biomarkers are reported by Figure 2. Multivariate logistic regression revealed that use of SGLT2i (OP = 0.92; p = 0.048), baseline serum levels of irisin ≤ 4.50 ng/ml (OR = 1.51; p = 0.001) and adropin ≤ 2.10 ng/ml (OR = 1.15; p = 0.001) along with and a ≤ 15% increase in the levels of these biomarkers (OR = 1.60; p = 0.001) and ≤ 6% (OR = 1.21; p = 0.001), respectively, remained an independent predictor for composite kidney endpoint. We noticed that irisin ≤ 4.50 ng/ml at baseline and a ≤ 15% increase in irisin serum levels added more valuable predictive information than the reference variable. However, the combination of irisin ≤ 4.50 ng/ml at baseline and ≤ 15% increase in irisin serum levels (area under curve = 0.91; 95% confidence interval = 0.87-0.95) improved the discriminative value of each biomarker alone. Conclusion: We suggest that low levels of irisin and its inadequate increase during administration of SGLT2i are promising predictors for unfavorable kidney outcome among patients with T2DM and concomitant HF.

Heart Failure – Chronic Heart Failure, Diagnostic Methods, Biomarkers

Circulating levels of erythrocytes-derived vesicles related to poor glycaemia control in heart failure patients with type 2 diabetes mellitus

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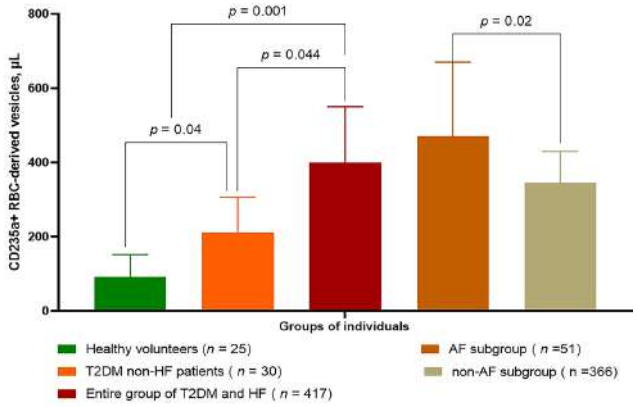
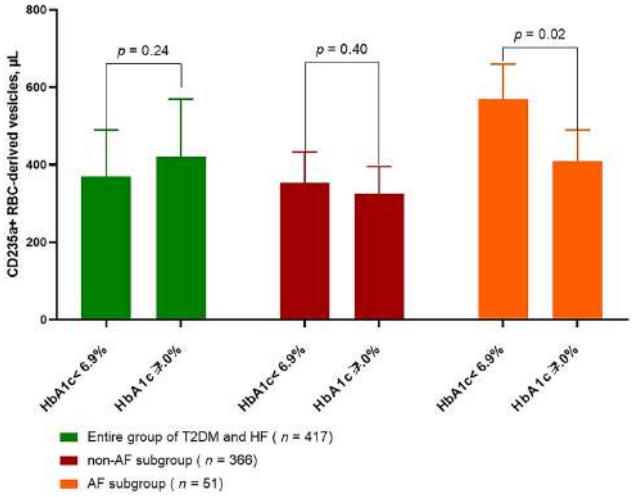
Background: Previous studies demonstrated that insulin resistance, hyperglycemia contribute to the development of a pro-thrombotic state characterized by increased platelet activation, activation of coagulation cascade and elevated number of extracellular vesicles (EVs) in type 2 diabetes mellitus (T2DM) patients. There is a less known impact of glycaemia control in T2DM patients with concomitant heart failure (HF) and atrial fibrillation (AF) on a number of erythrocytes-derived EVs. The aim of the study was to elucidate whether glucose control in T2DM patients with HF and AF affect a circulating number of erythrocytes-derived EVs.
Methods: The entire patient population composes of 417 patients (231 male, 55.4% and 186 female, 44.6%) with average age of 53 years as well as 25 healthy volunteers and 30 T2DM non-HF individuals. As inclusion, age ≥ 18 years, T2DM, established HF, and written consent to participate in the study was used. Patients after successful ablation procedure (mainly radiofrequency ablation) were included in the group non-AF in 6 weeks after procedure if cardiac rhythm is sinus. All patients were divided into two groups depending on criteria of poor glycemic control (HbA1c < 6.9% and ≥7.0%, respectively). Hemodynamics features, conventional biochemistry parameters and EVs measure were performed at the baseline. Flow cytometry was performed according to conventional protocol with FMO standards to detect and measure EVs.
Results: Circulating levels of CD235a+ PS+ erythrocytes-derived vesicles differed amongst T2DM patients depending on HF presentation when compared with healthy volunteers (Figure 1). Figure 2 illustrated the differences in circulating amount of CD235a+ PS+ RBC-derived vesicles in AF and non-AF patients with T2DM and HF depending on glycaemia control. There were significantly lower levels of CD235a+ PS+ RBC-derived vesicles were detected in those with HbA1c < 6.9% than in patients with HbA1c ≥ 7.0%. To note, there were no significant differences in circulating amount of CD235a+ PS+ erythrocytes-derived vesicles between patients in entire cohort (p = 0.24) and in non-AF sub-cohort (p = 0.40) with HbA1c < 6.9% and HbA1c ≥ 7.0%, respectively. The Receive Operation Characteristics curve analysis revealed that the well-balanced cut-off point for circulating amount of CD235a+ PS+ erythrocytes-derived vesicles (HbA1c ≥ 7.0% versus HbA1c < 6.9%) were 545 particles in μL (area under curve = 0.91, sensitivity = 74.2%, specificity = 90.3%; p = 0.0001). Multivariate linear regression yielded that NT-proBNP (OR = 1.07; 95% CI = 1.02-1.10, p = 0.04) and CD235a+ PS+ erythrocytes-derived vesicles ≥ 545 particles in μL (OR = 1.06; 95% CI = 1.01-1.11, p = 0.044) remained independent predictors for HbA1c ≥ 7.0%.
Conclusion: Poor glycaemia control is associated with elevated levels of CD235a+ PS+ EVs, which were found to be independent predictor for AF presentation in T2DM patients with HF.



