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The Emergency Department Management of Pulmonary Embolism

Rashmi U. Kothari, MD
Kalamazoo College of Medical Science
Borgess Research Institute
Goals

- PE is complication of venous thrombosis
- PE is very, very common
- Diagnosing only a very small % of PEs
- The classic symptoms are uncommon
20 y.o Male College Student with Hypotension & Questionable Syncope

- Found knocking at neighbors door
- BP=60/p P=125 R=24
- EMS with MAST-trousers
- PMH= none
Pulmonary Embolism
*3rd most common cause of death*

- Most common fatal missed diagnosis
- #2 cause of unanticipated death (after MI)
- #1 cause of unexpected death on ventilator
- #1 cause of death in orthopedics
- #1 cause of death in pregnancy

Papadakis: *JAMA* 1991; 265
Hecht: *Zentralbl Allg Pathol* 1984; 129
Fatal PE in-hospital

70% misdiagnosed antemortum

70% of PE cases unsuspected until autopsy

30% have PE suspected before death

Reference: Coon: Arch Surg 1976;111
Mayo inpatient PE deaths

*Autopsies between 1985 - 1989*

- Listed cause of death correct in only 32%
- Only 22% had a diagnostic workup for PE
- ‘Classic’ symptoms absent in most cases
- 64% had no prophylaxis
- 46% had inadequate prophylaxis

Missed PE: autopsy incidence

33 published autopsy studies

- 33 studies between 1980 - 1995
- 150,000 autopsies
- Fraction w/ missed diagnosis
  - 100% (highest)
  - 85% (average)
  - 55% (lowest)

References too numerous to list
Fatal PE: missed Dx by age

Dx missed in 90% of older patients

Inpatients vs out-of-hospital

No difference in the incidence of PE found at autopsy

Sperry: Hum Pathol 1990; 21
Mortality in PE
By treatment type

References:

Bell: Am Heart J 1982;103
The Urokinase Pulmonary Embolism Trial: Circulation 1973;47
Mortality reduction w/ heparin

1358 medical admissions randomized

Risk Factors for PE & DVT

- **Hypercoaguable state**
  - Protein S & C def
  - Pregnancy
  - Malignancy (colon & ovarian)
  - Anti-Thrombin III def*
  - BCP (>35 yo & smoker)

- **Venostasis**
  - Obesity
  - Heart disease (CHF, MI)
  - Immobilization

- **Vessel injury**
  - Surgery (especially pelvic surgery)
  - Trauma

Virchow’s Triad
## Risk Factors for PE

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Clinical Trial (n=117)</th>
<th>Autopsy* (n=92)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immobile</td>
<td>66 (56%)</td>
<td>56 (61%)</td>
</tr>
<tr>
<td>Surgery</td>
<td>63 (54%)</td>
<td>33 (36%)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>27 (23%)</td>
<td>36 (39%)</td>
</tr>
<tr>
<td>Thrombophlebitis</td>
<td>16 (14%)</td>
<td>22 (24%)</td>
</tr>
<tr>
<td>Trauma</td>
<td>12 (10%)</td>
<td>7 (8%)</td>
</tr>
<tr>
<td>Post-Partum &lt;3 mos.</td>
<td>5 (4%)</td>
<td>NA</td>
</tr>
<tr>
<td>No Risk Factors</td>
<td>21 (18%)</td>
<td>11 (12%)</td>
</tr>
</tbody>
</table>

Pathophysiology of PE

- **Majority caused by DVT**
  - 15-30X more common
  - 50-90% with pelvic/lower ext. clot

- Patent foramen ovale
- Air embolus (barotrauma, gyn surgery)
- Fat embolus (trauma)
## Incidence of PE in patients with DVT

<table>
<thead>
<tr>
<th>Level</th>
<th>No PE</th>
<th>Asymp. PE</th>
<th>Symp. PE</th>
<th>Total PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal (n=72)</td>
<td>40 (56.5%)</td>
<td>4 (6.5%)</td>
<td>28 (39%)</td>
<td>32 (45.5%)</td>
</tr>
<tr>
<td>Proximal (n=292)</td>
<td>160 (55%)</td>
<td>72 (25%)</td>
<td>60 (20%)</td>
<td>132 (45%)</td>
</tr>
<tr>
<td>Total (n=364)</td>
<td>200 (55%)</td>
<td>76 (21%)</td>
<td>88 (24%)</td>
<td>164 (45%)</td>
</tr>
</tbody>
</table>

