The OPTALYSE PE Trial – Reducing thrombolytic dose and treatment times with EKOS™ in the treatment of pulmonary embolism patients

Keith M. Sterling, M.D.
Director, Cardiovascular & Interventional Radiology
Inova Alexandria Hospital
Alexandria, VA, US
Associate Professor of Radiology
George Washington University School of Medicine
Washington, DC, US
Background

- 60-100K deaths in the US from DVT/PE\(^1\)
- Mortality from PE
  - Massive 25-65\%\(^2,3\)
  - Submassive PE 3-15\%\(^3,4\)
- Clinical decompensation in submassive PE 5\%\(^4\)
- RV:LV ratio > 0.9 independent predictor of mortality\(^5-8\)

\(^6\) Frémont B et al. Chest 2008; 133;558-362
\(^7\) Schoepf UJ et al. Circulation 2004; 110:3276-3280
Full-Dose Systemic Fibrinolysis for Submassive PE: Efficacy at the Cost of Safety

Goals of Catheter-Directed Therapy

- Recovery of right ventricular dysfunction
- Decrease in pulmonary vascular resistance and pulmonary artery pressure
- Increase in systemic arterial pressure
- Improvement of symptoms and survival
- Decrease the risk of developing chronic thromboembolic pulmonary hypertension (CTEPH)
- Minimize the bleeding risk associated with systemic therapy

Kucher N, Goldhaber SZ. Circulation 2006;112:e28-32
Possible candidates for Catheter-based Therapy

### Patient risk stratification (per AHA 2011 guidelines)

<table>
<thead>
<tr>
<th>Massive PE</th>
<th>Submassive PE</th>
<th>Minor/Nonmassive PE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High risk</strong></td>
<td><strong>Moderate risk</strong></td>
<td><strong>Low risk</strong></td>
</tr>
<tr>
<td>• Sustained hypotension (systolic BP &lt;90 mmHg for ≥15 min)</td>
<td>• Systemically normotensive (systolic BP ≥90 mmHg)</td>
<td>• Systemically normotensive (systolic BP ≥90 mmHg)</td>
</tr>
<tr>
<td>• Inotropic support</td>
<td>• Myocardial necrosis</td>
<td>• No RV dysfunction</td>
</tr>
<tr>
<td>• Pulselessness</td>
<td>• RV dysfunction</td>
<td>• No myocardial necrosis</td>
</tr>
<tr>
<td>• Persistent profound bradycardia (HR &lt;40 bpm with signs or symptoms of shock)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Risk Stratification – ESC

<table>
<thead>
<tr>
<th>Early mortality risk</th>
<th>Risk parameters and scores</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Shock or hypotension</td>
<td>PESI class III-V or sPESI ≥1&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>High</td>
<td>+</td>
<td>(+)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Intermediate</td>
<td>Intermediate–high</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Intermediate–low</td>
<td>–</td>
</tr>
<tr>
<td>Low</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Clinical scenarios

- Massive
  - Crashing
  - Not crashing
- Submassive
  - Bordering on massive
  - Significant RV dysfunction
  - Bordering on low risk
Background

- **ULTIMA**
  - Prospective multicenter randomized trial
  - Submassive PE
  - 30 patients USCDT
    - 10 mg (U) or 20 mg (B) r-tPA over 15 hours
  - 29 patients randomized to AC with UFH
- Confirmed that fixed dose USCDT regimen superior to AC alone in improving RV dysfunction without increase in bleeding complications

Background

- **SEATTLE II**
  - Prospective multicenter single-arm trial
  - Massive: 31 patients
  - Submassive: 119 patients
  - 24 mg r-tPA over 12 hours (B) or 24 hours (U)
  - 30% decrease in RV:LV ratio in patients treated with USCDT
  - Rapid reduction in PA HTN and PA obstruction
  - No ICH

