Kardiologia Polska 2018; 76, 7: 1081–1088; DOI: 10.5603/KP.a2018.0068 ISSN 0022–9032

ORIGINAL ARTICLE

Cryoballoon ablation of atrial fibrillation in patients with advanced systolic heart failure and cardiac implantable electronic devices

Patrycja Pruszkowska[1], Radosław Lenarczyk[1], Jakub Gumprecht[2], Ewa Jędrzejczyk-Patej[1], Michał Mazurek[1], Oskar Kowalski[1], Adam Sokal[1, 2], Tomasz Podolecki[1], Stanisław Morawski[1], Witold Streb[1], Katarzyna Mitręga[1], Zbigniew Kalarus[3]

[1]Department of Cardiology, Congenital Heart Diseases and Electrotherapy, Silesian Centre for Heart Diseases, Zabrze, Poland
[2]Kardio-Med Silesia, Zabrze, Poland
[3]Department of Cardiology, School of Medicine with the Division of Dentistry, Zabrze, Poland

Abstract

Background: Pulmonary vein isolation with cryoballoon catheter ablation (CCB) is an effective method of treatment in patients with atrial fibrillation (AF), but in patients with heart failure (HF) the role of CCB remains unknown.

Aim: The aim of the study was to assess the feasibility, effectiveness, and safety of CCB in patients with HF and cardiac implantable electronic devices (CIEDs), the impact of the procedure on symptoms, and echocardiographic parameters.

Methods: Thirty consecutive HF patients with left ventricular ejection fraction (LVEF) ≤ 40% and CIED, referred for CCB of AF, were included. Procedural parameters were compared to a group of 59 consecutive patients without cardiac diseases referred for CCB (control group).

Results: The number of veins ablated per patient was smaller and application was performed less frequently in the right inferior pulmonary vein in the HF group compared with the control group (66.7% vs. 88.1%; p = 0.01, respectively). In two (6.7%) patients from the HF group and in five (8.5%) from the control group procedure-related complications occurred (p = 0.76). After six months 21 HF patients (70%), after one year 13 (43%), and after 625 days only three (10%) were free from arrhythmia. AF burden was significantly reduced after six months compared to the pre-ablation period (18.5% vs. 52.9%; p = 0.001). New York Heart Association and European Heart Rhythm Association classes were both significantly (p < 0.001) reduced and LVEF was higher after six months in the HF patients.

Conclusions: Safety and feasibility of CCB for AF in HF patients with CIED are comparable to subjects with structurally normal heart; however, stable positioning of the balloon in the right inferior pulmonary vein may be more challenging. Although late recurrences are common, ablation reduces arrhythmia burden and leads to a long-term improvement of symptoms and echocardiographic indices.

Key words: atrial fibrillation, heart failure, pulmonary vein isolation, cryoballoon catheter ablation, cardiac implantable electronic device

Kardiol Pol 2018; 76, 7: 1081–1088

INTRODUCTION

With the turn of the 21st century, it became increasingly evident that heart failure (HF) emerged as one of the major medical, but also socio-economic challenges. It is also well known that HF is a significant cause of death and hospitalisation in developed countries. Even with the recent progress in management of cardiovascular disease, a 10-year survival for patients with HF is currently as poor as 27% [1].

Heart failure often coexists with atrial fibrillation (AF), and it has been demonstrated that HF predisposes to AF, and

Address for correspondence:
Ewa Jędrzejczyk-Patej, MD, Department of Cardiology, Congenital Heart Diseases and Electrotherapy, Silesian Medical University, Silesian Centre for Heart Diseases, ul. Skłodowskiej-Curie 9, 41–800 Zabrze, Poland, tel: +48 32 37 33 682, fax: +48 32 37 33 792, e-mail: ewajczyk@op.pl
Received: 18.09.2017 **Accepted:** 02.03.2018 **Available as AoP:** 07.03.2018

Table 1. Baseline characteristics of the heart failure group and the control group

Variable	Heart failure group (n = 30)	Control group (n = 59)	p
Male sex	25 (83%)	28 (47%)	0.001
Age [years]	63 (13)	60 (11)	0.74
NYHA class	2 (1–3)	1 (1–1)	< 0.001
Arrhythmia form:			
Paroxysmal AF	16 (53%)	51 (86%)	0.0018
Persistent AF	14 (47%)	8 (14%)	< 0.001
Comorbidities:			
Hypertension	16 (53%)	35 (59%)	0.47
Diabetes	16 (53%)	4 (7%)	< 0.001
CAD	15 (50%)	8 (14%)	< 0.001
Renal failure	4 (13%)	6 (10%)	0.33
HF aetiology:			
Ischaemic	15 (50%)	8 (14%)	< 0.001
Echocardiography:			
LVESD	52 (12%)	34 (7%)	< 0.001
LVEDD	63 (11%)	50 (7%)	< 0.001
LVEF	30 (10%)	55 (7%)	< 0.001
LA	44 (9%)	40 (8%)	0.015
Mitral regurgitation	1 (0%)	1 (0%)	0.39

