Pulmonary Embolism – It’s a Team Sport
Case Presentations and Discussion

Panelists:
Christopher Kabrhel, MD, MPH
Louis Chu, MD
Samuel Goldhaber, MD
Jeffrey L. Weinstein, MD
Barbara L. LeVarge, MD
Case 1

- 25 yo F, otherwise healthy, on oral contraceptives
- Long haul flight 3 days prior
- Sudden onset pleuritic chest pain and dyspnea
- Called EMS, arrives to ED with following VS:
  - BP 90/65, HR 133, RR 30, O2 89% RA, 94% NRB
- CTA chest shows saddle PE with moderate R heart strain
Pulmonary Embolism Response Team (PERT)
MGH PERT Activations

n=394 (initial 30 months)
now, n≈850

• Multidisciplinary virtual consults
  – Average length: 25 mins.
  – Range 5–15 physicians
  – Off-hours/weekends: 53%

Kabrhel, CHEST, 2016
MGH PERT Treatment

Treatment (%)

- Anticoags
- IV Lysis
- CDT
- Vortex
- Surgery
- ECMO
- IVC Filter

ED
ICU
Inpt

Deadmon, AEM, 2017
MGH PERT Treatment

Deadmon, AEM, 2016
Case 1

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• Called EMS, arrives to ED with following VS:
  – BP 90/65, HR 133, RR 30, O2 89% RA, 94% NRB
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ADVANCED MANAGEMENT

1) Systemically administered (via peripheral IV) thrombolysis:
   Full Dose (TPA 100 mg)
   Half Dose (TPA 50 mg)

2) Pharmacomechanical therapy with catheter-directed (ultrasound-facilitated) thrombolysis: TPA 24 mg

3) Surgical Embolectomy

4) IVC Filter
# LYSIS IN SUBMASSIVE PE: MORTALITY META-ANALYSIS

**Table:**

<table>
<thead>
<tr>
<th>Source</th>
<th>No. of Events</th>
<th>No. of Patients</th>
<th>No. of Events</th>
<th>No. of Patients</th>
<th>OR (95% CI)</th>
<th>Favors</th>
<th>Favors</th>
<th>Weight %</th>
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</thead>
<tbody>
<tr>
<td>Goldhaber et al,² 1993</td>
<td>0</td>
<td>46</td>
<td>2</td>
<td>55</td>
<td>0.16 (0.01-2.57)</td>
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<td>5.3</td>
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<tr>
<td>Konstantinides et al,³ 2002</td>
<td>4</td>
<td>118</td>
<td>3</td>
<td>138</td>
<td>1.58 (0.35-7.09)</td>
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<td>18.4</td>
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<tr>
<td>TIPES,²⁹ 2010</td>
<td>0</td>
<td>28</td>
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<td>30</td>
<td>0.14 (0.00-7.31)</td>
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<tr>
<td>Fasullo et al,¹¹ 2011</td>
<td>0</td>
<td>37</td>
<td>6</td>
<td>35</td>
<td>0.11 (0.02-0.58)</td>
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<td>15.1</td>
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<tr>
<td>MOPETT,¹⁰ 2012</td>
<td>1</td>
<td>61</td>
<td>3</td>
<td>60</td>
<td>0.35 (0.05-2.57)</td>
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<td>10.5</td>
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<tr>
<td>ULTIMA,³⁰ 2013</td>
<td>0</td>
<td>30</td>
<td>1</td>
<td>29</td>
<td>0.13 (0.00-6.59)</td>
<td></td>
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<td>2.7</td>
</tr>
<tr>
<td>TOPCOAT,⁹ 2014</td>
<td>1</td>
<td>40</td>
<td>1</td>
<td>43</td>
<td>1.08 (0.07-17.53)</td>
<td></td>
<td></td>
<td>5.3</td>
</tr>
<tr>
<td>PEITHO,⁸ 2014</td>
<td>6</td>
<td>506</td>
<td>9</td>
<td>499</td>
<td>0.66 (0.24-1.82)</td>
<td></td>
<td></td>
<td>40.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>12</strong></td>
<td><strong>866</strong></td>
<td><strong>26</strong></td>
<td><strong>889</strong></td>
<td><strong>0.48 (0.25-0.92)</strong></td>
<td></td>
<td></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>

Heterogeneity: \( \chi^2 = 7.63; P = .37; I^2 = 8\%

Overall effect: \( z = 2.22; P = .03 \)

**Intermediate-risk PE**

<table>
<thead>
<tr>
<th></th>
<th>Thrombolytics</th>
<th>Anticoagulants</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality (8)</td>
<td>12/866 (1.39)</td>
<td>26/889 (2.92)</td>
</tr>
<tr>
<td>Major bleeding (8)³</td>
<td>67/866 (7.74)</td>
<td>20/889 (2.25)</td>
</tr>
</tbody>
</table>

