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Endothelial progenitor cells and apoptotic endothelial cell-derived microparticles as biomarker of heart failure phenotypes

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Background: Chronic heart failure (HF) remains a leading cause of cardiovascular (CV) mortality and morbidity worldwide.

Aim: The aim of the study was to investigate whether the pattern of angiogenic endothelial progenitor cells (EPCs) and apoptotic endothelial cell-derived microparticles (EMPs) would be able to differentiate HF with reduced (HFrEF) and preserved (HFpEF) ejection fraction.

Methods: 164 chronic HF subjects met inclusion criteria. Patients with global left ventricular ejection fraction ≥50% were categorized as the HFpEF group (n=79) and those with ≤45% as the HFrEF group (n=85). Therefore, to compare the circulating levels of biological markers, 35 control subjects without HF were included in the study. All control individuals were age- and sex-matched chronic HF patients. The serum level of biomarkers was measured at baseline. The flow cytometric technique was used for predictably distinguishing circulating cell subsets depending on expression of CD45, CD34, CD14, Tie-2, and CD309 antigens and determining endothelial cell-derived micro particles. CD31+/annexin V+ was defined as apoptotic endothelial cell-derived MPs, MPs labeled for CD105+ or CD62E+ were determined as MPs produced due to activation of endothelial cells.

Results: In multivariate logistic regression model T2DM (R2=0.26; P=0.001), obesity (R2=0.22; P=0.001), previous MI (R2=0.17; P=0.012), galectin-3 (R2=0.67; P=0.012), CD31+/annexin V+ EMPs (R2=0.11; P=0.001), NT-proBNP (R2=0.11; P=0.046), CD14+CD309+ cells (R2=0.058; P=0.001), and CD14+CD309+ Tie-2+ cells (R2=0.044; P=0.028) were found as independent predictors of HFpEF. Using multivariate Cox-regression analysis adjusted etiology (previous myocardial infarction), cardiovascular risk factors (obesity, type 2 diabetes mellitus), we found that NT-proBNP (OR 1.08; 95% CI=1.03–1.12; P=0.001) and CD31+/annexin V+EMPs to CD14+CD309+ cells ratio (OR 1.06; 95% CI=1.02–1.11; P=0.02) were independent predictors for HFpEF.

Conclusion: We found that CD31+/annexin V+EMPs to CD14+CD309+ cells ratio added to NT-proBNP, clinical data and cardiovascular risk factors has exhibited the best discriminate value and higher reliability to predict HFpEF compared with NT-proBNP and clinical data/cardiovascular risk factors alone.

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