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>No. of pts</th>
<th>No. of high risk PEs (%)</th>
<th>tPA dose (mg)</th>
<th>tPA duration (hr)</th>
<th>RV:LV</th>
<th>PAP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chamsuddin (2008)</td>
<td>10</td>
<td>N/A</td>
<td>21.8</td>
<td>24.8±8.4</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Lin (2009)</td>
<td>11</td>
<td>2 (18)</td>
<td>17.2±2.4</td>
<td>17.4±5.2</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Engelhardt (2011)</td>
<td>24</td>
<td>5 (21)</td>
<td>33.5±15.5</td>
<td>19.7±8.1</td>
<td>1.33±0.24</td>
<td>1.0±0.13</td>
</tr>
<tr>
<td>Kennedy (2013)</td>
<td>60</td>
<td>12 (20)</td>
<td>35.1±11.1</td>
<td>19.6±6.0</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Engelberger (2013)</td>
<td>52</td>
<td>14 (27)</td>
<td>21.0±5.7</td>
<td>15.2±1.7</td>
<td>1.42±0.21</td>
<td>1.06±0.23</td>
</tr>
<tr>
<td>Quintana (2014)</td>
<td>10</td>
<td>2 (20)</td>
<td>18 (7-38)</td>
<td>20.8 (12-49)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Kuchler (2014)</td>
<td>30</td>
<td>0</td>
<td>20.8±3.0</td>
<td>15±1.0</td>
<td>1.28±0.19</td>
<td>0.99±0.17</td>
</tr>
<tr>
<td>Dumantepe (2014)</td>
<td>22</td>
<td>5 (26)</td>
<td>23 (16-35)</td>
<td>20.5 (14-25)</td>
<td>1.29±0.17</td>
<td>0.92±0.11</td>
</tr>
<tr>
<td>Bagla (2015)</td>
<td>45</td>
<td>0</td>
<td>24</td>
<td>12.8 (12-24)</td>
<td>1.59±0.54</td>
<td>0.93±0.17</td>
</tr>
<tr>
<td>Piazza (2015)</td>
<td>150</td>
<td>31 (21)</td>
<td>23.7±2.9</td>
<td>≈13.6 (12-24)</td>
<td>1.55±0.39</td>
<td>1.13±0.20</td>
</tr>
<tr>
<td>Nykamp (2015)</td>
<td>45</td>
<td>12 (27)</td>
<td>30.5 (14-66)</td>
<td>14.2±4.0</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Graif (2017)</td>
<td>24</td>
<td>3 (13)</td>
<td>27.1±11.3</td>
<td>23.9±8.8</td>
<td>1.6±0.25</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>483</strong></td>
<td><strong>89 (18.5)</strong></td>
<td><strong>25.7</strong></td>
<td><strong>16.2</strong></td>
<td><strong>1.49</strong></td>
<td><strong>1.05</strong></td>
</tr>
</tbody>
</table>

