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Improvement in ejection fraction after cryoballoon pulmonary vein isolation for atrial fibrillation in individuals with systolic dysfunction

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Abstract

Background Cryoballoon pulmonary vein isolation (PVI) is commonly used for rhythm control of atrial fibrillation (AF). Data are limited examining the outcomes of cryoballoon PVI in patients with systolic dysfunction. We evaluate the impact of cryoballoon PVI in patients with systolic dysfunction.

Methods We evaluated a single-center prospective registry of patients undergoing cryoballoon PVI between 8/2011 and 6/2016. Patients with systolic dysfunction (EF < 55%) between the time of AF diagnosis and their cryoballoon PVI procedure were assessed for AF recurrence at 6 months and 1 year post-procedure, with a 3-month blanking period.

Results Final analysis included 66 patients with systolic dysfunction undergoing cryoballoon PVI. An AF diagnosis for ≥ 1 year prior to PVI was present in 62.1% ($n = 41$), and 53.0% ($n = 35$) had systolic dysfunction for ≥ 1 year pre-procedure. The proportion of AF-free patients at 1 year was 51.5%. Of patients with echocardiograms performed at 1 year ($n = 43$), a greater proportion of individuals without AF recurrence had an improvement in EF of ≥ 10% than in those with AF recurrence (54.2% vs. 25.0%, $p = 0.039$). Of the patients who had systolic dysfunction at the time of the ablation (EF < 55%), there was a significant increase in EF post-procedure (36.5% pre-procedure vs. 48.3% post-procedure, mean change 11.8%, $p < 0.001$).

Conclusion In patients with systolic dysfunction, cryoballoon PVI provides an acceptable AF recurrence-free rate at 1 year. AF recurrence-free individuals were more likely to have improvement in EF. Further evaluation is needed to determine the potential role of early cryoballoon PVI in patients with a new diagnosis of systolic dysfunction and AF.

Keywords Atrial fibrillation · Cryoballoon · Systolic dysfunction · Ablation · Pulmonary vein isolation

1 Introduction

Cryoballoon pulmonary vein isolation (PVI) has emerged as a commonly used strategy for rhythm control in atrial fibrillation (AF). It has been shown to be non-inferior to radiofrequency ablation for treatment of paroxysmal AF [1]. It has been shown to have a favorable safety profile [1] and is associated with a reduction in healthcare resource use and payer costs [2]. Additionally, individuals treated with cryoballoon PVI have significantly fewer repeat ablation procedures, fewer re-hospitalizations, and improved quality of life scores compared with medical therapy [2].

There is accruing evidence that catheter ablation for maintenance of sinus rhythm has benefits over medical rate control or AV node ablation in heart failure (HF) patients [3–5]. The data evaluating AF outcomes after cryoballoon ablation, in particular, for AF in individuals with HF is more limited. In the present study, we evaluated the impact of cryoballoon PVI on AF outcomes in patients with systolic dysfunction. Furthermore, we sought to examine the association of change in LV function with AF recurrence on follow-up.

2 Methods

The study population included patients undergoing cryoballoon PVI with documented systolic dysfunction. We identified patients from a single-center prospective registry between August 2011 and June 2016 undergoing cryoballoon PVI for AF with documented reduced ejection fraction (EF < 55%). Baseline

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clinical characteristics and detailed medical history, including specific AF and HF history, were recorded for all patients. Assessment of LV systolic function was performed by two-dimensional echocardiographic evaluation prior to cryoablation. Electronic chart review was performed to ascertain the LVEF from the echocardiography testing at the time of AF diagnosis and at follow-up. The University of Pittsburgh Institution Review Board approved the study protocol. All patients provided written informed consent for the ablation procedure.

The cryoballoon PVI procedure has been previously described in detail [6–8]. In brief, all ablation procedures were performed with the patient under general anesthesia. The cases were performed using the Arctic Front Cryoballoon (Medtronic) via transseptal approach. In general, a strategy of two 180–240 s applications was applied to each vein with the endpoint of entrance and exit block in all pulmonary veins.

