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FGF23 but not soluble klotho is associated with diasease severity and progression in chronic heart failure

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Introduction: Elevated levels of the phosphatonin fibroblast growth factor 23 (FGF23) have been linked with cardiac remodeling and the advent and progression of heart failure (HF). In the kidney Klotho acts as essential coreceptor of FGF23. By contrast, circulating soluble Klotho (sKlotho), which is cleaved from the Klotho receptor appears to oppose the detrimental effects of FGF23 on the heart. We aimed to investigate the association of sKlotho with disease severity and progression in chronic HF.

Methods: Serum levels of C-term FGF23 (Ct-FGF23) and soluble Klotho (sKlotho) concentrations were measured in 287 patients with non-ischemic heart failure (age 48 ± 15 years; 69 % male; NYHA Class I 24.7 %, NYHA Class II 40.8 %, NYHA Class III/IV 34.5 %; LV-EF 32 % [IQR 21–47]; NT-proBNP 1180 ng/l [IQR 440–3128]).

Results: Median levels of Ct-FGF23 and sKlotho were 21.8 RU/ml (IQR 12.1–45.7) and 380 pg/ml (IQR 301–529), respectively. A dose-response relationship was found between median Ct-FGF23 levels and increasing NYHA class (I: 16.5 RU/ml, II: 20 RU/ml, III/IV: 38.4 RU/ml; $p < 0.001$) but not so for sKlotho (I: 380 pg/ml, II: 351 pg/ml, III/IV: 417 pg/ml; $p = 0.17$). Also, Ct-FGF23 but not sKlotho correlated with NTproBNP ($r = 0.307$, $p < 0.001$ and $r = -0.083$, $p = 0.176$).

No relationship was found for sKlotho with the combined endpoint of death or heart transplantation (hazard ratio 0.76 [0.45–1.2]; $p = 0.299$) wheras in tertile-based sex-stratified analysis, individuals in the third Ct-FGF23 tertile were 2.7 times (95 %CI 1.2–6.0; $p = 0.015$) more likely to reach an endpoint than were individuals in the first tertile.

Conclusions: In contrast to Ct-FGF23 soluble Klotho is not associated with disease severity and progression in chronic HF. Protective effects of sKlotho on the diseased heart may thus be mediated by local rather than systemic mechanisms.

V-3

Correlation between clinical response to cardiac resynchronization therapy and changes in frequency spectra of the first heart sound recorded with an endocardial acceleration sensor

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Introduction: There is an ongoing search for early prognostic markers in patients with cardiac resynchronization therapy (CRT). We initiated this study to prove our hypothesis that dyssynchrony of the left ventricle leads to a wide frequency distribution in the endocardial acceleration signal (EAS) of the first heart sound recorded with a sensor in the tip of the right atrial lead in CRT devices and that the frequency distribution becomes narrower during clinically successfull CRT.

Methods: Fourteen patients with chronic heart failure (LVEF ≤ 35 %, NYHA II–IV, QRS duration ≥ 130 ms in LBBB and ≥ 150 ms in non-LBBB, on stable optimal medical therapy) requiring CRT were enrolled. NYHA class, BNP, ECG, six-minute walk test, Kansas City cardiomyopathy questionaire (KCCQ) and echocardiographic measurements were documented at implantation (IMP), pre-hospital discharge (PHD), at 3 months (3M), at 6 months (6M) and at 12 months (12M) after implantation. The EAS was recorded for at least 3 consecutive cardiac cycles with different stimulation frequencies and different interventricular delays according to a standardized protocol at the same time points. The main frequency components were calculated using a Fourier analysis.

Results: The frequency distribution became significantly narrower (IMP [mean ± SD] 21.4 ± 16.5 Hz; PHD 19.3 ± 16.3 Hz; 3M 10.2 ± 5.0 Hz; 6M 11.4 ± 4.7 Hz; 12M 11.2 ± 4.3 Hz, respectively; IMP vs. 12M, $p < 0.001$) and the power of the main frequencies increased (area under the curve at IMP 19.0 ± 17.8 mW; PHD 24.6 ± 19.9 mW; 3M 33.0 ± 23.9 mW; 6M 23.1 ± 17.0 mW; 12M 33.6 ± 29.2 mW, respectively; IMP vs. 12M, $p < 0.001$) over time. Remarkably, there is a correlation between an improvement in NYHA class, KCCQ score and a narrower frequency distribution combined with an increased power of the main frequencies.

Conclusions: It is possible to determine the synchronicity of the ventricular wall motion during a cardiac cycle by analyzing the frequency distribution of the first heart sound with an EAS system. The observed correlation between a narrower frequency distribution combined with an increased power of the signal may be a marker of a beneficial clinical response to CRT. This method may enable continuous automatic monitoring of the reverse remodeling effect of CRT in the future.

V-4

Features of myocardium remodeling and type of diastolic dysfunction in patients with anemic syndrome on a background of chronic heart failure and chronic kidney disease

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Purpose: To examine the features of the remodeling of the myocardium and estimate the parameters of diastolic dysfunction in patients with anemia of varying severity that developed on the background of chronic heart failure (CHF) and chronic kidney disease (CKD).

Materials and methods: The study involved 90 patients with CHF II-IV FC (NYHA) of ischemic origin (mean age 71.42 ± 8.66 years), with anemia and CKD stage II-III. Causes of CKD were chronic pyelonephritis and diabetic nephropathy. Availability and CKD stages were determined according to the classification of the National Kidney Foundation U.S. (NKF) K/DOQ. Diagnosis of anemia was determined according to the criteria of the Medical Committee of Standards of Hematology (ICST, 1989). Mild anemia was diagnosted in 50 pts, moderate – 25 pts and severe – 12 pts. Types of remodeling were defined by Ganau classification. The nature of transmitral flow was determined by following parameters of left ventricular diastolic function: maximum peak velocity of early transmitral blood flow—E, cm/sec and the maximum speed of atrial systole—A, cm/sec;diastolic ratio—E/A.

Results: In patients with mild anemia, CHF and CKD concentric remodeling (CR) was found in 47 %, concentric hypertrophy (CG) in 53 %. The normal geometry and eccentric hypertrophy (EG) was not found in any patient. In patients with moderate anemia defined by CR in 23 % of patients, CG in 68 % pts and EG in 9 %. Study of the structural myocardial changes in patients with severe anemia showed the presence of EG in the majority of patients-72 %, CG in 28 %, CR was absent. The study of diastolic dysfunction (DD) showed the presence of transmitral flow changes in 20 % of patients, which is specific for pseudonormal type, a violation of relaxation in 80 % of patients. In patients with moderate anemia structural and functional features are characterized by heterogeneity, patients with DD type pseudonormalisation (24 %) prevailed, violation of relaxation was diagnosed in 15 % of pts, 27 % had DD of restrictive type. Patients with severe anemia mostly had restrictive type of DD