**Note:** The highlighted values indicate the average RV:LV and PAP values across all studies.
<table>
<thead>
<tr>
<th>Author (year)</th>
<th>No. of pts</th>
<th>No. of high risk PEs (%)</th>
<th>tPA dose (mg)</th>
<th>tPA duration (hr)</th>
<th>Bleeding comp</th>
<th>Mortality (1-6 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Minor</td>
<td>Major</td>
</tr>
<tr>
<td>Chamsuddin (2008)</td>
<td>10</td>
<td>N/A</td>
<td>21.8</td>
<td>24.8±8.4</td>
<td>2 (20)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Lin (2009)</td>
<td>11</td>
<td>2 (18)</td>
<td>17.2±2.4</td>
<td>17.4±5.2</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Engelhardt (2011)</td>
<td>24</td>
<td>5 (21)</td>
<td>33.5±15.5</td>
<td>19.7±8.1</td>
<td>2 (8)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Kennedy (2013)</td>
<td>60</td>
<td>12 (20)</td>
<td>35.1±11.1</td>
<td>19.6±6.0</td>
<td>1 (2)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Engelberger (2013)</td>
<td>52</td>
<td>14 (27)</td>
<td>21.0±5.7</td>
<td>15.2±1.7</td>
<td>11 (21)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Quintana (2014)</td>
<td>10</td>
<td>2 (20)</td>
<td>18 (7-38)</td>
<td>20.8 (12-49)</td>
<td>2 (20)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Kucher (2014)</td>
<td>30</td>
<td>0</td>
<td>20.8±3.0</td>
<td>15±1.0</td>
<td>3 (10)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Dumantepe (2014)</td>
<td>22</td>
<td>5 (26)</td>
<td>23 (16-35)</td>
<td>20.5 (14-25)</td>
<td>2 (9)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Bagla (2015)</td>
<td>45</td>
<td>0</td>
<td>24</td>
<td>12.8 (12-24)</td>
<td>4 (8.9)</td>
<td>2 (4.4)</td>
</tr>
<tr>
<td>Piazza (2015)</td>
<td>150</td>
<td>31 (21)</td>
<td>23.7±2.9</td>
<td>≈13.6 (12-24)</td>
<td>0 (0)</td>
<td>15 (1.0)</td>
</tr>
<tr>
<td>Nykamp (2015)</td>
<td>45</td>
<td>12 (27)</td>
<td>30.5 (14-66)</td>
<td>14.2±4.0</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Graif (2017)</td>
<td>24</td>
<td>3 (13)</td>
<td>27.1±11.3</td>
<td>23.9±8.8</td>
<td>0 (0)</td>
<td>2 (8.3)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>483</strong></td>
<td><strong>89 (18.5)</strong></td>
<td><strong>25.7</strong></td>
<td><strong>16.2</strong></td>
<td><strong>41 (9)</strong></td>
<td><strong>26 (5.4)</strong></td>
</tr>
</tbody>
</table>
Background

- FDA approval for treatment of acute PE in May 2014
- Broad adoption of SEATTLE II protocol
Case Example

- 54 y/o female presenting with acute onset of chest pain and syncope
- PE: HR 110/min, BP 82/50, SaO$_2$ 92% on 100% non-rebreather facemask
- Troponin I = 0.92 ng/ml (↑)
- BNP = 572 pg/ml (↑)
RV:LV Ratio = 2.5
PAP 59/18 (mean 32 mmHg)
- tPA 1mg/hr via each catheter x 12 hours
- Heparin 500 units/hr
- At 90 minutes post initiation of USCDT
  - HR 90/min, BP 114/72, SaO₂ 98% on 4L
  - Easier to breathe, speak
- Next morning
  - HR 74/min, BP 122/74, SaO₂ 99% on 2L
USCDT protocol

- Infusion ended at 4 am
  - Drug delivery ports converted to NS
  - Conversion to heparin moderate intensity protocol
- Follow up PA pressures measured through EKOS catheter at bedside after removing ultrasound core at 7 am
  - R PA = 24/10 (mean 15 mm Hg)
  - L PA = 23/10 (mean 14 mm Hg)
RV:LV Ratio = 0.7
Pre and Post USCDT

RV:LV = 2.5

RV:LV = 0.7
Follow up

- LOS = 3 days
- Discharged on Rivaroxaban
Background for OPTALYSE PE Study

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

- Pharmacologic studies\(^1,2\)
  - Clot lysis occurs rapidly after IV r-tPA
  - \(~90\%\) clot lysis within 90 minutes
  - Half-life of r-tPA is 3-4 minutes, but lytic effect between 7-12 hours
  - Ultrasound enhances the effect of r-tPA\(^3\)

- Clinical reports of symptomatic improvement by 2 hours post USCDT

---

\(^2\) Eisenberg PR et al. Thrombosis and Haemostasis 1987; 57: 35-40
\(^3\) Lauer CG et al. Circulation 1992; 86: 1257-1264
Optimum duration and dose of r-tPA with the acoustic pulse thrombolysis procedure for intermediate-risk (submassive) pulmonary embolism (OPTALYSE PE)
Purpose

- To explore optimal duration of the EkoSonic™ Endovascular System ultrasound-facilitated, catheter-directed thrombolysis (USCDT) and dose of r-tPA in patients with acute submassive pulmonary embolism (PE)
Patient Selection

