Real-world experience with cryoballoon ablation for treatment of atrial fibrillation in Poland: 24-month outcomes from the Cryo Global Registry

Krzysztof Kaczmarek[1], Marcin Kuniewicz[2, 3], Janusz Romanek[4, 5], Kelly A van Bragt[6], Valentine Obidigbo[6], Rachelle E Kaplon[6], Paweł Ptaszyński[1]

[1]Department of Electrocardiology, Medical University of Lodz, Łódź, Poland
[2]Department of Electrocardiology, The John Paul II Hospital, Kraków, Poland
[3]Department of Anatomy, Jagiellonian University Medical College, Kraków, Poland
[4]Cardiology Department with the Acute Coronary Syndromes Subdivision, Clinical Provincial Hospital No 2, Rzeszów, Poland
[5]Medical College, University of Rzeszów, Poland
[6]Cardiac Ablation Solutions, Medtronic, Inc., Mounds View, Minnesota, United States

Correspondence to:
Krzysztof Kaczmarek, MD, PhD, Department of Electrocardiology, Medical University of Lodz, Pomorska 251, 92–213 Łódź, Poland, phone +48 42 201 43 60, e-mail: krzysztof.kaczmarek@umed.lodz.pl

DOI: 10.33963/v.phj.100380

Received:
November 10, 2023

Accepted:
April 23, 2024

Early publication date:
April 29, 2024

INTRODUCTION

Pulmonary vein isolation (PVI) *via* catheter ablation is a well-established rhythm-control strategy for symptomatic atrial fibrillation (AF) [1]. A recent survey in electrophysiology centers in Poland identified widespread adoption of cryoballoon PVI [2]. Despite widespread adoption of cryoballoon ablation (CBA), local real-world evidence is limited. This sub-analysis of the "Cryo Global Registry" aims to evaluate the use, safety, and long-term efficacy of CBA in a cohort of patients treated in Poland.

METHODS

This analysis included all patients with paroxysmal AF (PAF) or persistent AF (PsAF) enrolled by 3 centers in Poland (Central Clinical Hospital of the Medical University of Lodz, Łódź, John Paul II Hospital, Kraków, and Clinical Provincial Hospital No 2, Rzeszów) in the Cryo Global Registry (NCT02752737). The patients underwent CBA using the Arctic Front (Advance)™ as described previously [3, 4]. An independent ethics committee approved the study at each center, and all patients provided written informed consent before participating. Procedures were conducted according to the standard of care. A dedicated, 15-F steerable sheath (FlexCath [Advance] Steerable Sheath; Medtronic, Inc.) was used to introduce a 23- or 28-mm CBA catheter into the left atrium *via* transseptal puncture and delivered to the targeted pulmonary vein (PV) with a J-tip guidewire or dedicated circular mapping catheter (Achieve [Advance], Medtronic, Inc.). Phrenic nerve monitoring was recommended during right-sided PVI. PVI was demonstrated by entrance and/or exit block following the ablation. Patients were followed up *via* telephone and/or in-person office visits according to the site standard-of-care protocol. Monitoring methods included Holter monitors, electrocardiogram recording, trans-telephonic monitors, or implantable cardiac devices. Annual visits were required.

Statistical analysis

Kaplan–Meier methods were used to estimate 12- and 24-month freedom from atrial arrhythmia (AA) recurrence. Event times were defined as ≥30-second recurrence of AF, atrial flutter, or atrial tachycardia following a 90-day blanking period, documented on a rhythm monitoring device. Patients who did not have an event were censored at their last reported study visit. Standard error was approximated with Greenwood's formula. A log-rank test was used to assess relationships in AA recurrence between patients receiving single vs. multiple freezes per vein. Kaplan–Meier methods were also used to estimate 12- and 24-month freedom from healthcare utilization (repeat ablation, rehospitalization, and cardioversion). Changes in quality-of-life (QoL; EQ-5D-3L questionnaire) [5] from baseline to 12- or 24-months were assessed with ANOVA, while changes in symptoms from baseline to 12 or

