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Single-Procedure Outcomes and Quality-of-Life Improvement 12 Months Post-Cryoballoon Ablation in Persistent Atrial Fibrillation

Results From the Multicenter CRYO4PERSISTENT AF Trial

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ABSTRACT

OBJECTIVES The CRYO4PERSISTENT AF (Cryoballoon Ablation for Early Persistent Atrial Fibrillation) trial aims to report long-term outcomes after a single pulmonary vein isolation (PVI)-only ablation procedure using the second-generation cryoballoon in persistent atrial fibrillation (PerAF) patients.

BACKGROUND Pulmonary vein isolation is recognized as the cornerstone of atrial fibrillation (AF) ablation, including ablation of PerAF.

METHODS The CRYO4PERSISTENT AF trial (NCT02213731) is a prospective, multicenter, single-arm trial designed to assess single-procedure outcomes of PVI using the cryoballoon. The primary endpoint was freedom from AF, atrial flutter, or atrial tachycardia ≥30 s after a 90-day blanking period. After enrollment, but before ablation, patients without 100% AF burden (18-h Holter monitoring or 3 consecutive electrocardiograms in a time frame ≥14 days) were excluded. Patients were followed at 3, 6, and 12 months, with 48-h Holter monitoring at 6 and 12 months. Quality of life and symptoms were evaluated at baseline and 12 months. Arrhythmia recurrence and adverse events were adjudicated by an independent committee.

RESULTS A total of 101 patients (62 ± 11 years of age, 74% men, left ventricular ejection fraction 56 ± 8%, left atrial diameter 43 ± 5 mm) meeting criteria, undergoing cryoballoon-based PVI, with follow-up data, were included. Kaplan-Meier estimate of freedom from AF, atrial flutter, or atrial tachycardia recurrence was 60.7% at 12 months. Compared with baseline, there were significantly fewer patients with arrhythmia-related symptoms at 12 months (16% vs. 92%; $p < 0.0001$). The symptom reduction was supported by significant improvement in 36-Item Short Form Health Survey composite scores and European Heart Rhythm Association score at 12 months. The only device related event was transient phrenic nerve injury in 2 (2%) patients, with resolution pre-discharge.

CONCLUSIONS Cryoballoon ablation for treatment of PerAF demonstrated 61% single-procedure success at 12 months post-ablation in addition to significant reduction in arrhythmia-related symptoms and improved quality of life. (Cryoballoon Ablation for Early Persistent Atrial Fibrillation [Cryo4 Persistent AF]; NCT02213731). (J Am Coll Cardiol EP 2018;■:■-■) © 2018 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

AAD = antiarrhythmic drug

AF = atrial fibrillation

AFL = atrial flutter

AT = atrial tachycardia

EHRA = European Heart Rhythm Association

PAF = paroxysmal atrial fibrillation

PerAF = persistent atrial fibrillation

PNI = phrenic nerve injury

PV = pulmonary vein

PVI = pulmonary vein isolation

QoL = quality of life

SF-36 = 36-Item Short Form Health Survey

Atrial fibrillation (AF) is the most common cardiac arrhythmia, and its incidence continues to grow with the progression of an aging demographic (1). The detrimental effects of this cardiac arrhythmia are an increased risk of stroke and a diminished quality of life (QoL) (2). Early ablation of AF in the paroxysmal AF (PAF) disease state is on average more effective than ablations that are performed in a much later AF state, such as persistent or long-standing persistent AF (PerAF), when compared according to outcomes (3). As the AF disease progresses, there is an increase of left atrial substrate involvement, greater left atrial wall fibrosis and left atrial dilation, greater proarrhythmic diversion circuits, and less conductive healthy tissue (4,5). Pulmonary vein isolation (PVI) remains the cornerstone of AF ablation therapy, and current consensus and guidelines recommend PVI ablation strategy for treatment of AF (2,4). Recent publications have demonstrated that PVI alone is effective for the treatment PerAF (6-10) and outcomes are comparable to a stepwise approach (11-13). Therefore, a PVI-only strategy may logically be preferred as a first treatment strategy in both the treatment of PAF and PerAF.

