15.3.1 - Biomarkers

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Predictive value of both irisin and apelin for heart failure with preserved ejection fraction in type 2 diabetes mellitus patients

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Background: Irisin is skeletal muscle-derived peptide, the expression of which is under close control of peroxisome proliferator-activated receptor-γ co-activator 1α. Apelin is a peptide having positive inotrope ability and acting as an autocrine regulator of cardiac and vascular reparation. Type 2 diabetes mellitus (T2DM) . The aim of the study was to investigate whether serum levels of both irisin and apelin predict HF with preserved ejection fraction (HFpEF) in patients with T2DM.

Methods: One hundred and eight HF patients with T2DM having HFpEF (EF>50%; n=58), HF with mildly reduced ejection fraction (HFmrEF, EF<40%; n=22), HF with reduced ejection fraction (HFrEF, EF<40%; n=28) aged from 41 to 62 years and 20 non-HF patients with T2DM. Healthy control group was consisted of 25 individuals matched with age and sex. All patients gave voluntary written informed consent to participate in the study. We polled at baseline demographic and anthropometric information, data for hemodynamic performances by B-mode echocardiography, Doppler and TDI, and the levels of biomarkers including irisin, apelin, N-terminal pro-brain natriuretic peptide (NT-proBNP) by ELISA.

Results: We found that the levels of irisin were significantly higher in HFpEF patients than in HFrEF individuals, whereas healthy volunteers and T2DM non-HF patients demonstrated lower concentrations of these peptides. On contrary, apelin levels were significantly increased in HF patients mainly with HFrEF. There were not significant differences between the levels of these biomarkers in HFrEF and HFmrEF (P=0.42 for all cases). Using ROC curve we revealed that cut-off points for irisin and apelin that distinguished HFpEF from HFrEF/HFmrEF were (6.50 ng/mL; AUC=0.78; 95% confidence interval [CI] = 6.85 - 10.66 ng/mL and 4.12 ng/mL, AUC=0.72; 95% CI=3.90-5.75 ng/mL, respectively). Then we divided all patients with HF having elevation of NT-proBNP > 750 pmol/mL into three subgroups depending on the biomarkers' levels. Patients from subgroup A had both irisin and apelin levels higher cut-off points, individuals from group B had higher concentration of one of two biomarkers, and patients from subgroup C demonstrated levels of both peptides lower cut-off points. Multivariate logistic regression analysis revealed that discriminative value of irisin and apelin to predict HFpEF in subgroup B (Hazard Ratio [HR]= 2.18; 95% CI=1.26-3.14; P=0.001) were substantially higher compared with subgroups A and C (HR = 1.03; 95% CI=1.00-1.05; P=0.64 and HR = 0.92; 95% CI=0.89-1.01; P=0.62, respectively). Adding irisin and apelin to NT-proBNP as independent variables to the predictive model sufficiently improved discriminative ability of whole model for HFpEF.

In conclusion: We found that multidirectional changes in the levels of irisin and apelin in T2DM patients had better predictive value for HFpEF that simultaneous increase and decrease in the circulating levels of these peptides.