NNT = 65

NNH = 18

(JAMA 2014; 311: 2414-2421)
<table>
<thead>
<tr>
<th>ENDPOINT</th>
<th>LYSIS</th>
<th>HEPARIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-Term Mortality</td>
<td>20%</td>
<td>18%</td>
</tr>
<tr>
<td>Chronic SOB or other symptoms</td>
<td>36%</td>
<td>30%</td>
</tr>
<tr>
<td>Incidence of CTEPH</td>
<td>2.1%</td>
<td>3.2%</td>
</tr>
</tbody>
</table>

(JACC 2017; 69: 1536-1544)
<table>
<thead>
<tr>
<th>Promise</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced Mortality and Recurrent PE: Short-Term</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Reduced Long-Term Mortality</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Reduced Long-Term Recurrent PE</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Improved Function and QOL</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Reduced Incidence of CTEPH</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>
Case 1

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Catheter Directed Thrombolysis

![Graph showing mean systolic PA pressure (mmHg) before and after catheter-directed thrombolysis (CDT) in three trials: PERFECT, SEATTLE II, and ULTIMA.](image)

- **PERFECT**
  - Baseline: 51.2 (n=92)
  - Post CDT: 37.2
  - (P<0.0001)

- **SEATTLE II**
  - Baseline: 51.4 (n=150)
  - Post CDT: 37.6
  - (P<0.0001)

- **ULTIMA**
  - Baseline: 52.3 (n=30)
  - Post CDT: 39.9
  - (P<0.0001)

*Kuo CHEST, 2015*
Catheter Directed Thrombolysis

- Proximal infusion of thrombolytic
- Mechanical Fragmentation
- Ultrasonic acceleration

- 12-24 hour treatment

- Theoretical benefits:
  - lower drug dose (10-20mg tPA)
  - Drug acts faster, clearing clot sooner
  - Less hemolysis
  - Monitor PA pressure

Cleaner®

EKOS®

Scmitz-Rode CVIR 1998
Questions for our experts related to thrombolysis
Case 2

- 63 yo M with small cell lung cancer
- Sent from Oncology clinic to Radiology to evaluate for LLE DVT
- US confirms DVT
- Code Blue called to Radiology as pt exiting
- VS: BP 74/46, HR 152, RR 32, O2 86%
- Point of care ultrasound shows a moderate pericardial effusion but no evidence tamponade with RV dilatation and McConnell’s sign
Contraindications to Thrombolysis

• Absolute
  – Prior intracranial hemorrhage
  – Intracranial malignant neoplasm or cerebrovascular disease (i.e. AVM)
  – Ischemic stroke within 3 months
  – Active bleeding or bleeding diathesis
  – Recent surgery involving brain or spinal canal
  – Recent significant closed-head trauma
  – Suspected aortic dissection

• Relative
  – Age >75 years
  – Pregnancy
  – Remote ischemic stroke (>3 months)
  – Major surgery within 3 weeks
  – Recent internal bleeding
  – Traumatic or prolonged CPR (>10 minutes)
  – Non-compressible vascular puncture
  – Current use of anticoagulation
  – Severe uncontrolled hypertension at presentation (>SBP 180 or DBP >110) or history of chronic, severe, poorly controlled hypertension
  – Dementia

Case 2

• 63 yo M with small cell lung cancer
• Sent from Oncology clinic to Radiology to evaluate for LLE DVT
• US confirms DVT
• Code Blue called to Radiology as pt exiting
• VS: BP 74/46, HR 152, RR 32, O2 86%
• Point of care cardiac ultrasound shows moderate pericardial effusion but no evidence tamponade with RV dilatation and McConnell’s sign
Who to treat

- Team sport – Multidisciplinary teams
- Guidelines lag
- Massive PE often = IV TPA
- Stable, submassive PE = anticoagulation
- Hi-risk submassive PE = ? CDT
  - RV strain (echo, CT)
  - Symptomatic patient
  - Elevated troponins, BNP
  - PESI Score?
**PESI Score**

**Table 8**

Pulmonary embolism severity index (PESI) score

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Points assigned</th>
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</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>Age, in years</td>
</tr>
<tr>
<td>Altered mental status*</td>
<td>+60</td>
</tr>
<tr>
<td>Systolic blood pressure &lt; 100 mmHg</td>
<td>+30</td>
</tr>
<tr>
<td>History of cancer</td>
<td>+30</td>
</tr>
<tr>
<td>Arterial oxygen saturation &lt; 90 %†</td>
<td>+20</td>
</tr>
<tr>
<td>Temp &lt; 36 °C</td>
<td>+20</td>
</tr>
<tr>
<td>Respiratory rate ≥ 30/min</td>
<td>−20</td>
</tr>
<tr>
<td>Pulse ≥ 110/min</td>
<td>−20</td>
</tr>
<tr>
<td>Male sex</td>
<td>+10</td>
</tr>
<tr>
<td>History of heart failure</td>
<td>−10</td>
</tr>
<tr>
<td>History of chronic lung disease†</td>
<td>+10</td>
</tr>
</tbody>
</table>

