

## February 2015 Tucson Pulmonary Journal Club: Fibrinolysis for PE

**Meyer G, Vicaut E, Danays T, et al. Fibrinolysis for patients with intermediate-risk pulmonary embolism. *N Engl J Med.* 2014;370(15):1402-11. [\[CrossRef\]](#) [\[PubMed\]](#)**

The role of fibrinolytic therapy among patients with intermediate-risk pulmonary embolism (PE) is controversial (1). When right ventricular dysfunction and myocardial injury are associated with PE, there is an increased risk of adverse events (2). However, the risk of bleeding with fibrinolytic therapy has previously been thought to outweigh the benefits among patients without overt hemodynamic collapse.

The Pulmonary Embolism Thrombolysis (PEITHO) trial was a multi-center, double-blind, placebo-controlled randomized trial designed to investigate the efficacy and safety of single-bolus injection with tenecteplase plus heparin anticoagulation versus heparin anticoagulation alone among normotensive patients with intermediate risk PE (3). The study included 1005 adult patients who were randomized within fifteen days of symptom onset; randomization occurred when both right ventricular dysfunction (echocardiography or spiral computed tomography) and myocardial injury (troponin I or T) were present. All patients were followed for 30 days. The primary outcome was death or hemodynamic collapse within 7 days of randomization. Safety outcomes included major extra cranial and intracranial hemorrhage within 7 days.

Fibrinolytic therapy was associated with less frequent hemodynamic collapse or death within 7 days of treatment (2.6% vs 5.6%,  $p=0.02$ ). The result was primarily driven by fewer instances of hemodynamic collapse in tenecteplase group (1.6% vs 5.0%,  $p=0.002$ ). At 30 days, there was no difference in mortality from any cause between the tenecteplase and usual care groups, 2.5% versus 3.2%, respectively ( $p=0.42$ ). However, tenecteplase therapy was associated with higher risk of major bleeding and stroke than usual care, 11.5% versus 2.4% ( $p<0.001$ ) and 2.4% versus 0.2% ( $p=0.003$ ), respectively. Subgroup analysis showed a trend towards increased bleeding in patients older than 75 years though this was not significant ( $p=0.09$ ).

PEITHO is a relatively large, expensive, randomized controlled trial that provides little guidance on the optimal care of patients with intermediate risk PE. While improvement in the composite outcome of death or hemodynamic decompensation was significant (Odds Ratio 0.44,  $CI_{95\%}$  0.23-0.87), the benefit was primarily driven by less frequent hemodynamic compromise. Furthermore, any treatment benefit must be weighed against a substantially increased risk of major bleeding (Odds Ratio 5.55,  $CI_{95\%}$  2.3-13.39) or stroke (Odds Ratio 12.10,  $CI_{95\%}$  1.57-93.39). Given that follow-up is limited to 30 days and no patient-reported/patient-centered outcomes are available, it is difficult to provide patients or clinicians with the evidence they need to weigh the risks and benefits. Until better data are available, thrombolytic therapy for intermediate risk PE still remains weakly supported due to unclear efficacy and high risks of major bleeding or stroke, particularly among older patients.

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### ***References***

1. Konstantinides S, Goldhaber SZ. Pulmonary embolism: risk assessment and management. *Eur Heart J*. 2012;33:3014-22. [\[CrossRef\]](#) [\[PubMed\]](#)
2. Konstantinides S. Acute pulmonary embolism. *N Engl J Med*. 2008;359:2804-13. [\[CrossRef\]](#) [\[PubMed\]](#)
3. Meyer G, Vicaut E, Danays T, et al; PEITHO Investigators. Fibrinolysis for patients with intermediate-risk pulmonary embolism. *N Engl J Med*. 2014;370(15):1402-11. [\[CrossRef\]](#) [\[PubMed\]](#)