

## **SUMMARY**

### **Introduction**

Heart Failure (HF) is diagnosed in approximately 26 million people worldwide. HF is a clinical syndrome consisting of cardinal symptoms that may be accompanied by signs with progressive abnormalities in a heart structure and/or function. The special group of patients with HF are those with systolic dyssynchrony and the symptomatic heart failure with reduced left ventricular ejection fraction. The dynamic development of invasive electrotherapy methods, such as implantation of: the cardiac resynchronization therapy with defibrillator (CRT-D), the cardiac resynchronization therapy pacemaker (CRT-P), together with the optimal medical treatment, gives the possibility to improve the quality and length of life of those patients. The increase in a cardiac output (CO-cardiac output) achieved with CRT, by optimizing the synchronization of myocardial contraction, correlates positively with a perfusion of other organs. Moreover, the low-resistance renal circulation, receiving approximately  $\frac{1}{4}$  of CO, requires special attention. The need for an improved monitoring of the patient status in ambulatory setting requires the use of newer and more precise biomarkers.

### **Aim of the study**

The aim of the study was to prospectively evaluate the effect of cardiac resynchronization therapy on the kidney function. The scope of the research were patients after CRT implantation at 12-month follow-up with the assessment of cardiac function and survival. The classical diagnostic methods were utilized along with biomarkers. The assumption was done that the improvement in left ventricular systolic function correlates positively with an increase in the organ perfusion.

### **Materials and methods**

The study covered the population of 89 people. The patients had been diagnosed with a heart failure that met the criteria for implantation of a CRT-D or CRT-P, or upgrade of an existing pacemaker to resynchronization therapy (according to the ESC 2013/2016 Guidelines). During the 12-month follow-up 14 patients died and 15 were disqualified from the study for other reasons. After 12 months the detailed evaluation with the use of laboratory and imaging methods was performed.

As the result, 74 patients were analyzed for a baseline assessment of the cardiac and renal function parameters such as: LVEF (left ventricular ejection fraction), IVCmax (maximum inferior vena cava width), NT-proBNP (the N-terminal pro-B-type natriuretic peptide), sCr (serum creatinine), UACR (urine albumin to creatinine ratio), eGFR CKD-EPI (glomerular filtration rate according to the eGFR CKD-EPI formula), and UNCR (urine neutrophil to creatinine ratio).

Following the clinical severity by New York Heart Association related to the classification of heart failure and etiology of HF ischemic and nonischemic, patients have been divided into subgroups. In addition to that, mortality has been analyzed by the type of implanted device (CRT-D, CRT-P), electrodes (bipolar or quadripolar), clinical stage of HF according to NYHA, comorbidity of T2DM and etiology of HF. 12 months, after the implantation procedure standard laboratory (blood count, sCr, eGFR-CKD-EPI, C-reactive protein) and NYHA, LVEF, IVCmax, NT-proBNP, UACR, UNCR, NGAL parameters have been compared to the initial testing results in a population of 60 patients.

## **Results**

1. There was no correlation in the incidence of death between the type of the device (CRT-D vs CRT-P), type of left ventricular electrodes, etiology of heart failure, or coexistence of T2DM. Patients who died before the end of the study had been hospitalized for HF decompensation nearly two and a half times more frequent comparing to patients examined one year after implantation and survived.
2. The evaluation prior to CRT implantation indicated that ischemic etiology of heart failure is associated with more severe kidney disease comparing to nonischemic. This finding is based on statistically significant results of parameters such as: sCr, eGFR-CKD-EPI.

3. Clinical severity of the disease regarding NYHA classes (I-IV amb.) correlated positively with the severity of kidney failure related to parameters UNCR and IVCmax.
4. Comparing initial examination vs 12 month period after implantation in the population of 60 people, the analysis of following parameters such as: QRS complex width, NYHA class, LVEF and NT-proBNP, IVCmax width, resulted with the statistically significant change within the studied group of patients. It gives us evidence of good response to the resynchronization therapy. In addition to the kidney function testing there was a statistically significant decrease in UACR in the overall study population. In the subdivision into ischemic and nonischemic etiologies of HF, a statistically significant decrease in UACR was demonstrated only in the nonischemic etiology population of heart failure ( $p=0,0001$ ). Furthermore, the statistically significant improvement in LVEF and decrease in NT-proBNP was found in both subgroups after 12 months.
5. In the population of patients without T2DM a significant decrease in UNCR was observed after 12 months comparing initial laboratory results.

## **Conclusions**

1. No influence on the death incidence in presented population has been found within the type of the device, left ventricular electrodes, etiology of heart failure, or coexistence of T2DM.
2. Parameters such as: IVCmax or UNCR can be used to assess the severity of the cardiorenal syndrome between NYHA classes, but sCr, eGFR-CKD-EPI can concern HF etiology. Furthermore, the obtained results have prognostic value in these groups of patients.
3. Based on the UNCR results, patients without T2DM and in lower NYHA class indicated less glomerular damage within the distal tubule and better expressed regenerative processes. Further studies are needed to confirm the clinical efficacy of UNCR for diagnostic purposes in HF patients.
4. The results obtained in the evaluation of the change in IVCmax width demonstrated, that this test is a readily available, inexpensive and simple indirect marker of cardiovascular compensation. Therefore, the usage of this parameter as a prognostic marker in chronic type II cardiorenal syndrome should be considered.

5. Current study demonstrates the effect of cardiac resynchronization therapy on the reduction of albuminuria, that is associated with a kidney function improvement. Moreover, it can be concerned as more sensitive prognostic marker, than another cardiac and renal laboratory and imaging findings in the CRS type II.
6. Determination of UACR from morning urine sample, particularly in a group of patients with heart failure of nonischemic etiology (independently of eGFR laboratory test), allows to more accurate assessment of the kidney function in a population of patients with type II cardiorenal syndrome and implanted CRT.