In the randomized FIRE AND ICE trial, cryoballoon demonstrated noninferiority for treatment of patients with drug-refractory PAF compared with radiofrequency ablation, while demonstrating fewer repeat ablations and reinterventions (14,15). Further, although a handful of recent publications have reported cryoballoon PVI-only outcomes in PerAF patients (6-10), there is a lack of consistency in documentation of PerAF and objective patient selection (i.e., required documentation of 100% AF burden pre-ablation), resulting in undebatable inhomogeneity across patients evaluated in these studies.

The CRYO4PERSISTENT AF clinical trial (NCT02213731) was designed to prospectively assess the 12-month single procedure outcomes of PV antrum isolation using the cryoballoon in PerAF patients with documentation of 100% AF burden pre-ablation. Acute outcomes, QoL (36-Item Short Form Health Survey [SF-36]), European Heart Rhythm Association (EHRA) score, and 12-month outcomes were evaluated after a single PVI-only cryoballoon ablation procedure.

METHODS

STUDY DESIGN. The CRYO4PERSISTENT AF (Cryoballoon Ablation for Early Persistent Atrial Fibrillation) trial is a prospective, multicenter, single-arm, interventional post-market trial of patients with PerAF. Patients underwent a single cryoballoon ablation procedure without additional empirical lesions or complex fractionated atrial electrogram ablations. A total of 11 sites in Germany, France, and Greece participated in the study (Online Table S1). The study was approved by each site's ethics review board, registered on ClinicalTrials.gov (NCT02213731), and conducted in accordance with the Declaration of Helsinki.

INCLUSION AND EXCLUSION CRITERIA. Patients 18 to 80 years of age were required to have a diagnosis of symptomatic PerAF ≤12 months, 100% AF burden of 7 to 180 days as documented on a electrocardiography recording, or AF requiring cardioversion. In addition, study participants were required to have failed or refused a prescription of at least 1 antiarrhythmic drug (AAD). Major exclusion criteria included long-standing PerAF, prior left atrial ablation, a percutaneous coronary intervention or myocardial infarction ≤3 months, left atrial diameter ≥50 mm, or a stroke or transient ischemic attack ≤6 months. All patients provided written informed consent before study enrollment. After enrollment, but before ablation, 100% AF burden was required to be recorded on an 18-h Holter or 3 consecutive electrocardiography recordings in a time frame ≥14 days. If 100% AF burden was not demonstrated, the patient was required to be exited from the trial before ablation. Ablation was to occur within 30 days of enrollment and patients were managed in this period according to standard of care.

ABLATION PROCEDURE. Within 6 months before the cryoballoon procedure, a transthoracic

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All authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Clinical Electrophysiology* author instructions page.