Reference: Monreal: Chest 1992102:677
PE from calf vein DVT
Common and often fatal

References:
Moreno-Cabral Surgery 1976;80
Havig: Acta Chir Scand 1977;478
Autopsy source of PE

Isolated calf veins in 1/3 of cases

33%

67%

Other

Chronic pulmonary HTN

In 70% of those with recurrent PE

Reference: Riedel: Chest 1982;81
512 autopsy cases
With isolated upper-extremity DVT

Catheter-associated DVT

One-year autopsy study of PE

- Autopsies with catheter DVT at one hospital
- 10 fatalities from massive PE
- Source of embolus:
  - Innominate vein
  - Subclavian vein
  - Superior vena cava

Muller: Dtsch Med Wochenschr 1976; 101
PE from catheter-related DVT

20 cases of upper-extremity DVT associated with indwelling catheters

- 6/20 had PE
- 1 died from massive PE
Pathophysiology (cont)

- Obstructs pulmonary vasculature
- Increased physiologic deadspace in lung
- Increases PA & RV pressures
  - May cause Mitral regurg & cor pulmonale
- Poor filling of L Ventricle causing hemodynamic compromise/collapse
## Clinical Presentation

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Clinical Trials(^1)</th>
<th>Autopsy(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>84%</td>
<td>59%</td>
</tr>
<tr>
<td>Pleuritic Chest Pain</td>
<td>74%</td>
<td>8%</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>27%</td>
<td>3%</td>
</tr>
<tr>
<td>Apprehension</td>
<td>59%</td>
<td>17%</td>
</tr>
<tr>
<td>Cough</td>
<td>53%</td>
<td>3%</td>
</tr>
</tbody>
</table>

\(^1\)UPET & USPET

## Signs of PE

<table>
<thead>
<tr>
<th>Sign</th>
<th>Clinical Trials</th>
<th>Autopsy *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachypnea &gt;16</td>
<td>92%</td>
<td>66%</td>
</tr>
<tr>
<td>Tachypnea &gt;20</td>
<td>70%</td>
<td>NA</td>
</tr>
<tr>
<td>Tachycardia &gt;100</td>
<td>30%</td>
<td>54%</td>
</tr>
<tr>
<td>Fever &gt;37.5 °C</td>
<td>43%</td>
<td>30%</td>
</tr>
<tr>
<td>Low. Ext. edema</td>
<td>24%</td>
<td>26%</td>
</tr>
<tr>
<td>Homan’s sign</td>
<td>4%</td>
<td>NA</td>
</tr>
</tbody>
</table>

PE & asymptomatic DVT
2/3 with PE have no DVT symptoms

Reference: Walsh: J Obstet Gynaecol Br Commw 1974; 81
Clinical Dx of DVT unreliable
50% false positives and negatives

In asymptomatic patients and in patients with pain, tenderness, and unilateral leg swelling

Reference: Richards: Arch Int Med 1976; 136
ED Evaluation of PE

- Prospective, all pleuritic chest pain (n=173)
- EKG, CXR, V/Q,
- Angio (low, intermed., & high prob V/Q)
- 23% had PE

- Immobilization, hx DVT, phlebitis, effusion*
- 20% had none of these risk factors*

Laboratory Tests

- CXR
- EKG
- ABG
- D-Dimer
Chest X-ray

- Non-specific & insensitive

- Findings:
  - Normal 30%
  - Elevated hemi-diaphragm 50%
  - Focal infiltrate (w/in 3 days) 30-50%
    indistinguishable from pneumonia
  - Effusion 40-50%
  - Atelectasis 50-60%

- Classic findings:
  - Hampton’s hump
  - Westermark Sign 7%
Electrocardiogram

- Poor sensitivity & specificity
- Findings:
  - Tachycardia
  - Non-specific ST-T wave changes
  - Rt or Lt axis deviation
  - P-pulmonale
  - Atrial fibrillation
  - S₁Q₃T₃
  - S₁S₂S₃

PO$_2$ in Patients with & without PE (no prior history of Cardiac or Pulmonary disease)

Reference: Stein Chest 1991:100:598
Arterial Blood Oxygen

- 0% predictive value
- 17% $\text{PO}_2 > 80 \text{ mmHg}$
- 5% $\text{PO}_2 > 100 \text{ mmHg}$
ABG does not predict PE  
(120 possible PE, 54 with PE)