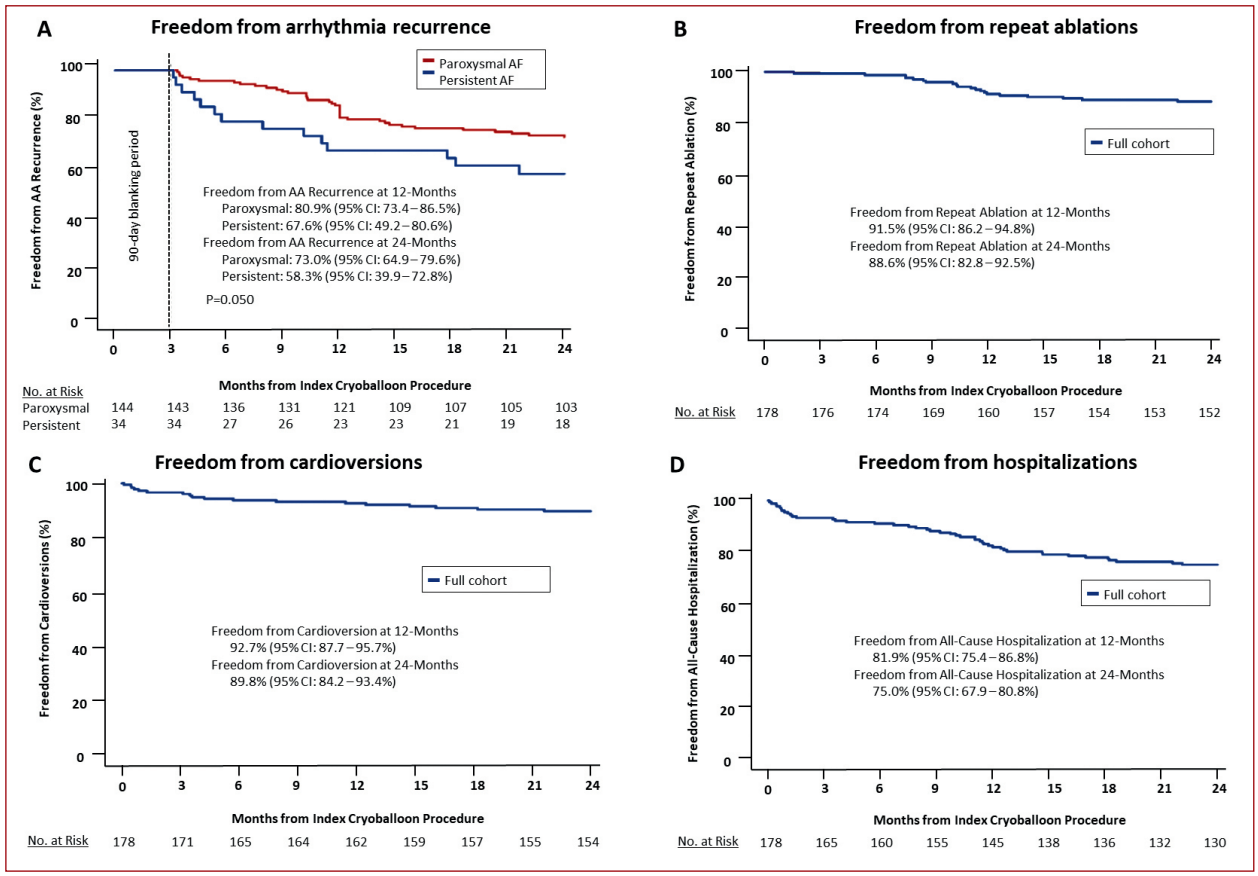

Figure 1. Freedom from: AA recurrence after a 90-day blanking period (**A**), repeat ablation (**B**) cardioversion (**C**), and all-cause hospitalization (**D**) in patients with paroxysmal and persistent AF lasting 24 months

Abbreviations: AA, atrial arrhythmia; AF, atrial fibrillation; CI, confidence interval

24 months were assessed using generalized estimating equations with logit link function. Values of P <0.05 were considered significant.

