

## Thrombolytics for Pulmonary Embolism

- Alteplase is a thrombolytic agent that binds to fibrin in a clot and converts plasminogen to plasmin.
- Pharmacokinetics:
  - Duration:
    - ~80% cleared within 10 minutes
    - Fibrinolytic activity persists for up to 1 hour after termination of infusion
  - Half-life:
    - ~ 5 minutes
- Typical IV dosing for pulmonary embolism (found in Lexicomp):
  - Submassive/Hemodynamically stable:
    - 100mg over 2 hours\*
  - Massive/Hemodynamically unstable:
    - 100mg over 2 hours\*
  - Pulmonary embolism associated with cardiac arrest
    - 50mg bolus over 2 minutes
    - Repeat second 50mg bolus 15 minutes later if return of spontaneous circulation (ROSC) not achieved

\*Initiate or resume parenteral anticoagulation near the end or immediately following the alteplase infusion when partial thromboplastin time or thrombin time returns to twice normal or less

- Literature:
  - **Moderate Pulmonary Embolism Treated with Thrombolysis [PMID 23102885]**
    - Enrolled 121 patients with submassive PE
    - Intervention: thrombolytic vs placebo
    - Dosing: tPA 0.5 mg/kg (max 50mg) given as 10mg bolus followed by remaining dose over 2 hours
    - Outcomes:
      - Composite primary outcome of pulmonary hypertension or recurrent PE was lower in the thrombolytic group (16% vs 63%;  $p < 0.001$ ; NNT 2)
      - Recurrent PE was not significant, but lower in the thrombolytic group (0% vs 5%;  $p = 0.08$ )
  - **Half-Dose versus Full-Dose Alteplase for Treatment of Pulmonary Embolism [PMID 29979222]**
    - Retrospective cohort study with 3768 patients
    - Intervention: half-dose (50mg) vs full-dose (100mg) alteplase for pulmonary embolism
    - Outcomes:
      - No difference cerebral hemorrhage (0.5% vs 0.4%;  $p = 0.67$ ); GI bleeding (1.6% vs 1.6%;  $p = 0.99$ ), blood loss anemia (6.9% vs 4.6%;  $p = 0.11$ ); use of blood products ( $p > 0.05$ ) or fibrinolytic adverse events (2.6% vs 2.8%;  $p = 0.82$ )
      - Treatment escalation occurred more often in patients in the half-dose group (53.8% vs 41.4%;  $p < 0.01$ )
      - Hospital mortality was similar (13% vs 15%;  $p = 0.3$ )