ORIGINAL ARTICLE

A quality of life, clinical and biochemical improvements after catheter ablation of persistent arrhythmia in patients with structural heart disease and arrhythmia-mediated cardiomyopathy

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ABSTRACT

Background: Arrhythmia-mediated cardiomyopathy (AMC) is an essential clinical situation that is commonly underdiagnosed. Successful arrhythmia control leads to improvement in health-related quality of life (HRQoL) and heart failure (HF) symptoms in patients with structural heart disease (SHD).

Aims: The study aimed to evaluate the impact of catheter ablation (CA) of persistent arrhythmia on HRQoL, biochemical and clinical parameters HF in patients with SHD and AMC.

Methods: Patients with SHD, on optimal medical treatment, with persistent arrhythmia and strong suspicion of AMC, scheduled for CA were prospectively enrolled. Study procedures included: HRQoL measurement (the Minnesota Living with Heart Failure Questionnaire [MLHFQ] and the EuroQol Research Foundation [EQ-5D-3L] questionnaire), biomarkers (N-terminal pro-B-type natriuretic peptide [NT-proBNP], troponin T [TnT], matrix metalloproteinase-9 [MMP-9], soluble suppression of tumorigenesis-2 [sST2], tissue inhibitor of matrix metalloproteinase-1 [TIMP-1]), transthoracic echocardiography and clinical assessment.

Results: At 6 months, 30/35 (86%) patients were free of persistent arrhythmia. Patients who underwent successful CA had a significant improvement in HRQoL: MLHFQ (median [interquartile range, IQR], –22 [–28; –11]; *P* <0.001), EQ5D-3L score (mean [standard deviation], 21.8 (16.8); *P* <0.001); EQ5D-3L index (median [IQR], 0.09 (0.05; 0.18); *P* <0.001). A significant decrease in injury biomarkers was observed: NT-proBNP (median [IQR], –414 [–1397; –318] pg/ml; *P* <0.001), TnT (median [IQR], –2.27 (–8.52; 0.55) ng/l; *P* <0.01) but not in fibrosis biomarkers: (median [IQR], sST2: 2.20 [–5.4; 4.3] ng/ml; *P* = 0.741, MMP-9: 34 [–376; 283] ng/ml; *P* = 0.881, TIMP-1: 11.1 [–17.1; 31.9] ng/ml; *P* = 0.215). There was a significant increase of left ventricular ejection fraction (LVEF) (mean [SD], 9.8 [5.9] %; *P* <0.01).

Conclusions: Successful CA significantly improved clinical status, LVEF, and HRQoL of patients with SHD and AMC.

Key words: arrhythmia-mediated cardiomyopathy, biomarkers, catheter ablation, quality of life, structural heart disease

WHAT'S NEW?

This is the first study to assess the influence of catheter ablation in patients with structural heart disease and arrhythmia-mediated cardiomyopathy on the quality of life (QoL), clinical and heart failure (HF) biomarkers. A successful ablation procedure leads to significant improvements in QoL and left ventricular ejection fraction. There was a decrease in HF biomarkers related to myocardial stress, but no reduction in fibrosis biomarkers. Therefore, optimal medical treatment of HF should be continued.

INTRODUCTION

Identifying, correcting, and stabilizing the causes of heart failure (HF), together with standard recommended HF treatment, improve prognosis and the quality of life in HF patients [1–3]. HF is commonly accompanied by arrhythmia that 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 and arrhythmia-mediated cardiomyopathy

Arrhythmia-induced cardiomyopathy (AIC) is a form of dilated cardiomyopathy, which is partially or completely reversible once the underlying arrhythmia is controlled [4–6]. Both long-standing supraventricular and ventricular arrhythmias can be the cause of cardiomyopathy [7, 8]. The sooner the appropriate treatment is implemented the better chance to achieve complete restoration of left ventricular (LV) function [4, 5, 9]. It is very important to include AIC in the differential diagnosis in patients 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 HF, and a successful treatment leads to a complete recovery of the heart muscle. Type 2 of AIC is known as arrhythmia-mediated cardiomyopathy (AMC) and is present in patients with underlying structural heart disease (SHD) [1]. In these patients, new onset of arrhythmia leads to deterioration of previously impaired LV function and an increase in HF symptoms. Elimination of arrhythmia in patients with SHD can lead to symptoms improvement measured by the New York Heart Association (NYHA) functional classification and to the increase of left ventricular ejection fraction (LVEF). SHD is defined as any structural abnormalities found in imaging studies, i.e. echocardiography or cardiovascular magnetic resonance (CMR) [10, 11].

Health-related quality of life (HRQoL)

The quality of life is an important factor influencing daily functioning of patients with chronic heart failure. Patient care, effective treatment of potentially reversible causes of HF exacerbation, significantly affect daily activities of patients in society. Many studies have shown improvement in the quality of life (QoL) in patients undergoing invasive procedures, while there are no data on the effects of ablation procedures in patients with structural heart disease whose conservative treatment has been ineffective [12, 13]. A QoL assessment, which is undeniably relevant to every single patient, is rarely conducted as an endpoint for effective arrhythmia treatment in patients with initially reduced LVEF.

