Right Heart Strain in Life-Threatening Pulmonary Embolism

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Incomplete Information
Incomplete Information

• **CT #1:**
  - Multiple large acute pulmonary emboli
  - Upper, lower & middle right pulmonary artery branches

• **CT #2:**
  - Small acute pulmonary embolism segmental branch right upper lobe
Case #1

- 43yo f
- Dyspnea x 1mo
- Preceded by URI sx
- 36° C, 140/64, 84, 18
- SpO2 99% RA
- Lungs CTAB
- No edema

EKG #1
**Labs #1**

<table>
<thead>
<tr>
<th>Calcium</th>
<th>Magnesium</th>
<th>NT-proBNP</th>
<th>Troponin I</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.7</td>
<td>2.0</td>
<td>58</td>
<td>≤0.017</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Lactate</th>
<th>D-dimer</th>
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</thead>
<tbody>
<tr>
<td>1.6</td>
<td>5.09</td>
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Diff:
- PMN’s 65%
- Lymph’s 26%

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**Echo #1**
Questions

1. Classify this patient's PE:
   a) Massive
   b) Submassive
   c) Low-risk

2. How would you treat this patient's PE?
   a) Heparin
   b) LMWH
   c) Systemic thrombolysis
   d) Catheter-directed thrombolysis
   e) Embolectomy
Case #2

- 74yo m
- Cardiac arrest x 10 min
- Non-shockable
- COPD, CAD, HTN, CKD, PAD & DVT

EKG #2
Labs #2

<table>
<thead>
<tr>
<th>136</th>
<th>98</th>
<th>30</th>
<th>124</th>
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<tbody>
<tr>
<td>6.1</td>
<td>23</td>
<td>2.8</td>
<td></td>
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</tbody>
</table>

Calcium 8.6
Magnesium 1.9
NT-proBNP 15,970
Troponin I 0.060

<table>
<thead>
<tr>
<th>10.1</th>
<th>8.3</th>
<th>238</th>
</tr>
</thead>
<tbody>
<tr>
<td>27.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ABG:
pH 7.3
pCO2 55
pO2 377
Lactate 8.1

Diff:
PMN’s 65%
Lymph’s 26%

Echo #2
Echo #2: TAPSE

Echo #2: Tricuspid Regurg
Questions

• 1. Classify this patient’s PE:
   a) Massive
   b) Submassive
   c) Low-risk

Questions

• 2. How would you treat this patient’s PE?
   a) Heparin
   b) LMWH
   c) Systemic thrombolysis
   d) Catheter-directed thrombolysis
   e) Embolectomy
Objectives

• Understand hemodynamic principles of providing optimal supportive care & risk-stratifying patients with PE
  1. Reduce PVR
  2. Optimize RV preload
  3. Increase afterload
  4. Improve RV systolic function
  5. Avoid intubation

• Have your mind blown!
  • Hint: it has nothing to do with t-PA!

Definitions: Intermediate-High Risk

• Massive PE:
  • Pulmonary embolism in a pt with persistent hypotension or shock

• Submassive PE:
  • Pulmonary embolism in normotensive pt with signs of Right Ventricular strain/failure
Size is not Everything

- **Traditional thinking:**
  - Massive: >50% pulmonary vascular bed

- **Contemporary thought:**
  - Outcome & risk:
    1. Clot burden
    2. Cardiopulmonary reserve

Wood et al. Chest 2002
Who is High Risk?

• Hypotension or shock
  • 3x-7x mortality increase

• Normotensive patients (relative importance):
  • SpO2<95% (100)
  • Substernal CP (76.5)
  • HR>96 (34.6)
  • Shock index>0.9 (19.7)
  • RR>22 (17.1)

• Syncope

Biomarkers

• **BNP**: Kucher et al. Circ ’03
  • 73 consecutive pts with acute PE
  • 20 pts w/ adverse clinical events, median BNP 194.2 vs 39.1 in pts w/o
  • Discriminatory level 90 (OR 8.0)

• **Troponin**: Kline et al ’06
  • 10/51 pts w/ adverse outcome had + troponin
  • Sensitivity 20%
  • Specificity 92%
  • High NPV in hosp-death
Electrocardiography (not just S1Q3T3)

• Comparison ECG vs TTE:
  • RBBB
  • S1Q3 +/- T3
  • TWI V1-V3

• 130/386 pts with RV strain:
  • 12/386 (3%) died during hospitalization, 8 with RV strain (p=0.025)

Vanni S et al. Am J Med '09

Echocardiography

• 30-day deaths:
  – Right heart failure

• 2 small cohort studies:
  PPV 4% & 5%

• ICOPER, RV hypokinesis
  – 1035 pts SBP>90, echo within 24h
  – 405 pts w/ RV hypokinesis
  – 30 day mortality:
    -9% w/ RV hypokinesis
    • -3.6% in pts w/o hypokinesis

