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Title: Baseline hemodynamic predictors of treatment response in pulmonary arterial hypertension

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Body: **PURPOSE:** Pulmonary arterial hypertension (PAH) is a progressive disease characterized by an increase in pulmonary vascular resistance (PVR), by right ventricular dysfunction, and ultimately, right heart failure and death. Although PVR can be reduced by vasodilator treatment, PVR remains elevated above normal in the vast majority of patients, and prognosis remains poor. The purpose of this study was to identify baseline hemodynamic predictors of treatment response in patients with PAH. **METHODS:** A retrospective data set of 3107 patients undergoing right heart catheterization was analyzed. 1094 patients were classified as post-capillary and 137 as pre-capillary PH. Of these, 23 patients had idiopathic PAH (iPAH). Hemodynamic cut-offs for the discrimination between iPAH and post-capillary PH were determined by ROC curves. A prospective data set of 541 PAH patients receiving treprostinil or placebo was utilized for the validation of hemodynamic cut-offs. **RESULTS:** ROC analysis identified mPCWP of 12mmHg (area under the curve [AUC] 0.99) and diastolic pressure gradient (DPG) of 20mmHg (AUC 0.97) as the best hemodynamic values for the differentiation between iPAH and post-capillary PH. Patients with mPCWP <12mmHg, DPG >20mmHg or a combination of both had a significant improvement in hemodynamics under treprostinil compared to corresponding placebo groups, with a decrease in PVR of 3.1WU [1.3, 4.9], 2.9WU [1.0, 4.7] and 3.6WU [1.5, 5.8], respectively. By contrast, hemodynamics did not improve in patients with mPCWP ≥12mmHg or DPG ≤20mmHg, or both. **CONCLUSION:** An mPCWP of less than 12 and a DPG of over 20mmHg identify PAH patients who are likely to have a significant benefit under vasodilator treatment.