

**Determinants of the long-term haemodynamic course and late sequelae after acute intermediate-risk pulmonary embolism: results from a randomized thrombolysis trial**

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**Background:** Following pulmonary embolism (PE), patients may report persisting or progressive functional limitation, with or without echocardiographic (echo) signs of pulmonary hypertension and right ventricular (RV) dysfunction. The incidence and determinants of this continuum of “post-PE impairment”, with chronic thromboembolic pulmonary hypertension (CTEPH) as its most severe clinical manifestation, are largely unknown.

**Methods:** We performed a post-hoc analysis of the dataset of the PEITHO trial, in which 1,006 patients with acute intermediate-high risk PE were randomized to tenecteplase or placebo (on top of standard anticoagulation) and followed for 6 months. Long-term (at least 2-year) clinical and echo follow-up (FU) was part of the third protocol amendment, signed by 28 of the 76 study sites. This analysis included patients who had complete 6-month and long-term FU data. Complete echo recovery at 6 months was defined by normalization of all of the following: 1) estimated systolic pulmonary artery pressure, 2) RV end-diastolic diameter and RV/left ventricular diameter ratio, and 3) RV free wall motion. Post-PE impairment at long-term FU was defined 1) as confirmed diagnosis of CTEPH, or 2) by the presence of persisting/new-onset exertional dyspnoea (NYHA class II-IV) combined with intermediate or high echo probability of pulmonary hypertension as per 2015 ESC Guidelines.

**Results:** Of 219 patients with complete FU data, 112 received tenecteplase and 107 placebo. At 6-months, 15 (6.8%) patients reported severe dyspnoea, and 86 (39.2%) had incomplete echo recovery. At long-term FU, 29 (14.5%) patients were diagnosed with post-PE impairment, with CTEPH confirmed in 6 of these cases (2.7%). By univariable analysis, age >68 years at baseline (OR 3.4; 95% CI 1.4–8.0), NYHA class II-IV at 6 months (OR 3.2; 1.3–7.7), and incomplete echo recovery at 6 months (OR 4.8; 1.8–12.6), but not thrombolytic treatment (15.5% versus 13.4%; OR 1.2; 0.5–2.6), were associated with post-PE impairment. At multivariable analysis, incomplete echo recovery at 6 months was confirmed as an independent predictor (adjusted OR 7.1, 95% CI 2.1–23.8) of long-term outcome.

**Conclusions:** In the present analysis from the PEITHO trial, 14.5% of patients presented with post-PE impairment over long-term FU, with a 2.7% rate of confirmed CTEPH. The absence of complete echocardiographic recovery 6 months after acute PE, but not early thrombolytic treatment, was a predictor of long-term functional impairment. These results may have implications for developing patient FU protocols after

acute PE.