Main Inclusion Criteria

- 18-75 years of age AND
- CTA evidence of proximal PE (unilateral or bilateral) AND
- Acute PE (symptom duration ≤14 days) AND
- Submassive PE (RV:LV diameter ≥ 0.9 and hemodynamically stable)

Main Exclusion Criteria

- No recent history of stroke, TIA, head trauma, active bleeding from a major organ, major surgery, or catheter-based pharmacomechanical treatment for PE
- No high-risk for catastrophic bleeding
Randomized to 1 of 4 treatment groups

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Treatment Duration (h)</th>
<th>Total dose tPA one/two catheters (mg)</th>
<th>tPA infusion rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>4/8</td>
<td>2 mg/h/catheter</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>4/8</td>
<td>1 mg/h/catheter</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>6/12</td>
<td>1 mg/h/catheter</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>12/24</td>
<td>2 mg/h/catheter</td>
</tr>
</tbody>
</table>
Material and Methods

- Eligible subjects received treatment with USCDT within 48h of the diagnostic CTA
Primary Endpoints

- **Efficacy**
  - Reduction of RV:LV by >0.2 on CTA 48h after starting treatment

- **Safety**
  - Major bleeding events within 72h after initiating the procedure (ISTH criteria)
Secondary Efficacy Endpoints

- Technical success of APT procedure as assessed by Adjudication Committee
- Change in baseline echo parameters (4h, 48h, 30d, 90d, 365d post APT procedure)
  - RV:LV ratio
  - TAPSE
  - Estimated RVSP
  - Collapse of the IVC with respiration
- Change in thrombus burden by MMS as assessed by CTA at 48h post APT procedure
- 6MWD with BORG score and requirement for oxygen therapy
- QOL as measured by PROMIS PF-6 and PEmb-QOL at all post-hospitalization visits
Secondary Safety Endpoints

- Technical procedural complications
- Symptomatic recurrent PE
- All-cause mortality
Analysis Flow Diagram

101 patients
- Randomized
- 17 centers
- Enrollment 6/2015-10/2016
- Intention to Treat (ITT) group

100 patients
- Treated with APT procedure

86 patients
- With bilateral catheters to treat bilateral disease

83 patients
- In modified per protocol (mPP) analysis
- 3 excluded for receiving additional r-tPA

77 patients
- Complete, technically adequate echo data
## Study Population

<table>
<thead>
<tr>
<th>Demographics</th>
<th>2hr; 2 mg/hr/catheter</th>
<th>4hr; 1 mg/hr/catheter</th>
<th>6hr; 1 mg/hr/catheter</th>
<th>6hr; 2 mg/hr/catheter</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>28</td>
<td>27</td>
<td>28</td>
<td>18</td>
<td>101</td>
</tr>
<tr>
<td>Age (y)</td>
<td>56</td>
<td>57</td>
<td>59</td>
<td>59</td>
<td>57.6</td>
</tr>
<tr>
<td>Female</td>
<td>43%</td>
<td>44%</td>
<td>61%</td>
<td>39%</td>
<td>48%</td>
</tr>
<tr>
<td>Caucasian</td>
<td>57%</td>
<td>52%</td>
<td>68%</td>
<td>61%</td>
<td>59%</td>
</tr>
<tr>
<td>BMI (k/m²)</td>
<td>36</td>
<td>36</td>
<td>40</td>
<td>29</td>
<td>35.8</td>
</tr>
<tr>
<td>Diabetes</td>
<td>39%</td>
<td>37%</td>
<td>39%</td>
<td>17%</td>
<td>35%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>57%</td>
<td>67%</td>
<td>79%</td>
<td>56%</td>
<td>65%</td>
</tr>
</tbody>
</table>
### Study Population