RESULTS

Between April 2018 and September 2019, 178 patients were enrolled. Patients had a mean age of 60 with a standard deviation (SD) of 10 years; 70.8% were male and 80.9% had PAF (Supplementary material, *Table S1*). The mean (SD) times of the procedure, left atrial dwell, and total fluoroscopy were 78 (22), 64 (22), and 28 (34) minutes, respectively. The median (Q1–Q3) number of cryoapplications per vein was 1 (1-1). CBA procedures were completed primarily under conscious sedation (98.3%), without pre-procedural imaging, 3D electroanatomical mapping, intracardiac echocardiography, or esophageal monitoring. Phrenic nerve monitoring was conducted in 172 cases (96.6%). Acute procedural success (defined as isolating all targeted pulmonary veins [PVs]) was achieved in 173 patients (97.2%). A subset of patients underwent prior ablation for atrial flutter (9.0%) and PVI (1.7%). In total, 175 (98.3%) patients completed a 12-month follow-up, and 171 (96.1%) completed a 24-month follow-up. The median (Q1–Q3) rate of office visits was 2.0 (2.0–4.0) during 24 months of follow-up. Rhythm monitoring was conducted ≥1 time during follow-up in 121 (68.0%) patients (Supplementary material, *Figure S1*).

Freedom from AA recurrence and healthcare utilization are depicted in Figure 1. All 44 cases of rehospitalization were cardiovascular-related, of which 28 (63.6%) were due to AF recurrence. The relationship between freedom from AA recurrence and single freeze attitude was examined. Unadjusted analysis showed no difference in freedom from recurrence between patients receiving a single freeze in all PVs vs. patients receiving multiple freezes in at least one PV (P = 0.42; Supplementary material, *Figure S2*). Anti-arrhythmic drugs (AADs) prescription in PAF patients decreased from baseline (77.0%) to 24 months (63.9% on discharge, 46.1% at 12- and 51.8% at 24-months). In the PsAF subpopulation, AAD use was maintained throughout the follow-up period (73.5% on discharge, 64.7% at 12- and 75.0% at 24-months). In total, 4 system- or procedure--related serious adverse events occurred in 4 patients (2.2%) during the index ablation procedure (one cardiac tamponade, one vascular pseudoaneurysm, and two instances of phrenic nerve paralysis). Both persisted after discharge, with resolution at 238 and 260 days post-onset.

Symptom and QoL data were available at baseline, 12- and 24-months in 171 (96.1%) patients. At baseline, 4 (2.3%) patients reported being free of predefined symptoms

(palpitations, dizziness, rapid heartbeat, dyspnea, fatigue, syncope), which increased to 100 (58.5%) and 108 patients (63.2%) at 12- and 24-months, respectively (P <0.01). The mean (SD) EQ-5D-3L index score increased from 0.84 (0.14) at baseline to 0.89 (0.12) at 12 months and 0.87 (0.14) at 24 months (P <0.01).

DISCUSSION

In this multicenter registry, the vast majority of CBA was performed as the index ablation procedure. One-year outcomes in the Polish cohort (80.9% and 67.6% in PAF and PsAF, respectively) were slightly lower than reported for global (86.4% and 70.9% in PAF and PsAF, respectively) and European (83.3% and 71.6% in PAF and PsAF, respectively) cohorts of the Cryo Global Registry [3, 4]. Observed differences in efficacy outcomes may be related to differences in study populations, standard-of-care monitoring methods, and AAD prescription post-ablation. Sixty-eight percent of patients received rhythm monitoring at least once, which likely resulted in underreporting of (asymptomatic) AA recurrence. In our analysis, the rate of AAD use was higher than in global and European cohorts of the Cryo Global Registry [3, 4]. However, frequent use of AADs on discharge corresponds with a 2020 survey of Polish electrophysiology centers [2]. Further analysis showed significant heterogeneity in the rate of AAD prescription among participating Polish centers (Supplementary material, *Table S2*). Known risk factors for recurrence in Polish patients undergoing CBA are left atrial enlargement in combination with left ventricular wall thickening, patent foramen ovale, and left atrial appendage flow velocity [6–8]. Independent risk factors for CBA were not assessed in this analysis, but a single freeze attitude was analyzed and did not affect the outcome.

