

**Assessment of pulmonary endothelial function during invasive testing in children and adolescents with idiopathic pulmonary arterial hypertension**

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Introduction: IPAH may be associated with pulmonary endothelial dysfunction, however data regarding the impact of endothelial dysfunction on severity and prognosis of this disease are limited. The purpose of our study was to assess pulmonary endothelial function by vasodilator response to Acetylcholine (Ach) administered in segmental pulmonary arteries in children with idiopathic pulmonary arterial hypertension (IPAH). We hypothesized a relation between pulmonary endothelial response to Ach, severity of the disease and clinical outcome.

Methods: 43 children and adolescents (mean age  $10.4 \pm 5.5$  years) with IPAH were included in the study. Changes in pulmonary blood flow in response to Ach were determined using intravascular Doppler flow measurements. Pulmonary flow reserve (PFR) was calculated as the ratio of pulmonary blood flow velocity in response to Ach relative to baseline values.

Results: Mean PFR of all patients was  $1.58 \pm 0.1$ . Mean follow up after catheterization was  $55.7 (\pm 41.9)$  months. Freedom from serious cardiovascular events (lung transplantation or death) was 83% after 2 years, 76% after 3 years, and 57% after 5 years. PFR correlated with WHO functional class and long-term response to calcium channel blocker therapy. Receiver-operating characteristic curve revealed a PFR of 1.4 as best cut-off value. Kaplan-Meier analysis demonstrated PFR  $<1.4$  as highly predictive for cardiovascular events (Log rank (Mantel Cox) Chi square 12.49;  $p < 0.0001$ ).

Conclusions: Our study demonstrates a strong relation between pulmonary endothelial response to Ach and prognosis of children with IPAH. As an adjunct to the usual testing protocol, this method provides additional information for therapeutic guidance.