<table>
<thead>
<tr>
<th>Signs/Symptoms</th>
<th>2hr; 2 mg/hr/catheter</th>
<th>4hr; 1 mg/hr/catheter</th>
<th>6hr; 1 mg/hr/catheter</th>
<th>6hr; 2 mg/hr/catheter</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>86</td>
<td>89</td>
<td>100</td>
<td>100</td>
<td>93</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>54</td>
<td>33</td>
<td>46</td>
<td>28</td>
<td>42</td>
</tr>
<tr>
<td>Hypoxemia</td>
<td>18</td>
<td>33</td>
<td>25</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td>Chest pain</td>
<td>54</td>
<td>41</td>
<td>46</td>
<td>44</td>
<td>47</td>
</tr>
<tr>
<td>DVT (US)</td>
<td>43</td>
<td>41</td>
<td>36</td>
<td>56</td>
<td>43</td>
</tr>
</tbody>
</table>

*All values in percentages*
<table>
<thead>
<tr>
<th>Tx Group</th>
<th>N</th>
<th>RV/LV Change at 48h (%)</th>
<th>p-value*; 1-sided</th>
<th>MMS % Change; p-value**; 2-sided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm 1: 2hr; 2 mg/hr/catheter</td>
<td>27</td>
<td>-0.40 (24); 0.0046</td>
<td>-6%; 0.0083</td>
<td></td>
</tr>
<tr>
<td>Arm 2: 4hr; 1 mg/hr/catheter</td>
<td>26</td>
<td>-0.35 (23); 0.0039</td>
<td>-9%; 0.0002</td>
<td></td>
</tr>
<tr>
<td>Arm 3: 6hr; 1 mg/hr/catheter</td>
<td>27</td>
<td>-0.42 (26); 0.0006</td>
<td>-14%; &lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Arm 4: 6hr; 2 mg/hr/catheter</td>
<td>18</td>
<td>-0.48 (26); 0.0179</td>
<td>-26%; 0.0006</td>
<td></td>
</tr>
</tbody>
</table>

*100 patients treated (ITT)
mPP = 83 patients (Bilateral only)

<table>
<thead>
<tr>
<th>Tx Group</th>
<th>N</th>
<th>RV/LV Change at 48h (%)</th>
<th>p value*, 1-sided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm 1: 2hr; 2 mg/hr/catheter (8 mg)</td>
<td>21</td>
<td>-0.46 (27);</td>
<td>0.0030</td>
</tr>
<tr>
<td>Arm 2: 4hr; 1 mg/hr/catheter (8 mg)</td>
<td>21</td>
<td>-0.40 (25);</td>
<td>0.0014</td>
</tr>
<tr>
<td>Arm 3: 6hr; 1 mg/hr/catheter (12 mg)</td>
<td>24</td>
<td>-0.44 (27);</td>
<td>0.0006</td>
</tr>
<tr>
<td>Arm 4: 6hr; 2 mg/hr/catheter (24 mg)</td>
<td>16</td>
<td>-0.52 (27);</td>
<td>0.0145</td>
</tr>
</tbody>
</table>
## Mean Change in RV:LV Diameter Ratio from Baseline to 4h – 365 d

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>4 hours</th>
<th>48 hours</th>
<th>30 days</th>
<th>90 days</th>
<th>365 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>2hrs (2mg/hr/catheter)</td>
<td>27</td>
<td>-0.17 ± 0.15</td>
<td>-0.23 ± 0.22</td>
<td>-0.34 ± 0.25</td>
<td>-0.37 ± 0.23</td>
<td>-0.36 ± 0.20</td>
</tr>
<tr>
<td>4hrs (1mg/hr/catheter)</td>
<td>26</td>
<td>-0.17 ± 0.17</td>
<td>-0.24 ± 0.19</td>
<td>-0.35 ± 0.17</td>
<td>-0.37 ± 0.20</td>
<td>-0.44 ± 0.19</td>
</tr>
<tr>
<td>6hrs (1mg/hr/catheter)</td>
<td>27</td>
<td>-0.13 ± 0.23</td>
<td>-0.17 ± 0.21</td>
<td>-0.33 ± 0.19</td>
<td>-0.34 ± 0.22</td>
<td>-0.37 ± 0.15</td>
</tr>
<tr>
<td>6hrs (2mg/hr/catheter)</td>
<td>18</td>
<td>-0.25 ± 0.37</td>
<td>-0.29 ± 0.32</td>
<td>-0.37 ± 0.39</td>
<td>-0.43 ± 0.41</td>
<td>-0.32 ± 0.13</td>
</tr>
</tbody>
</table>