Importantly, real-world use of cryoablation in Poland was associated with a low rate of serious system- or procedure-related adverse events (2.2%), comparable to previous reports from the Cryo Global Registry (2.6%–4.7%) [3, 4, 9]. We acknowledge that phrenic nerve monitoring was not conducted in 6 cases, which could have led to underreporting of the rate of transient phrenic nerve injury reported here.

In conclusion, these data demonstrate that real-world use of CBA in Poland is associated with a favorable longer-term impact on healthcare utilization and improvement in symptom burden and QoL over 24 months, with a low rate of serious system- or procedure-related adverse events.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/polish_heart_journal.

Article information

Conflict of interest: KK and PP declare lecturer and consultant fees from Medtronic. KAvB, VO, and REK are employed by, and stockholders, of Medtronic. MK and JR declare no conflict of interest.

Funding: None.

REFERENCES

1. Hindricks G, Potpara T, Dagres N, et al. Corrigendum to: 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021; 42(40): 4194, doi: 10.1093/eurheartj/ehab648, indexed in Pubmed: 34520521.
2. Wojdyła-Hordyńska A, Baran J, Mazurek M, et al. Results of a survey concerning atrial fibrillation ablation strategies in Poland. Kardiol Pol. 2020; 78(10): 974–981, doi: 10.33963/KP.15407, indexed in Pubmed: 32486629.
3. Chun KR, Okumura K, Scazzuso F, et al. Safety and efficacy of cryoballoon ablation for the treatment of paroxysmal and persistent AF in a real-world global setting: Results from the Cryo AF Global Registry. J Arrhythm. 2021; 37(2): 356–367, doi: 10.1002/joa3.12504, indexed in Pubmed: 33850577.
4. Földesi C, Misiková S, Ptaszyński P, et al. Safety of cryoballoon ablation for the treatment of atrial fibrillation: First European results from the cryo AF Global Registry. Pacing Clin Electrophysiol. 2021; 44(5): 883–894, doi: 10.1111/pace.14237, indexed in Pubmed: 33813746.
5. EQ-5D-3L: EuroQol Research Foundation. https://euroqol.org/eq-5d-instruments/eq-5d-3l-about/ (accessed: November 9, 2023).
6. Warmiński G, Urbanek P, Orczykowski M, et al. Association of left atrial enlargement and increased left ventricular wall thickness with arrhythmia recurrence after cryoballoon ablation for atrial fibrillation. Kardiol Pol. 2022; 80(11): 1104–1111, doi: 10.33963/KP.a2022.0191, indexed in Pubmed: 35950547.
7. Kosztin A, Merkel E, Merkely B. Association of left atrial enlargement and increased left ventricular wall thickness with arrhythmia recurrence after cryoballoon ablation for atrial fibrillation. Kardiol Pol. 2022; 80(11): 1070–1071, doi: 10.33963/KP.a2022.0277, indexed in Pubmed: 36477905.
8. Kiełbasa G, Bednarek A, Bednarski A, et al. Patent foramen ovale and left atrial appendage flow velocity predict atrial fibrillation recurrence post cryoballoon ablation. Kardiol Pol. 2021; 79(7-8): 756–764, doi: 10.33963/KP.a2021.0004, indexed in Pubmed: 34002841.
9. Kimura M, Kobori A, Nitta J, et al. Cryoballoon ablation for paroxysmal atrial fibrillation in Japan: 2-year safety and efficacy results from the Cryo AF Global Registry. J Interv Card Electrophysiol. 2022; 64(3): 695–703, doi: 10.1007/s10840-022-01132-0, indexed in Pubmed: 35119586.