At the time of the procedure, the operator recorded the pre-procedure EF. Retrospective chart review was performed to evaluate the EF at the time of AF diagnosis and at follow-up. Patient follow-up was as per standard protocol with outpatient visits at 6 weeks, 3 months, 6 months, 1 year, and yearly thereafter post-procedure. Echocardiograms were performed at follow-up at the discretion of the primary electrophysiologist. Electrocardiograms were performed at follow-up visits. Event monitors were applied routinely at 6 months or if there were recurrent symptoms. Retrospective chart review of all ECGs, event monitors, office visits, hospitalizations, and ED visits was performed to assess clinical outcomes post-procedure. We defined recurrence as an episode of atrial arrhythmia (atrial fibrillation, atrial tachycardia, atrial flutter) documented on an event monitor lasting 30 s, recurrence of typical symptoms, or any ECG-documented atrial arrhythmia during follow-up or hospitalization. Arrhythmias occurring in the first 3 months after the ablation (blanking period) were censored.

The baseline and post-procedure characteristics were compared between individuals with recurrence at 1 year and individuals without recurrence at 1 year. Continuous variables are presented as means ± SD, and categorical variables as percentages and absolute frequencies. The Kaplan-Meier survival analysis was used to ascertain AF-free survival. Statistically significant differences between groups were defined as a p value < 0.05. Statistical analysis was performed using STATA (version 14.0, Statacorp LP).

3 Results

Final analysis included 66 patients who were 58.4 ± 10.0 years old, 52% with hypertension, 17% with diabetes, 9% female, CHA_2DS_2VASc 1.7 ± 1.2, lowest EF pre-procedure 34.8%, 65% persistent AF, and 62% with AF > 1 year pre-procedure (Table 1). The 1-year AF recurrence-free survival rate was 51.5% ($n = 34$) (Fig. 1). Of those who were AF-free at 1 year, 23.5% were still taking anti-arrhythmic drug; however, 87.5% of those individuals had previously failed the anti-arrhythmic drug prior to ablation. When comparing the individuals with AF-recurrence at 1 year to those without, there were no significant differences in baseline characteristics (Table 1). When looking specifically at the patients who had systolic dysfunction (EF < 55%) at the time of the procedure ($n = 42$), there was a significant increase in EF post-procedure (36.5% pre-procedure vs. 48.3% post-procedure, mean change 11.8%, $p < 0.001$) (Fig. 2).

When comparing the EF during follow-up post cryoballoon PVI between the individuals with and without recurrence at 1 year, there were no significant differences between EF measurements at 1 year (Table 2). However, a greater proportion of individuals without AF recurrence had an improvement in EF of ≥ 0% than in those with AF recurrence (54.2% vs. 25.0%, $p = 0.039$) (Table 2).

4 Discussion

The main findings of our study were that in our cohort of 66 individuals with systolic dysfunction undergoing cryoballoon PVI, the recurrence-free rate at 1 year was 51.5%. Improvement of EF > 10% post cryoballoon PVI was associated with recurrence-free survival. The patients who had systolic dysfunction at the time of the procedure saw a significant (11.8%) increase in systolic function after cryoballoon PVI. Based on these findings, cryoballoon provides an acceptable AF recurrence-free rate at 1 year and was associated with an improvement in EF. Our findings were similar to a large multicenter cohort ($n = 484$) of persistent AF with a 1-year recurrence-free rate of 63.9% and an 18-month recurrence-free rate of 51.5% [9].

Heart failure (HF) and AF are common comorbid conditions [10]. Development of one disease process after the other was associated with a worse prognosis [10]. For example, the presence of AF in individuals with systolic HF is associated with an increased risk of all-cause mortality and heart failure progression [11]. There are many potential reasons for the conditions to be so frequently comorbid. The two disease processes share many risk factors such as hypertension, age, diabetes, valvular disease, ischemic disease, and obesity. Atrial fibrillation may also predispose individuals to HF via a tachycardia-related myopathy. Heart failure also predisposes individuals to AF via a variety of mechanisms including increased filling pressure, left atrial sizes, fibrotic changes, and neurohormonal activation [12].

