Novel potential diagnostic targets revealed by plasma proteomic analysis in chronic thromboembolic pulmonary hypertension

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Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is associated with poor outcome if untreated, although it is a curable form of pulmonary hypertension (PH). Successful treatment requires an optimized diagnostic work-up.

Purpose: The aim of this study was to identify non-invasive biomarkers that might serve as new diagnostic parameters in the multifaceted pathophysiology of CTEPH.

Methods: The biomarker profile of 64 CTEPH patients who underwent balloon pulmonary angioplasty (BPA) was analyzed prior to and after therapy and compared with that of a healthy control group (CG1, n=25) at baseline. Proteomes were analyzed by semiquantitative screening based on a proximity extension assay of three high-throughput, multiplex immunoassay panels. Serum levels of a subset of biomarkers identified in the screening were additionally measured by immunochemical methods.

Results: Fifty protein biomarkers were found to differ between CTEPH patients and CG1. Eight biomarkers changed significantly after therapy. The overlap of these two groups revealed six targets that were all upregulated in CTEPH at baseline and modifiable by treatment. In this group of biomarkers, the levels of DCN (decorin), HGF (hepatocyte growth factor), BNP (B-type natriuretic peptide), and PAPP-A (papalysin-1) decreased after therapy, whereas SPON-1 (spondin-1) and MEPE (matrix extracellular phosphoglycoprotein) further increased at follow-up. The differences in these biomarkers in CTEPH as well as the dynamics after therapy were confirmed and quantified in enzyme-linked immunosorbent assays.

Conclusions: This study identified 6 biomarkers that might serve as new diagnostic parameters or constitute new therapeutic targets in CTEPH. Further prospective studies will be necessary to determine the specific pathophysiological role of each marker.