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Metabolomic profile of patients with new onset heart failure; more microvascular dysfunction in patients with preserved ejection fraction compared to reduced ejection fraction - the PREFERS Study

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On behalf: PREFERS Study group

Topic(s):
Heart Failure with Preserved Ejection Fraction

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Background: Heart failure with preserved (HFpEF) and reduced (HFrEF) ejection fraction are both associated with metabolic derangements which may have different pathophysiological implications

Purpose: To identify metabolites and pathways differentially altered with the potential to differentiate HFpEF from HFrEF.

Methods: In the PREFERS Stockholm study (Preserved and Reduced Ejection Fraction Epidemiological Regional Study) 121 endogenous plasma metabolites were assessed by targeted mass spectrometry. Partial Least Squares Discriminant Analysis (PLS-DA) was used to identify metabolites differentially altered in new onset HF divided into HFpEF (EF ≥50%, n=46) versus HFrEF (EF<40%, n=75) patients. Multivariable logistic regression was used to assess independent associations between HF group and selected metabolites, including sex, age and eGFR as co-variates.

Results: Compared to HFrEF, HFpEF patients were older; 77 vs 65 years (p<0.001), more often female 54% vs 46% (p=0.004) with hypertension 60% vs 40% (p<0.001) and diabetes 63% vs 37% (p=0.007), and lower NT-proBNP 720 vs 1295 ng/L (p=0.014) and eGFR 63 vs 72 mL/min/1.73 m² (p<0.001).

HFpEF patients had higher levels of hydroxyproline, cysteine, symmetric dimethyl arginine, alanine, kynurenine and acylcarinitines and lower levels of cAMP, lysPC, L-carnitine, arginine, cGMP, serine and lactate (Figure). HFpEF was independently associated with reduced levels of cGMP (OR 0.98 [95% CI: 0.97–0.99; p=0.008]), serine (0.97 [0.95–1.00; 0.047]) and cAMP (0.97 [0.94–0.99; 0.009]).

Conclusions: In new onset HF patients, HFpEF was associated with decreased cGMP, cAMP and serine indicating increased oxidative stress, impaired innate immune function and myocardial hypertrophy. HFpEF patients displayed a distinct metabolic profile reflecting increased endothelial dysfunction, hypoxia, inflammation and myocardial fibrosis pointing towards more involvement of microvascular dysfunction compared to HFrEF.

Figure 1
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Metabolomic profile of patients with new onset heart failure; more microvascular dysfunction in patients with preserved ejection fraction compared to reduced ejection fraction - the PREFERS Study

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Figure 1