Biomarkers

Natriuretic peptides (NP) are still universal biomarkers used in the evaluation of patients with HF in terms of diagnosis, risk stratification, and prediction of cardiovascular deaths. However, there are other biomarkers describing pathophysiological processes [14, 15]. They can be divided into the following subgroups: markers of overload (N-terminal pro-B-type natriuretic peptide (NT-proBNP), soluble suppression of tumorigenesis-2 (sST2), markers of cardiac injury (troponin T [TnT], creatine kinase–myocardial band [CKMB]), markers of extracellular matrix turnover (matrix metalloproteinase-9 [MMP-9], sST2, tissue inhibitor of matrix metalloproteinase-1 [TIMP-1]) [15]. Although it is assumed that reverse remodeling is associated with cellular and molecular changes, it is unclear how they exactly contribute to the restoration of LV function [14, 16]. In a more precise evaluation of the related mechanisms, cardiac stress biomarkers including NT-proBNP, high sensitivity TnT, or sST2 (a member of the interleukin 1 receptor family expressed by cells in response to myocardial stress) are employed [17]. Extracellular compartment fibrosis is one of the integral components of negative remodeling. Evaluation of this process can additionally provide information about the recovery of LV function. There are no data about specific biomarkers related to AMC, and there is a lack of data on how catheter ablation procedures influence biomarker changes during the reverse remodeling process in patients with AMC and concomitant SHD.

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

METHODS

Study design

A single-center, prospective, cohort study was conducted in a tertiary-care cardiac center. The study protocol was approved by the local Institutional Review Board and was in full compliance with the Declaration of Helsinki. Written informed consent was obtained from all patients recruited into the study.

Study population

The study group comprised consecutive patients with HF symptoms referred for arrhythmia ablation in the 2nd Department of Heart Arrhythmia in the National Institute of Cardiology between October 2018 and July 2020. Patients were on optimal medical treatment of HF [1]. Patients were recruited if they: (1) were >18 years old; (2) had drug-refractory persistent supraventricular arrhythmias or drug-refractory ventricular arrhythmias with premature ventricular contractions (PVC) burden of >10% PVC/day; (3) had LVEF ≤50%; (4) had NT-proBNP >125 pg/ml; (5) had NYHA functional class ≥II; (6) had previously been diagnosed with SHD defined as any structural abnormalities on transthoracic echocardiography (TTE) or CMR (e.g. ischemic or non-ischemic cardiomyopathy, history of valve surgery, history of myocarditis). Exclusion criteria were: (1) lack of informed consent to participate in the study; (2) non-optimal medical treatment of HF; (3) secondary cause of exacerbation of arrhythmia (ischemic, valvular, uncontrolled hypertension, hyperthyroidism); (4) non-compliance.

Study procedures

Clinical assessment

Before ablation, 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. An echocardiographer certified by EACVI (the European Association of Cardiovascular Imaging) performed all 2D TTEs for this investigation. The biplane method of disks (modified Simpson's rule) was used for the assessment of LVEF. The echocardiographer was blinded to catheter ablation outcomes.

Health-related quality of life assessment:

HRQoL was analyzed using a generic EuroQol Research Foundation EQ-5D-3L score and a questionnaire specific for HF Minnesota Living with Heart Failure Questionnaire (MLHFQ).

The EQ-5D is a descriptive system that comprises five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression [18]. We have used the EQ-5D-3L version of the questionnaire that uses a 3-tier evaluation (no problem, some problem, extreme problem) for every dimension. The responses for every dimension can be combined into a 5-digit number, which describes the respondent's actual health status. The obtained 5-digit number can be converted into a single summary index using specific formulas (the EQ-5D-3L index). In the study, we used the Polish EQ-5D value set which was validated in a specific study using the time trade-off method [19].

The second part of EQ-5D was the EQ-VAS scale, which asked respondents to rate their health using a 20-cm long analog on a scale from 0 to 100. Endpoints are characterized as "best imaginable health state" and "worst imaginable health state."

The MLHFQ is a reliable and valid patient-oriented measure of the adverse effects of HF on a patient's life [20]. MLHFQ scores range from 0 to 105. Higher scores are associated with worse symptoms. The questionnaire contains 21 questions describing the adverse effect of heart failure on different dimensions: physical, emotional, and socioeconomic. A change of ≥5 points is considered clinically meaningful [20, 21].

Biomarkers

Blood samples for biomarkers analysis were taken from peripheral veins before the procedure and during a 6-month follow-up visit. All mentioned biomarkers were analyzed in a local laboratory. NT-proBNP, TnT concentrations were measured immediately after blood collection on a fully-automated Cobas e601 analyzer (Roche Diagnostics, Basel, Switzerland), whereas blood samples for MMP-9, TIMP-1, sST-2 assessment were centrifuged and frozen to -80° C for further analysis using Quantikine ELISA kits (R&D Systems). All reagent kits were used following the manufacturer's recommendations.

