
<td>53</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>30</td>
</tr>
<tr>
<td>Sweating</td>
<td>27</td>
</tr>
<tr>
<td>Chest Pain, nonpleuritic</td>
<td>14</td>
</tr>
<tr>
<td>Syncope</td>
<td>13</td>
</tr>
</tbody>
</table>
Clinical Features

Signs with Angiographically Proven PE

<table>
<thead>
<tr>
<th>Sign</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachypnea &gt; 20/min</td>
<td>92</td>
</tr>
<tr>
<td>Rales</td>
<td>58</td>
</tr>
<tr>
<td>Accentuated S2</td>
<td>53</td>
</tr>
<tr>
<td>Tachycardia &gt; 100/min</td>
<td>44</td>
</tr>
<tr>
<td>Fever &gt; 37.8</td>
<td>43</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>36</td>
</tr>
<tr>
<td>S3 or S4 gallop</td>
<td>34</td>
</tr>
<tr>
<td>Thrombophlebitis</td>
<td>32</td>
</tr>
<tr>
<td>Lower extremity edema</td>
<td>24</td>
</tr>
</tbody>
</table>

Diagnostic Test

- **Imaging Studies**
  - CXR
  - V/Q Scans
  - Spiral Chest CT
  - Pulmonary Angiography
  - Echocardiography

- **Laboratory Analysis**
  - CBC, ESR, Hgb/Hct,
  - D-Dimer
  - ABG’s
  - Cardiac Biomarkers

- **Ancillary Testing**
  - EKG
  - Pulse Oximetry
Diagnostic Testing
- CXR’s

Chest X-Ray Myth:

“You have to do a chest x-ray so you can find *Hampton’s hump or a Westermark sign.*”

Reality:

Most chest x-rays in patients with PE are nonspecific and insensitive

Chest X-ray Eponyms of PE

• **Westermark's sign**
  – A dilation of the pulmonary vessels proximal to the embolism along with collapse of distal vessels, sometimes with a sharp cutoff.

• **Hampton’s Hump**
  – A triangular or rounded pleural-based infiltrate with the apex toward the hilum, usually located adjacent to the hilum.
Radiographic Eponyms
- Hampton’s Hump, Westermark’s Sign

- Hampton’s Hump
- Westermark’s Sign

Diagnostic Testing
- EKG’s

♥ EKG

- **Most Common Findings:**
  - Tachycardia or nonspecific ST/T-wave changes

- **Acute cor pulmonale or right strain patterns**
  - Tall peaked P-waves in lead II (P pulmonale)
  - Right axis deviation
  - RBBB
  - S1-Q3-T3 (occurs in only 20% of PE patients)
Diagnostic Testing
- Pulse Oximetry

• **The Pulse Oximetry Myth:**

  – “You must do a pulse oximetry reading, since patients with pulmonary embolism are hypoxemic!”

• **Reality:**

  – Most patients with a PE have a normal pulse oximetry, and most patients with an abnormal pulse oximetry will not have a PE.

Diagnostic Testing
- ABG’s

• **The ABG/ A-a Gradient myth:**

  – “You must do an arterial blood gas and calculate the alveolar-arterial gradient. Normal A-a gradient virtually rules out PE”.

• **Reality:**

  – The A-a gradient is a better measure of gas exchange than the pO2, but it is nonspecific and insensitive in ruling out PE.
Diagnostic Testing

- **Echocardiography**
  - Consider in every patient with a documented pulmonary embolism
    - EKG maybe helpful in demonstrating right heart strain
  - Early fibrinolysis can reduce mortality 50%!

---

**High sensitivity D Dimer**

- The measurement of the degradation products of cross-linked fibrin (D-dimer) circulating in plasma is a **highly sensitive** but **nonspecific screening** test for suspected venous thromboembolism.

- **Quantitative test** have 80-85% sensitivity, and 93-100% **negative predictive value**

- Elevated levels are present in nearly all patients with embolism but are also associated with **many other circumstances, including advancing age, pregnancy, trauma, the postoperative period, inflammatory states, and cancer**. The role of D-dimer testing is therefore limited to the ruling out of embolism.