* p≤0.0002
Mean Change in RV:LV Diameter Ratio from Baseline to 4h – 365 d

At 365d, the mean RV/LV ratio was in the 0.7 range for all cohorts.
## 6-minute walk distance

<table>
<thead>
<tr>
<th>Tx Group</th>
<th>30 d</th>
<th>90 d</th>
<th>365 d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm 1: 2hr; 2 mg/hr/catheter</td>
<td>351.6</td>
<td>352.2</td>
<td>383.3</td>
</tr>
<tr>
<td>Arm 2: 4hr; 1 mg/hr/catheter</td>
<td>336.0</td>
<td>411.3</td>
<td>362.3</td>
</tr>
<tr>
<td>Arm 3: 6hr; 1 mg/hr/catheter</td>
<td>343.1</td>
<td>375.9</td>
<td>417.0</td>
</tr>
<tr>
<td>Arm 4: 6hr; 2 mg/hr/catheter</td>
<td>327.3</td>
<td>348.2</td>
<td>357.9</td>
</tr>
</tbody>
</table>
6-minute walk distance

Cohort 1
Cohort 2
Cohort 3
Cohort 4
### Follow up interval

<table>
<thead>
<tr>
<th>Tx Group</th>
<th>30 d</th>
<th>90 d</th>
<th>180 d</th>
<th>270 d</th>
<th>365 d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm 1: 2hr; 2 mg/hr/catheter</td>
<td>37.98 ± 24.9</td>
<td>23.80 ± 21.5</td>
<td>18.30 ± 18.7</td>
<td>16.42 ± 19.2</td>
<td>18.47 ± 20.5</td>
</tr>
<tr>
<td>Arm 2: 4hr; 1 mg/hr/catheter</td>
<td>28.49 ± 22.3</td>
<td>15.11 ± 17.6</td>
<td>13.62 ± 19.9</td>
<td>13.24 ± 20.1</td>
<td>15.87 ± 18.2</td>
</tr>
<tr>
<td>Arm 3: 6hr; 1 mg/hr/catheter</td>
<td>25.13 ± 18.8</td>
<td>20.76 ± 20.6</td>
<td>19.84 ± 8.1</td>
<td>18.80 ± 19.4</td>
<td>15.67 ± 21.2</td>
</tr>
<tr>
<td>Arm 4: 6hr; 2 mg/hr/catheter</td>
<td>25.63 ± 26.9</td>
<td>20.89 ± 12.3</td>
<td>17.50 ± 24.9</td>
<td>22.76 ± 29.1</td>
<td>15.16 ± 19.8</td>
</tr>
</tbody>
</table>

- Dedicated PE QOL questions
- The PEmb-QOL questionnaire contains 6 dimensions: frequency of complaints, ADL limitations, work related problems, social limitations, intensity of complaints and emotional complaints
- Understanding PEmb-QoL – Lower scores indicate better outcome
PEmb-QOL

Cohort 1  | Cohort 2  | Cohort 3  | Cohort 4
---------|-----------|-----------|-----------
          | 30d       | 365d      |
---------|-----------|-----------|-----------
Cohort 1 |           |           |
Cohort 2 |           |           |
Cohort 3 |           |           |
Cohort 4 |           |           |

30d  | 365d
### PROMIS-PF-6b QOL

<table>
<thead>
<tr>
<th>Tx Group</th>
<th>30 d</th>
<th>90 d</th>
<th>180 d</th>
<th>270 d</th>
<th>365 d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm 1: 2hr; 2 mg/hr/catheter</td>
<td>42.00</td>
<td>45.54</td>
<td>46.29</td>
<td>48.40</td>
<td>45.67</td>
</tr>
<tr>
<td>Arm 2: 4hr; 1 mg/hr/catheter</td>
<td>43.86</td>
<td>49.71</td>
<td>49.19</td>
<td>51.03</td>
<td>48.18</td>
</tr>
<tr>
<td>Arm 3: 6hr; 1 mg/hr/catheter</td>
<td>44.53</td>
<td>47.14</td>
<td>47.54</td>
<td>45.98</td>
<td>47.26</td>
</tr>
<tr>
<td>Arm 4: 6hr; 2 mg/hr/catheter</td>
<td>41.40</td>
<td>45.58</td>
<td>44.81</td>
<td>42.84</td>
<td>44.21</td>
</tr>
</tbody>
</table>