Ablation procedure

Ablation procedures were performed by experienced physicians certified either by the European Heart Rhythm Association (EHRA) or the Heart Rhythm Section of the Polish Society of Cardiology. Indications for ablation procedure were persistent supraventricular arrhythmia or ventricular arrhythmia with PVC burden of at least 10%/day, with symptoms of HF and clinical suspicion of arrhythmic component of HF worsening [22, 23]. In our group in the cases of ventricular arrhythmias, we performed radiofrequency ablation (RFA) using the 3D mapping system Ensite Precision (Abbott/St. Jude Medical, St. Paul, MN, US). In 11 of 13 (85%) patients with persistent atrial fibrillation (AF), cryoballoon ablation was performed. In the other 2 patients (15%), the ablation procedure was performed with the 3D mapping system Ensite Precision. RF ablation of other supraventricular arrhythmias (macro-reentrant atrial tachycardia (MRAT), typical atrial flutter) was performed in a group of 14 (8 patients using the 3D mapping system, 6 patients with classic fluoroscopy) (Figure 1).

Follow-up

Follow-up visits were conducted 3 and 6 months after ablation. HRQoL was measured after 3 and 6 months while TTE, 24-hour ECG Holter, and biomarkers analysis were repeated after 6 months. The efficacy of catheter ablation was determined by clinical symptoms, 12 lead ECG, and 24-hour Holter monitoring, interrogation of implantable cardiac devices if feasible. Successful ablation was defined according to the type of baseline arrhythmia. In the case of ventricular arrhythmias, successful ablation was de-

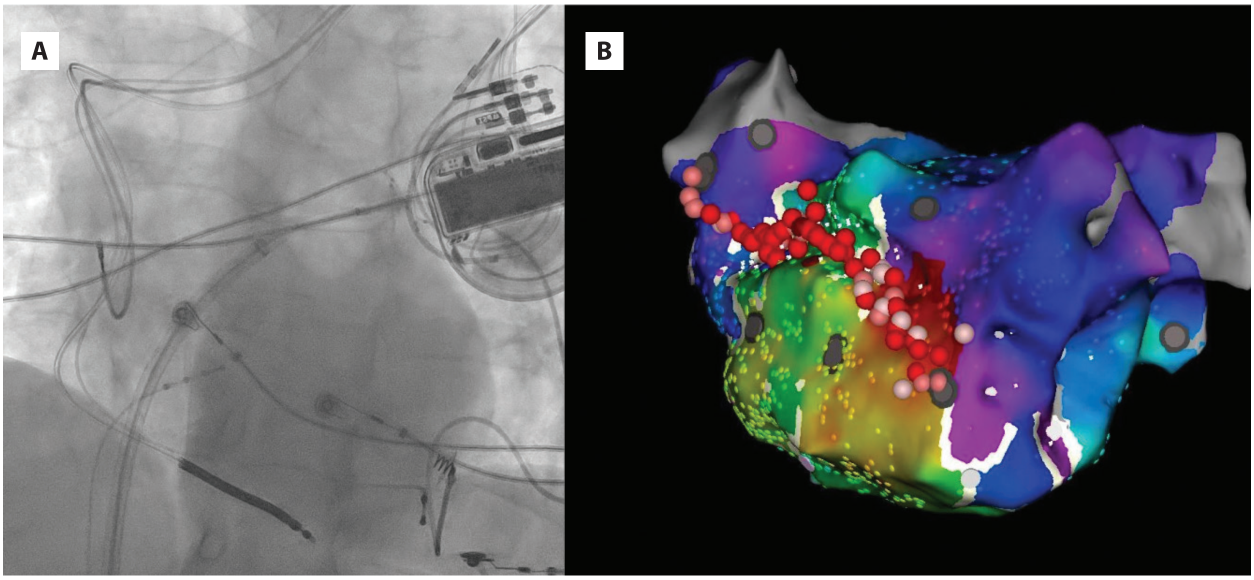

Figure 1. A. Cryoballoon ablation in a patient with cardiac resynchronization therapy (CRT-D). **B.** 3D activation map of left atrial macro-reentrant tachycardia, red dots — radiofrequency ablation application points between the mitral valve and the right superior pulmonary vein

fined as the reduction of PVC burden by 80%. In the case of supraventricular arrhythmias, successful ablation was defined as the lack of sustained arrhythmia or episodes lasting longer than 30 s in 24-hour ECG Holter monitoring or device interrogation.

Statistical analysis

Descriptive statistics for categorical variables are expressed as counts and percentages and for continuous variables are expressed in terms of mean (standard deviation [SD]) or median (interquartile range [IQR]). Continuous variables were tested for normal distribution with the use of the Shapiro-Wilk test. The significance of within-group differences was analyzed by one-way analysis of variance (ANOVA) with repeated measures and Tukey's *post hoc* test, non-parametric Friedman's test, paired Student's t-test, or Wilcoxon signed-rank test, as appropriate. The significance of differences between the 2 groups was analyzed by unpaired Student's t-test or the Mann-Whitney test. The categorical variable was compared using the χ^2 test. A two-sided *P*-value <0.05 was considered to be statistically significant. All analyses were performed using the SAS software, version 9.4 (SAS Institute, Inc., Cary, NC, US).