Data are shown as number (percentage), mean (standard deviation) or median (range). AF — atrial fibrillation; CAD — coronary artery disease; HF — heart failure; LA — left atrium; LVEDD — left ventricular end-diastolic diameter; LVESD — left ventricular end-systolic diameter; LVEF — left ventricular ejection fraction; NYHA — New York Heart Association

vice versa. It has been estimated that development of AF is associated with increased risk of death among HF patients [2, 3]. AF can be especially devastating in HF subjects with cardiac resynchronisation therapy defibrillators (CRT-Ds) and implantable cardioverter-defibrillators (ICDs). On top of diminishing cardiac output and predisposing to thromboembolism, AF is a potent trigger of inadequate ICD interventions, the most common being ineffective biventricular pacing in subjects with CRT devices. The negative prognostic impact of both abovementioned complications has been well documented.

Despite the serious consequences of AF, data concerning interventions directed towards rhythm control in patients with HF who developed this arrhythmia are still limited. Accordingly, current guidelines recommend a very cautious approach to AF in HF patients, referring at best to medical therapy, or to atrioventricular junction ablation [4]. To the best of our knowledge, no data exist on the value of cryoballoon technology for AF ablation in patients with advanced HF, especially in those implanted with cardiac implantable electronic devices (CIEDs). Moreover, reporting on success rates, none of the previous studies on AF ablation in HF is based on arrhythmic data retrieved from devices' memory and transmitted day-by-day with home-monitoring technology (minimising risk of data loss). The aim of this study was to assess the safety, feasibility, and success-rates of cryoballoon pulmonary vein (PV) isolation for AF in a set of patients with advanced HF and CIED.

METHODS

Study population

The studied population consisted of 30 consecutive HF patients with left ventricular ejection fraction (LVEF) ≤ 40% and previously implanted dual chamber ICD (n = 16) or CRT-D, who were referred to our centre for ablation of paroxysmal (n = 16) or persistent AF between September 2012 and May 2015. To be included, patients had to have at least one 5-min episode of AF recorded by CIED within the last six months, and at least one of the following: significant symptoms of arrhythmia, inadequate ICD interventions, or substantial loss of CRT pacing. The most common indication for ablation was symptomatic arrhythmia (74% had ≥ 3 points in European Heart Rhythm Association [EHRA] scale), followed by AF-provoked inadequate interventions of ICD (58%) and a drop in CRT pacing < 95% (33% of CRT patients). Thirty-nine per cent of patients had concurrently two indications, and 6% had all three. Baseline characteristics of the HF group are shown in Table 1. The study complied with the Declaration of Helsinki

and was approved by the Institutional Review Board. Written, informed consent was obtained from all study participants.

The control group was formed to compare feasibility, course, and safety of cryoablation procedures in HF subjects with those performed in patients with structurally normal hearts. This group consisted of 59 consecutive patients without symptoms or signs of HF, with LVEF ≥ 45% (55% ± 7%), who underwent cryoablation for AF within the same period (September 2012 to May 2015) as HF patients. To be qualified for ablation, patients needed to have symptomatic AF and should have undergone failed, not tolerated, or not accepted antiarrhythmic drug therapy. Exclusion criteria were LVEF < 45%, signs or symptoms of HF, any implanted CIED, and significant valvular disease. Control patients had smaller diameters of the left ventricle and left atrium and higher LVEF. Controls presented with paroxysmal AF (93% vs. 29% in HF group, $p < 0.05$; Table 1).

Cryoablation procedure

All cryoablation procedures both in HF patients and in the control group were performed by the same four experienced operators (> 100 cryoablation procedures performed by each at the time of study initiation in 2012), in identical clinical settings. Patients were kept on oral anticoagulants in a low therapeutic range of international normalised ratio (2.0–2.5) on the day of the procedure or were bridged with intravenous unfractionated heparin.

Under superficial sedation and with the use of local anaesthetics, a single transseptal puncture of the intraatrial septum was performed with the aid of pressure tracings from the needle-tip and under fluoroscopic guidance. Transseptal Brockenbrough needle (BRK or BRK-1) and 8 F vascular sheath — dilator set (63 cm long, Moullins-type) were used. Heparin was given routinely immediately after transseptal puncture and again during the procedure, under the control of activated clotting time values aiming at levels 300 to 350 s. After the puncture was accomplished the transseptal sheath was exchanged for a 12 F steerable Flex Cath access sheath (Medtronic, Minneapolis, MN, USA), the tip of which was positioned within the ostia of successive PVs, starting with left superior one. Cardio CryoAblation Catheters Arctic Front with balloon diameter of 28 mm, and since mid-2014 second-generation Arctic Front Advance (Medtronic, Minneapolis, MN, USA) catheters, were used for ablation. The occlusion of PVs was assessed by operators based on fluoroscopic evaluation of contrast leak around the inflated balloon positioned at the ostial aspect of the PV. To avoid phrenic nerve palsy, high-amplitude right phrenic nerve pacing from the superior cava vein was performed during right-sided ablations. The ablation was stopped immediately in the case of reduced phrenic nerve capture.

