Catheter Based Therapy for PE: Who and How?

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Disclosures

- PERT Consortium (501c3): Board of Directors
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- Recor Medical: Research Funds to the Institution
- Astra Zeneca: Advisory Board
Risk Stratification

Massive (High)
Submassive (Int-high)
(Int-low)
Lower Risk

OHCA

Estimated prevalence (%)

5
10
20
25
40

Estimated mortality (%)

>30
7-10
5-8
3
<3
>1

OHCA

shock, hypotension

10%

50%

RVD + TnT/BNP
RVD – TnT/BNP
no RVD + TnT/BNP
no RVD – TnT/BNP
asymptomatic

Rationale for Advanced Therapy

Outcomes in Pulmonary Embolism

- Sudden Death
- Cardiac Arrest
- Shock
- Emboli in transit
- Syncope
- Stratification by RV dysfunction?

Mortality

- Hemodynamically stable - RV Normal

Severity

- Embolism Size
- Cardiopulmonary Status

Wood KE. Critical Care Clinics 2011;27(4):885-906
Can We Prevent This?
PE Therapeutic Options: All Over the Map

- Anticoagulation
- IV Thrombolysis
- Catheter Directed Thrombolysis
- Pharmaco-Mechanical Catheter Treatment
- IVC Filter
- Surgical Embolectomy
- ECMO
Thrombolysis for Pulmonary Embolism and Risk of All-Cause Mortality, Major Bleeding, and Intracranial Hemorrhage

A Meta-analysis

Figure 3. Odds of Mortality in Patients With Intermediate-Risk Pulmonary Embolism Treated With Thrombolytic Therapy vs Anticoagulation

<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>Thrombolitics OR (95% CI)</th>
<th>Favors Thrombolitics</th>
<th>Favors Anticoagulants</th>
<th>Weight, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldhaber et al, 1993</td>
<td>0</td>
<td>46</td>
<td>2</td>
<td>55</td>
<td>0.16 (0.01-2.57)</td>
<td></td>
<td></td>
<td>5.3</td>
</tr>
<tr>
<td>Konstantinides et al, 2002</td>
<td>4</td>
<td>118</td>
<td>3</td>
<td>138</td>
<td>1.58 (0.35-7.09)</td>
<td></td>
<td></td>
<td>18.4</td>
</tr>
<tr>
<td>TIPES, 2010</td>
<td>0</td>
<td>28</td>
<td>1</td>
<td>30</td>
<td>0.14 (0.00-7.31)</td>
<td></td>
<td></td>
<td>2.7</td>
</tr>
<tr>
<td>Fasullo et al, 2011</td>
<td>0</td>
<td>37</td>
<td>6</td>
<td>35</td>
<td>0.11 (0.02-0.58)</td>
<td></td>
<td></td>
<td>15.1</td>
</tr>
<tr>
<td>MOPETT, 2012</td>
<td>1</td>
<td>61</td>
<td>3</td>
<td>60</td>
<td>0.35 (0.05-2.57)</td>
<td></td>
<td></td>
<td>10.5</td>
</tr>
<tr>
<td>ULTIMA, 2013</td>
<td>0</td>
<td>30</td>
<td>1</td>
<td>29</td>
<td>0.13 (0.00-6.59)</td>
<td></td>
<td></td>
<td>2.7</td>
</tr>
<tr>
<td>TOPCOAT, 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, 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>Total</td>
<td>12</td>
<td>866</td>
<td>26</td>
<td>889</td>
<td>0.48 (0.25-0.92)</td>
<td></td>
<td></td>
<td>100.0</td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi_\nu^2 = 7.63; P = .37; I^2 = 8\%$
Overall effect: $z = 2.22; P = .03$
### Table 2. Absolute Risk Metrics of Outcomes of Major Interest