Previous literature has shown PVI to be superior to AV node ablation with biventricular pacing in patients with atrial fibrillation and heart failure [3]. In the AATAC trial, catheter ablation has been shown to be superior to amiodarone in patients with HF and persistent AF [4]. Finally, when compared

Table 1 Baseline characteristics by recurrence of AF at 1 year post cryoballoon PVI

Characteristic	Overall $n = 66$	Recurrence at 1 year $n = 32$	No recurrence at 1 year $n = 34$	p value
Age	58.4 ± 10.0	57.5 ± 11.5	59.2 ± 8.3	0.484
BMI	31.1 ± 5.6	31.6 ± 6.3	30.8 ± 5.0	0.604
Hypertension	52% (34)	50% (16)	53% (18)	0.815
Diabetes	17% (11)	22% (7)	12% (4)	0.278
Stroke	3% (2)	0% (0)	6% (2)	0.169
Female	9% (6)	13% (4)	6% (2)	0.357
Coronary artery disease	18% (12)	19% (6)	18% (6)	0.909
Peripheral vascular disease	13% (8)	7% (2)	18% (6)	0.161
CHADS2VA2Sc	1.7 ± 1.2	1.6 ± 1.4	1.7 ± 1.1	0.456
Serum creatinine level, mg/dL	1.05 ± 0.6	0.96 ± 0.2	1.15 ± 0.9	0.887
Tobacco use	21% (14)	16% (5)	27% (9)	0.289
Lowest EF	34.8 ± 9	35.7 ± 9	34.0 ± 10	0.441
Persistent AF	65% (43)	63% (20)	68% (23)	0.348
AF > 1 year pre-procedure	62% (41)	56% (18)	68% (23)	0.347
EF at time of procedure	43.6 ± 10	44.9 ± 11	42.3 ± 10	0.314
LA dimension (cm)	4.4 ± 0.7	4.3 ± 0.6	4.4 ± 0.8	0.753
LVEDD (cm)	5.3 ± 0.7	5.1 ± 0.7	5.4 ± 0.7	0.739
LVESD (cm)	3.9 ± 0.7	3.7 ± 0.6	4.1 ± 0.8	0.77
Medications				
ACEI/ARB	57% (37)	50% (16)	62% (21)	0.417
Beta-blocker	73% (48)	66% (21)	80% (27)	0.215
Digoxin	16% (10)	17% (5)	15% (5)	0.833
Diuretic	29% (19)	38% (12)	21% (7)	0.133
Antiarrhythmic	71% (47)	72% (23)	71% (24)	0.909
Aspirin	44% (29)	31% (10)	55% (19)	0.077
Anticoagulant	91% (60)	91% (29)	91% (31)	0.939
Statin	38% (25)	36% (12)	38% (13)	0.822

Values are presented as mean ± SD or %

BMI, body mass index; *EF*, ejection fraction; *AF*, atrial fibrillation; *LA*, left atrium; *LVEDD*, left ventricular end diastolic diameter; *LVESD*, left ventricular end systolic diameter; *cm*, centimeters

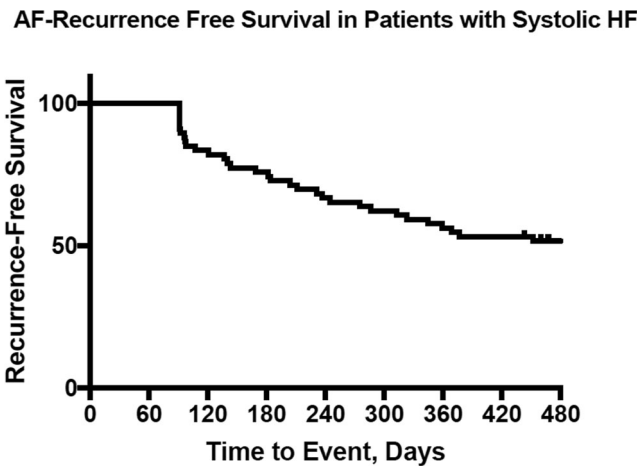

Fig. 1 AF recurrence-free survival after cryoballoon PVI in individuals with systolic dysfunction