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echocardiogram was required for the collection of left atrial size, left ventricular ejection fraction, left ventricular hypertrophy, and mitral valve impairment. A transesophageal echocardiogram was required within 7 days before the procedure to assess for left atrial thrombus. Cryoballoon procedural techniques have been previously described in detail (16,17). In brief, cryoablation was performed under conscious or general sedation, without use of 3-dimensional mapping. Heparin was administered before the transseptal puncture and maintained at activated clotting time levels ≥300. A 15-F steerable sheath (FlexCath Steerable Sheath, Medtronic, Minneapolis, Minnesota) was used to introduce the cryoballoon catheter system into the left atrium. A cryoballoon (Arctic Front Advance Cryoballoon Catheter, Medtronic, Minneapolis, Minnesota) was then advanced through the FlexCath sheath, and positioned at the antrum of each PV guided by the circular mapping catheter (Achieve Mapping Catheter, Medtronic, Minneapolis, Minnesota). The ablation strategy was PVI using only the cryoballoon, neither focal cryoablation nor radiofrequency could be used, and additional left atrial empirical lesions or complex fractionated atrial electrogram ablations were not allowed. Right atrial flutter ablations could be performed using radiofrequency energy. For PVI, the protocol recommended 240-s cryoapplications using a freeze-thaw-freeze technique, with a bonus freeze after PVI which, at the time of the trial, was the current operator consensus for cryoablation application duration. To minimize the risk of phrenic nerve injury, right phrenic nerve pacing was performed by an electrode catheter in the superior vena cava and capture was confirmed by palpation and intermittent fluoroscopy. Application of cryoenergy was terminated immediately upon attenuation or loss of phrenic nerve capture. PVI was confirmed using the Achieve mapping catheter. Whenever possible, the electrodes of the circular mapping catheter were positioned as close as possible to the PV antrum to monitor for real-time PVI. Use of computed tomography or magnetic resonance imaging, intracardiac echocardiography, esophageal temperature monitoring, compound motor action potential, or other adjunctive phrenic nerve monitoring was left to the discretion of the operator. Systemic anticoagulation with warfarin or a new oral anticoagulant was recommended for at least 2 months following the AF ablation procedure. The protocol recommended that antiarrhythmic medications were used, when necessary, during the 90-day post-cryoablation procedure blanking period and discontinued thereafter.

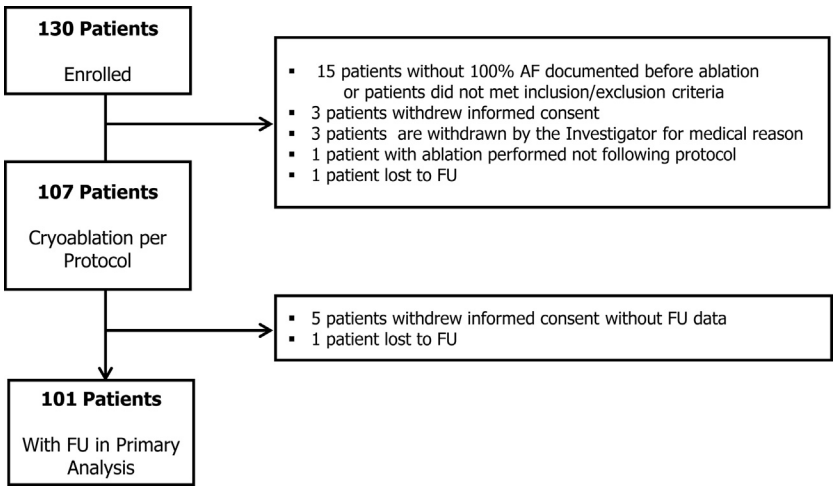
PATIENT FOLLOW-UP AND ENDPOINTS. Post-ablation, patients had in-office follow-up visits at 3, 6, and 12 months. During each visit patients were assessed for their relevant clinical history, and underwent a physical examination and a 12-lead electrocardiogram. Serial ambulatory electrocardiogram monitoring was performed using a 48-h Holter monitor at 6-month and 12-month visits. Recurrence of AF, AFL, or AT was reported when there was a documented episode of AF, AFL, or AT lasting ≥30 s (both symptomatic and asymptomatic) outside the 90-day blanking period. Ablation success was reported after a single procedure (which defines any repeat ablation post-index ablation procedure as a clinical trial failure) and without use of direct-current cardioversion outside of the blanking period. QoL measurements were assessed by 2 tools, the SF-36 version 2 questionnaire and the EHRA score of AF-related symptoms at the 6-month and 12-month visits. Arrhythmia-related symptoms were also evaluated at baseline, 6 months, and 12 months. An independent core lab-adjudicated arrhythmia recurrences and adverse events were adjudicated by an independent safety committee.

