Fibrinolysis in Intermediate Risk PE

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Topic	**Thrombosis**	
Citation of Paper:	**Fibrinolysis for Patients with Intermediate-Risk Pulmonary Embolism (PEITHO Trial**) NEJM 370;15 april 10, 2014 PMID: 24716681	
Clinical Question:	In patients with intermediate-risk PE (signs of RV dysfunction* and cardiac injury) does thrombolysis improve clinical outcomes?	
PICO	P:	normotensive adult patients with intermediate-risk pulmonary embolism: (1) right ventricular dysfunction on echocardiography (see footnote) or computed tomography **AND** (2) positive troponin I or T
	I:	tenecteplase (full bolus dose over 5-10 seconds based on weight: >60kg=30 mg; >90kg=50mg) plus heparin started immediately after randomization
	C:	placebo plus heparin
	O:	1- **Primary outcome** was death or hemodynamic decompensation ** (or collapse) within 7 days 2- **Secondary outcomes**: (1) death < 7 days after randomization, (2) hemodynamic decompensation < 7 days, (3) confirmed symptomatic recurrence of PE < 7 days, (4) death < 30 days, (5) major adverse events < 30 days
Methods	randomized, double-blind trial, intention to treat analysis	
Results	**1- Primary outcome:** Death or hemodynamic decompensation: 2.6% with TNK vs. 5.6% with placebo (OR=0.44; 95%CI, 0.23 to 0.87; P = 0.02) **(NNT = 33)** **2- Adverse events/Harm: a)** Extracranial bleeding 6.3% (TNK); vs. 1.2% (placebo) (P<0.001) **(NNH=20)**; **b)** Stroke: TNK: 12 patients (2.4%) (hemorrhagic=10/12); vs. Placebo: 1 patient (0.2%) (hemorrhagic=1/1) (P = 0.003) **(NNH=45)**.	
Conclusion	Normotensive patients with intermediate-risk pulmonary embolism benefit from treatment with a single intravenous bolus of tenecteplase, but at a higher risk of ICH.	
Take Home Point	Normotensive patients with intermediate-risk pulmonary embolism benefit from treatment with a single intravenous bolus of tenecteplase (but effect driven by decrease in hemodynamic collapse) and with a higher risk of ICH. More studies are ongoing about the use of reduced doses of TNK. In June 2014, a meta-analysis was published in JAMA.	
Caveats	1- Were the hemorragic complications due to previous LMWH or fondaparinux given before randomization? 2- In the present trial, the efficacy of thrombolysis was mainly driven by the prevention of hemodynamic decompensation more than its effect on mortality 3- To reduce risk of ICH in patients over 75 years, should we adopt a policy to reduce dose by 50%? (NB. In a recently published prehospital trial of TNK in STEMI, there were no cases of intracranial hemorrhage when the dose was reduced by 50% in patients 75 years of age or older. (PMID: 23473396 Full text click here). 4- A reduced dose strategy also has merit: see MOPETT trial.	

***Definition of RV Failure**

At least one of the following echocardiographic criteria were needed to confirm right ventricular dysfunction:

• Right ventricular end-diastolic diameter > 30 mm (parasternal long-axis or short-axis view);

• right-to-left ventricular end-diastolic diameter > 0.9 (apical or subcostal 4-chamber view);
• hypokinesis of the right ventricular free wall (any view);
• tricuspid systolic velocity > 2.6 m/s from the apical or subcostal 4-chamber view.

****Definition of Hemodynamic Failure**
Hemodynamic decompensation (or collapse) was defined as:
• need for cardiopulmonary resuscitation; **OR**
• systolic blood pressure < 90 mm Hg for at least 15 min, **OR**
• drop of systolic blood pressure by at least 40 mm Hg for at least 15 min with signs of endorgan hypoperfusion (cold extremities or low urinary output < 30 mL/h or mental confusion); **OR**
• need for catecholamine administration to maintain adequate organ perfusion and a systolic blood pressure of > 90 mm Hg (including dopamine at the rate of > 5 micrograms / kg per minute).