Two applications of 300 s each (240 s each with the second-generation balloons) were performed within every vein. Electrical vein isolation was not confirmed with any mapping catheter, and ablation endpoint for every vein was at least one application with minimal temperature ≤ –45°C, lasting for at least half of the application time. If the first two applications were unsuccessful (inability to achieve or maintain –45°C for sufficient time), a third or ultimately a fourth application was performed within the vein. With second-generation balloons one application of 240 s was allowed if the minimal temperature achieved was < –50°C. Irrespectively of the ablation catheter used, the application was stopped immediately in case of temperature drop < –60°C.

Data collection and follow-up

Apart from medical history, physical examination, and routine biochemistry, echocardiographic measurements, 6-min walking distance, and maximal oxygen consumption were assessed one day prior to ablation in every HF patient. The patients were discharged routinely one day after the ablation. After six-months, the patients were readmitted to hospital, and the assessment of medical history, device check-up, echocardiographic measurements, 6-min walking distance, and maximal oxygen consumption was repeated. All echocardiographic measurements were performed in our department by an echocardiography-experienced cardiologist dedicated for this study. Subsequently, the patients were followed in outpatient settings every six months.

Remote rhythm monitoring

All the subjects from the HF group were monitored remotely (Medtronic devices; CareLink Monitor or Biotronik; CardioMessenger II), and every episode of arrhythmia was noted by researchers on the second day after its occurrence. Implanted CRT-D and ICD devices (Consulta™ CRT-D, Maximo™II CRT-D, Protecta™ CRT-D, InSyncSentry™7298, Medtronic, Minneapolis, MN, USA; Lumax 340HF-T, Biotronik, Berlin, Germany) detected an atrial high-rate episode if the atrial rate was higher than the programmed value (171 bpm for Medtronic and 200 bpm for Biotronik devices) and the episode persisted longer than the minimum programmed count (nominal value for Medtronic and Biotronik). Nominal programmed atrial sensitivity was set to 0.3 to 0.5 mV with bipolar sensing configuration. Two experienced cardiologists assessed every recorded and transmitted episode on the basis of intracardiac electrograms. Those episodes were classified as AF (irregular atrial activity > 350 bpm), atrial flutter (regular atrial activity 240–350 bpm), or no tachyarrhythmia. A three-month postprocedural blanking period was assumed in all the patients, and after this period every episode of AF or flutter lasting ≥ 30 s was considered a recurrence of arrhythmia, irrespective of symptoms.

Statistical analysis

The continuous parameters were presented as median ± interquartile range or as mean ± standard deviation, depending

Table 2. Procedural details in both groups

Variable	Heart failure group (n = 30)	Control group (n = 59)	p
Procedure duration [min]	110 (35)	115 (45)	0.46
Fluoroscopy time [min]	14.9 (7.8)	17.3 (11.6)	0.54
Radiation exposure [mGy]	187 (325)	207 (437)	0.97
Number of veins frozen/patient	4 (1)	4 (0)	0.03
Number of cryoapplications/patient	8 (2)	7 (2)	0.79
Number of inflations without freeze/patient	1 (2)	1 (2)	0.23
Total freeze duration [s]	1853 (268)	1920 (355)	0.08
Total inflation duration without freeze [s]	154 (60)	173 (87)	0.55
Minimal temperature achieved [°C]:			
Left superior PV	–54 (12)	–51 (11)	0.06
Left inferior PV	–50 (11)	–46 (11)	0.31
Right superior PV	–54 (9)	–51 (12)	0.08
Right inferior PV	–50.5 (9.5)	–47 (12)	0.28
Ablation of cavo-tricuspid isthmus	3 (10%)	9 (15.3%)	0.49
AF during procedure	6 (20%)	11 (18.6%)	0.88
Conversion to sinus rhythm	1 (3.3%)	4 (6.8%)	0.51
Conversion to atrial flutter/tachycardia	1 (3.3%)	2 (3.4%)	0.98
Periprocedural complications:	2 (6.7%)	5 (8.5%)	0.76
Cardiac tamponade	1 (3.3%)	1 (1.7%)	0.62
Phrenic nerve palsy	1 (3.3%)	4 (6.8%)	0.51

Data are shown as number (percentage) or mean (standard deviation). PV — pulmonary vein; other abbreviations — see Table 1

on normality of distribution; categorical variables were presented as numbers and percentages. A comparison between the groups was performed with χ^2 test, Student t test or Mann-Whitney U test, as appropriate. Statistical significance was set at $p < 0.05$.