RESULTS

Between October 2018 and July 2020 40 consecutive patients with persistent arrhythmia, who were strongly suspected of having AMC, were prospectively screened for the study participation. Out of these 36 patients were finally enrolled in the study. The reasons for exclusions were: 3 patients refused to participate, one patient was disqualified from ablation due to persistent thrombus in the left atrial appendage. One patient withdrew from the study due to acute coronary syndrome 2 months after the ablation, hence 35 patients finished 6 months follow-up period and were included in the final analysis. Clinical characteristics of the enrolled patients are summarized in Table 1. The most common cause of AMC was persistent AF (13 patients, 37.1%), followed by MRAT (8 patients, 22.9%), PVC (8 patients, 22.9%), and typical atrial flutter (6 patients, 17.1%). Acute ablation success was achieved in 32 patients. Three patients with PVC had failed ablation with no reduction in PVC burden nor symptoms of amelio-

Table 1. Baseline of the study participants characteristics

Number of patients, n	35
Age, years, mean (SD)	65.9 (8.7)
Gender	
Males, n (%)	28 (80)
Females, n (%)	7 (20)
Cardiomyopathy	
Ischemic, n (%)	13 (37)
Non-ischemic, n (%)	22 (62.9)
Comorbidities	
Hypertension, n (%)	27 (77.1)
Chronic kidney disease defined as eGFR <60 ml/min, n (%)	17 (48.6)
Diabetes, n (%)	5 (14.3)
History of valve interventions (percutaneous/surgery), n (%)	6 (17.1)
Cardiac implantable electronic device	
Permanent pacemaker, n (%)	5 (14.3)
ICD/CRT-D, n (%)	9 (25.7)
Dominant arrhythmia	
Premature ventricular contractions, n (%)	8 (22.9)
Persistent atrial fibrillation, n (%)	13 (37.1)
Persistent atrial tachycardia, n (%)	14 (40)
New York Heart Association functional class	
Class II, n (%)	14 (40)
Class III, n (%)	21 (60)
Baseline treatment	
β-blocker, n (%)	33 (94)
ACE-inhibitor/ARB, n (%)	34 (97)
MRA, n (%)	18 (51)
Loop diuretics, n (%)	20 (57)
Amiodarone, n (%)	8 (23)

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CRT-D, cardiac resynchronization therapy with a defibrillator; eGFR, estimated glomerular filtration rate; ICD, implantable cardioverter-defibrillator; MRA, mineralocorticoid receptor antagonists

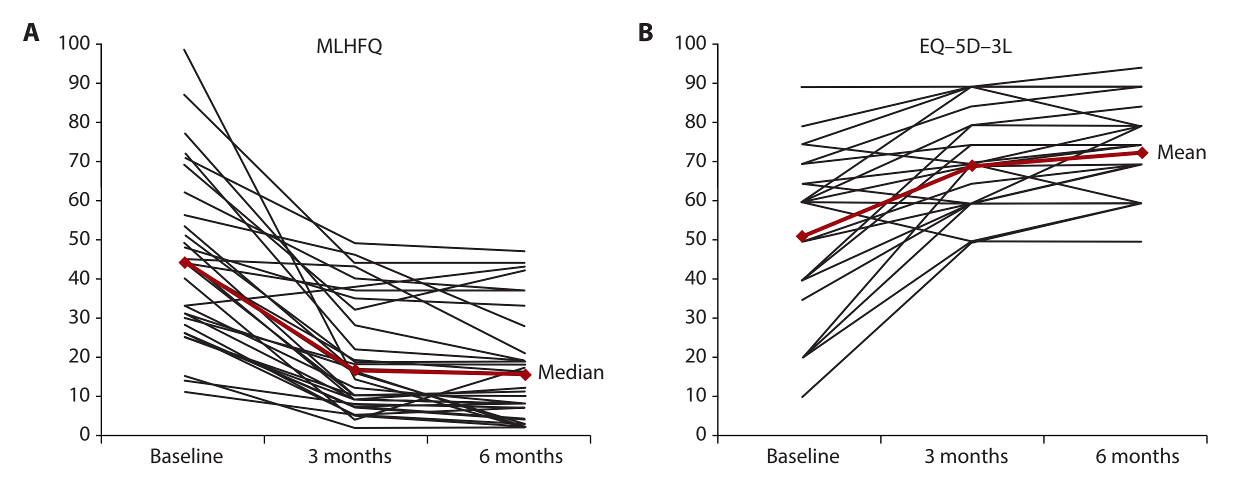

Figure 2. Health-related quality of life (HQRoL) improvements after a successful ablation procedure. Changes of HRQoL: **A.** Minnesota Living with Heart Failure Questionnaire (MLHFQ) and **B.** EuroQol Research Foundation questionnaire (EQ-5D-3L) for individual patients are indicated with blue lines. Red lines represent median (MLHFQ) or mean (EQ-5D-3L) values

