Catheter-based Pulmonary Interventions: Advancing The Science In PE Treatment – What Do We Need To Know, And How Will We Learn

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Massive PE

Massive
Submassive
Prospective Registry Randomized Controlled Trial

Massive
Submassive
Low-risk
Rescue
Prevent mortality and hemodynamic decompensation (?)
Prevent progression to above (AC)

Intravenous thrombolysis
Thrombolytics contraindicated
Thrombolytic failure
Surgical embolectomy
Rescue
Catheter Directed Therapy
The case that launched the Cornell PERT

- 30+ year old man s/p transcranial resection of a pituitary tumor
- Developed post-op seizures, found to have intracranial frontal lobe hemorrhage
- Several days after operation, developed hypotension and hypoxia
- CT chest, PE protocol was ordered

Clot in transit (IVC) and large pulmonary embolus in right main PA

Further history

- Had systolics of ~90 mm Hg x 1 hour
- Progressively more altered and tachycardic
- Referred for potential thrombolysis
- Brought to IR suite, was started on pressors

Initial pulmonary angiogram

Spot images of the Cleaner device (FDA approved for AV fistula work)

Post Cleaner pictures

Radiology Case. 2014 Feb; 8(2):30-36
**CATHETER THERAPIES**

Best analysis done so far – Kuo et al. 2009

<table>
<thead>
<tr>
<th>Major Complications</th>
<th>Clinical Success</th>
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</thead>
<tbody>
<tr>
<td>2.4% (CI: 1.9%, 4.3%)</td>
<td>86.5% (CI: 82.2%, 90.2%)</td>
</tr>
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What does the data (not) tell us?

- Techniques are available to remove thrombus or create a channel through occluded pulmonary arteries
- Can be used if systemic lysis is contraindicated
- (not): whether catheter-based therapy is better than the other therapies
- (not): whether it should be used in combination with other therapies
- (not): which patients should get catheter-based therapy and which should get surgery
- (not): which catheter-based techniques are most effective (and safe)?

Back of the envelope calculation: RCT not feasible for Massive PE

- 800 bed hospital
- 200 PE's per year
- 5% Massive = 10 per year
- Assume 40% enrollment
- 4 massive PE's per year/institution
- Randomize them to what? IV lytics vs surgery vs interventional therapy? 3 arm study? What is the effect size, and how would you power it?
What does a Massive PE Prospective Registry look like?

- Detailed baseline characteristics
- Every patient is included
- Detailed intervention (device, fibrinolytic drug, surgical intervention, ECMO)
- 7 and 30 day outcomes, followed for 1 year

ICOPER (1999) alerted the world to RV dysfunction

PEITHO – the trial to answer all uncertainty?

<table>
<thead>
<tr>
<th>PEITHO Trial Outcomes</th>
<th>Tirofiban (n = 168)</th>
<th>Placebo (n = 168)</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome (died)</td>
<td>13 (7.8)</td>
<td>24 (14.3)</td>
<td>0.48 (0.23-0.95)</td>
<td>0.02</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>6 (3.6)</td>
<td>9 (5.4)</td>
<td>0.54 (0.25-1.17)</td>
<td>0.10</td>
</tr>
<tr>
<td>Hemodynamic decompen</td>
<td>sion</td>
<td>6 (3.6)</td>
<td>3 (1.8)</td>
<td>0.35 (0.14-0.86)</td>
</tr>
</tbody>
</table>

Systemic thrombolysis has a questionable risk-benefit profile in patients with submassive PE
ULTIMA – CDT reduced RV/LV ratio to a greater extent than heparin at 24 hours*

PERFECT: Consistent PA Pressure reduction

Optalyse: All CDT groups associated with a reduction in the RV/LV ratio at 48 hours

| TABLE 3: RV/LV Diameter Ratio by CTA |
|-------------------|-------|-------|-------|-------|
|                   | Arm 1 | Arm 2 | Arm 3 | Arm 4 |
| RV/LV diameter ratio at baseline | 1.47 ± 0.30 | 1.43 ± 0.30 | 1.49 ± 0.37 | 1.51 ± 0.38 |
| Percentage change from baseline at 48 h | -20.2 ± 15.9 | -26.1 ± 16.0 | -26.1 ± 16.0 | -25.5 ± 16.0 |
| p value (2-tailed Student’s t test comparing with baseline) | 0.0000 | 0.0000 | 0.0000 | 0.0000 |

Safety: SEATTLE 2 and Optalyse had major bleeds

| TABLE 5: Major Bleeding Within 72 h |
|-------------------|-------|-------|
|                   | m (%) | Events (%) |
| Arm 1             | 27 (0) | 0 (0)   |
| Arm 2             | 27 (3.7) | 2 (1.4) |
| Arm 3             | 28 (3.6) | 1 (0.3) |
| Arm 4             | 16 (2.1) | 2 (1.1) |
| All patients      | 100 (4.0) | 5 (5.0) |
Clot extraction minus fibrinolytic

What does the data (not) tell us?

- CDT probably reduces the RV/LV ratio at 24 hours (ULTIMA)
- CDT associated with a reduction in the RV/LV ratio at 48 hours (SEATTLE 2, OPTALYSE)
- Major bleeding is seen with CDT (SEATTLE 2, OPTALYSE)
- (not): what the short and long-term clinical outcomes are following CDT for submassive PE
- (not): whether CDT should be routinely used for submassive PE
- (not): what the optimal dose/duration of thrombolytic drug is
- (not): whether non-lytic techniques are efficacious and safe

>1600 patients have been randomized in systemic lytic trials. 59 have been randomized in a single, non-US, CDT trial

The PERT CDT roller coaster

Pulmonary Embolism – Thrombus Removal with Catheter-Directed Thrombolysis: PE-TRACT

- RCT of CDT vs. No-CDT in the setting of submassive PE
- Short-term and Long-term clinically relevant outcomes, important to patients and providers
- 414 patients
- 30 sites-50 sites

Massive | Submassive

Prospective Registry | Randomized Controlled Trial
Thank you!
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