Kucher N et al. Arch Int Med '05
High Risk Features

1. Hypoxemia (SpO₂ <95%)
2. ECG:
   i. RBBB
   ii. S₁Q₃T₃
   iii. T wave inversions (anterior/inferior)
3. Elevated troponin
4. Elevated BNP
5. Abnormal Echo:
   i. RV dilation (RV:LV>1.0)
   ii. RV hypokinesis
   iii. Paradoxical Septal motion (D-sign)
   iv. Tricuspid Regurgitation
   v. TAPSE (<17mm)

EKG + Echo

Vanni S et al. Am J Med '09
Complexities of the RV

Wood et al. Chest '02

RV Death Spiral

Marti et al Eur Heart J 2014
Management Principles

1. Clot Dissolution/Extraction
   I. Systemic thrombolysis
   II. Directed thrombolysis
   III. Mechanical retrieval
   IV. Embolectomy

2. Hemodynamic Support
   I. Pulmonary Vascular resistance
   II. Preload
   III. Afterload
   IV. Contractility

Management Principles

1. Hemodynamic Support
   I. Pulmonary Vascular resistance
   II. Preload
   III. Afterload
   IV. Contractility

2. Clot Dissolution/Extraction
   I. Systemic thrombolysis
   II. Directed thrombolysis
   III. Mechanical retrieval
   IV. Thrombectomy
Hemodynamic Support

1. Decrease Pulmonary Vascular Resistance
2. Optimize LV preload
3. Increase LV afterload
4. Improve RV Contractility

Wood et al. Chest 2002

RV Exquisitely Sensitive to Afterload

Friedman 2014.
RV CO = LV CO

Remember the Septum

↑ Pulmonary Vascular Resistance

1. High pCO2/low pH in pulmonary artery
2. Low mixed venous O2 (SVO2)
3. High sympathetic tone: α-receptor agonism
4. High plateau pressures
5. *Endothelial injury
6. Hypoxic vasoconstriction
7. Micro- & Macrothrombosis
Decrease Pulmonary Vascular Resistance

- Relieving **Obstruction:**
  - THE CLOT
- **Neurohumoral** effects
  - Thromboxane A2
  - Platelet activating factor
  - Serotonin
  - C3a, C5a, thrombin

Inhaled Nitric Oxide

- Weak evidence
- cGMP pathway $\rightarrow$ smooth muscle relaxation
  1. Vasodilation
  2. Bronchodilation
  3. Antiinflammatory effect
- **10-20ppm**
  - Improves V/Q mismatch
  - Reduce shunting
Addressing the Clot

1. Systemic Thrombolysis
2. Cather-directed:
   i. Lysis
   ii. Extraction
3. Surgery:
   i. Embolectomy
The Modern Era (post-2012)

- **MOPETT**: ½ dose t-PA submassive PE
  - RV dysfunction resolved
  - Almost no bleeding
- **TOPCOAT**: tenecteplase
  - Stopped early, composite endpoint
  - Global health assessment improved
- **PEITHO**: tenecteplase
  - 1000 pts; “great caution”; composite endpoint
  - NNT: 33 & NNH: 55

SEATTLE II Study
Seattle II: Conclusions

- **Safe:**
  - 0 ICH's
- Early hemodynamic improvement
- Worthy of further study
- Submassive PE pts die infrequently
Hemodynamic Support

1. Decrease Pulmonary Vascular Resistance
2. Optimize LV preload
3. Increase LV afterload
4. Improve RV Contractility

Wood et al. Chest 2002

\[ r = 0.89 \]
Diuretics?!??

Diuretics in Normotensive Patients With Acute Pulmonary Embolism and Right Ventricular Dilatation
Jilien Temaite, MD; Romain Gallet, MD; Armand Mekontso-Dessap, MD; Guy Meyer, MD, PhD; Bernard Maire, MD, PhD; Alexandre Bansal, MD; Priscille Jurzak, MD; Pascal Gueret, MD, PhD; Jean-Luc Debois Randé, MD, PhD; Pascal Lim, MD, PhD

Background: The benefit of load expansion is controversial in acute pulmonary embolism (PE). The aim of this study was to evaluate the benefit of furosemide in cases of normotensive acute PE.