STATISTICAL ANALYSIS. Statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, North Carolina) and R statistical software version 3.2.5 (Foundation for Statistical Computing, Vienna, Austria). Categorical variables were summarized as count and percentage. Continuous data are reported as mean ± SD. Baseline information and relevant medical history were summarized. The Kaplan-Meier method was used to estimate 12-month freedom from AF, AFL, or AT ≥30 s after a 90-day blanking period. Subjects with a primary endpoint >12 months from index cryoablation had their time to primary endpoint set to 12.0 months, and subjects without a primary endpoint whose last visit is >12 months from index cryoablation were censored at 12.0 months. Major adverse events as defined and adjudicated as clinically relevant, device or procedure related, and occurring within 31 days of ablation were summarized. McNemar's test was used to compare arrhythmia-related symptom data at baseline and 12 months. A paired *t* test was used for SF-36 QoL and the EHRA score of AF-related symptoms. All p values < 0.05 were considered significant.

RESULTS

PATIENTS. Enrollment of patients began on December 2014 and ended May 2016. A total of 130

FIGURE 1 Patient Selection and Disposition



Flow chart detailing patient selection and disposition in the Cryo4Persistent trial beginning with enrollment. AF = atrial fibrillation; FU = follow-up.

patients were enrolled. The final analysis cohort included 101 patients. Failure to meet the 100% AF burden pre-ablation criteria was the primary reason for patient exclusion. Patients' disposition and baseline characteristics are detailed in Figure 1 and Table 1, respectively.

PROCEDURAL CHARACTERISTICS. All 101 patients underwent a single PV antrum isolation at the time of cryoballoon index ablation. No additional left atrial empirical lesions or complex fractionated atrial electrogram ablations were performed. PVI was achieved in 98% (99 of 101) of patients as confirmed by entrance or exit block and sinus rhythm post-procedure was achieved in 100% of patients. The 28-mm cryoballoon was used in all procedures. The additional use of the 23-mm balloon was applied in 2 (2.0%) patients for 1 application (right superior pulmonary vein) and 4 applications (left superior pulmonary vein, left inferior pulmonary vein, right inferior pulmonary vein, right superior pulmonary vein). The frequency of time to isolation visualization was as follows; left superior pulmonary vein 56.7%, left inferior pulmonary vein 58.3%, right superior pulmonary vein 48.0%, and right inferior pulmonary vein 47.9%. Index procedural characteristics are summarized in Table 2.

PRIMARY ENDPOINT: 12-MONTH FREEDOM FROM AF, AT, OR AFL. During study follow-up, 95.5% (274 of 287) of expected in-office follow up visits were attended. At 12 months, the Kaplan Meier estimate of PVI-only single-procedure freedom from all atrial arrhythmia (AF, AFL, or AT) recurrence was 60.7% (1-sided lower 95% confidence interval: 51.1%) (Figure 2). Thirty-three patients had a primary endpoint failure event and among these patients, 17 patients had a repeat ablation procedure (5 cryoablation, 12 radiofrequency), at a mean of 203.5 days. In the remaining 16 patients at the time of endpoint failure: 1 patient had a direct-current cardioversion and antiarrhythmic medication increased, 6 patients had a direct-current cardioversion, 1 patient had antiarrhythmic medication increased, and no immediate treatment was prescribed for 8 of 16 patients. Although discontinuation of AAD therapy was not a protocol requirement and not considered a treatment failure, the authors observed a decrease in AAD use during study follow-up. Of patients in sinus rhythm, 11 (12.4%) patients remained on AADs between 3 and 6 months, and at 12 months 3 (5.9%) patients were prescribed AADs.