to medical treatment, catheter ablation has been shown be effective at restoring sinus rhythm as well as improving LV function, functional capacity, and HF symptoms in the CAMTAF trial [5]. Most recently in the pivotal CASTLE-AF trial, catheter ablation for atrial fibrillation in patients with systolic heart failure was shown to be associated with a significantly lower rate of death from any cause or HF hospitalization when compared to medical therapy. Overall, ablation strategies for individuals with AF and HF appear to be a reasonable and effective treatment strategy.

The findings of our study suggest that specifically cryoballoon PVI as a treatment option for individuals with AF and comorbid systolic HF is a reasonable option for treatment of AF. Additionally, successful treatment of AF using this treatment strategy may improve outcomes from a HF standpoint as well. Our study adds to the growing body of evidence for benefit of treatment with ablation for patients with AF, and systolic HF may improve hospitalization rates,

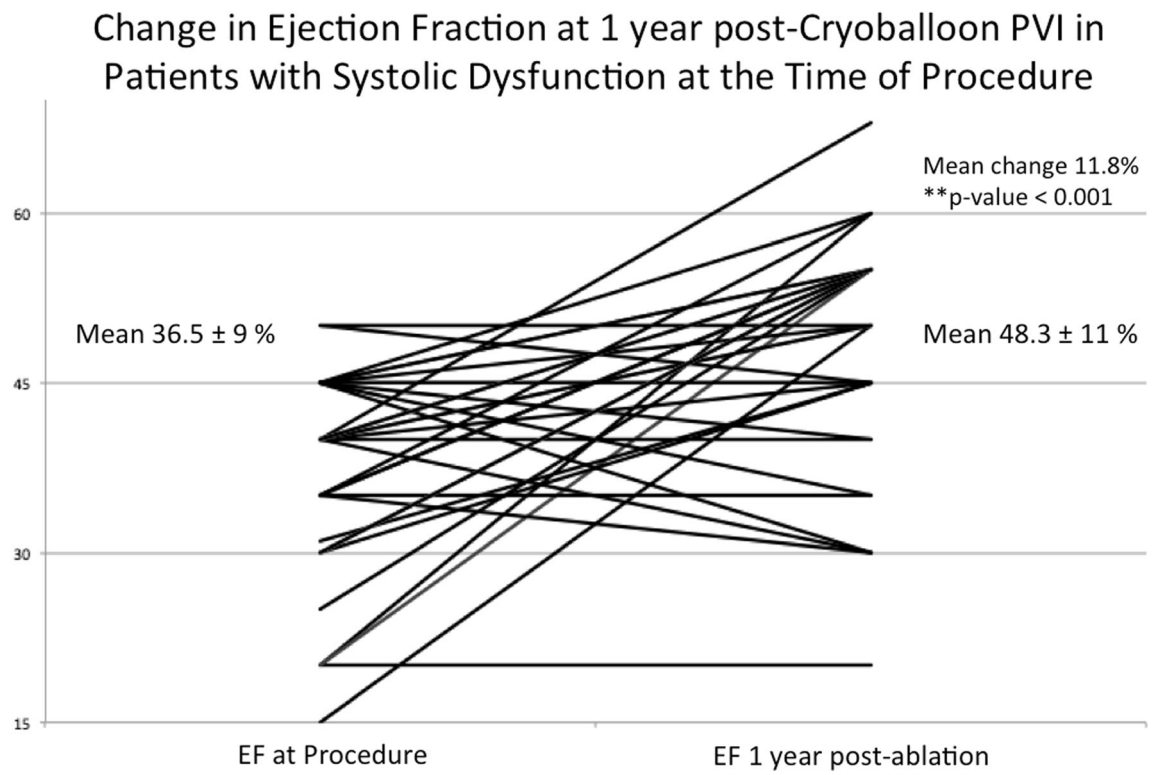

Fig. 2 Change in EF at 1 year post-cryoballoon PVI in patients with systolic dysfunction at the time of procedure

mortality, LV function, functional capacity, and HF symptoms [4, 5, 13]. To our knowledge, our study is the first to evaluate the impact of successful treatment of AF with cryoballoon PVI in patients with comorbid systolic HF and AF. Certainly, for some of our cohort, the mechanism for improvement in EF in individuals with AF-free recurrence at 1 year includes a decrease in tachycardia-mediated etiology [14, 15].