<table>
<thead>
<tr>
<th>PO$_2$</th>
<th>Incidence of PE below level</th>
<th>Incidence of PE above level</th>
</tr>
</thead>
<tbody>
<tr>
<td>80 mm Hg</td>
<td>45/101 (44.6%)</td>
<td>9/19 (47.4%)</td>
</tr>
<tr>
<td>70 mm Hg</td>
<td>39/87 (44.8%)</td>
<td>15/33 (45.5%)</td>
</tr>
<tr>
<td>65 mm Hg</td>
<td>29/69 (42%)</td>
<td>25/51 (49%)</td>
</tr>
</tbody>
</table>

A-a Gradient

- A-a grad = (Calc PO$_2$) - (Measured PO$_2$)
- A-a grad = 150 - (PCO$_2$ / .8) - PO$_2$
- Normal = 10 - 20

- 23% will have normal A-a gradient
A-a Gradient in Patients with & without PE (no prior history of Cardiac or Pulmonary disease)

Reference: Stein Chest 1991:100:598
D-Dimer

- A degradation product of fibrin
- Monoclonal Ab test (RIA* & latex)
- NPV 90% (misses 1/10)
- PPV 30% (incorrect 7/10)
Lower Extremity Dopplers

- PPV=78% NPV=88%
- Advantages
  - noninvasive
  - inexpensive
- Disadvantages
  - diff. with acute on chronic
  - worse PPV & NPV if asymp
  - leg pain
  - casts
  - calf DVT’s (52% sens)
# Ventilation Perfusion Scans

## Clinical Probability

<table>
<thead>
<tr>
<th></th>
<th>80-100%</th>
<th>20-79%</th>
<th>0-19%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hi</td>
<td>96%</td>
<td>88</td>
<td>56%</td>
</tr>
<tr>
<td>Int</td>
<td>66%</td>
<td>28%</td>
<td>16%</td>
</tr>
<tr>
<td>Low</td>
<td>40%</td>
<td>16%</td>
<td>4%</td>
</tr>
<tr>
<td>Nl</td>
<td>0%</td>
<td>6%</td>
<td>2%</td>
</tr>
</tbody>
</table>

73% had Int/Low prob scans
High prob scans have PPV 88%

![Lung Perfusion]

Lung Perfusion images: Rt Lat, Anterior, Lt Lat, LPO, Posterior, RPO

*Source undetermined*

**PIOPED 90**
Ventilation Perfusion Scan

- **PIOPED, ‘90**
  - Interobserver agreement for V/Q readings 95%, 92%, 94% for high, VLP, & NL scans but dropped to 75% & 70% for IP & LP scans

- **Schugler et al ‘94**
  - 78% of intermediate scans & 92 % of low probability scans had no further testing
  - But 35% of the former and 20% of the latter received anticoag.
  - Leaving the decision to anticoagulate based on clinical grounds

- **Stein et al ‘91**
  - Clinical evaluation of PE is non-specific
Pulmonary Angiogram

- **Advantages**
  - gold standard

- **Disadvantages**
  - invasive, $$$$
  - internists reluctance

- **PIOPED ‘90**
  - 2.5% mortality
  - 66% interobserver agreement for subsegmental PE’s

- **Stein ‘92**
  - 6% morb., 0.5% mortality

- **Sustman ‘82 12% requiring PA underwent procedure**

Source undetermined
CT Angiograms

- Remy-Jardin, *Radiology* ‘96
  - 75 conseq. Pts referred for PA prospectively
  - Sensitivity 91%, specificity 78%, PPV 100%, NPV 89%
  - 188 central PE’s on CT corresponded to PA
  - Found isolated subsegmental clots in 5% on PA