IMPROVEMENT OF ARRHYTHMIA-RELATED SYMPTOMS, QoL, AND NEW YORK HEART ASSOCIATION FUNCTIONAL CLASSIFICATION. At 12 months post-ablation, 16% of patients had arrhythmia-related symptoms as compared with 92% at baseline ($p < 0.0001$). Arrhythmia-related symptom reduction was statistically significant 12 months post-ablation for all symptoms except syncope (2% to 0%): dizziness (14% to 2%), palpitations (68% to 8%), rapid heartbeat (27% to 5%), dyspnea (53% to 6%), and fatigue (42% to 4%) (all $p < 0.01$) (Figure 3A). The reduction of symptoms was supported by

TABLE 1 Patients' Baseline Characteristics

Demographics	N = 101
Male	75 (74.3)
Age, yrs	61.8 ± 10.5
PerAF onset, days	120.6 ± 98.0
CHA_2DS_2-VASc	1.6 ± 1.3
BMI, kg/m^2	28.2 ± 4.2
Systolic BP, mm Hg	129.9 ± 14.0
Diastolic BP, mm Hg	82.0 ± 11.1
LAD, mm	43 ± 5
LVEF, %	56 ± 8
Coronary artery disease	5 (5.0)
Hypertension	63 (62.4)
Type II diabetes	5 (5.0)
Dyslipidemia	20 (19.8)
Smoking	22 (21.8)
Alcoholism	4 (4.0)
Prior DCCV <12 Months	51 (50.5)
Prior stroke/transient ischemic event	4 (4.0)
NYHA functional classification	
Subject does not have heart failure	46 (45.5)
I	23 (22.8)
II	26 (25.7)
III	5 (5.0)
IV	0 (0)
Not reported	1 (1.0)

Values are n (%) or mean ± SD.

BMI = body mass index; BP = blood pressure; CHA_2DS_2-VASc = congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65–74 years, sex category; DCCV = direct-current cardioversion; LAD = left atrial diameter; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PerAF = persistent atrial fibrillation.

TABLE 2 Index Procedural Characteristics

Procedure Characteristics	N = 101
Cryoballoon applications (per patient)	6.1 ± 2.2
Mean application duration (per vein), s	213.9 ± 28.8
Nadir balloon temperature, °C	−55.2 ± 6.1
Time to isolation when observed, s	
LSPV	54.5
LIPV	44.3
RSPV	38.6
RIPV	48.3
28-mm balloon use	101 (100)
Achieve mapping catheter use	101 (100)
Conscious sedation	57 (56.4)
Phrenic nerve pacing	101 (100)
Esophageal monitoring	50 (49.5)
3D mapping	0 (0)
Right atrial flutter ablation	8 (7.9)
Lab occupancy time, min	133.1 ± 51.3
Procedure time, min	53.2 ± 22.2
Elapsed fluoroscopy, min	17.7 ± 11.5

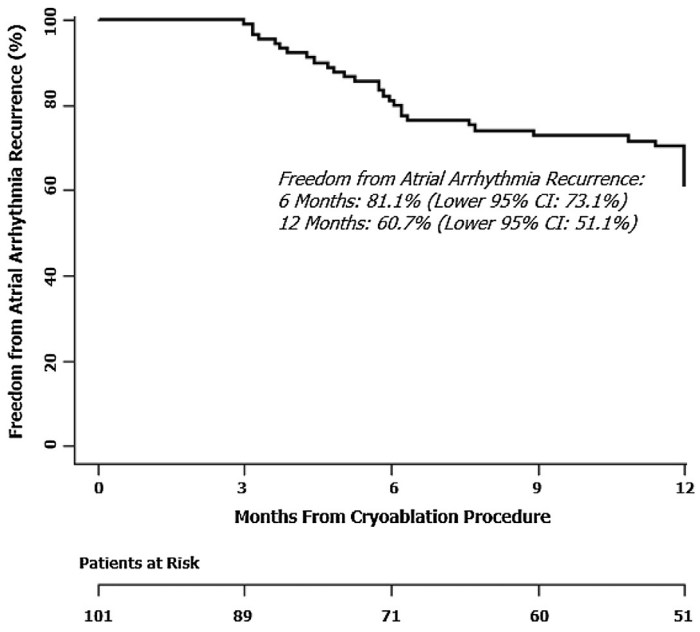
Values are mean ± SD or n (%) unless otherwise indicated.

