Plasma Extracellular Matrix and Inflammatory Proteins as Biomarkers for Diagnosis, Differentiation and Risk Assessment in Pulmonary Arterial Hypertension

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Abstract

**Background:** Pulmonary arterial hypertension (PAH) is a rare but serious disease that may lead to right heart failure and premature death. Diagnosis is often delayed due to non-specific symptoms. Extracellular matrix (ECM) and inflammatory proteins are implicated in vascular remodeling and may be involved in PAH development. The discovery of new biomarkers related to PAH development, that could be utilized as new diagnostic tools and for risk stratification, could lead to earlier diagnosis and treatment initiation, and improve patient outcome.

**Aim and Method:** The aim was to investigate plasma levels of matrix metalloproteinases (MMPs), proteoglycans and inflammatory proteins to determine whether they may be used to differentiate PAH patients from other causes of dyspnea. Patients ≥ 18 years under investigation for dyspnea, with baseline right heart catheterizations (RHC) and enrolled in the Lund Cardio Pulmonary Registry, were included. The proteins’ levels were analyzed with proximity extension assays and related to hemodynamic data from the RHCs. In total, 152 patients with PAH (n=48), CTEPH (n=20), HFrEF-PH (n=33), HFpEF-PH (n=36), HF without PH (n=15), and healthy controls (n=20) were evaluated.

**Preliminary results:**

**Paper I** investigated MMPs as biomarkers for differentiation of PAH. Plasma MMP-7 was found to be higher in PAH compared to controls (P < 0.0001) and lower than the other disease groups (P < 0.0081). MMP-7 may be used to identify PH and differentiate patients with PAH from healthy controls, HF and other causes of PH.

**Paper II** investigated proteoglycans and inflammatory proteins as biomarkers for differentiation of PAH. Prolargin was higher in patients with PAH than in healthy controls (P < 0.003), but lower than in the other studied disease groups (P < 0.001). Prolargin may be used for differentiation of PAH. Furthermore, prolargin correlated with mean right atrial pressure, NT-proBNP and cardiac index, implicating that it may also be a marker of impaired heart function.

**Significance:** The results suggest that MMP-7 and prolargin are two potential future biomarker candidates that could be included in a multi-marker panel to enable earlier PAH diagnosis and treatment initiation, to improve outcome for patients with PAH.

**Publications**

**Accepted:**


Submitted:


**Other co-authorship papers not included in the present thesis**
