Biomarker correlates of coronary microvascular dysfunction and diastolic dysfunction in heart failure with preserved ejection fraction

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Topic(s):
Heart Failure with Preserved Ejection Fraction

Citation:
Background. Limited data is available on the pathophysiological mechanisms and the role of underlying coronary microvascular (CMD) in heart failure with preserved ejection fraction (HFpEF). Therefore, we studied biomarker profiles associated with CMD and associations between left ventricular systolic and diastolic dysfunction and structural derangements in HFpEF.

Methods. We measured 268 biomarkers from different pathophysiological domains (e.g. inflammation, oxidative stress) in 192 patients with stable HFpEF from the prospective PROMIS-HFpEF study. Coronary flow reserve (CFR) was measured with adenosine stress transthoracic Doppler echocardiography. Elastic net regression analyses combined with network and pathway overrepresentation analyses were used to identify key pathophysiological biomarkers and mechanisms associated with CFR as well as global longitudinal strain (GLS), lateral E’ and left atrial volume indexed to body surface area (LAVi).

Results. In total, 11 biomarkers were significantly associated with CFR with the strongest predictors being N-terminal pro B-type natriuretic peptide (NT-proBNP), growth differentiation factor 15 (GDF15), insulin-like growth factor binding protein 1 (IGFBP1) and surfactant protein D (PSPD). Only NT-proBNP was significantly associated with both CFR, LAVi, lateral E’ and GLS (P <0.001 for all). Network analyses showed that Pappalysin-1 (PAPPA) was an important hub (Figure A). Insulin-like growth factor receptor pathways and T-cell migration were most strongly associated with CFR (Figure B) in pathway overrepresentation analyses.

Conclusions. In HFpEF, CMD is associated with a unique biomarker profile, related to T-cell migration and insulin-like growth factor receptor signaling. These data highlight IGF signaling and immune cell trafficking as distinct pathophysiological correlates of CMD in HFpEF.
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