- **Patient-Reported Outcomes Measurement Information System – Physical Function**
- PROMIS-PF includes the functioning of one’s upper extremities (dexterity), lower extremities (walking or mobility), and central regions (neck, back), as well as activities of daily living, such as running errands.
- Understanding PROMIS-PF – Higher scores indicate better outcomes
## Recurrent PE and Mortality

<table>
<thead>
<tr>
<th>Tx Arm</th>
<th>N</th>
<th>30 d</th>
<th>365 d</th>
<th>30 d</th>
<th>365 d</th>
<th>30 d</th>
<th>365 d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm #1</td>
<td>27</td>
<td>0</td>
<td>1 (3.7)b</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Arm #2</td>
<td>27</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (3.7)d</td>
<td>1 (3.7)e</td>
<td>1 (3.7)e</td>
</tr>
<tr>
<td>Arm #3</td>
<td>28</td>
<td>0</td>
<td>0</td>
<td>1 (3.6)c</td>
<td>1 (3.6)c</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Arm #4</td>
<td>18</td>
<td>1 (5.6)a</td>
<td>1 (5.6)a</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>All</td>
<td>100</td>
<td>1 (1)</td>
<td>2 (2)</td>
<td>1 (1)</td>
<td>2 (2)</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

**Analysis performed on intention to treat population**

- **a** Death attributed to cardiac arrest. No follow up imaging or autopsy.
- **b** Death attributed to complications of COPD and multi-organ failure 177 days post USCDT procedure.
- **c** Recurrent symptomatic PE within 30 d (patient was off anticoagulation).
- **d** Recurrent symptomatic PE at 9 months post USCDT.
- **e** Patient presented with acute symptoms, but no diagnostic imaging performed prior to treatment with systemic tPA.
## Major Bleeding within 72 Hours after Initiating the Procedure

<table>
<thead>
<tr>
<th>Tx Arm</th>
<th>N</th>
<th>N (%)</th>
<th>Events (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm #1</td>
<td>27</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Arm #2</td>
<td>27</td>
<td>1 (3.7)¹</td>
<td>2 (7.4)</td>
</tr>
<tr>
<td>Arm #3</td>
<td>28</td>
<td>1 (3.6)²</td>
<td>1 (3.6)</td>
</tr>
<tr>
<td>Arm #4</td>
<td>18</td>
<td>2 (11.1)³⁴</td>
<td>2 (11.1)</td>
</tr>
<tr>
<td>All</td>
<td>100</td>
<td>4 (4)</td>
<td>5 (5)</td>
</tr>
</tbody>
</table>

¹ 61 y/o female experienced anemia secondary to facial trauma caused by syncopal event; later received additional 50mg systemic tPA post study treatment and experienced ICH.

² 35 y/o female experienced anemia secondary to bleeding uterine fibroid after receiving 12mg additional tPA after study treatment.

³ 75 year old male with history of platelet abnormality, pancytopenia and labile hypertension experienced ICH and died 11 days after study procedure while in rehab facility.

⁴ 50 y/o male with S/P splenectomy 2 months prior to presentation. Experienced hemoperitoneum post procedure secondary to splenic artery pseudoaneurysm. Treated successfully with coil embolization.
Case Example

- 50 y/o female presents to the ED with CP, SOB and syncope
- BP 102/51 HR 116/min O2 sat 94% on RA
- Troponin I = 2.13 ng/ml (↑)
- CTA: Saddle and Bilateral PE
- RV:LV = 1.6
sPAP = 42 mmHg
- tPA 1mg/hr via each catheter x 6 hours
- Heparin 500 units/hr
3 hours post infusion patient reports noticeably less SOB