Univariate and multivariate regression models were used to select parameters associated significantly with procedure duration and fluoroscopy exposure. The parameters significantly related to these variables in univariate models were subsequently included into multivariate models. Multivariate Cox regression models were constructed to identify independent predictors of arrhythmia recurrence. All parameters that differed significantly between the groups with and without recurrence were included into a multivariate model.

RESULTS

Procedural details

A total of 110 veins were cryoablated in HF patients and 225 in the control group. The number of veins cryoablated per patient was smaller in the HF group (3.67 vs. 3.83/patient; $p = 0.03$). This was due to a lower proportion of HF patients, in whom application was less often performed in the right inferior PV (66.7% vs. 88.1% in the control group; $p = 0.01$), as a result of intraprocedural dislocation of a steerable sheath to the right atrium during attempts to cannulate the vein. All remaining veins were ablated in similar proportions of HF and control patients (left superior 100% in both groups, left inferior 100% vs. 98% and right superior vein 100% vs. 95%, respectively; $p = 1.0$, $p = 0.47$, $p = 0.22$, respectively). Procedure duration, fluoroscopy time, and radiation exposure were similar in both groups (Table 2). Compared to the control group, total duration of all cryoapplications showed a tendency to be shorter in the HF group ($p = 0.08$), and minimal temperature achieved during freezing showed a tendency to be lower, especially in left superior ($p = 0.06$) and right superior veins ($p = 0.08$). The target temperature (–45°C) for the desired period of time (120–150 s, depending on balloon generation) was achieved in HF group in 87% of left superior veins (vs. 74% in controls), 77% of left inferior (vs. 72%), 80% of right superior (vs. 68%), and 80% of the right inferior PV (vs. 65%; all $p = 0.16$, 0.61, 0.24, 0.15, respectively).

In two (6.7%) patients from the HF group and five (8.5%) from the control group, procedure-related complications occurred ($p = 0.76$). Cardiac tamponade requiring percutaneous drainage occurred in 3.3% of patients from the HF group and in 1.7% from the control group ($p = 0.62$). After percutaneous pericardiocentesis, further clinical course was uneventful and these patients were discharged home. Intraoperative phrenic

Table 3. Factors associated with procedure and fluoroscopy duration in the heart failure group

Variable	Univariate HR (95% CI)	p	Multivariate HR (95% CI)	p
Procedure duration:				
Age (per 1 year)	0.73 (9.52–1.04)	0.09		
CRT-D (vs. ICD)	0.98 (0.68–1.41)	0.91		
NYHA class (per 1 class)	0.97 (0.67–1.40)	0.86		
Hypertension	0.73 (0.51–1.03)	0.08		
Coronary heart disease	1.48 (1.06–2.06)	0.03	1.29 (0.93–1.76)	0.14
Diabetes	0.73 (0.51–1.03)	0.08		
Chronic kidney disease	0.80 (0.56–1.15)	0.22		
Persistent AF (vs. paroxysmal)	1.53 (1.09–2.14)	0.02	1.21 (0.87–1.68)	0.29
AF duration (per year)	0.88 (0.61–1.28)	0.52		
Symptoms (per 1 EHRA class)	1.03 (0.71–1.49)	0.88		
LVEF (per 1%)	0.91 (0.63–1.33)	0.64		
LVEDD (per 1 mm)	0.89 (0.61–1.29)	0.52		
RV diameter (per 1mm)	1.28 (0.90–1.83)	0.17		
LA diameter (per 1 mm)	0.82 (0.57–1.18)	0.28		
Mitral regurgitation (per 1 grade)	1.29 (0.90–1.85)	0.17		
Tricuspid regurgitation (per 1 grade)	1.73 (1.27–2.36)	0.002	1.57 (1.16–2.13)	0.008
Prior cardiac surgery	0.78 (0.57–1.16)	0.19		
Fluoroscopy duration:				
Age (per 1 year)	0.87 (0.60–1.25)	0.45		
CRT-D (vs. ICD)	0.95 (0.65–1.37)	0.78		
NYHA class (per 1 class)	1.24 (0.86–1.78)	0.26		
Hypertension	0.85 (0.59–1.22)	0.38		
Coronary heart disease	1.42 (1.0–2.01)	0.05	1.17 (0.88–1.57)	0.48
Diabetes	0.85 (0.59–1.22)	0.38		
Chronic kidney disease	0.93 (0.64–1.35)	0.72		
Persistent AF (vs. paroxysmal)	1.52 (1.09–2.13)	0.02	1.12 (0.82–1.51)	0.46
AF duration (per year)	1.02 (0.71–1.48)	0.90		
Symptoms (per 1 EHRA class)	1.09 (0.76–1.59)	0.62		
LVEF (per 1%)	0.81 (0.56–1.17)	0.27		
LVEDD (per 1 mm)	0.84 (0.58–1.21)	0.36		
RV diameter (per 1 mm)	1.43 (1.02–2.08)	0.04	1.26 (0.96–1.67)	0.11
LA diameter (per 1 mm)	0.85 (0.59–1.22)	0.38		
Mitral regurgitation (per 1 grade)	1.29 (0.90–1.85)	0.17		
Tricuspid regurgitation (per 1 grade)	1.89 (1.43–2.52)	< 0.001	1.74 (1.32–2.30)	< 0.001
Prior cardiac surgery	0.84 (0.59–1.22)	0.37		