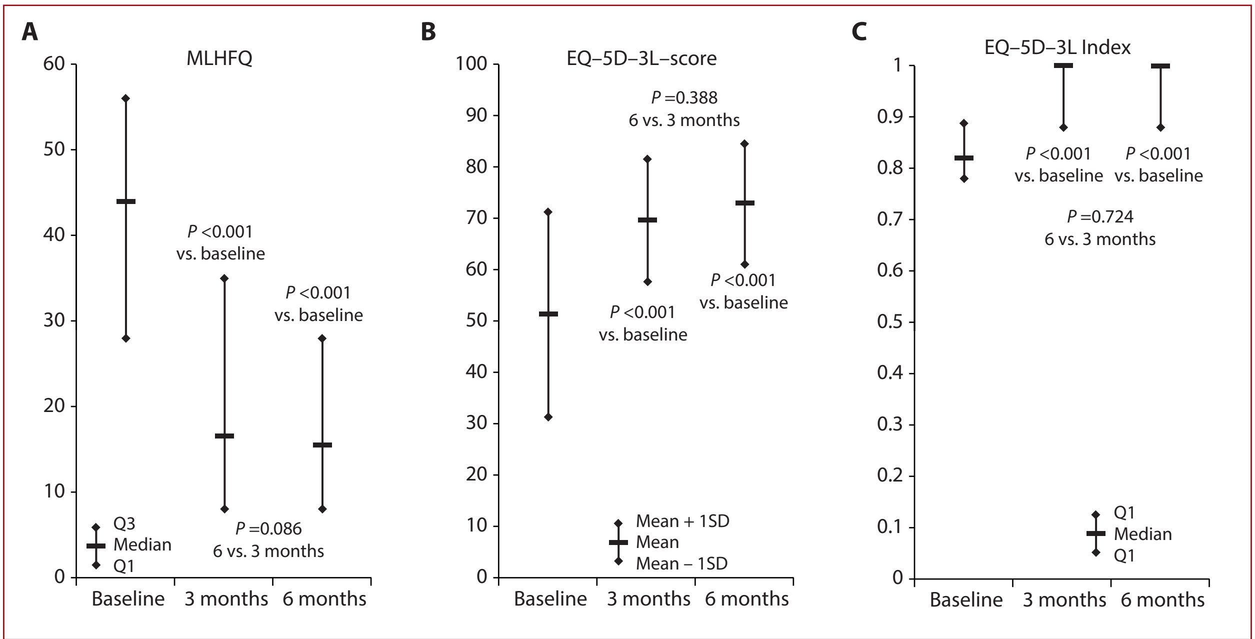

Figure 3. Results of a health-related quality of life assessment: **A.** MLHFQ; **B.** EQ-5D-3L index; **C.** EQ-5D-3L score. In **A** and **B** bars represent mean values, whiskers represent SD, in **C** bars represent median values, whiskers represent interquartile ranges (IQR)

Abbreviations: see Figure 2

ration. In another two patients, arrhythmia returned during the follow-up period (AF in both cases) and after an initial improvement, HF symptoms returned, and the patients were scheduled for a redo procedure.

HRQoL

The HRQoL results are presented in Figures 2, 3, and Table 2. A significant improvement vs. baseline was observed after three and six months both in EQ-5D-3L and MLHFQ and there was no significant difference between measurements at 3 and 6 months suggesting a rapid and sustained improvement after ablation. At 6 months, 32 out of 35 (91%) patients reported improvement of ≥5 points on MLHFQ. HRQoL improvements were more pronounced in the successful ablation cohort, but there was also some improvement in the failed ablation cohort.

LVEF, HF, biomarkers

Table 3, Figures 2, and 4 present the effect of catheter ablation on biomarkers, patients' clinical status, and echocardiographic parameters. After successful ablation, both NT-proBNP and TnT (biomarkers related to LV overload or injury) decreased significantly, but MMP-9 and TIMP-1 levels (biomarkers related to fibrosis) did not change. Patients who underwent successful catheter ablation had also a significant improvement of the NYHA functional class (P <0.001). Successful procedure was related to a significant improvement in both clinical and echocardiographic

Table 2. Results of generic (EQ-5D-3L) and HF-specific (MLHFQ) HRQoL measurements at baseline, 3 months, and 6 months. The successful ablation group (n = 30) and the whole cohort (n = 35)