<table>
<thead>
<tr>
<th>Outcome of Interest (No. of Studies Reporting)</th>
<th>No. of Events/No. of Patients, Absolute Event Rate (%)</th>
<th>No. Needed to Treat or Harm</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality (16)</td>
<td>Thrombolytic Group 23/1061 (2.17) Anticoagulant Group 41/1054 (3.89)</td>
<td>NNT = 59</td>
<td>.01</td>
</tr>
<tr>
<td>Major bleeding (16)*</td>
<td>Thrombolytic Group 98/1061 (9.24) Anticoagulant Group 36/1054 (3.42)</td>
<td>NNH = 18</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ICH (15)</td>
<td>Thrombolytic Group 15/1024 (1.46) Anticoagulant Group 2/1019 (0.19)</td>
<td>NNH = 78</td>
<td>.002</td>
</tr>
<tr>
<td>Recurrent PE (15)</td>
<td>Thrombolytic Group 12/1024 (1.17) Anticoagulant Group 31/1019 (3.04)</td>
<td>NNT = 54</td>
<td>.003</td>
</tr>
<tr>
<td>Age &gt;65 y</td>
<td>Thrombolytic Group All-cause mortality (5) 14/673 (2.08) Anticoagulant Group 24/658 (3.65)</td>
<td>NNT = 64</td>
<td>.07</td>
</tr>
<tr>
<td></td>
<td>Major bleeding (5)* 87/673 (12.93) Anticoagulant Group 27/658 (4.10)</td>
<td>NNH = 11</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age ≤65 y</td>
<td>Thrombolytic Group All-cause mortality (11) 9/388 (2.32) Anticoagulant Group 17/396 (4.29)</td>
<td>NNT = 51</td>
<td>.09</td>
</tr>
<tr>
<td></td>
<td>Major bleeding (11)* 11/388 (2.84) Anticoagulant Group 9/396 (2.27)</td>
<td>NNH = 176</td>
<td>.89</td>
</tr>
<tr>
<td>Intermediate-risk PE</td>
<td>Thrombolytic Group All-cause mortality (8) 12/866 (1.39) Anticoagulant Group 26/889 (2.92)</td>
<td>NNT = 65</td>
<td>.03</td>
</tr>
<tr>
<td></td>
<td>Major bleeding (8)* 67/866 (7.74) Anticoagulant Group 20/889 (2.25)</td>
<td>NNH = 18</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Note: * denotes difference between the treatment and control group is significant at the tails.
Weighing Benefits & Risks of PE Intervention

- Prevent early mortality
- Improve symptoms
- Prevent CTEPH

- Major Bleeding
- ICH
- Precipitate Decompensation
Theoretical Advantages for Local Lytic

- Higher local concentration
- Lower overall dose
- Ability to fragment clot if desired
- PA pressure monitoring
Options for CDT

**Cragg-McNamara**
- 4-5 F
- 100 cm catheter length
- 5-10 cm infusion length
- $100-200

**Unifuse**
- 4-5 F
- 100 cm catheter length
- 5-10 cm infusion length
- $100-200

**EKOS**
- 5F
- 100 cm catheter length
- 5-10 cm infusion length
- $2000-3000
Catheter-Directed Thrombolysis

4-24 hour treatment
↓ lytic dose (8-24 mg TPA)
? Bleeding impact
? thrombus resolution impact
Faster than passive catheter-directed alone (?)
Who Knows?

Longer Infusion

Reduced Dose
## All Studies – Major Bleeding Comparison

<table>
<thead>
<tr>
<th></th>
<th>Non-ICH Major Bleed</th>
<th>No Bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Catheter-Directed Lysis</strong></td>
<td>31</td>
<td>525</td>
</tr>
<tr>
<td><strong>Systemic Lysis</strong></td>
<td>83</td>
<td>948</td>
</tr>
</tbody>
</table>

\[ P = 0.08 \]

Piazza, et al. JACC Intvn. 2015
Piazza et al. JACC Intvn 2018
Giri, et al. Manuscript in Press
### All Studies – ICH Comparison

<table>
<thead>
<tr>
<th></th>
<th>ICH</th>
<th>No ICH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter-Directed Lysis</td>
<td>6</td>
<td>550</td>
</tr>
<tr>
<td>Systemic Lysis</td>
<td>15</td>
<td>1009</td>
</tr>
</tbody>
</table>

**P = 0.64**

Piazza et al. JACC Intvn 2018.
CDT Trade-Offs

**Pros**
- Lower Dose
- Can halt infusion
- Less off-target exposure (theoretical)
- Better Clot Penetration (theoretical)

**Cons**
- Longer Infusion
- Technical Expertise
- Resource Intensive
- Deep Vein Access (not absolutely required)
- Can Destabilize Patient Acutely


- We do not know the ICH risk with CDT (though we hope it is less than systemic lysis)
- The non-ICH major bleeding rate may be similar with CDT compared to systemic lysis
- No randomized comparative studies of CDT vs ST exist and few observational studies exist
1) You are more likely to feel better sooner

2) The cost of this is a higher risk of bleeding and a small but real risk of ICH

3) We cannot promise you that this will make you live longer or prevent the development of long-term dyspnea or pulmonary hypertension from your PE
Sample Devices for PE Intervention

(A) AngioVac cannula. (B) Diagram of AngioVac insertion and reinfusion circuit. It has been inserted into the right internal jugular vein. Blood and thrombus is aspirated through the filter cannula, allowing clot capture utilizing a centrifugal pump. (C) Example of thrombus captured in the filter cannula. Images from AngioVac.

(A) The flow restoration catheter (FRC) is used to aspirate clots and is pulled through the aspiration guide catheter (AGC) utilizing (B) the retraction aspirator device (RAD). Images from Inari Medical.

