THROMBOLYSIS FOR PULMONARY EMBOLISM


Take home points:
1. RV dysfunction may be a predictor of worse clinical outcomes in acute PE
2. If you are going to use tPA in massive or submassive PE, know the inclusion and exclusion criteria and how to give it
3. Tx for submassive PE with tPA doesn’t provide a mortality benefit at 30 days but prevents escalation of treatment; therefore, use it judiciously and on a case-by-case basis

Massive pulmonary embolism:
- For purposes of thrombolysis, massive PE is characterized by hypotension (cardiogenic shock)
- Size of PE on imaging study does not correlate well with clinical outcome
- FDA approved indication for thrombolysis though data is scant
- Give tPA 100 mg IV over 2 hours followed by heparin up to 14 days after onset of symptoms (but the earlier the better)

Submassive pulmonary embolism:
- Characterized by PE with signs of R heart dysfunction or failure
- R heart failure is the usual cause of death from PE; therefore RV dysfunction may be an important warning sign of a bad outcome
- Recent NEJM trial looked at using thrombolysis for “submassive” PE (RCT, 256 pts.)

Inclusion criteria for tPA in submassive PE:
- Acute PE on radiographic study (CT chest or V/Q scan) and
  - RV dysfunction on echo (RVE + loss of IVC collapse on inspiration without LV or MV dz) or
  - Pulmonary HTN on echo (TR jet > 2.8 m/s) or
  - Precapillary pulmonary HTN on R heart cath (mean PA > 20 mmHg, PCWP < 18 mmHg) or
  - New ECG signs of RV strain (S1Q3T3 or RBBB or T wave inversion in V1-4)

Exclusion criteria for tPA in submassive PE:
- Age > 80
- Hemodynamic instability (SBP < 90 mmHg)
- Onset of symptoms > 96 hours
- Thrombolytic treatment, major surgery, or biopsy < 7 days ago; major trauma < 10 days ago
- CVA, TIA, craniocerebral trauma, or neurosurgery < 6 months ago
- GI bleeding < 3 months ago
- Uncontrolled HTN
- Known bleeding disorder or diabetic retinopathy
- Current therapy with oral anticoagulant; Current pregnancy or lactation
- Life expectancy < 6 months because of underlying disease

How was tPA given? In this trial, tPA was given differently then in massive PE
- IV bolus 10 mg then 90 mg infusion over 2 hours
- 5000 U heparin bolus given before tPA and heparin infusion started concomitantly with tPA

What were the outcomes?
- See table on the back of this page for main outcomes
- Escalation of treatment defined as catecholamine infusion (dopamine had to be > 5 mcg/kg/min) for hypotension, secondary thrombolysis, worsening respiratory failure, intubation, CPR, surgical/catheter embolectomy
- Hemorrhagic complications: only 1% (previous trials 6% tPA vs. 2% with heparin alone)
Heparin plus alteplase vs heparin plus placebo for acute submassive pulmonary embolism‡

<table>
<thead>
<tr>
<th>Outcomes at 30 d</th>
<th>Alteplase</th>
<th>Placebo</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined endpoint§</td>
<td>11%</td>
<td>25%</td>
<td>55% (21 to 75)</td>
<td>8 (5 to 24)</td>
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<tr>
<td>Clinical deterioration</td>
<td>10%</td>
<td>25%</td>
<td>59% (25 to 78)</td>
<td>7 (5 to 20)</td>
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<tr>
<td>All-cause mortality</td>
<td>3.4%</td>
<td>2.2%</td>
<td>56% (~60 to 513)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

‡Abbreviations defined in Glossary: RRR, RRI, NNT, NNH, and CI calculated from data in article.

§In-hospital death or clinical deterioration requiring escalation of treatment.