Further validation of the impact of cryoballoon PVI on individuals with AF and systolic HF in a larger, multicenter cohort with longer follow-up is needed. The recent Castle-AF trial suggests that catheter ablation for AF in individuals with HF over medical therapy may decrease mortality and heart failure hospitalization; however, the study did not evaluate cryoballoon specifically [13]. Cryoballoon ablation has been shown to decrease procedure time and hospital length of stay when compared to radiofrequency ablation [16]. Therefore, if we see similar outcome benefits in patients with comorbid AF and HF undergoing cryoballoon treatment as radiofrequency catheter ablation, it may represent a favorable treatment option for individuals with HF and AF. It is important to note that our study did not routinely include additional lesion sets in patients to address non-PV triggers which potentially impacts outcomes and our study cohort had a slightly higher average baseline EF than the recent Castle-AF trial.

Our study does have several potential limitations. It is a retrospective observational study of a prospective registry involving only a single center and, thus, generalizability may be limited. We did not have a standardized protocol for evaluating EF; the EF measurements were obtained at the discretion of the patient's primary electrophysiologist and/or cardiologist and, thus, there may be some variability in outcome measurements. Additionally, patients were not continuously

Table 2 Changes in ejection fraction by recurrence of AF at 1 year post cryoballoon PVI

	Overall ($n = 66$)	No recurrence at 1 year ($n = 34$)	Recurrence at 1 year ($n = 32$)	p value
Lowest EF	34.8 ± 9.0	34.0 ± 9.4	35.7 ± 8.5	0.441
EF at time of AF diagnosis	37.8 ± 10.3	35.6 ± 10.9	40.2 ± 9.2	0.098
EF at time of procedure	43.6 ± 10.4	42.3 ± 9.6	44.9 ± 11.2	0.383
EF at 1 year	48.7 ± 10.3	48.7 ± 10.5	48.7 ± 10.4	0.934
EF improved > 10%	39.6%	54.2%	25.0%	0.039

Values are presented as mean ± SD or %

EF, ejection fraction; *AF*, atrial fibrillation

monitored for recurrence of AF; however, patients were monitoring using patient-reported symptomatic recurrence in addition to auto-triggered event monitors and ECGs. Of the AF recurrence-free patients at 1 year, 25.8% were still taking anti-arrhythmic drugs. This may be due to some hesitation by the provider to discontinue the medication given underlying heart failure. However, it is important to note that of the patients still taking anti-arrhythmic drugs, 82.4% of them were on anti-arrhythmic drugs that were previously ineffective, and it is also important to note that there were no significant differences in anti-arrhythmic drug use at 1 year when compared to the group with AF-recurrence at 1 year (23.5% vs. 28.1%, $p = 0.675$).

5 Conclusions

Overall, our study adds evidence to the growing body of literature that AF ablation, particularly cryoballoon ablation, is a favorable treatment strategy in individuals with comorbid AF and systolic dysfunction. Individuals in our cohort with systolic dysfunction undergoing cryoballoon PVI had a moderate AF recurrence-free rate at 1 year of 52%. Specifically, these individuals with AF-free recurrence at 1 year post-cryoballoon PVI were more likely to have significant improvements in EF.

Compliance with ethical standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This was a retrospective review of a prospectively managed database.

Conflict of interest Norman Wang, Boston Scientific funding; Evan Adelstein, Medtronic funding; Samir Saba, Boston Scientific and Medtronic funding; and SJ, Medtronic funding. Remaining authors have no conflicts of interest to disclose.

The study was approved by the University of Pittsburgh Institutional Review Board.

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