	Baseline	3 months	6 months	Δ 3 - baseline	Δ 6-baseline	ANOVA *P*-value	*Post-hoc*, *P*-value		
							6 m vs. baseline	3 m vs. baseline	6 m vs. 3 m
All patients, n = 35									
MLHFQ, median (IQR)	45 (30–60)	19 (9–40)	18 (8–42)	–21 (–36–[–10])	–22 (-28–[–11])	<0.001	<0.001	<0.001	0.091
EQ-5D-3L score, mean (SD)	49.7 (19.0)	66.9 (13.8)	69.7 (13.7)	17.1 (15.6)	20.0 (16.4)	<0.001	<0.001	<0.001	0.437
EQ-5D-3L index, median (IQR)	0.82 (0.77–0.88)	0.93 (0.80–1.00)	0.93 (0.82–1.0)	0.07 (0.00–0.15)	0.07 (0.00–0.15)	<0.001	<0.001	<0.001	0.546
Successful ablation group, n = 30									
MLHFQ, median (IQR)	44 (28–56)	16.5 (8–35)	15.5 (8–28)	–21.5 (–36–[–12])	–24 (–36–[–14])	<0.001	<0.001	<0.001	0.742
EQ-5D-3L score, mean (SD)	51.2 (20.0)	69.7 (12.0)	73.0 (11.6)	18.5 (15.8)	21.8 (16.8)	<0.001	<0.001	<0.001	0.388
EQ-5D-3L index, median (IQR)	0.82 (0.78– 0.89)	1.00 (0.88– 1.00)	1.00 (0.88–1.0)	0.10 (0.00–0.18)	0.09 (0.05–0.18)	<0.001	<0.001	<0.001	0.089

Abbreviations: IQR, interquartile range; SD, standard deviation, other — see Table 1 and Figure 2

Table 3. Summary of clinical and biochemical parameters at baseline and 6 months. Successful ablation group (n = 30) and the whole cohort (n = 35)

Parameter	Baseline	6 months	Δ 6 months-baseline	*P*-value
All patients, n = 35				
Biomarkers				
NT-proBNP, pg/ml, median (IQR)	1115 (525–2648)	396 (188–1312)	–412 (–757–[–274])	<0.001
TnT, ng/l, median (IQR)	15.0 (9.7–37.0)	13.6 (7.8–24.4)	–1.94 (–5.90–0.66)	0.019
sST2, ng/ml, median (IQR)	24.3 (18.0–31.7)	23.3 (14.7–30.0)	1.77 (–6.0–[–4.3])	0.761
MMP-9, ng/ml, median (IQR)	704 (574–859)	802 (459–1038)	13.8 (–376–362)	0.773
TIMP-1, ng/ml, median (IQR)	169 (144–220)	181 (154–208)	10.3 (–17.7–31.9)	0.221
Echocardiography				
LVEF, %, mean (SD)	37.4 (9.1)	46.3 (10.3)	8.9 (6.4)	<0.001
LVESD, mm, mean (SD)	42.9 (7.9)	41.0 (8.2)	–1.9 (7.0)	0.116
LVEDD, mm, mean (SD)	57.5 (7.3)	56.4 (6.2)	–1.1 (6.1)	0.273
NYHA functional classification				
Class I, n (%)	0 (0)	10 (28.6)	10 (28.6)	
Class II, n (%)	12 (34.3)	21 (60.0)	9 (25.7)	
Class III, n (%)	23 (65.7)	4 (11.4)	–19 (54.3)	
Successful ablation group, n = 30				
Biomarkers				
NT-proBNP, pg/ml, median (IQR)	945 (521–2382)	347 (177–983)	–414 (–1397–[–318])	<0.001
TnT, ng/l, median (IQR)	15.5 (8.2–28.8)	13.0 (7.4–22.1)	–2.27 (–8.52–0.55)	<0.001
sST2, ng/ml, median (IQR)	23.3 (16.9–31.3)	22.5 (14.3–30.0)	2.20 (–5.4–4.3)	0.741
MMP-9, ng/ml, median (IQR)	726 (574–832)	774 (459–1030)	34 (–376–283)	0.881
TIMP-1, ng/ml, median (IQR)	168 (141–202)	180 (162–192)	11.1 (–17.1–31.9)	0.215
Echocardiography				
LVEF, %, mean (SD)	37.9 (9.0)	47.7 (8.9)	9.8 (5.9)	<0.001
LVESD, mm, mean (SD)	42.7 (8.0)	40.5 (7.9)	–2.2 (6.5)	0.069
LVEDD, mm, mean (SD)	57.7 (7.7)	55.9 (6.3)	–1.8 (6.2)	0.117
NYHA functional classification				
Class I, n (%)	0 (0)	10 (33.3)	10 (33.3)	
Class II, n (%)	11 (36.7)	20 (66.7)	9 (30.0)	
Class III, n (%)	19 (63.3)	0 (0)	–19 (63.3)	

Abbreviations: LVEF, left ventricular ejection fraction; LVESD, left ventricular end systolic diameter; LVEDD, left ventricular end diastolic diameter; NT-proBNP, N-terminal pro–B--type natriuretic peptide; NYHA, New York Heart Association

outcomes. In four patients (11.4 % of patients, three with persistent AF and one with typical atrial flutter), the LVEF improved above 35%, and those patients were no longer eligible for an implantable cardioverter-defibrillator (ICD) in the primary prevention of sudden cardiac death (SCD). No improvements on TTE were recorded in patients with failed ablation. In the successful ablation group, 25 patients (83.3 %) improved by a minimum of one NYHA functional class. All 5 patients with unsuccessful ablation did not improve in the NYHA functional class.