(A) The 6- to 8-F straight or angled aspiration catheter (CAT6 or CAT8, respectively) is advanced to the thrombus and aspiration performed with the (B) ACER pump. Wires may be inserted into the catheter and utilized in a gentle back-and-forth motion to clear the catheter of thrombus. Images from Penumbra, Inc.

(A) Infusion catheter (A), which contains 3 lumens: 1 each for the inner ultrasound cable, drug infusion, and normal saline as a coolant. The inner cable (B) is shown with ultrasound crystals (arrows). Ultrasound energy separates fibrin strands, allowing for enhanced thrombus penetration of fibrinolytic agent. Images from Ekos Corporation.
Get Ready for PE Devices with Limited Data

- Be careful with embolectomy devices in intermediate risk patients
- Minimal comparative evidence of safety/efficacy versus conservative strategies
- We do not know that these therapies influence long-term CTEPH/CTED
- Reserve for patients who are “on-the-edge” and have bleeding contraindications
High Risk PE patients

Very High Mortality
(30-60% at 30-90 days)

Very Different Approach
High Risk PE patients - Paradigm Shift

First Question:
Should I institute emergent mechanical circulatory support?

1) No life-threatening comorbidities
2) Reasonable Age (<80)
3) Escalating Pressors or In-Hospital Arrest
Bridge to Definitive Therapy
66 year old male smoker w/ HTN p/w 2 weeks dyspnea, CP, dizziness, LE edema → acutely worse

Vitals
BP 88/73
HR 106-120
Sat 89%, RR>30

s/p IVF and 100% o2
BP 107/89
HR 101
Sat 100%

Lactate 5.5
Trop wnl, Cr wnl
HgB 9.2
NTproBNP 236

EKG: Sinus Tach. RBBB. LAFB
Right heart Strain

Bilateral PE involving R/L main PA and into lobar and segmental branches

LLL infarct
Notable ROS

- No bleeding hx
- No recent travel
- No Surgery
- No immobilization
- NO personal or Fam Hx of VTE or SCD

HAS-BLED = 1

PESI Class V, Very High Risk: 10.0-24.5% 30-day mortality
PERT TEAM Consulted.

How would you proceed?

- Therapeutic Anticoagulation/Heparin
- Systemic Thrombolysis
- Surgical Embolectomy
- Catheter Directed Thrombolysis
- Catheter Based Embolectomy
26F Gore Dryseal: R Fem Vein
16F ECMO Cannula: Left Fem Vein
Admitted to CT SICU
Off Pressors

MvO2 22%

2 Pressor Shock and Respiratory Failure

Placed on emergent VA ECMO via existing femoral arterial and venous sheaths
**What would you offer?**

(Patient supported with VA ECMO)

<table>
<thead>
<tr>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continue Therapeutic Anticoagulation/Heparin</td>
</tr>
<tr>
<td>Systemic Thrombolysis</td>
</tr>
<tr>
<td>Surgical Embolectomy</td>
</tr>
<tr>
<td>Catheter Directed Thrombolysis</td>
</tr>
<tr>
<td>Catheter Based Embolectomy</td>
</tr>
</tbody>
</table>
Hospital Day #1 on bifemoral VA ECMO

Antegrade Perfusion 7F cannula (micropuncture)

5F Cragg-McNamara valved infusion catheters in Right and Left interlobar pulmonary arteries

-6F Right Basilic Vein
-6F Left common femoral vein
Penn Catheter Directed Thrombolysis

- 1-3mg Alteplase/catheter bolus
- 1mg/catheter/hr x 6 hours
- 0.5mg/hr thereafter, based upon response
- Labs q 4hr, CBC, PTT ~ 40-50 (continue low dose heparin), Fibrinogen >100-150
- Stop Alteplase, pull venous sheaths 30-40 minutes later, 5 min hemostasis, Lovenox STAT and BID
Hospital Day #1 (continued)

- Patient Returned to CT-SICU from cath lab

- Within 6 hours patient had return of pulsatility, pressors weaned off

- After 24 mg Alteplase, infusion catheters and sheaths removed

- Patient restarted on therapeutic dose unfractionated heparin

- LE Duplex:
  - Acute DVT L femoral vein
  - Acute and Chronic DVT R and L popliteal
Hospital Day #4

- Decannulated from VA ECMO and Extubated
Bard Denali IVC Filter (Retrievable)
Discharged to home Hospital Day #13

- Ambulatory
- Off Oxygen
- Xarelto
6 week follow up with Pulmonary Clinic (PERT Follow up)
Retrieved at 8 weeks
Thank You

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  - Robert Schainfeld, MD
  - Michael Jaff, DO

- PERT Consortium
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  - Victor Tapson – Cedar Sinai
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