6 hours post infusion
- Heparin moderate intensity protocol
- BP 124/86 HR 96/min SaO₂ 98% RA
- sPAP = 23 mmHg

TTE
- RV:LV = 0.64

Discharged on Day #3 on Rivaroxaban
Case Example #2

- 70 y/o male with history of prior DVT/PE in setting of postoperative period following neck surgery
- Sedentary to due chronic back and knee pain
- SOB x 2 days
- Vitals stable
- Troponin I = 0.4ng/ml, BNP = 504 pg/ml
- ECG normal
RV:LV = 1.41
OPTALYSE PE tPA at 2 mg/hr x 2 h = 8 mg
OPTALYSE PE

tPA at 2mg/hr x 2 h = 8 mg

Pre-USCDT
RV:LV = 1.41

Post-USCDT
RV:LV = 1.12
Case Example #3

- 82 y/o male with sudden onset of CP and SOB
- SaO2 89% → 94% Non-rebreather
- BP 110/64 mm Hg, HR 90/min
- Lactic acid = 4.5 mmol/l
- Troponin I = 0.63 ng/ml
- BNP = 493 pg/ml
- AKI: eGFR = 44
- Admitted to telemetry
- Started on anticoagulation with UFH moderate intensity protocol
- Foley catheter placed for strict I/Os
- Experienced hematuria due to traumatic catheter placement
- Hgb: 14.7 → 10.2 g/dl
- CBI with clearing
- AC continued
- Worsening respiratory status with need for non-rebreather for SaO2 > 90%

- Initial TTE
  - RV:LV = 1.8
  - TAPSE = 8 mm
  - RVSP = 41 mm Hg
- R PAP = 77/19 mmHg (µ = 38 mm Hg)
- L PAP = 35/21 (µ = 26 mm Hg)
- Bilateral 12 cm EkoSonic™ catheters
- tPA at 1 mg/hr x 6 hours
- UFH 500 units/hr
Follow up

RV:LV = 0.8

Clinical

- SOB resolved
- SaO2 98% on 3L NC
- RVSP: 20 mm Hg
- Urine cleared
- Discharged on Eliquis
- LOS = 4 days
Case Example #4

- 46 y/o male presenting to ED with CP and SOB
- BP 116/72 HR 98/min O2 sat 92% on RA
- Troponin I = 0.32 ng/ml (↑)
- Lactic acid 6.6 mmol/L (↑)
- CTA: Saddle and Bilateral PE
- RV:LV = 1.7
- PAP = 56/21 mmHg
- Bilateral 12 cm EkoSonic™ catheters
- tPA at 1 mg/hr x 6 hours
- UFH 500 units/hr
No ICU bed available at the time
- Infusion and monitoring in the CVIR Recovery room
- Symptomatic improvement at 2 hours
- 6 hour post PAP = 33/12 mmHg
- 48 hour CTA: RV:LV = 0.8
- Discharged on Day #3 on Rivaroxaban
OPTALYSE PE conclusions

- Statistically significant reduction in RV:LV in all 4 treatment groups
- Lower-dose, shorter duration USCDT appears to be as effective as the regimens employed in other USCDT studies
- Reduced dose and treatment duration with r-tPA minimizes risk of major bleeding
- Very low long-term mortality
- Improved quality of life
Impact of OPTALYSE PE Treatment Regimen

- Potential use of USCDT in patients with relative contraindication to lytic therapy
- Change treatment duration with comfort that effective
- Potential to avoid ICU stay
What’s Next

- KNOCKOUT PE worldwide trial
- 1500 patients with acute submassive PE treated with USCDT
Thank you

- keith.sterling@inova.org
- (703) 504-7950
The OPTALYSE PE Trial – Reducing thrombolytic dose and treatment times with EKOS™ in the treatment of pulmonary embolism patients

Keith M. Sterling, M.D.
Director, Cardiovascular & Interventional Radiology
Inova Alexandria Hospital
Alexandria, VA, US
Associate Professor of Radiology
George Washington University School of Medicine
Washington, DC, US