Circulating levels of EVs



EVs in AF and non-AF patients

Heart Failure – Chronic Heart Failure, Diagnostic Methods, Biomarkers

Novel biomarkers associated with worsening renal function among patients hospitalized for acute heart failure

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Background: Worsening renal function is associated with poor prognosis in patients with heart failure. Osteopontin (OPN) and Matrix extracellular phosphoglycoprotein (MEPE) are both proteins involved in bone mineralization processes and have also been implicated in renal function. Ostepontin has been associated with kidney function markers worsening and a higher risk for adverse outcomes in patients with chronic kidney disease, and MEPE has been shown to promote renal phosphate excretion by influencing FGF23 expression.
Purpose: To explore if MEPE and OPN are associated with worsening renal function in patients with acute heart failure.
Methods: Worsening renal function was defined as an increase in plasma creatinine of >26.5 mmol/L, or 50% higher than the admission concentration within 48 hours of admission. OPN and MEPE were analyzed using a proximity extension assay in 324 patients, of whom 321 had complete data. Logistic regression analyses were performed to explore the associations between MEPE, OPN and worsening renal function. The model was adjusted for age, sex, systolic blood pressure, NT-proBNP, NYHA-classification, prevalent diabetes and treatment with diuretics and RAAS-blockade. Correlations were assessed using Spearman's correlations.
Results: The study population characteristics are presented in Table 1. Mean age was 74.5 years (±12.1) and 32.3% were women. In the fully adjusted logistic regression analyses MEPE and OPN were significantly associated with worsening renal function (OR 2.89; 95%CI 1.56-5.34; p < 0.001, and OR 1.91; 95%CI 1.11-3.31; p = 0.020, respectively). Furthermore, both MEPE and OPN were significantly correlated with each other (Spearman rho 0.52, p < 0.001). MEPE was correlated with Cystatin C (Spearman rho 0.52; p < 0.001), and with estimated glomerular filtration rate (eGFR) (Spearman rho -0.55; p < 0.001). OPN was also correlated with Cystatin C (Spearman rho 0.59; p < 0.001) and with eGFR (Spearman rho -0.57; p < 0.001).