A total point score for a given patient is obtained by summing the patient’s age in years and the points for each applicable predictor. Points assignments correspond with the following risk classes: Class I (very low risk): ≤65; Class II (low risk): 65–85; Class III (intermediate risk): 86–105; Class IV (high risk): 106–125; Class V (very high risk): >125

† Chronic obstructive pulmonary disease

‡ With and without supplemental oxygen administration

* Altered mental status was defined as confusion, disorientation, somnolence, lethargy, stupor, or coma

Simplified PESI

- Age > 80
- History of Cancer
- Chronic Cardiopulmonary Disease
- Pulse > 110
- CHF
- SBP < 100
- SaO2 < 90%

0 factors is low risk, everything else is high risk

Case 2

- 63 yo M with small cell lung cancer
- Confirmed LLE DVT
- Code Blue called to Radiology
- VS: BP 74/46, HR 152, RR 32, O2 86%
- Moderate pericardial effusion on ultrasound
- Patient brought to the ED and started on IVF and Levophed for blood pressure support.
- The pt received 2 L crystalloids and is on maximum dose of Levophed with continued hypotension, current 80/57.
Patient Selection

- Classic Indications:
  - Hemodynamic instability despite 2 pressors
  - Failed thrombolytic therapy
  - Contraindication to thrombolytic therapy

- Expanded indications:
  - Good surgical candidates with submassive PE and significant RV strain
Surgical Embolectomy

Video: Beyer E. “Acute Pulmonary Embolism”
https://www.youtube.com/watch?v=3OX3-h9zHV0
Surgical Embolectomy

Right

Left
Outcomes After Surgical Pulmonary Embolectomy for Acute Pulmonary Embolus: A Multi-institutional Study

W. Brent Keeling, MD, Thor Sundt, MD, Marzia Leacche, MD, Yutaka Okita, MD, Jose Binongo, PhD, Yi Lasajanak, MSPH, Lishan Aklog, MD, and Omar M. Lattouf, MD, for the SPEAR Working Group

Table 3. Postoperative Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>All (n = 214), n (%)</th>
<th>Massive (n = 38), n (%)</th>
<th>Submassive (n = 176), n (%)</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative transfusion</td>
<td>93 (43.5)</td>
<td>29 (76.3)</td>
<td>64 (36.4)</td>
<td>5.42</td>
<td>2.43–12.08</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Septicemia</td>
<td>8 (3.7)</td>
<td>3 (7.9)</td>
<td>5 (2.8)</td>
<td>3.01</td>
<td>0.76–12.48</td>
<td>0.12</td>
</tr>
<tr>
<td>Permanent Stroke</td>
<td>10 (4.7)</td>
<td>3 (7.9)</td>
<td>7 (4.0)</td>
<td>2.23</td>
<td>0.59–8.44</td>
<td>0.24</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>26 (12.1)</td>
<td>7 (18.4)</td>
<td>19 (10.8)</td>
<td>1.92</td>
<td>0.76–4.90</td>
<td>0.17</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>14 (6.5)</td>
<td>4 (10.5)</td>
<td>10 (5.7)</td>
<td>2.07</td>
<td>0.64–6.70</td>
<td>0.23</td>
</tr>
<tr>
<td>Prolonged ventilation</td>
<td>60 (28.0)</td>
<td>16 (42.1)</td>
<td>44 (25.0)</td>
<td>2.18</td>
<td>1.054–4.52</td>
<td>0.04</td>
</tr>
<tr>
<td>Postoperative dialysis</td>
<td>3 (1.4)</td>
<td>0</td>
<td>3 (1.7)</td>
<td>0.64</td>
<td>0.03–13.18</td>
<td>0.77</td>
</tr>
<tr>
<td>Renal failure</td>
<td>24 (11.2)</td>
<td>5 (13.2)</td>
<td>19 (10.8)</td>
<td>1.33</td>
<td>0.48–3.71</td>
<td>0.59</td>
</tr>
<tr>
<td>Reexploration for hemorrhage</td>
<td>18 (8.4)</td>
<td>6 (15.8)</td>
<td>12 (6.8)</td>
<td>2.63</td>
<td>0.94–7.37</td>
<td>0.07</td>
</tr>
<tr>
<td>In-hospital Mortality</td>
<td>25 (11.7)</td>
<td>9 (23.7)</td>
<td>16 (9.1)</td>
<td>3.13</td>
<td>1.28–7.69</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Outcomes

