Single-Center, Retrospective, Observational Analysis of Patients with Submassive Pulmonary Embolism (PE) Receiving Catheter-Directed Thrombolysis

John A. Phillips, M.D.
OhioHealth Heart and Vascular Physicians
Columbus, Ohio USA
Disclosure

I have the following potential conflicts of interest to report:

- Consulting: Cook Medical, Endologix, Aztra-Zenica, Boston Scientific, Gore, Jansen
Pulmonary Embolism

• According to The US Surgeon General 100,000-180,000 deaths/yr *
• 20% die during first 24 hours
• 11% die within first 3 months
• Up to 10% who survive have chronic pulmonary hypertension

Not All PE are Created Equal

• Patients diagnosed with PE are often risk-stratified
  – Based on hemodynamic instability
    • Massive vs submassive
  – Right ventricular function
    • High-risk vs. low-risk submassive

• RV dysfunction = predictor of adverse early outcome

• ICOPER registry revealed RV hypokinesis as independent predictor of 30-day mortality

Intermediate-Risk PE

• ‘Submassive’ PE
• High-risk features without overt hemodynamic compromise
  – RV dysfunction (CTPE or echo)
    • RV dilation (RV diameter/LV diameter >0.9) echo or CT
    • RV systolic dysfunction on echo
  – Elevated cardiac biomarkers (troponin I or T)
  – “High–risk” Clinical markers:
    • Hypoxic
    • Tachycardia
Intermediate-Risk PE

• Data suggests this population has 3-15% mortality rate  

• Optimal treatment method not well delineated

• PEITHO trial suggested full-dose systemic thrombolysis (single-bolus TNK):
  – Reduced hemodynamic decompensation
  – Increased major bleeding and stroke  
Ultrasound-assisted Thrombolysis (SEATTLE II)

- Single-arm, low dose lysis acute (massive - 31pts) and submassive PE (119)
- RV/LV ratio ≥0.9
- 24 mg TPA (1mg/hr) or 1mg/hr (bilateral)
- Primary outcome change in chest CT RV/LV ratio @ 48hr
- Primary safety = major bleeding at 72 hr

Piazza G. et al. JACC Card Interventions. 24 August 2015
Seattle II

- RV/LV diameter ratio 1.55 vs. 1.13 (p<0.0001)
- Mean sPA decrease 51.4 vs. 36.9 mmHg
- One GUSTO-defined severe groin bleed, HoTN
- 16 ‘moderate’ events in 15 pts (10%)
- No ICH
Intermediate-Risk PE

• Is there a role for single bolus, low-dose, catheter-directed thrombolysis (CDT) in the intermediate-risk (submassive PE) population?
  – Safe
    • Major bleeding complications
  – Effective
    • Unload the RV
  – Cost
    • Pig tail catheter verses ultrasound catheter(s) with control unit
CDT for Submassive PE at Riverside Methodist Hospital

- February 2013-April 2014, **29 normotensive patients** with **acute pulmonary embolism**, deemed intermediate-risk (**RV dysfunction or elevated cardiac biomarkers**)

Brought to catheterization suite for assessment of PA pressure and administration of a single bolus of Tenecteplase (TNK) via a catheter in the pulmonary artery or RV outflow tract
Statistical Methods

- Demographics and clinical characteristics of pts described using means, SD, medians
- Ranges for continued variables
- Frequencies and percentages for categorical variables
- Change in PA pressure was evaluated using a paired t-test
- Statistical significance was set at $p<0.05$
<table>
<thead>
<tr>
<th>Demographic and Clinical Characteristics</th>
<th>n=29</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placement of inferior vena cava (IVC) filter, n (%)</td>
<td>17 (58.6)</td>
</tr>
<tr>
<td>Troponin level, n (%)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>17 (58.6)</td>
</tr>
<tr>
<td>Negative</td>
<td>10 (34.5)</td>
</tr>
<tr>
<td>Not applicable</td>
<td>2 (6.9)</td>
</tr>
<tr>
<td>Pre-intervention RV dysfunction, n (%)</td>
<td>28 (96.6)</td>
</tr>
<tr>
<td>PA pressure prior to treatment, mean (SD)(^a)</td>
<td>50.3 (12.3)</td>
</tr>
<tr>
<td>PA pressure after treatment, mean (SD)(^b)</td>
<td>44.1 (11.2)</td>
</tr>
<tr>
<td>Change in PA pressure, mean (SD)(^c)</td>
<td>-7.7 (8.2)</td>
</tr>
<tr>
<td>Thrombolytic dose, mg, n (%)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2 (6.9)</td>
</tr>
<tr>
<td>10</td>
<td>8 (27.6)</td>
</tr>
<tr>
<td>15</td>
<td>7 (24.1)</td>
</tr>
<tr>
<td>20</td>
<td>12 (41.4)</td>
</tr>
<tr>
<td>Length of stay, median (range)</td>
<td>3.0 (1.0 – 23.0)</td>
</tr>
<tr>
<td>Had follow up transthoracic echocardiogram (TTE), n (%)(^d)</td>
<td>21 (72.4)</td>
</tr>
<tr>
<td>RV function on follow up TTE(^e)</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>19 (90.5)</td>
</tr>
<tr>
<td>Abnormal &lt;30 days</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Abnormal ≥ 30 days</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Death related to procedure(^f)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>
CDT for Submassive PE at Riverside Methodist Hospital

- Average Age: 59.6 years
- 19 Male
- 10 Female
- Length of stay 3.0 days (median), 4.6 days (average)
- Average dose of TNK = 15 mg
  - Majority received 20 mg (~ 1/3 the systemic dose)
PA pressure change

- Pulmonary artery systolic pressure (pre-intervention)
  - 24 recorded
  - Range: 29 mm Hg to 75 mm Hg
    - Average 50.3 mm Hg
- Mean -7.7 mmHg (SD:8.2) p=0.004
Alive at Discharge

• 29/29 (100%) of patients were alive at discharge

• 1 patient died 2 weeks later unrelated to procedure (complications of leukemia)
Major Adverse Events for all Patients Treated with TNK

- No significant bleeding complications requiring transfusion
- No reported intracranial hemorrhage
Non-Procedure Related Event

• Major Adverse Events
  – One received 10 mg TNK for submassive PE, discharged on Xarelto 3 days later.
    • Returned 17 days later with acute, embolic stroke.
RV Function Assessment

- Of 29 alive at discharge:
  - 20 had one month echo (69%)
  - 5 lost to follow-up
  - 3 without repeat echo, no reported dyspnea at follow-up
  - 1 had repeat echo within 24 hours
RV Function Assessment at 30 days

• 19/20 (95%) normal reported RV function

• 1/20 ‘mildly’ reduced RV function
  – Had highest initial PA systolic pressure of true submassive group, 75 mmHg
Conclusion

- In this patient population, single-bolus low-dose CDT with TNK was observed to be safe and seemed to help mitigate against RV dysfunction at 30 days

    - Further trials are needed, including randomized clinical trials
      - Single bolus vs. ultrasound assisted
      - Route?
        - IV vs. Catheter-Assisted
Thank You
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