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Safety and efficacy of cryoballoon versus radiofrequency ablation for atrial fibrillation in elderly patients: A real-world evidence

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ABSTRACT

Background: There are limited data describing the experience of radiofrequency (RF) vs. cryoballoon (CB) ablation for atrial fibrillation (AF) among elderly patients in the United States.

Methods: We conducted a retrospective analysis of patients ≥ 75 years of age undergoing index RF vs. CB ablation between January 2014 and May 2020 at our center. The choice of ablation technique was left to the operator's discretion. Major complications and efficacy, defined as freedom from any atrial tachyarrhythmia (ATA) lasting ≥ 30 s after one year of follow-up, were assessed in patients with index RF vs. CB ablation.

Results: In our cohort of 186 patients, the median age was 78 (76–81) years, 54.8% were men, and 39.2% had persistent AF. The median CHA₂DS₂-VASc score was 4 (3–4), while the median duration of AF was 3 (1–7) years. The majority (n = 112, 60.2%) underwent RF ablation. The median procedure time was significantly lower in CB group (197 vs 226.5 min, $p < 0.01$). The incidence of complications was similar in the two sub-groups (RF: 1.8% vs. CB: 2.7%, $p = 0.67$). Similarly, arrhythmia-free survival rate on antiarrhythmic drugs at 1-year follow-up remained statistically comparable (63.4% vs. 68.9%, $p = 0.33$) between patients receiving RF vs. CB ablation.

Conclusion: The safety and efficacy of RF vs. CB ablation for AF remained comparable in our cohort of patients older than 75 years. CB ablation was associated with a shorter procedure time.

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1. Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia in clinical practice leading to significant morbidity and mortality. Pulmonary vein isolation (PVI) via catheter ablation (CA) has become an effective procedure for AF management, and given the association of AF with increasing age, a rising proportion of patients of advanced age are receiving this procedure. There have been significant advancements in ablation techniques over the last decade. Cryoballoon (CB) ablation has recently emerged as an effective strategy for the treatment of symptomatic paroxysmal AF (PAF) [1]. CB ablation has been reported to be associated with shorter procedure time and comparable safety and efficacy as compared to radiofrequency (RF) ablation in randomized

controlled trials (RCTs) [2,3]. Interestingly, these RCTs were conspicuous for the exclusion of patients with advanced age. While several studies have reported data regarding the safety and efficacy of CB vs. RF ablation of AF in elderly patients from Asia [4,5], there is a paucity of such data from the United States (US). Accordingly, the objective of our study was to provide real-world evidence of the safety and efficacy of CB vs. RF AF ablation in a contemporary cohort of patients at our center.

2. Methods

2.1. Patient selection

We conducted a single-center, retrospective cohort study comprised of patients enrolled in an IRB-approved, prospectively populated clinical database of AF ablation patients. The included study patients were at least 75 years of age and underwent their index AF ablation using either RF or CB ablation technique at our center between January 2014 and May 2020. The demographics,

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clinical history, procedural data, complications, and outcomes were recorded for each case. Patients were excluded if they had prior CA of AF, LA thrombus detected on pre-procedural transesophageal echocardiography (TEE) or computed tomography (CT) scan, and advanced comorbidities and frailty precluding CA.

2.2. Peri-procedural management

Antiarrhythmic drug (AAD) management was left to the discretion of the operator. Pre-procedure TEE was performed only for the patients presenting in AF at the time of ablation as per institutional practice. All patients underwent a preprocedural computed tomography (CT) scan to assess the left atrium (LA) and pulmonary vein (PV) anatomy in detail. Catheter ablation in patients on warfarin was performed without cessation of warfarin, and patients on direct oral anticoagulants (DOACs) held anticoagulation for 12–24 h prior to the ablation procedure, with resumption 4 h post-procedure. Anticoagulation was continued for a minimum of 3 months following the ablation procedure for all patients unless contraindicated. The choice of ablation technique was left to the discretion of the operator. All ablation procedures were performed under general anesthesia. Femoral site access was obtained, and intravenous heparin was administered to maintain activated clotting times >350 s.

2.3. RF ablation

After performing a double transseptal puncture, a Lasso or PentaRay mapping catheter (Biosense-Webster, Diamond Bar, California) was positioned in the left atrium. An electroanatomic map of the left atrium was obtained using the CARTO system (Biosense-Webster) and superimposed on a pre-acquired CT scan. Right-sided phrenic nerve pacing was performed by placing a catheter against the phrenic nerve at or above the level of the superior vena cava. A 4-mm open-tip irrigated RF catheter with a contact force sensor (Thermocool SmartTouch, Biosense-Webster) was then positioned in the left atrium: PVI was performed using a real-time automated display of RF application points (Visitag, Biosense-Webster) with predefined catheter stability settings. Additional ablation sets were performed at the discretion of the operator in patients with persistent AF (PsAF), non-PV focal triggers initiating AF, or macroreentrant atrial tachycardia or atrial flutter, in accordance with 2017 HRS consensus guidelines [1]. Non-PV ablation consisted of lesions involving the roof, floor, posterior wall, mitral isthmus, cavotricuspid isthmus (CTI), and other linear lesions. Starting energy delivery parameters were 25–40 W on the posterior wall and 35–45 W at other sites. Target contact force was between 5 and 20 g at all sites. Esophageal temperature was monitored, and the RF delivery paused if the esophageal temperature increased by 0.5 °C. Electric isolation of PVs was confirmed by entrance block to individual PVs, assessed by PentaRay catheter positioned at the PV antrum.

