A Novel Lipidomics Approach to Predicting Pulmonary Hypertension in Human Heart Failure

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Pulmonary hypertension (PH) in heart failure with preserved ejection fraction (HFpEF) is associated with high morbidity and mortality; however, the pathophysiology of disease is unknown. Polyunsaturated Fatty Acid (PUFA) metabolites play a vital role in cardiovascular health by regulating balance between anti-inflammation and pro-resolution processes. An imbalance of these metabolites can lead to PH. We hypothesize that a PUFA-derived mediator score can be created using lipidomics analysis to accurately predict PH in patients with HFpEF. Pulmonary venous and arterial serum samples were collected during right heart catheterization from 88 HFpEF patients without PH (control, n=40), HFpEF with isolated postcapillary PH (pc-PH, n=30), and HFpEF with combined post- and precapillary PH (cpc-PH, n=18). A total of 143 PUFA metabolites were analyzed by mass spectroscopy with Multiple Reaction Monitoring. A series of regression models was conducted to assess which metabolites were predictive of PH. Low arterial 7(S)-Maresin1, a pro-resolution molecule, was significantly more predictive of HFpEF with pc-PH (p=0.0003) and HFpEF with cpc-PH (p=0.004) when compared to control. Low venous 11(12)-EpETrE, an anti-inflammatory molecule, was more predictive of HFpEF with pc-PH (p=0.02) compared to control. Elevated arterial 19(R)- OH PGF2 alpha and 20-OH PGF2 alpha both pro- and anti-inflammatory molecules, were more significant predictors of HFpEF with cpc-PH compared to pc-PH (p=0.006). These findings support the hypothesis that distinct PUFA metabolites play a significant role in mediating PH in HFpEF. Our study introduces a novel lipidomics framework and approach for the diagnostic assessment of PH in patients with HFpEF.

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