VIII. Streszczenie w języku angielskim

Introduction

Despite the continuous development of modern diagnostic and therapeutic methods, heart failure (HF) remains a major challenge for healthcare systems in Poland and worldwide and is widely recognized as the epidemic of the 21st century. This fact encourages the constant search for new cardiovascular risk factors and markers that may have potential preventive and therapeutic significance.

Aim of the study

The main objective of the study was to evaluate the serum concentrations of Klotho protein and fibroblast growth factor 23 (FGF-23) in patients diagnosed with HF, taking into account the severity and etiology of the disease. An additional aim was to determine possible correlations between the concentrations of Klotho protein and FGF-23 and selected clinical, laboratory, and echocardiographic parameters, as well as the extent of coronary atherosclerosis. The study also analyzed the overall mortality of the patients during a long-term observation period.

Materials and methods

The study included 250 patients (192 males and 58 females) diagnosed with HF, hospitalized at the Department of Invasive Cardiology of the University Clinical Hospital in Białystok between January and July 2016. The control group consisted of 20 patients (16 males and 4 females) who did not meet the criteria for HF diagnosis and exclusion criteria from the study. The median age in the study group was 71 years. Both groups were predominantly male, accounting for 76.8% and 80% of the population, respectively. Depending on the severity of HF based on the left ventricular ejection fraction, the study group was divided into three subgroups (HFpEF, HFmrEF, HFrEF) according to the ESC recommendations for the diagnosis and treatment of HF. Depending on the etiology of HF, the study group was also divided into patients with significant coronary artery disease, valvular heart disease, and dilated cardiomyopathy. The concentrations of Klotho protein and FGF-23 in the serum were determined using the ELISA immunoenzymatic method. A

detailed analysis of selected clinical, echocardiographic, and laboratory parameters was performed in the study group and the control group. The results of measurements and analyzed parameters were subjected to statistical analysis. Overall and cardiovascular mortality was assessed as of December 31, 2022. The data were obtained from the database of the Data Sharing and Certification Department of the Ministry of Digitization in Warsaw.

Results

The median concentration of FGF-23 in the study group was 83.64 RU/mL, which was higher than in the control group ($p=0.002$). The median concentration of Klotho protein in the study group was 629.25 pg/mL, which did not differ significantly from the control group ($p=0.32$). The concentrations of FGF-23 and Klotho protein did not depend on the severity and etiology of HF or the extent of coronary atherosclerosis. A positive correlation was found between FGF-23 concentration and clinical severity based on the NYHA scale ($R=0.335$, $p<0.001$), BNP concentration ($R=0.401$, $p<0.0001$), as well as phosphorus ($R=0.279$, $p<0.0001$) and creatinine ($R=0.368$, $p<0.0001$) levels. Furthermore, the concentration of FGF-23 negatively correlated with the left ventricular ejection fraction (LVEF) ($R=-0.160$, $p=0.011$), glomerular filtration rate (GFR) ($R=-0.454$, $p<0.0001$), and serum Klotho protein levels ($R=-0.176$, $p=0.005$).

During long-term follow-up, a total of 69 patients (33.33%) from the study group died, with over two-thirds of the cases being cardiovascular deaths. It was demonstrated that patients with the highest levels of FGF-23 in the serum had a higher risk of mortality (HR=8.864; 95% CI: 3.094-25.393; $p<0.0001$), which persisted even after adjusting for age, LVEF, and GFR (HR=7.150; 95% CI: 2.438-20.974; $p<0.0001$). The study also found a high discriminatory ability of FGF-23 serum levels (AUC=0.752; 95% CI: 0.672-0.832; $p<0.0001$), with the highest value observed in patients with valvular heart disease (AUC=0.846; 95% CI: 0.703-0.989; $p<0.0001$).

Conclusions

1. In contrast to Klotho protein levels, FGF-23 levels show significant differences in the studied group of HF patients compared to the reference group without heart failure.

2. Serum FGF-23 levels correlate with the degree of left ventricular systolic dysfunction but are independent of the etiology of heart failure and the extent of atherosclerotic changes in coronary arteries.

3. FGF-23 levels increase proportionally with the severity of clinical status, correlating with the severity of HF assessed by the NYHA scale and BNP levels. These findings suggest the potential utility of measuring FGF-23 levels in daily clinical practice.

4. Fibroblast growth factor 23, rather than Klotho protein, is a strong independent predictor of death from cardiovascular causes in patients with HF.

5. Serum FGF-23 levels exhibit a high discriminatory ability, especially in patients with valvular heart disease, potentially aiding in the identification of patients at particularly high risk of serious cardiovascular events.