2.4. CB ablation

Cryoballoon ablation was performed exclusively with the second-generation cryoballoon catheter with a 23 or 28 mm balloon (Arctic Front Advance, Medtronic). Pre and post-ablation LA mapping was performed at the discretion of the operator and consisted of either electroanatomical mapping with the CARTO system (Biosense-Webster, Diamond Bar, California), PV angiography, and fluoroscopic mapping only, or some combination of both. Lesion application was again at the discretion of the operator, but in the majority of cases, consisted of at least two 180-s freezes to each PV. Goal temperatures were between –35 and –55°C.

Freezes were aborted if the esophageal temperature fell below 28 °C or if phrenic nerve pacing showed diminution of diaphragmatic excursion during right-sided PV lesion delivery. Assessment of PV isolation was made after 20 min waiting period, either with the Achieve catheter or a designated EAM mapping catheter.

2.5. Outcome assessment

Arrhythmia recurrence and peri-procedural complications were ascertained based on monitoring strategies suggested in consensus document [1]. Arrhythmia recurrence was defined as any AF or atrial tachyarrhythmia (AT) sustained for >30 s recorded by a surface electrocardiogram or rhythm monitoring device after a 90-day blanking period. Procedure-related complications, including vascular complications, major bleeding, phrenic nerve palsy, cerebral embolism, pericardial effusion/tamponade, atri-esophageal fistula, or extended hospitalization (>48 h) were assessed. All patients were observed in the hospital for a minimum of one-night post-ablation. Routine follow-up (history, exam, and electrocardiography) was performed at the outpatient clinic or by a local cardiologist at 3, 6, and 12 months, and additionally, if prompted by symptoms. Holters or event monitors were arranged for patients in whom symptoms suggestive of AF developed in the post-blanking phase of follow-up. Pacemaker interrogation records were also used for arrhythmia recurrence monitoring when available. AAD therapy, if present at the time of ablation, was discontinued at the 3-month follow-up visit based on the operator's discretion. Outcomes were assessed via electronic health record reviews or phone interviews.

2.6. Statistical analysis

Continuous data were analyzed using the student's t-test for normally distributed data and the Mann-Whitney test for non-normally distributed data. Categorical data were analyzed using the χ^2 test. Values are presented as mean \pm standard deviation or median and interquartile range (Q1-Q3) according to distribution for continuous data and count and percentage for categorical data unless otherwise stated. The cumulative probability of survival free from atrial arrhythmia was displayed according to the Kaplan–Meier method, with comparisons of cumulative event rates by the log-rank test. Follow-up for all patients was censored at one year after ablation. A p-value of <0.05 was considered statistically significant. Analyses were performed using SPSS Statistics version 23.0 (IBM Corporation, Armonk, New York) and STATA Version 13 (Stata Corp, College Station, TX).

3. Results

3.1. Patient characteristics

Our study included a total of 186 patients (Fig. 1), of whom 112 (60.2%) underwent RF ablation, and 74 (39.7%) underwent CB ablation (Table 1). The median age of the study patients was 78 (76–81) years, 138 patients belonged to the age group of 75–80 years and the remaining 48 patients were older than 80 years. A total of 102 (54.8%) were men. The median time since AF was first diagnosed was 3 (1–7) years. 113 (60.8%) of all patients had PAF, while 73 (39.2%) had PsAF. A greater proportion of the patients with PAF (71.6 vs. 53.6%, $p = 0.01$) were included in the CB ablation cohort. The median body mass index (BMI) was 27.7 (24.2–31.7) kg/m², and the median CHA₂DS₂-VASc score was 4 (3–4). A history of hypertension was documented in 139 (74.7%) patients, diabetes mellitus (DM) and congestive heart failure (CHF) in 31 (16.7%) patients each, stroke/transient ischemic attack (TIA) in 19 (10.2%)