Univariate and multiple regression models were used. CI — confidence interval; CRT-D — cardiac resynchronisation therapy defibrillator; ICD — implantable cardioverter-defibrillator; EHRA — European Heart Rhythm Association; HR — hazard ratio; LV — left ventricle; RV — right ventricle; other abbreviations — see Table 1

nerve palsy occurred in five patients (3.3% of the HF group vs. 6.8% of controls; p = 0.51) but resolved spontaneously in all subjects without additional interventions between seven days and 12 months in the HF group, and one to 12 months in the control group.

Considering the HF group only, ablation and fluoroscopy duration were higher in patients with coronary heart disease, persistent AF, and tricuspid regurgitation; fluoroscopy was also longer in those with enlarged right ventricle (Table 3). Severe regurgitation of the tricuspid valve was the only independent

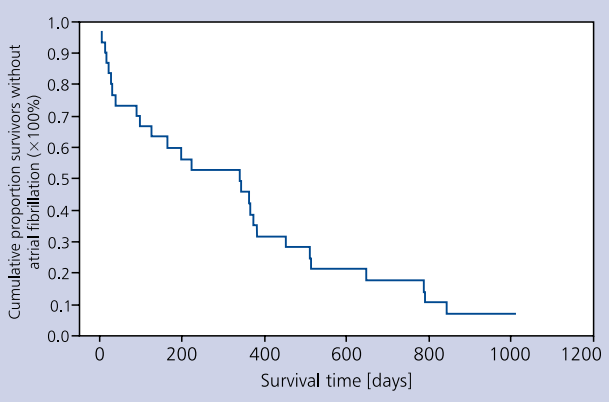

Figure 1. Kaplan-Meier curves of atrial fibrillation recurrence after cryoablation in the heart-failure group

predictor of longer procedure (adjusted hazard ratio [HR] 1.57; p = 0.008) and longer fluoroscopy use (HR = 1.74; p < 0.001).

Efficacy of ablation and arrhythmia burden

At six-month follow-up, 21 (70%) out of 30 patients in the HF group were free from AF episodes, but after a median of 625 days (20.5 months) only three (10%) subjects remained free of arrhythmia recurrence. In the population with arrhythmia recurrence seven (23.3%) subjects had persistent/chronic AF, while 20 patients had paroxysmal arrhythmia. Up to one year after ablation, 13 (43.3%) patients did not present AF episodes. Median time to the arrhythmia recurrence was 223 days (31–425 days). The Kaplan-Mayer curve of cumulative survival without arrhythmia recurrence is shown in Figure 1. AF burden was significantly lower six months after ablation compared to the pre-ablation period (18.5% vs. 52.9%; p = 0.001), but this effect declined gradually, and at a median of 625 days the follow-up AF load (29.4%) was only borderline lower than before ablation (p = 0.05).

Symptoms, functional indices, echocardiographic parameters, and outcomes

Six months after ablation, the HF group improved clinically — New York Heart Association (NYHA) and EHRA classes were both significantly (p < 0.001) lower compared to the baseline. This effect persisted during a median of 625 days of follow-up (Table 4). LVEF increased significantly (p = 0.007) within six months of ablation (37% vs. 30%), and this effect was still present after a median of 625 days. There were no statistical differences in functional tests: 6-min walking distance and maximal oxygen consumption during ergospirometry test six months post-ablation remained comparable to the baseline (Table 4).

DISCUSSION

To the best of our knowledge, this is the first study comparing the safety and feasibility of cryoballoon PV ablation in patients with HF to those with structurally normal heart.

