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Targeted proteomics of right heart adaptation to pulmonary arterial hypertension

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High plasma HGF levels are associated with right heart maladaptive phenotype and prognosis in PAH. HGF and c-Met RV expression are both increased. Assessing plasma HGF levels might identify patients who warrant closer follow-up and intensified therapy. https://bit.ly/3djiy9O

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ABSTRACT No prior proteomic screening study has centred on the right ventricle (RV) in pulmonary arterial hypertension (PAH). This study investigates the circulating proteomic profile associated with right heart maladaptive phenotype (RHMP) in PAH.

Plasma proteomic profiling was performed using multiplex immunoassay in 121 (discovery cohort) and 76 (validation cohort) PAH patients. The association between proteomic markers and RHMP, defined by the Mayo right heart score (combining RV strain, New York Heart Association (NYHA) class and N-terminal pro-brain natriuretic peptide (NT-proBNP)) and Stanford score (RV end-systolic remodelling index, NYHA class and NT-proBNP), was assessed by partial least squares regression. Biomarker expression was measured in RV samples from PAH patients and controls, and pulmonary artery banding (PAB) mice.

High levels of hepatocyte growth factor (HGF), stem cell growth factor-β, nerve growth factor and stromal derived factor-1 were associated with worse Mayo and Stanford scores independently from pulmonary resistance or pressure in both cohorts (the validation cohort had more severe disease features: lower cardiac index and higher NT-proBNP). In both cohorts, HGF added value to the REVEAL score in the prediction of death, transplant or hospitalisation at 3 years. RV expression levels of HGF and its receptor c-Met were higher in end-stage PAH patients than controls, and in PAB mice than shams.

High plasma HGF levels are associated with RHMP and predictive of 3-year clinical worsening. Both HGF and c-Met RV expression levels are increased in PAH. Assessing plasma HGF levels might identify patients at risk of heart failure who warrant closer follow-up and intensified therapy.