15.3.1 - Biomarkers

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Elevated levels of apelin predict favorable clinical course of heart failure in type 2 diabetes mellitus patients

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Funding Acknowledgements: Type of funding sources: None.

Background: Apelin is a regulatory peptide having positive inotrope and reparative abilities. Type 2 diabetes mellitus (T2DM) is common comorbidity that is associated to occurrence of HF mainly HF with preserved ejection fraction (HFpEF). The discriminative potency of conventional cardiac biomarkers such as natriuretic peptides in HFpEF was found to be sufficiently lower compared to HF with reduced / mildly reduced ejection fraction (HFrEF / HFmrEF). The aim of the study was to investigate whether serum levels of apelin predict HF in patients with T2DM.

Methods: A total of 108 HF patients (left ventricular ejection fraction [LVEF] <60%) with T2DM were prospectively involved in the study. Entire HF population consisted of 58 HFpEF patients and 50 HFmrEF / HFrEF aged from 41 to 62 years. Cardiac hemodynamic performances were obtained by B-mode echocardiography, Doppler and TDI. The levels of apelin, N-terminal pro-brain natriuretic peptide (NT-proBNP), high sensitive troponin T (hs-TnT) were measured by ELISA. Combined end-point for the study were defined as all-cause death and any non-fatal cardiovascular event or HF hospitalization during 52 weeks.

Results: The combined end-point occurred in 37 patients (34.3%) from entire population. The levels of apelin in patients who had the combined end-point were significantly lower (3.55 ng/mL, 95% confidence interval [CI]=3.12-3.95 ng/mL) compared with those who did not meet it (5.60 ng/mL; 95% CI = 4.10-7.10 ng/mL; P=0.001). ROC curve revealed that the best-balanced cut-off point for apelin levels, which predicted combined end-point occurrence, was 3.88 ng/mL (AUC=0.82; P=0.001). Cox regression showed that apelin levels > 3.55 ng/mL (Odds Ratio [OR]= 2.02; 95% CI=1.14-3.25; P=0.001), LVEF< 49% (OR=1.48; 95% CI=1.22-1.68, P = 0.001), NT-proBNP > 785 ng/mL (OR =2.08; 95% CI = 1.03–4.12; P = 0.001), global longitudinal strain < -8.6% (OR =2.02; 95% CI = 1.09–3.10; P = 0.001), hs-TnT > 0.4 ng/mL (OR=1.98; 95% CI=1.10-2.93; P=0.001), estimated glomerular filtration rate <60 mL/min/1.73 m2 (OR=1.46; 95% CI=1.09-2.55; P=0.001) and history of atrial fibrillation (OR=1.14; 95% CI=1.02-1.80; P=0.001) predicted the combined end-point. After adjustment for HFpEF, apelin levels > 3.55 ng/mL (OR=2.03; 95% CI=1.10-3.20; P=0.001) and NT-proBNP > 785 ng/mL (OR =2.10; 95% CI = 1.05–3.80; P = 0.001) remain independent predictors for the combined end-point. The addition of apelin to the ABC model (NT-proBNP > 785 ng/mL) improved the relative integrated discrimination indices by 10.5% and net-reclassification improvement for 11.5% for combined end-point. Kaplan – Meier curve showed that patients having the levels of apelin >3.55 ng/mL demonstrated better clinical course of HF compared with those who had lower apelin levels (log rank test p=0.001).

In conclusion: We found that apelin levels >3.55 ng/mL regardless of NT-proBNP had positive discriminative ability for clinical course of HF in T2DM patients.