**Angiography**

<table>
<thead>
<tr>
<th>CT Findings</th>
<th>Negative</th>
<th>Positive</th>
<th>Inconclusive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>25</td>
<td>1</td>
<td>0</td>
<td>26</td>
</tr>
<tr>
<td>Positive</td>
<td>0</td>
<td>39</td>
<td>0</td>
<td>39</td>
</tr>
<tr>
<td>Inconclusive</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Suboptimal</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>32</strong></td>
<td><strong>43</strong></td>
<td><strong>0</strong></td>
<td><strong>75</strong></td>
</tr>
<tr>
<td>Embolism status</td>
<td>PA of Central Vessels Only</td>
<td>PA of All Vessels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------------</td>
<td>---------------------------</td>
<td>-------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CT</td>
<td>PE</td>
<td>No PE</td>
<td>Total</td>
</tr>
<tr>
<td>Embolism present</td>
<td></td>
<td>6</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Embolism absent</td>
<td></td>
<td>1</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>7</td>
<td>13</td>
<td>20</td>
</tr>
</tbody>
</table>
CT Angiograms

- General Observations
  - Sensitivities 53-97%
  - Specificity 78-97%

- Advantages
  - Cost
  - Fast
  - Close proximity to ED
  - Alternative Dx

- Disadvantages
  - ? Misses subseg. PE’s
  - Not standard of care; yet
  - IVP dye

Source undetermined
Treatment

- **Unfractionated Heparin**
  - 5000 U bolus followed by 1250 U/hr
  - Maintain aPTT 2 - 2.5 normal
  - Recommend concurrent heparin tx for 48 hr when starting Coumadin
  - Most recommend 3 - 6 months of coumadin, or longer if they have a clotting disorder  
    Agnelli et al., *Int’l J. of Card.*; 1998

- **LMWH**
  - Prospective randomized study have found nadroparine as safe and effective as unfrac. heparin for submassive PE
  - Similar double blinded studies using tinzaprin
  
    Thery et al., *Circ.*; 1992 & Simonnneau et al, Haemostasis; 1996
Thrombolytic Therapy

Studies

- Jerjes-Sanchez et al., *J Thrombosis*; 1995
  - Pts with hypotension & CHF were randomized to anticoag or thrombolytics and anticoag
  - Stopped after 8 pts b/c all 4 anticoag alone died, & all 4 thrombolytics and anticoag survived

- Wolfe et al., *Am Heart J*; 1994
  - 101 pts (nl BP, RV dysfxn) randomized to rt-PA plus heparin or heparin alone
  - No rt-PA pts had recurrent PE or died
  - Of the 55 receiving heparin alone, 5 recurrent PE (2 fatal)
Thrombolytic Therapy of PE

- **Standard Regimen***
  - 100 mg tPA infusion over 2 hours

- **Unstable patients**
  - .6mg/kg (max=50mg) over 15 min

*FDA approved
The bad news about thromboembolic disease

- Most DVT’s are asymptomatic
- Most DVT’s produce PE
- Most PE’s are asymptomatic
- DVT & PE causes death and disability
  even when there are no recognizable symptoms
## Risk Factors for PE in patients without Cardiac or Pulmonary disease

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>PE (n=117)</th>
<th>No PE (n=248)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immobile</td>
<td>66 (56%)</td>
<td>81 (33%)*</td>
</tr>
<tr>
<td>Surgery</td>
<td>63 (54%)</td>
<td>78 (31%)*</td>
</tr>
<tr>
<td>Malignancy</td>
<td>27 (23%)</td>
<td>38 (15%)</td>
</tr>
<tr>
<td>Thrombophlebitis</td>
<td>16 (14%)</td>
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</tr>
<tr>
<td>Trauma</td>
<td>12 (10%)</td>
<td>25 (10%)</td>
</tr>
<tr>
<td>Post-Partum &lt;3 mos.</td>
<td>5 (4%)</td>
<td>8 (3%)</td>
</tr>
</tbody>
</table>

*p < .001

Stein Chest 1991:100:598
Paradoxical embolism

Source most often in the calf

Electrocardiogram

- Normal Sinus or Sinus Tachycardia  80%
- QRS axis change
  - Acute RAD  15%*
  - RBBB  8%
- T-wave abnormality  40%*
- Depressed ST  25%
- Elevated ST  16%*

Mayo et al., *Radiology*; 1997
- 139 nonconseq. pts. underwent CT, V/Q, & PA (if indicated)
- 16% were outpts
- 46/139 pts had a PE and 93/139 did not
  - High prob V/Q in 30/46 (sens 65%)
  - + CT in 40/46 (sens 87%), - CT in 88/93 (spec 95%)
- Overall, V/Q correct in 103/139 (74%) pts & CT was correct in 128/139 (92%) of cases
- Interobserver agreement (K) 0.61 for V/Q and 0.85 for CT