Our data suggest that cryoablation of AF is comparably feasible and safe in patients with HF and in subjects with normal heart; however, higher frequency of balloon dislocations is to be expected in HF patients. Indeed — in our series the number of veins ablated per patient was smaller in the HF group due to the lower proportion of patients in whom

Table 4. Results of ablation in the heart failure group

Variable	Before ablation	Six months after ablation	During median 625 days of follow-up	p#	p+	p*
AF burden [%]	52.9 (83.4)	18.5 (10)	29.4 (99)	0.001	0.40	0.053
NYHA class	2.0 (1.0)	2.0 (1.0)	2.0 (1.0)	< 0.001	0.96	< 0.001
	Mean 2.26	Mean 1.7	Mean 1.69			
EHRA class	3.0 (1.0)	1.0 (0)	1.0 (0)	< 0.001	0.16	< 0.001
LVEF [%]	30 (10)	37 (13)	35 (14)	0.007	0.87	0.002
LVEDD [mm]	63 (11)	61 (12)	59 (12)	0.2	0.19	0.19
6MWT [m]	392.5 (108)	410 (121)		0.92		
VO_2max [mL/kg/min]	17.0 (9.8)	16.5 (7.5)		0.92		
Number of patients without AF	0	21	3			

Continuous variables are presented as median (range). 6MWT — six-minute walk test distance, VO_2max — maximal oxygen consumption; other abbreviations — see Tables 1 and 3
#p for comparison of variables before ablation and six months after ablation
+p for comparison of variables six months after ablation and during long-term follow-up
*p for comparison of variables before ablation and during long-term follow-up

the application was performed in the right inferior PV. This might be due to tortuous PV, altered vein anatomy, and/or dilated left atria in HF patients, leading to suboptimal catheter alignment. Apart from the right inferior vein, all remaining veins were ablated in similar proportions in HF and control patients. Procedure duration, fluoroscopy time and radiation exposure were similar in both groups, which is comparable to published data. In the meta-analysis, which compared first- to second-generation cryoballoons, the mean procedure duration was 112 min and fluoroscopy time was 20 min [5].

In our series of patients, serious procedure-related complications occurred in the same proportion in both groups. Similar rates (4.5%) were reported in a randomised trial performed in highly experienced centres [6]. In the meta-analysis of AF ablation in patients with systolic dysfunction of the left ventricle, rates of major procedure-related complications ranged from 3.6% to 4.8% and were similar to complication-rates in the general AF population [7]. The incidence of the most serious complication (cardiac tamponade) in our groups: 3.3% and 1.7%, respectively, was comparable to the rates previously reported [8, 9].

An interesting finding was that severe tricuspid regurgitation of tricuspid valve was the only independent predictor of longer procedure duration (adjusted HR 1.57) and longer fluoroscopy use (HR 1.74). Severe tricuspid regurgitation and high right atrial pressure lead to right atrial enlargement and change the anatomical relations. This may make transseptal puncture more challenging because of difficulties in proper positioning of the transseptal sheet and needle, which in turn may lead to longer procedure and higher fluoroscopic exposure.

Our data on effectiveness of ablation indicate that by using a very restrictive criterion of recurrence (arrhythmia episode of ≥ 30-s duration detected by CIED), arrhythmia-free survival was satisfying until six months after the procedure (70%) but declined sharply, reaching 43% after one year and only 10% after 20 months of ablation. Similarly, AF burden, reduced significantly in the early postprocedural period and relapsed gradually during a long-term observation. This relapse demonstrated, however, a relatively slow pace, and 20 months after ablation the arrhythmia load was still lower than before the procedure (with borderline significance). These findings are intuitively rational — after initial success (due to electrical vein isolation), AF may recur gradually with time due to ongoing slow progression of underlying heart disease and accompanying atrial dilatation, fibrosis, slowing of conduction velocity, etc. However, even transient reduction in arrhythmia burden may translate into symptomatic and echocardiographic benefit, especially in HF patients. It was shown previously that arrhythmia burden influenced outcomes in HF patients [10]. What is more, only four patients in our group underwent a second procedure, which translates into 1.13 procedures/patient. In the recent meta-analysis on catheter ablation of AF in HF patients, efficacy after a single procedure ranged from 36% to 44% (mean value 40%) [8]. In the CAMTAF trial the success rate after a single procedure was 38% after one year, and after a mean of 1.7 ± 0.7 procedures per patient it rose to 73%. In that trial more than 50% of patients needed the second procedure. Moreover, the number of patients free of AF decreases during long-term follow up [11, 12]. In a recently published randomised study with a very long observation period, 12 years after ablation only 19 out of 68 patients (27.9%) remained free of any relapse of atrial tachyarrhythmia [13]. These data are in line with our results, although in our HF population the proportions of AF-free patients are lower both at six months and after one year.