3D = 3-dimensional; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

significant improvement in the mental and physical composite SF-36 scores and EHRA score at 12 months. The mean normalized SF-36 physical component score improved by 7.1 (46.9 to 53.9 points; $p < 0.0001$) and the mental component score improved by 3.3 (47.3 to 50.6 points; $p = 0.008$) (Figure 3B). In addition, the EHRA score decreased from 2.1 to 1.3 ($p < 0.01$) during patient follow-up (Figure 3C). New York Heart Association improvement of 1 functional class was observed in 31.3% of patients, 2 functional classes in 13.3% of patients, and 3 functional classes in 2.4% of patients from baseline to 12 months.

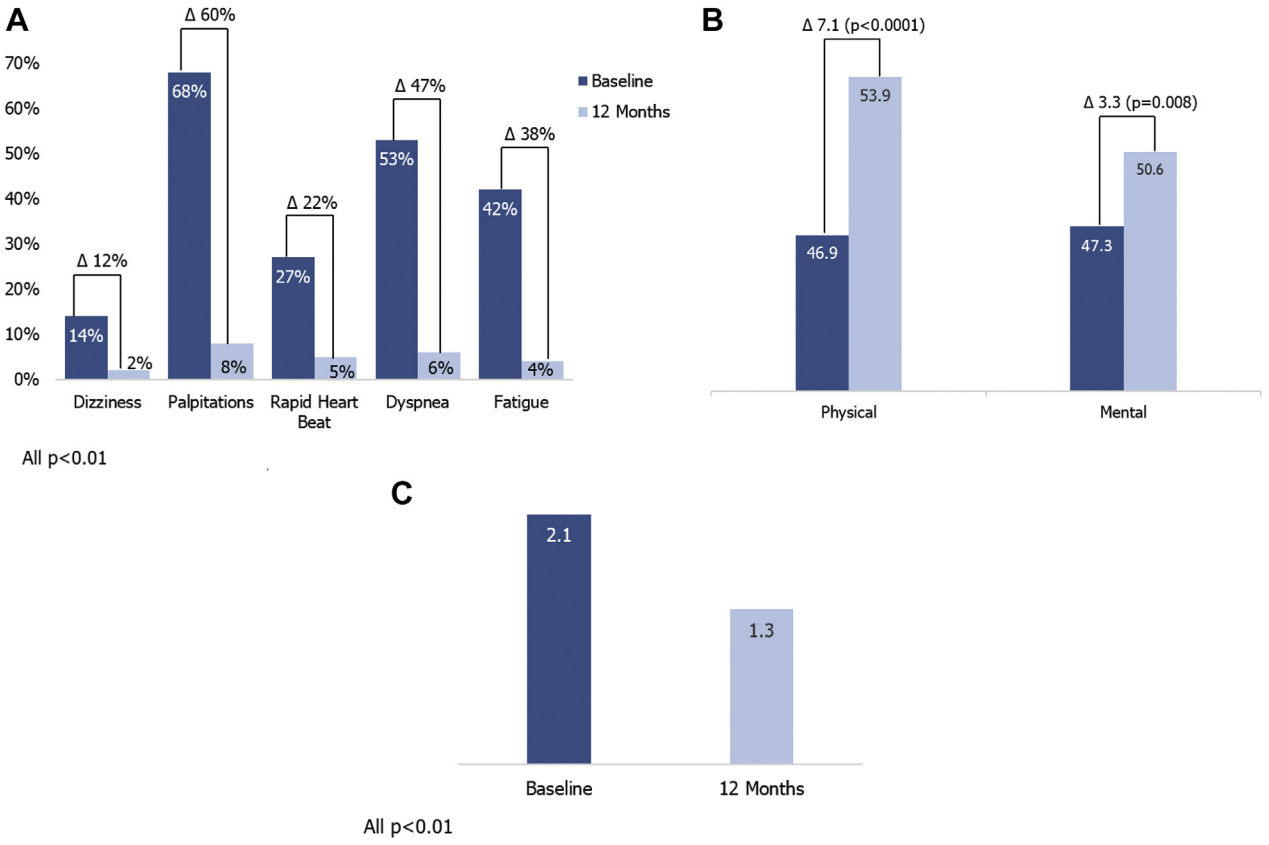
COMPLICATIONS. Major adverse events occurred in 4 of 101 (4.0%) patients as summarized in Table 3. There were 2 reports of vascular pseudoaneurysm, 1 transient ST-segment elevation event, and 1 pericardial effusion not requiring intervention. Procedure-related stroke or transient ischemic attack, PV stenosis, atrioesophageal fistula, persistent phrenic nerve injury (PNI), and death were not observed. The

