

Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare but severe complication of acute pulmonary embolism (APE). Identifying patients at risk during the acute phase remains challenging. As CTEPH may arise from acute-on-chronic thromboembolic events, combining biochemical markers with echocardiographic evidence of chronicity may facilitate early risk stratification.

Purpose: Our goal was to determine whether biochemical markers combined with transthoracic echocardiography (TTE) will identify APE patients requiring intensified follow-up for CTEPH development.

Methods: We followed APE patients for whom baseline D-dimer and NT-proBNP concentrations were available, and who had TTE performed. All patients were followed up in an outpatient clinic. Patients with persistent dyspnoea underwent further evaluation for CTEPH, confirmed by right heart catheterisation demonstrating elevated mean pulmonary artery pressure >20 mmHg.

Results: We included 342 patients, of whom 22 (6.4%) developed CTEPH during follow-up. They had higher median baseline NT-proBNP (1860 vs 550 ng/L, $p < 0.05$) and lower, though not statistically significant, D-dimer (4210 vs 5330 mcg/L, $p = 0.1$) concentrations. They differed in D-dimer/NT-proBNP ratio (DD/NT-proBNP; 2.9 vs 12.0 mcg/ng, $p < 0.001$), providing high negative predictive value of 98.3% (95% CI 95.7-99.7%) for subsequent CTEPH diagnosis at a threshold of 10 mcg/ng, increasing two-fold CTEPH incidence rate in the remaining group (20/171 cases, OR 11.2, 95%CI 2.6-48.6; $p = 0.0013$). Mean tricuspid regurgitation peak gradient (TRPG) was also higher in patients developing CTEPH (46.5 vs. 32 mmHg, $p < 0.001$). Combining TRPG ≥ 36 mmHg with the DD/NT-proBNP cutoff point allowed designing a two-step decision model, which narrowed down cohort to 87 patients, with 17 CTEPH cases (19.5% positive predictive value).

Conclusion: Patients with DD/NT-proBNP ratio above 10 mcg/ng constitute a group of low risk of CTEPH development. Patients with lower ratios and TRPG ≥ 36 mmHg warrant close surveillance, as approximately one in five may develop CTEPH.