Midterm benefits of surgical pulmonary embolectomy for acute pulmonary embolus on right ventricular function

William Brent Keeling, MD, Bradley G. Leshnower, MD, Yi Lasajanak, MSPH, Jose Binongo, PhD, Robert A. Guyton, MD, Michael E. Halkos, MD, Vinod H. Thourani, MD, and Omar M. Lattouf, MD

- Improvement in RV function/hemodynamics

<table>
<thead>
<tr>
<th>TABLE 4. Postoperative echocardiographic data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative (n = 21)</td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Moderate or greater ventricular dysfunction</td>
</tr>
<tr>
<td>Moderate or greater tricuspid regurgitation</td>
</tr>
<tr>
<td>Pulmonary artery systolic pressure (mm Hg)</td>
</tr>
<tr>
<td>Tricuspid valve regurgitant velocity (m/s)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 5. Midterm echocardiographic follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative value (n = 21)</td>
</tr>
<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td>Moderate or greater ventricular dysfunction</td>
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<tr>
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<td>Pulmonary artery systolic pressure (mm Hg)</td>
</tr>
<tr>
<td>Tricuspid valve regurgitant velocity (m/s)</td>
</tr>
</tbody>
</table>

Source: Keeling WB et al. JTCVS.2016.
Questions?
Case 3

• 56 yo male with history of DVTs on lifelong anticoagulation for underlying pro-thrombotic state presented to ED with traumatic SDH
• Coumadin reversed with prothrombin complex concentrate
• Taken emergently to OR for SDH evacuation
• Peri-Arrest in ICU POD 1
Damage control: shock in acute PE

**Definitive therapy**

Preload optimization:
- RV dilation $\rightarrow$ leftward septal shift $\rightarrow$ cardiovascular collapse
- Minimize fluid resuscitation unless clearly hypovolemic

RV afterload reduction:
- Intubation is a high risk event (be prepared for cardiac arrest)
- Do not allow hypoxemia/hypercarbia, but high alveolar pressure is bad
- Inhaled nitric oxide or epoprostenol might help

Inotropy support

Maintain aortic/RCA perfusion pressure
- Low SVR is poorly tolerated (more septal shift, poor coronary perfusion)
- Support SVR with vasopressors (usually mixed $\alpha/\beta$)
Right ventricular auto-aggravation

- ↑ RV dilation
- ↑ tricuspid valve regurgitation
- ↑ leftward septal shift

- ↑ RV afterload

- ↓ RV output

- ↓ LV preload
- ↓ LV output

- Cardiogenic shock

- ↑ RV wall stress
- ↑ RV oxygen demand
- ↑ RV ischemia
- ↓ RV oxygen supply
- ↓ coronary perfusion
Cardiogenic shock

- Excessive intravenous fluids
- Hypothermia
- Positive pressure ventilation, alveolar overdistension
- Atelectasis
- Hypoxemia, hypercarbia
- Pain, sympathetic nervous system
- Systemic vasodilators (agents lowering LV afterload)

- ↑ RV dilation
- ↑ RV wall stress
- ↑ tricuspid valve regurgitation
- ↑ leftward septal shift
- ↑ RV afterload

- ↓ RV output
- ↓ LV preload
- ↓ LV output
- ↑ RV oxygen demand
- ↑ RV ischemia
- ↓ RV oxygen supply
- ↓ coronary perfusion

Myocardial depressants

- Systemic vasodilators (agents lowering LV afterload)
Case 3

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- Coumadin reversed with prothrombin complex concentrate
- Taken emergently to OR for SDH evacuation
- Peri-Arrest in ICU POD 1- markedly dilated RV on bedside ECHO
Which Catheter to Choose?

• PERFECT registry did not find statistically significant difference USAT vs Regular lysis catheters*
  – PA pressure reduction
  – Infusion time
  – Total tPA dose

• Only EKOS is FDA approved for pulmonary lysis
  – Uses Ultrasound to facilitate/accelerate lysis, fibrin disaggregation
  – ULTIMA, SEATTLE II used USAT

Massive PE
Post CT
Post CT
Post CT
Questions for our panel?
Additional Slides
Impeller System

Amplatz® Catheter

Skaf, Am J Card, 2007
Rheolytic Thrombectomy

- AngioJet®
- Hydrolyzer®
- Oasis®
Angiovac® / Vortex®
Inari® Flowtriever®

- 22 F sheath
- 3 Nitinol discs
- FLARE Study Ongoing
Penumbra® Indigo®

- 6F and 8F Aspiration catheter
- Suction pump
- Separator wire
- 3 different tips