FIGURE 2 Freedom From Atrial Fibrillation, Atrial Flutter, Atrial Tachycardia Recurrence



Kaplan-Meier curve of time to first atrial fibrillation, atrial flutter, or atrial tachycardia recurrence. Subjects with a primary endpoint >12 months from index cryoablation had their time to primary endpoint set to 12.0 months. CI = confidence interval.

FIGURE 3 Arrhythmia-Related Symptoms, QoL, and EHRA AF Symptom Score



(A) Arrhythmia-related symptoms reduction (baseline to 12 months). **(B)** 36-Item Short Form Health Survey (SF36) quality-of-life (QoL) improvement (baseline to 12 months). **(C)** European Heart Rhythm Association (EHRA) atrial fibrillation (AF) symptom score reduction (baseline to 12 months).

only cryoballoon-related complication reported was transient PNI that occurred in 2 (2.0%) patients with resolution before discharge and was not classified as a major adverse event.

TABLE 3 Major Adverse Events

Major events	N = 101
Vascular pseudoaneurysm	2 (2.0)
Transient ST-segment elevation	1 (1.0)
Pericardial effusion/tamponade	1 (1.0)
PNI at discharge	0 (0.0)
Stroke/TIA	0 (0.0)
Pulmonary vein stenosis	0 (0.0)
AE fistula	0 (0.0)
Death	0 (0.0)
Total	4 (4.0)

Values are n (%).
AE = atrioesophageal; PNI = phrenic nerve injury; TIA = transient ischemic attack.

DISCUSSION

The results of this study complement earlier findings (7-10) and appear to suggest that a PVI-only approach using exclusively the cryoballoon is a reasonable first line ablation strategy for the treatment of symptomatic PerAF as recommended in the 2016 European Society of Cardiology Guidelines and 2017 Heart Rhythm Society/EHRA Consensus statement (2,4).

To our knowledge, this is the first multicenter, international, prospective evaluation of PVI-only, single-procedure outcomes, using a second-generation cryoballoon in an objectively defined cohort of PerAF patients with confirmation of 100% AF burden at the time of ablation. At the time of patient recruitment, patients were classified as having PerAF based on initial physician diagnosis. During pre-ablation arrhythmia monitoring, patients who failed to document 100% AF burden were exited to ensure the most conservative evaluation of success in this PerAF

patient cohort. Longer duration or continuous monitoring would have been ideal; however, this protocol was aimed to improve the selection of patients included in this study.

In this context, the present multicenter evaluation of the second-generation cryoballoon paired with the Achieve mapping catheter for PVI-only ablation in PerAF patients demonstrated 60.7% freedom of all atrial arrhythmia recurrences 12 months after a single procedure on or off AADs. The significant decrease in the use of AADs during study follow-up is promising. Between 3 and 6 months of follow-up, 12.4% of patients in sinus rhythm remained on AADs and this decreased to 5.9% at 12 months. Although the specific detail on AAD use was not collected, we believe this decision may have been patient facilitated out of fear of recurrence and associated symptoms. Furthermore, the cryoballoon demonstrated a low (4%) incidence of major adverse events, with no clinical sequelae, and no patients experienced PNI at hospital discharge.