DISCUSSION

The main findings of our study were: (1) a clear and significant improvement in HRQoL in patients with AMC undergoing ablation procedure; (2) a rapid and sustained effect on HRQoL during 6-month follow-up; (3) a significant decrease in overload and injury biomarkers levels but no change in fibrosis biomarkers levels; (4) significant clinical and echocardiographic improvement after successful catheter ablation, which in 4 patients led to removing the indication for ICD in primary prevention.

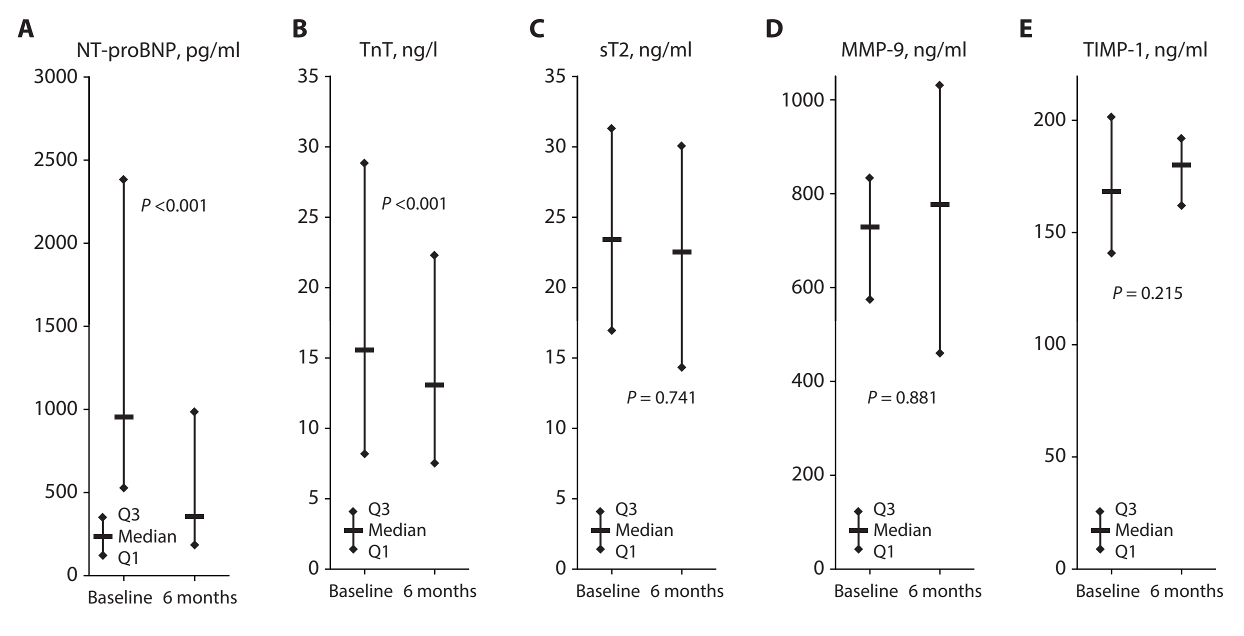

Figure 4. Changes in heart failure biomarkers during 6-month follow-up in patients who underwent a successful ablation procedure: **A.** NT-proBNP; **B.** TnT; **C.** sST-2; **D.** MMP-9; **E.** TIMP-1. Bars represent median values, whiskers represent interquartile ranges (IQR)

Abbreviations: MMP-9, matrix metalloproteinase-9; NT-proBNP, N-terminal pro-B-type natriuretic peptide; TIMP-1, tissue inhibitor of matrix metalloproteinase-1; TnT, troponin T

HRQoL improvement

According to the our knowledge, currently there are no published data concerning the HRQoL of patients with SHD and AMC and how it changes after successful catheter ablation. Due to a wide representation in clinical studies, we decided to choose two questionnaires: the generic EQ-5D--3L and HF-specific MLHFQ. The results obtained in the study indicate a clear improvement in HRQoL, which was already statistically significant in the 3-month period following the procedure and continued in the further 6-month follow-up period. All patients after successful ablation reported improvement in HRQoL (Tables 3 and 4). Also, in some patients whose ablation procedures were considered ineffective, improvement in HRQoL was observed. However, HRQoL achieved significantly lower values than in patients after successful catheter ablation (Δ-5.8 after 6 months). The improvement in HRQoL among patients with ineffective ablation procedures can be explained by better control of arrhythmias after the ablation procedure, e.g. in the case of supraventricular arrhythmias (greater effectiveness of anti-arrhythmic drugs after ablation to control the rhythm) and in the case of ventricular arrhythmias (reduction in the arrhythmia burden, but not meeting the criteria for the effectiveness of the treatment). A subanalysis of the CABANA trial found that patients with AF and heart failure who underwent catheter ablation had a significant improvement in the quality of life evaluated with the AF Effect on Quality of Life (AFEQT) summary score and the Mayo AF-Specific Symptoms Inventory (MAFSI) frequency score [24]. Gupta et al. [25] showed in a recent study that patients undergoing AF ablation procedures showed a significant improvement in QoL, which translated into the overall cost of medical care and a decrease in the hospitalization rate over a 12-month follow-up.