High sensitivity D Dimer

- For D-dimer $<500\text{ng/mL}$, negative predictive value (NPV) $91\,\text{-}99\%$

- For D-dimer $>500\text{ng/mL}$, sens=$93\%$, spec=$25\%$, and positive predictive value (PPV) = $30\%$

High sensitivity D Dimer

- Use of D-dimer test alone to rule out PE may not appropriate

- Patients with normal D-Dimer combined with low pretest clinical probability of PE could be safely discharged without further evaluation (NPV $>99.5\%$)
High sensitivity D Dimer

Disorders associated with increased plasma levels of fibrin D-dimer

- Arterial thromboembolic disease
- Myocardial infarction
- Stroke
- Acute limb ischemia
- Atrial fibrillation
- Intracardiac thrombus
- Venous thromboembolic disease
- Deep venous thrombosis
- Pulmonary embolism
- Disseminated intravascular coagulation
- Preeclampsia and eclampsia
- Abnormal fibrinolysis; use of thrombolytic agents
- Cardiovascular disease, congestive failure
- Severe infection/sepsis/inflammation
- Surgery/trauma (eg, tissue ischemia, necrosis)
- Systemic inflammatory response syndrome
- Vasoocclusive episode of sickle cell disease
- Severe liver disease (decreased clearance)
- Malignancy
- Renal disease
- Nephrotic syndrome (eg, renal vein thrombosis)
- Acute renal failure
- Chronic renal failure and underlying cardiovascular disease
- Normal pregnancy
- Venous malformations

Advanced risk stratification: laboratory markers

- Cardiac biomarkers, including **troponins and natriuretic peptides**, have emerged as promising tools for risk assessment of patients with acute PE.
Advanced risk stratification: laboratory markers

1. **Troponins**:–

- Cardiac troponins are the most sensitive and specific biomarkers of myocardial cell damage, reflecting microscopic myocardial necrosis.

- Elevations of troponin levels in PE patients are mild and of short duration compared with elevations in patients with acute coronary syndromes. *(Circulation. 2003;108.2191-2194.)*

Advanced risk stratification: laboratory markers

- In acute PE, troponin levels correlate well with the extent of right ventricular dysfunction. Some PE patients have initially negative troponin test results but may show a release of troponin 6 to 12 hours later.
Advanced risk stratification: laboratory markers

- Release of troponin can occur in patients with PE in the absence of angiographic coronary artery disease.

- An abrupt increase in right ventricular wall tension with compression of the right coronary artery and direct myocardial micro-injury is a possible explanation.


Advanced risk stratification: laboratory markers

• **Natriuretic Peptides:** Similar to cardiac troponins, elevations in BNP and NTproBNP are associated with right ventricular dysfunction in acute PE.

Mechanism of cardiac biomarker level elevation in pulmonary embolism.

Kucher N, and Goldhaber SZ Circulation. 2003;108:2191-2194

Other Novel Biomarkers

• Heart-type fatty acid-binding protein (H-FABP) is a small cytoplasmic protein which diffuses rapidly into the circulation following myocardial cell damage. It may provide relevant prognostic information in non-high-risk PE.

• Cardiac expression of growth differentiation factor-15 (GDF-15), a distant member of the transforming growth factor-ß cytokine family, also increases sharply after pressure overload or myocardial ischaemia.

• Both biomarkers appear promising and deserve further evaluation in external patient cohorts.

Ventilation/perfusion scan [V/Q scan]

- Ventilation–perfusion scanning is most likely to be diagnostic in the absence of cardiopulmonary disease.

- A normal perfusion lung scan effectively rules out acute pulmonary embolism.


Ventilation/perfusion scan [V/Q scan]

- However, if the clinical story strongly suggests pulmonary embolism despite a Nondiagnostic ventilation–perfusion scan, the Diagnosis should be rigorously pursued.

Ventilation/perfusion scan [V/Q scan]

• If the ventilation–perfusion scan is **nondiagnostic** in a patient with a **low clinical** probability of acute pulmonary embolism or in a patient with a **moderate clinical probability** but negative results on d-dimer testing, **no additional testing or Therapy is indicated**.

• Preferred test in pregnant patients


Helical (Spiral) Computed Tomography (CT)

• Contrast-enhanced CT arteriography has advantages over ventilation–perfusion scanning, including speed, characterization of nonvascular structures, and detection of venous thrombosis.

• If a patient has either acute or chronic renal insufficiency, caution in using contrast agents is imperative, given the possibility of inducing nephropathy associated with contrast material.

• CT arteriography has the **greatest sensitivity and specificity** for detecting emboli in the **main, lobar, or segmental pulmonary arteries**.

Spiral (Helical) Chest CT

• **Advantages**
  – Noninvasive and Rapid
  – Alternative Diagnosis

• **Disadvantages**
  – Costly (£ 2400 - 2800/scan)
  – Risk to patients with borderline renal function
  – Hard to detect subsegmental pulmonary emboli

Pulmonary Angiography

• “Gold Standard”
  – Performed in an Interventional Cath Lab

• Positive result is a “cutoff” of flow or intraluminal filling defect

• “Court of Last Resort”
Conclusion and outlook

• Although case fatality rates appear to have dropped over the past two decades, acute PE continues to pose a serious burden on health and survival.

• Rapid and accurate risk stratification is of paramount importance to ensure the highest quality of care.

• We must first classify patients as ‘stable’ or ‘unstable’, i.e. distinguish between high-risk and non-high-risk PE. This dichotomy will help us to optimize patient management.