Methods and Results: We retrospectively included 70 consecutive normotensive patients (systolic blood pressure ≥90 mmHg) admitted for acute PE with right ventricular dilatation. Overall, 40 patients were treated during the first 24 h by repeated bolus of furosemide (70-424 mg, range 40-1650 mg) and 30 patients received isosorine: saline solution (1.8-5.9 mL). Severity of hemodynamic status was similar in both groups, but patients in the furosemide group were older and had a greater creatinine level. At 24 h, only the furosemide group had a decreased shock index (0.80±0.32 vs. 0.63±0.16, P=0.0001) with improved systolic blood pressure (119±18 vs. 131±17 mmHg, P=0.0001), and creatinine levels. After treatment, there were fewer patients with simplified pulmonary embolism severity index ≥1 in the diuretic group (46% vs. 55%, P=0.03) than in the fluid expansion group (47% vs. 54%, P=0.001). Finally, oxygen requirement at 24 h decreased only in the diuretic group (73% to 47%, P=0.004), and in-hospital survival without death and PE-related shock were similar between the 2 groups.

Conclusions: In normotensive PE with RV dilatation, diuretics may improve hemodynamics and oxygenation requirement. (Circ 2013; 17; 2612–2618)

Really doctor, diuretics?

- Nonrandomized
- Retrospective
- Submassive PE
- N=70
- Physician discretion
- Lasix 40mg
  - Repeat q4h if urine o/p <0.5ml/kg
Ternacle et al. ‘14

• **Endpoints:**
  - Echocardiographic improvement
  - Shock index
  - PESI

<table>
<thead>
<tr>
<th></th>
<th>Lasix (n=40)</th>
<th>Normal Saline (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Troponin elevation</td>
<td>70%</td>
<td>64%</td>
</tr>
<tr>
<td>NT-proBNP</td>
<td>77%</td>
<td>67%</td>
</tr>
<tr>
<td>LVEF</td>
<td>57%</td>
<td>58%</td>
</tr>
<tr>
<td>Mean dose</td>
<td>78±42mg</td>
<td>1.6±0.9L</td>
</tr>
</tbody>
</table>

Ternacle et al. ‘14

![Graph showing changes in shock index and systolic blood pressure (SBP) with RV/LV ratio 1](image)
Airway Management

- Avoid Intubation
  - If possible
- ↓ afterload (meds)
- ↓↓ preload to RV & LV
- ↑↑ pulmonary vascular resistance (PPV)
- All hands on deck:
  - pressors
Hemodynamic Support

1. Decrease Pulmonary Vascular Resistance
2. Optimize LV preload
3. Increase LV afterload
4. Improve RV Contractility

Wood et al. Chest 2002

3. Increase LV Afterload

- **Goal**: optimize perfusion to RV through RCA
  - Limit RV ischemia
  - \( \text{RV CPP} = \text{MAP} - \text{RV Pressure} \)
  - \( \text{RV Pressure} = \text{PA pressure} \)
- **Vasopressors**:
  - \( \uparrow \) afterload
  - \( \uparrow \) venous return
RV Exquisitely Sensitive to Afterload

Friedman 2014.

Vascular Pressure in mmHg

RV perfused in Diastole & Systole

RV perfused in Diastole & Systole
Vasopressors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cardiac Output</th>
<th>Pulmonary Vascular Resistance</th>
<th>Systemic Vascular Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine</td>
<td>+</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>-</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>++</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

Hemodynamic Support

1. Decrease Pulmonary Vascular Resistance
2. Optimize LV preload
3. Increase LV afterload
4. Improve RV Contractility

Wood et al. Chest 2002
Septal Dyskinesia
Tricuspid Regurgitation
4. Improve RV Contractility

- After BP improves
  1. Dobutamine
     - Max 5μg/kg/min
     - Synergistic with iNO
  
- Low CO state:
  - Cool, low ScVo2, narrow pulse pressure
Inotropes

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<tbody>
<tr>
<td>Dobutamine</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>++</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>Milrinone</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Dopamine</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
</tr>
</tbody>
</table>

VA ECMO

A

B

VC

AC

RR
Summary

- Post-diagnosis risk stratification:
  - Biomarkers, echo, EKG, hypoxemia, BP
- Aggressive early or watch and wait?
  - Mortality low
- To lyse or not to lyse?
  - Weak data

Hemodynamic Optimization:
1. Reduce pulmonary vascular resistance (iNO)
2. Don’t worsen the preload
3. Increase systemic vascular resistance (NE)
4. Increase RV contractility

You can make the difference

Catch-up Phenomenon

References

- Tilburt, CD et al. Comparison by Controlled Clinical Trial of Streptokinase and Heparin in Treatment of Life-Threatening Pulmonary Embolism. British Medical Journal, 1974, 4, 343-347
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• Kline JA, et al. Surrogate Markers for Adverse Outcomes in Normotensive Patients with Pulmonary Embolism. Critical Care Medicine, 2006, vol. 34, no. 11,2772-2780.