Fibrinolysis for Patients with Intermediate-Risk Pulmonary Embolism

Abstract:

Background The role of fibrinolytic therapy in patients with intermediate-risk pulmonary embolism is controversial. Methods In a randomized, double-blind trial, we compared tenecteplase plus heparin with placebo plus heparin in normotensive patients with intermediate-risk pulmonary embolism. Eligible patients had right ventricular dysfunction on echocardiography or computed tomography, as well as myocardial injury as indicated by a positive test for cardiac troponin I or troponin T. The primary outcome was death or hemodynamic decompensation (or collapse) within 7 days after randomization. The main safety outcomes were major extracranial bleeding and ischemic or hemorrhagic stroke within 7 days after randomization. Results Of 1006
patients who underwent randomization, 1005 were included in the intention-to-treat analysis. Death or hemodynamic decompensation occurred in 13 of 506 patients (2.6%) in the tenecteplase group as compared with 28 of 499 (5.6%) in the placebo group (odds ratio, 0.44; 95% confidence interval, 0.23 to 0.87; P=0.02). Between randomization and day 7, a total of 6 patients (1.2%) in the tenecteplase group and 9 (1.8%) in the placebo group died (P=0.42). Extracranial bleeding occurred in 32 patients (6.3%) in the tenecteplase group and 6 patients (1.2%) in the placebo group (P<0.001). Stroke occurred in 12 patients (2.4%) in the tenecteplase group and was hemorrhagic in 10 patients; 1 patient (0.2%) in the placebo group had a stroke, which was hemorrhagic (P=0.003). By day 30, a total of 12 patients (2.4%) in the tenecteplase group and 16 patients (3.2%) in the placebo group had died (P=0.42). Conclusions In patients with intermediate-risk pulmonary embolism, fibrinolytic therapy prevented hemodynamic decompensation but increased the risk of major hemorrhage and stroke. (Funded by the Programme Hospitalier de Recherche Clinique in France and others; PEITHO EudraCT number, 2006-005328-18; ClinicalTrials.gov number, NCT00639743.) In a randomized trial, 1006 patients with intermediate-risk pulmonary embolism were assigned to tenecteplase or placebo in addition to standard heparin therapy. The tenecteplase group had a lower rate of hemodynamic decompensation but more frequent major hemorrhage and stroke. Acute pulmonary embolism occurs frequently and may cause death or serious disability. Acute right ventricular pressure overload at diagnosis is an important determinant of the severity and early clinical outcome of pulmonary embolism. High-risk pulmonary embolism is characterized by overt hemodynamic instability and warrants immediate advanced therapy, including consideration of fibrinolysis. In contrast, for patients presenting without systemic hypotension or hemodynamic compromise, standard anticoagulation is generally considered adequate treatment.