#### SUMMARY

#### 1. Introduction

Identifying, correcting and stabilizing the causes of heart failure (HF) together with standard recommended HF treatment improve prognosis and the quality of life (QoL) in HF patients. HF is commonly accompanied by arrhythmia which seems to be an important contributor to HF worsening, increased mortality, hospitalization and morbidity rates, hence if possible it should always be adequately corrected. Arrhythmia induced cardiomyopathy (AIC) is a form of dilated cardiomyopathy, which is partially or completely reversible once the underlying arrhythmia is controlled. It is very important to include AIC in differential diagnosis in patient with HF symptoms, especially in those with a previous diagnosis of structural heart disease (SHD). There are two types of AIC. Type I is diagnosed when arrhythmia is the only cause of heart failure and a successful treatment leads to a complete recovery of heart muscle. Type II of AIC is known as arrhythmia-mediated cardiomyopathy (AMC) and is present in patients with underlying SHD. In these patients a new onset of arrhythmia leads to deterioration of previously impaired left ventricular (LV) function and an increase in HF symptoms. Successful arrhythmia control leads to improvement in health-related quality of life (HRQoL) and HF symptoms in patients with SHD. Worsening of HF symptoms associated with arrhythmia negatively influence HRQoL. Elimination of arrhythmia in patients with SHD can also lead to symptoms improvement measured in New York Heart Association (NYHA) functional classification and to the increase of left ventricular ejection fraction (LVEF). The structural heart disease (SHD) is defined as any structural abnormalities found in imaging studies i.e. echocardiography or cardiovascular magnetic resonance (CMR).

The HRQoL is an important factor influencing daily functioning of patients with chronic HF. Patient care, an effective treatment of potential reversible causes of HF exacerbation significantly affect daily activity of the patient in society. Many studies have shown improvement of the HRQoL in patients undergoing invasive procedures, while there are limited data on the effects of ablation procedures in patients with structural heart disease whose conservative treatment has been ineffective.

# 2. Aim of the study

The main aims of the study were to evaluate the impact of catheter ablation of persistent arrhythmia on HRQoL, biochemical and clinical parameters of HF in patients with SHD and AMC.

## 3. Material and methods

The study group comprised consecutive patients with HF symptoms referred for arrhythmia ablation in the II Department of Heart Arrhythmia in the National Institute of Cardiology between October 2018 and July 2020. Patients were on optimal medical treatment of HF. Before ablation procedure all patients were stratified according to the NYHA functional classification and underwent a clinical assessment that included: a detailed medical history, which excluded secondary causes of arrhythmia exacerbation and confirmed ineffectiveness of drug therapy, 12-lead electrocardiogram (ECG), chest radiography, TTE, 24-hour baseline ECG Holter monitoring. HRQoL was analyzed using generic EuroQol Research Foundation EQ-5D-3L score and a questionnaire specific for HF Minnesota Living With Heart Failure Questionnaire (MLHFQ). Ablation procedures were performed by experienced physicians certified either by European Heart Rhythm Association (EHRA) or Heart Rhythm Section of the Polish Society of Cardiology. Indications for ablation procedure were persistent supraventricular arrhythmia or ventricular arrhythmia with PVC burden of minimum 10%/day, with symptoms of HF and clinical suspicion of arrhythmic component of HF worsening.

### Follow-up

Patients were followed in out-patient clinic. Follow-up visits were scheduled 3 and 6 months after the ablation. Patients were asked to complete HRQoL questionnaires after 3 and 6 months. Transthoracic echocardiography, 24-hour ECG Holter were repeated after 6 months. Blood samples for biomarkers analysis were taken after 6 months after ablation procedure. During follow-up visits clinical symptoms, 12 lead ECG, and 24-hour Holter monitoring, interrogation of implantable cardiac devices if feasible were assessed. Successful ablation of ventricular arrhythmias was defined as the reduction of PVC burden by minimum of 80%. Successful ablation of supraventricular arrhythmias was defined as the lack of sustained arrhythmia or episodes lasting longer than 30 s in 24 hours ECG Holter monitoring or device interrogation.

#### 4. Results

40 consecutive patients who met inclusion criteria were prospectively enrolled. Finally 35 patients finished 6 months follow-up period and were included in the final analysis. A midterm success rate of catheter ablation was 86 % (30 out of 35 procedures).

## 4.1. Health-related quality of life

A significant improvement vs baseline was observed after three and six months both in EQ-5D-3L and MLHFQ (p<0.001 in all variables). There was no relevant differences between measured values at 3 and 6 months. Patients who underwent successful catheter ablation had a significant improvement in HRQoL: MLHFQ (median (Q1;Q3): -24 (-36;-12), p<0.001), EQ5D-3L Score (mean ( $\pm$ SD): 21.8  $\pm$  16.8), p<0.001); EQ5D-3L index (median (Q1;Q3): 0.09 (0.05;0.18), p<0.001). At 6 months, 32 out of 35 (91%) patients reported improvement of  $\geq$  5 points on MLHFQ. There was also some HRQoL improvement in the failed ablation cohort but it was less pronounced.

### 4.2. Echocardiography

In patients after successful ablation procedure there was increase in left ventricular ejection fraction (LVEF) by (mean ( $\pm$  SD)): 9.8 %  $\pm$  5.9 % (p<0.001). Four patients (11.4 % of patients, three with persistent AF and one with typical atrial flutter) improved their LVEF above 35%. Those patients did not meet the criteria for implantable cardioverter-defibrillator (ICD) in the primary prevention of sudden cardiac death (SCD) anymore.

# 4.3. Clinical function and biomarkers of heart failure

Successful ablation procedure lead to relevant decrease in overload and injury biomarkers: NT-proBNP (median (Q1;Q3): -414pg/ml (-1397;-318), p<0.001), hsTnT (median (Q1;Q3): -2.27ng/ml (-8.52;0.55), p<0.001), but not in fibrosis biomarkers (median (Q1;Q3), sST2: 2.20ng/ml (-5.4;4.3), p=0.741, MMP-9: 34ng/ml (-376;283), p=0.881, TIMP-1: 11.1ng/ml; (-17.1;31.9), p=0.215). In patients after successful ablation procedure there was significant in clinical outcomes measured in NYHA functional class. In 25 patients (83,3%) there was increase by minimum one functional class. No improvements in the NYHA functional class were seen in all 5 patients who underwent unsuccessful catheter ablation.

#### 5. Conclusions

The main findings were:

- 1) Early and sustained improvement in HRQoL during 6-month follow-up in patients after catheter ablation,
- 2) Relevant decrease in NT-proBNP and hsTnT, but no change in fibrosis biomarkers' levels,
- 3) Successful ablation procedure lead to significant improvement in LVEF. Relevant improvement in clinical parameters measured in NYHA functional class was also observed.

Piok Gordnieguyls