European Respiratory Society
Annual Congress 2012

Abstract Number: 673

Publication Number: P962

Abstract Group: 4.3. Pulmonary Circulation and Pulmonary Vascular Disease

Keyword 1: Biomarkers **Keyword 2:** Inflammation **Keyword 3:** Pulmonary hypertension

Title: Human pentraxin 3 (PTX3) as a novel biomarker for the diagnosis of pulmonary arterial hypertension

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Body: Background Although inflammation is an important feature of pulmonary arterial hypertension (PAH), the usefulness of local inflammatory markers as biomarkers for PAH is unknown. In this study, we tested plasma concentrations of human pentraxin 3 (PTX3), a local inflammatory marker, would be a useful biomarker for detecting PAH. Methods Plasma PTX3 concentrations were evaluated in 50 PAH patients (27 with idiopathic PAH, 17 with PAH associated with connective tissue disease (CTD-PAH), and six with congenital heart disease), 100 age and sex-matched healthy controls, and 34 disease-matched CTD patients without PAH. Plasma concentrations of B-type natriuretic peptide (BNP) and C-reactive protein (CRP) were also determined. Results Mean PTX3 levels were significantly higher in all PAH patients than in the healthy controls (4.40±0.37 vs. 1.94±0.09 ng/mL, respectively; $P < 0.001$). Using a threshold level of 2.84 ng/mL, PTX3 yielded a sensitivity of 74.0% and a specificity of 84.0% for the detection of PAH. In CTD-PAH patients, mean PTX3 concentrations were significantly higher than in CTD patients without PAH (5.02±0.69 vs. 2.40±0.14 ng/mL, respectively; $P < 0.001$). There was no significant correlation between plasma levels of PTX3 and BNP or CRP. Receiver operating characteristic (ROC) curves for screening PAH in patients with CTD revealed that PTX3 (area under the ROC curve 0.866) is superior to BNP. Using a PTX3 threshold of 2.85 ng/mL maximized true-positive and false-negative results (sensitivity 94.1%, specificity 73.5%). Conclusion Plasma concentrations of PTX3 are more excellent than BNP in the detection of PAH, especially in patients with CTD.