LVEF improvement

An important observation was the improvement of LVEF and the reduction of the dimensions of the heart chambers. The mean (SD) LVEF value before the procedure was 36.7% (9.2), while after the procedure it increased to 45.1% (9.9) within 6 months. In our study, the improvement of LVEF above 35% in 4 patients deserves special attention (persistent atrial fibrillation ablation in 3 patients, typical atrial flutter ablation in one patient). Those patients did not meet the criteria for implantation of the ICD in the primary prevention of sudden cardiac death anymore. It was already described by Penela et al. [26] that successful PVC ablation could remove the indication for ICD in primary prevention. In the CAMERA MRI study, in the AF ablation group, the proportion of patients with LVEF <35% decreased from 52 to 9% (9). Due to a small group of patients and a short follow-up period, further studies with a larger group of patients and a longer follow-up period are needed to assess whether the implantation of the ICD system can be safely avoided. Wojdyła-Hordyńska et al. [27] showed in their study an increase in LVEF by mean (SD) 11.5% (11) in the group of patients with SHD undergoing PVC ablation. The CAMERA-MRI study showed a significant increase in LVEF by mean (SD) 18% (13) in the group of patients with reduced LVEF undergoing ablation procedure for persistent AF [9]. Results from our study are also in agreement with the study conducted by Pruszkowska et al. [28], where in patients with systolic heart failure a mean (SD) improvement in LVEF from 30% (10) to 37% (13) following cryoballoon ablation for AF was observed. It is also worth noting that patients with systolic heart failure benefit from catheter ablation for AF in terms of all-cause mortality, reduction in the AF burden, and improvement in LVEF, which was shown in the CASTLE-AF trial [29].

Biomarkers

The reduction of myocardial injury was reflected by a concomitant reduction of NT-proBNP and TnT, but not sST2. It is important to underline that our study group presented stable LV dysfunction, so the baseline myocardial stress markers concentrations were lower than reported by other authors [30].

Our study showed no changes in biomarkers of fibrosis (Table 3). However, it should be noted that the lack of reduction of collagen turnover markers may not be associated with a full myocardial recovery, but rather with myocardial remission. So as the myocardial remission process is insufficient to fully prevent the recurrence of HF, optimal pharmacological treatment, using angiotensin-converting enzyme inhibitors (ACE-i) and mineralocorticoid receptor antagonists (MRA) agents as the anti-fibrotic therapy, should be recommended [31]. Recently Stegman et al. [32] showed that CMR study could be very helpful in distinguishing patients with arrhythmia-induced vs arrhythmia-mediated cardiomyopathy. The highest probability of a complete LVEF recovery was found in patients with late gadolinium enhancement (LGE) negativity and opposite left ventricular end-diastolic volume index (LVEDVI) category defined as values below the normal range. Patients with AMC exhibited larger LV volumes and a higher likelihood of positive LGE. The lack of improvement in biomarkers of fibrosis (MMP-9, TIMP-1) may also result from the severity of primary heart disease, which cannot be cured by the elimination of arrhythmia. We enrolled patients with confirmed SHD but, unfortunately, CMR was not part of our protocol as we expected a high proportion of patients with cardiac implantable electronic devices (CIED). Therefore, we were not able to quantify the amount of fibrosis localized in the myocardium before ablation.

Previously conducted studies showed that sST2 concentrations were significant predictors of mortality, all-cause hospitalization, mortality due to cardiovascular disease, and hospitalization for cardiovascular disease using a cut-off point of 35 ng/ml [33]. At baseline, only 5 patients (4 with successful and 1 with unsuccessful ablation procedures) had sST2 concentrations above 35 ng/ml. After six months in the group with successful ablation, sST2 decreased below 35 ng/ml in 3 out of 4 patients. It should also be taken into account that these new markers were measured in blood samples taken from peripheral veins and not directly from the myocardium. Further work in this area, e.g. on animal models, should be considered.

Study limitations

This was a relatively small, single-center prospective study. We were interested in the effectiveness of catheter ablation among patients with SHD and AMC, and, therefore, patients with persistent supraventricular arrhythmia who underwent electrical cardioversion as part of the preparation/qualification process for the invasive procedure ware not included in the study. However, the obtained results, in particular in terms of improving the HRQol, LVEF, were highly significant, and we believe that recruiting more patients would not significantly affect the above results. CMR was not included as part of the study protocol due to the expected high proportion of patients with CIEDs, so information on the LGE was not available.

CONCLUSIONS

Our study showed a significant improvement in the quality of life and LVEF in patients with structural heart disease and arrhythmia-mediated cardiomyopathy undergoing successful catheter ablation procedures. Levels of biomarkers related to myocardial stress decreased, but levels of biomarkers of fibrosis remained high despite the successful procedure.

Article information

Conflict of interest: MMF, AM, and MP received proctoring fees from Abbott and Medtronic. There is no conflict of interest declared by other authors.

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