Additionally, it is a well-known phenomenon that more strict and meticulous screening of arrhythmia recurrence results in a lower success rate. In most of the studies on efficiency, the analysis was based on a 12-lead ambulatory electrocardiogram monitoring, which lasted 24 to 48 h and was repeated every three months. Currently used implantable devices allow recognition of AF with a high hit rate and specificity [14]. In our study all the subjects from the HF group were monitored remotely on a 24/7 basis, and every episode of arrhythmia was noted first by the device and then by researchers on the day after its occurrence.

In our study the ablation was followed by the improvement in subjective symptoms and echocardiographically assessed function of left ventricle. Nearly all studies evaluating the impact of AF ablation on HF reported improvement of left ventricular function, exercise capacity, and symptoms. The mean absolute improvement in LVEF ranged from 0.05% to 0.21% after 6 to 12 months, according to various authors [8, 15–17]. The NYHA score was significantly reduced in an ablation group compared to a medication group; at six months the NYHA score was 1.6, and this result was sustained after one year [12]. Our data indicate that this effect is still present and probably even more exaggerated in the HF population.

This was a non-randomised study with all the drawbacks associated with such a study design. Pulmonary vein isolation was not verified during the procedure, and instead a temperature-guided approach was used during the ablation. However, recently published data indicate that those two approaches may be comparable in terms of safety and effectiveness. In our population, we performed pure PV ablation. It is highly probable that in the setting of advanced HF with a high degree of atrial fibrosis, and anatomical and electrical remodelling, additional ablation lines and ablation of continuous fractionated atrial electrograms might be of significant value in restoring and maintaining sinus rhythm [18]. The results of multivariate analysis may be affected by insufficient events per covariate (generally, 10 events per covariate are recommended). Nonetheless, in a lot of studies with low incidence of events similar multivariate analyses were also used.

In conclusion, the safety and feasibility of cryoballoon PV ablation in HF patients with CIED and in subjects with

structurally normal heart are comparable; however, stable positioning of the balloon in the right inferior PV may be more challenging in the former group. This treatment modality can be adopted as a standard clinical practice. Moreover, although late recurrences are common, ablation reduces arrhythmia burden and leads to a long-term improvement of symptoms and echocardiographic indices of left ventricular performance. Large-scale multicentre studies are needed to evaluate the efficacy of AF ablation and the impact on mortality in HF patients.

Conflict of interest: *Patrycja Pruszkowska — consultant fees from Medtronic, Biotronik, St. Jude Medical and Boston Scientific; Radosław Lenarczyk — consultant fees and lecturer for Biotronik, Medtronic, St. Jude Medical, Boston Scientific, Cordis Webster, Boehringer Ingelheim; Jakub Gumprecht — no conflict of interests reported; Ewa Jędrzejczyk-Patej — consultant fees from Medtronic, Biotronik, St. Jude Medical and Boston Scientific; Michał Mazurek — consultant fees from Medtronic, Biotronik, St. Jude Medical and Boston Scientific; Oskar Kowalski — consultant fees from Medtronic, Biotronik, St. Jude Medical and Boston Scientific; Adam Sokal — travel reimbursements and consultant fees from Boston Scientific, Medtronic, St. Jude Medical and Biotronik, lecturers bureau from Medtronic, Boston Scientific and Impulse Dynamics; Tomasz Podolecki — consultant fees from St. Jude Medical, Adamed, Abbott; Stanisław Morawski — financial support for attending cardiology congresses from Biotronic; Witold Streb — no conflict of interests reported; Katarzyna Mitręga — lecturers bureau from AMGEN, MSD; Zbigniew Kalarus — no conflict of interests reported.*

