Pulmonary Emboli: Diagnosis Based on Suspicion and Management in 2017

Gregory Piazza, MD, MS
Cardiovascular Division
Brigham and Women’s Hospital
December 8, 2017
Disclosures

• EKOS/BTG- grant/research support
• Daichii-Sankyo- grant/research support
• BMS- grant/research support
• Janssen- grant/research support
• Thrombosis Research Institute- grant/research support
Objectives

• Review the critical pathways for pulmonary embolism (PE) diagnosis and risk stratification

• Highlight evidence-based strategies for effective management of acute PE

• Explore emerging concepts in the advanced care of PE patients
PE Epidemiology: High Mortality and Risk of Readmission

Major Risk Factors for PE

**Inherited**
- Thrombophilias
- Family history

**Lifestyle**
- Smoking
- Stress
- Diet/obesity

**Acquired**
- Age
- Malignancy
- Recent surgery, trauma, hospitalization, immobility
- Chronic medical illness

**Inflammatory**
- Acute and chronic infection
- Chronic inflammatory diseases
Chronic Thromboembolic Pulmonary Hypertension


Critical Pathways for PE Diagnosis

Suspected PE

- History, physical examination, chest x-ray, and electrocardiogram

Consider clinical setting and assess clinical probability

- Outpatient with low OR intermediate clinical probability
  - D-dimer
    - Normal: No PE
    - Elevated: Chest CT
      - Normal: No PE
      - Positive: Treat for PE

- Inpatient OR outpatient with high clinical probability
  - Chest CT
    - Normal: No PE
    - Positive: Treat for PE
Spectrum of Disease

**Massive PE (~5%)**
- Hypotension, syncope, cardiogenic shock, cardiac arrest
- Respiratory failure
- Often fatal if aggressive care not instituted

**Catastrophic PE (<1%)**
- “Super-massive PE”
- Refractory cardiogenic shock
- Ongoing CPR

**Submassive PE (~25%)**
- Normotensive
- Right ventricular (RV) dysfunction is present
- Increased risk of adverse outcomes

**PE with normal BP and RV function (~70%)**
- Normotensive
- Normal RV function
- Excellent prognosis with anticoagulation alone
Risk Stratification Tools for PE

CT RV-to-LV Diameter Ratio
Stein PD, et al. Am J Cardiol 2010;106:558

Echocardiography

Troponin
2014 ESC Guidelines: Risk Stratification of Acute PE

NOACs for VTE: Meta-Analysis

Systemic Fibrinolysis

In a series of 104 patients with acute PE treated with fibrinolysis:
- 20 patients had major bleeding
- 1 patient had a fatal bleed (intracranial hemorrhage)
- 1 patient required surgery to stop the bleeding
- 7 patients had bleeding >3 units

Chatterjee S, et al. JAMA 2014;311:2414
Ultrasound-Facilitated, Catheter-Directed Embolectomy

The SEATTLE II Paradox

While most patients have normalization of RV size on chest CT, the average observed reduction in angiographic obstruction (modified Miller score) is only 30%.

This paradox suggests that symptomatic improvement and reduction in RV size may be achieved by mechanisms in addition to reduction in proximal pulmonary artery obstruction.

SEATTLE-3D: Small, Not Large Vessel Response Correlates with RV Recovery

Small Vessel Fractions Show Significant Correlations

- ΔRV10/ΔTBV: $R^2 = 0.2756$
- ΔRV15/ΔTBV: $R^2 = 0.3417$

Large Vessel Fractions DO NOT Show Significant Correlations

- ΔRV40/ΔTBV: $R^2 = 3E-05$
- ΔRV45/ΔTBV: $R^2 = 3E-05$
OPTALYSE PE: Optimizing US-Facilitated Catheter-Directed Fibrinolysis

**Objective:** Answer Questions from SEATTLE II and ULTIMA

- Can we lower the fibrinolytic dose to improve safety without compromising efficacy?
- Can we improve efficiency and decrease cost by reducing infusion time?

**Multi-Center, 100-Submassive PE Patient, Randomized, Controlled Trial**

- 8 mg/2 hrs
- 8 mg/4 hrs
- 12 mg/6 hrs
- 24 mg/6 hrs

**Study End Points**

- Change in CT RV-to-LV ratio from baseline to 48 hours
- Change in Miller Index from baseline to 48 hours
- Treatment success (composite end point)
- Major bleeding at 72 hours

**Mean Change in CT-Measured RV-to-LV Ratio from Baseline to 48 Hours**

- 8 mg/2 hrs (N = 26): -0.4
- 8 mg/4 hrs (N = 26): -0.35
- 12 mg/6 hrs (N = 27): -0.42
- 24 mg/6 hrs (N = 16): -0.48

*P<0.05 for all

**Overall Major Bleeding Rate = 3%**

**Intracranial Hemorrhage Rate = 2%**

Presented at American Thoracic Society 2017
Inferior Vena Cava Filters

Ahmed O, et al. CHEST. 2017;151:1402
PE Response Teams

Acute PE Patient in the Emergency Department, on Inpatient Service, or in Intensive Care

PERT Team Activation via Paging System

PERT Evaluation by On-Call Physician

Web-Based Video Conference

Discussion and Consensus

Options and Recommendations Presented to the Patient, Family, and Care Team

Table 1. Pulmonary embolism response team (PERT) midterm report card.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Grade (yes, possibly, no, incomplete)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced heterogeneity of PE care</td>
<td>Incomplete</td>
<td>No data available</td>
</tr>
<tr>
<td>Facilitate access to advanced therapies for those with increased risk of adverse outcomes</td>
<td>Possibly</td>
<td>Studies provide indirect evidence that PERTs increase access to advanced therapies such as systemic fibrinolysis, catheter-directed embolectomy, and mechanical circulatory support⁷,⁸</td>
</tr>
<tr>
<td>More appropriate use of interventional therapies for PE</td>
<td>Incomplete</td>
<td>No data available; however, the PERT model has been associated with increased utilization of interventional therapies for PE⁷,⁸</td>
</tr>
<tr>
<td>Improved clinical outcomes</td>
<td>Incomplete</td>
<td>No data available</td>
</tr>
<tr>
<td>Reduced length of stay and costs associated with PE care</td>
<td>Incomplete</td>
<td>No data available</td>
</tr>
<tr>
<td>Overall</td>
<td>Incomplete</td>
<td>Data beyond those from descriptive studies are required</td>
</tr>
</tbody>
</table>

Dudzinski D and Piazza G. Circulation. 2016;133:98
Giri JS and Piazza G. Vasc Med. 2017; in press
Summary Points

• Risk stratification is a critical component of PE diagnosis.

• Determining the optimal anticoagulation regimen should consider risk of recurrence, risk of bleeding, and patient preference.

• Selection of advanced therapies depends on assessment of the patient’s risk of adverse outcomes and major bleeding.