The QoL and arrhythmia-related symptom reduction results are equally encouraging. At 12 months post-ablation, 16% of patients had arrhythmia-related symptoms as compared with 92% at baseline ($p < 0.0001$). Arrhythmia-related symptom reduction was statistically significant 12 months post-ablation for all symptoms ($p < 0.01$) except syncope, which was too uncommon to allow for comparison (2 cases pre-ablation vs. 0 cases post-ablation). Furthermore, the reduction of symptoms was supported by significant improvement in SF-36 physical and mental composite scores and EHRA score from baseline to 12 months. To our knowledge, this is also the first time that a significant and clinically meaningful (18,19) QoL improvement (>5 in the physical component) has been so clearly demonstrated in a global cohort of patients with symptomatic PerAF.

Arrhythmia symptoms and QoL were evaluated in this trial to elucidate whether the clinical improvement that is frequently reported after an AF ablation, even in patients that experience an arrhythmia recurrence, is objectively observable, or if it is rather subjective. It could be reasonable to suggest, although unproven, that all patients (both successes and clinical trial failures) experienced AF burden and symptom reduction, as supported by the QoL outcomes. Consequently, some patients might be considered a "clinical success" despite an isolated arrhythmia recurrence, which was defined as a clinical trial failure.

Finally, the results of the present analysis are consistent with previously reported data (7-10) and particularly the recently published results from the 1STOP investigators. Tondo et al. (9) reported on real-world outcomes after single-procedure PVI-only outcomes in PerAF and long-standing PerAF patients followed according to standard of care at their respective institutions. In their evaluation, Tondo et al. demonstrated 63.9% freedom from atrial fibrillation at 12 months post-ablation, and a 4.3% acute or periprocedural complication rate. Furthermore, in context with the FIRE AND ICE trial, and while study designs are not directly comparable, we are encouraged by a relatively small (approximately 10%) decrease in freedom from AF in patients with more advanced disease progression.

This is the first multicenter, international, prospective study specifically designed to address the role of cryoablation in the management of PerAF. In this cohort of PerAF patients, a single-cryoballoon PVI-only ablation was an effective treatment for over 60% of patients with predicable procedure times and a low major device and procedure related complication rate. These findings make a significant contribution to the body of clinical evidence that support a PVI-only ablation as a reasonable treatment option for patients with PerAF.

STUDY LIMITATIONS. The present study is a single-arm study with no control group. However, bias in patient selection and subjective PerAF classification was mitigated by a rigorous inclusion-exclusion protocol. QoL and arrhythmia-related symptom reduction could have been influenced by multiple procedures and management of comorbidities and slight differences in operator or institutional ablation or monitoring protocols are relevant. We recommend future randomized studies, including pre- and post-ablation AF burden monitoring with implantable loop recorders or other devices, to evaluate PerAF outcomes in a comparative cohort of technologies as arrhythmias' burden reduction may be more clinically meaningful than a ≥30-s AF or AT recurrence.

CONCLUSIONS

This is the first multicenter prospective study to report safety, efficacy, and QoL outcomes after a single-procedure PVI-only ablation strategy using a second-generation cryoballoon in PerAF patients with documented 100% AF burden pre-ablation. This study demonstrates a 61% single-procedure success rate at 12 months post-ablation with a highly significant reduction in arrhythmia-related symptoms, and improved QoL. These outcomes are combined with a

beneficial safety profile and considerably short procedure times.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Cryoballoon PVI-only catheter ablation is an effective treatment option for patients with PerAF. This study demonstrated single-procedure success of 61% with patients experiencing a significant reduction in arrhythmic symptoms and an improved QoL.

TRANSLATIONAL OUTLOOK: Randomized studies with 100% AF burden monitoring comparing ablation technologies in terms of efficacy and safety are needed.

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APPENDIX For a supplemental table, please see the online version of this article.