References

1. Taylor CJ, Roalfe AK, Iles R, et al. Ten-year prognosis of heart failure in the community: follow-up data from the Echocardiographic Heart of England Screening (ECHOES) study. Eur J Heart Fail. 2012; 14(2): 176–184, doi: 10.1093/eurjhf/hfr170, indexed in Pubmed: 22253455.
2. Wang TJ, Larson MG, Levy D, et al. Temporal relations of atrial fibrillation and congestive heart failure and their joint influence on mortality: the Framingham Heart Study. Circulation. 2003; 107(23): 2920–2925, doi: 10.1161/01.CIR.0000072767.89944.6E, indexed in Pubmed: 12771006.
3. Ozierański K, Kapłon-Cieślicka A, Peller M, et al. Clinical characteristics and predictors of one-year outcome of heart failure patients with atrial fibrillation compared to heart failure patients in sinus rhythm. Kardiol Pol. 2016; 74(3): 251–261, doi: 10.5603/KP.a2015.0180, indexed in Pubmed: 26365943.
4. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Europace. 2016; 18(11): 1609–1678, doi: 10.1093/europace/euw295.
5. Pandya B, Sheikh A, Spagnola J, et al. Safety and efficacy of second-generation versus first-generation cryoballoons for treatment of atrial fibrillation: a meta-analysis of current evidence. J Interv Card Electrophysiol. 2016; 45(1): 49–56, doi: 10.1007/s10840-015-0075-4, indexed in Pubmed: 26582572.
6. Spragg DD, Dalal D, Cheema A, et al. Complications of catheter ablation for atrial fibrillation: incidence and predictors. J Cardiovasc Electrophysiol. 2008; 19(6): 627–631, doi: 10.1111/j.1540-8167.2008.01181.x, indexed in Pubmed: 18462327.
7. Anselmino M, Matta M, D'Ascenzo F, et al. Catheter ablation of atrial fibrillation in patients with left ventricular systolic dysfunction: a systematic review and meta-analysis. Circ Arrhythm Electrophysiol. 2014; 7(6): 1011–1018, doi: 10.1161/CIRCEP.114.001938, indexed in Pubmed: 25262686.
8. Cappato R, Calkins H, Chen SA, et al. Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. Circ Arrhythm Electrophysiol. 2010; 3(1): 32–38, doi: 10.1161/CIRCEP.109.859116, indexed in Pubmed: 19995881.
9. Dagres N, Hindricks G, Kottkamp H, et al. Complications of atrial fibrillation ablation in a high-volume center in 1,000 procedures: still cause for concern? J Cardiovasc Electrophysiol. 2009; 20(9): 1014–1019, doi: 10.1111/j.1540-8167.2009.01493.x, indexed in Pubmed: 19490383.
10. Lenarczyk R, Jędrzejczyk-Patej E, Szulik M, et al. Atrial fibrillation in cardiac resynchronization recipients with and without prior arrhythmic history. How much of arrhythmia is too much? Cardiol J. 2015; 22(3): 267–275, doi: 10.5603/CJ.a2014.0102, indexed in Pubmed: 25563708.
11. Lodziński P, Kiliszek M, Koźluk E, et al. Does a blanking period after pulmonary vein isolation impact long-term results? Results after 55 months of follow-up. Cardiol J. 2014; 21(4): 384–391, doi: 10.5603/CJ.a2013.0144, indexed in Pubmed: 24142681.
12. Hunter RJ, Berriman TJ, Diab I, et al. A randomized controlled trial of catheter ablation versus medical treatment of atrial fibrillation in heart failure (the CAMTAF trial). Circ Arrhythm Electrophysiol. 2014; 7(1): 31–38, doi: 10.1161/CIRCEP.113.000806, indexed in Pubmed: 24382410.
13. Bertaglia E, Senatore G, De Michieli L, et al. Twelve-year follow-up of catheter ablation for atrial fibrillation: A prospective, multicenter, randomized study. Heart Rhythm. 2017; 14(4): 486–492, doi: 10.1016/j.hrthm.2016.12.023, indexed in Pubmed: 27989681.
14. Jędrzejczyk-Patej E, Lenarczyk R, Mazurek M, et al. Can we rely on machines? Device-detected atrial high rates correspond well with atrial arrhythmias in cardiac resynchronization recipients. Europace. 2016; 18(3): 436–444, doi: 10.1093/europace/euv095, indexed in Pubmed: 26017467.
15. Wilton SB, Fundytus A, Ghali WA, et al. Meta-analysis of the effectiveness and safety of catheter ablation of atrial fibrillation in patients with versus without left ventricular systolic dysfunction. Am J Cardiol. 2010; 106(9): 1284–1291, doi: 10.1016/j.amjcard.2010.06.053, indexed in Pubmed: 21029825.
16. Hsu LF, Jaïs P, Sanders P, et al. Catheter ablation for atrial fibrillation in congestive heart failure. N Engl J Med. 2004; 351(23): 2373–2383, doi: 10.1056/NEJMoa041018, indexed in Pubmed: 15575053.
17. Trulock KM, Narayan SM, Piccini JP. Rhythm control in heart failure patients with atrial fibrillation: contemporary challenges including the role of ablation. J Am Coll Cardiol. 2014; 64(7): 710–721, doi: 10.1016/j.jacc.2014.06.1169, indexed in Pubmed: 25125304.
18. Iacopino S, Mugnai G, Takarada K, et al. Second-generation cryoballoon ablation without the use of real-time recordings: A novel strategy based on a temperature-guided approach to ablation. Heart Rhythm. 2017; 14(3): 322–328, doi: 10.1016/j.hrthm.2016.11.023, indexed in Pubmed: 27871986.

Cite this article as: Pruszkowska P, Lenarczyk R, Gumprecht J, et al. Cryoballoon ablation of atrial fibrillation in patients with advanced systolic heart failure and cardiac implantable electronic devices. Kardiol Pol. 2018; 76(7): 1081–1088, doi: 10.5603/KP.a2018.0068.