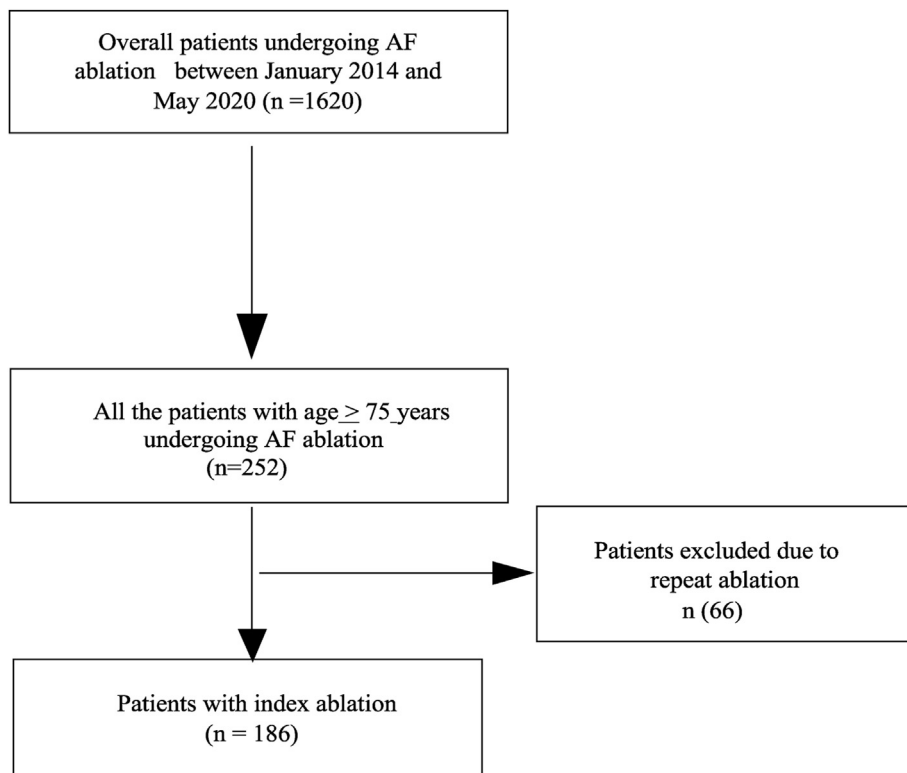


Fig. 1. Flow chart outlining the patient selection.

Table 1
Baseline characteristics, for all patients and by RF ablation vs. CB ablation.

Characteristics	Total (n = 186)	RF ablation (n = 112)	CB ablation (n = 74)	p-value
Age (years)	78 (76–81)	78 (76–81)	77.5 (76–80)	0.63
Male, n (%)	102 (54.8)	59 (52.7)	43 (58.1)	0.46
Body mass index (kg/m ²)	27.7 (24.2–31.7)	27.9 (24.0–31.8)	26.8 (24.3–30.9)	0.56
AF type				0.01
Paroxysmal, n (%)	113 (60.8)	60 (53.6)	53 (71.6)	
Persistent, n (%)	73 (39.2)	52 (46.4)	21 (28.4)	
Duration of AF (years)	3 (1–7)	3 (1–6)	3 (0.5–7.5)	0.60
Congestive heart failure, n (%)	31 (16.7)	19 (17)	12 (16.2)	1.00
Hypertension, n (%)	139 (74.7)	75 (67)	64 (86.5)	<0.01
Diabetes mellitus, n (%)	31 (16.7)	21 (18.8)	10 (13.5)	0.34
Stroke/TIA, n (%)	19 (10.2)	10 (8.9)	9 (12.2)	0.47
Vascular disease, n (%)	47 (25.3)	28 (25)	19 (25.7)	0.91
CHA ₂ DS ₂ -VASc score	4 (3–4)	4 (3–4)	4 (3–4)	0.74
Obstructive sleep apnea, n (%)	16 (8.6)	12 (10.7)	4 (5.4)	0.20
Chronic kidney disease, n (%)	13 (7)	7 (6.3)	6 (8.1)	0.62
Chronic obstructive pulmonary disease, n (%)	9 (4.8)	6 (5.4)	3 (4.1)	1.00
PPM, n (%)	17 (9.1)	8 (7.1)	9 (12.2)	0.24
LA diameter by TTE (cm)	4.34 ± 0.74	4.35 ± 0.74	4.31 ± 0.75	0.72
LV ejection fraction by TTE (%)	60 (55–64)	60 (50–60)	60 (55–65)	<0.01
Anticoagulation				0.81
None, n (%)	7 (3.8)	5 (4.5)	2 (2.7)	
Direct oral anticoagulant, n (%)	150 (80.6)	90 (80.4)	60 (81.1)	
Coumadin, n (%)	29 (15.6)	17 (15.2)	12 (16.2)	
Antiarrhythmic				
Class I, n (%)	7 (3.8)	3 (2.7)	4 (5.4)	0.43
Class III, n (%)	61 (32.8)	32 (28.6)	29 (39.2)	0.13

AF: atrial fibrillation, PPM: permanent pacemaker, LA: left atrial, LV: left ventricle, TTE: transthoracic echocardiogram.

patients, and OSA in 16 (8.6%) patients. A higher proportion of the patients in the CB ablation group were hypertensive (86.5 vs. 67%, $p < 0.01$). Other baseline comorbidities remained comparable between the groups. A total of 17 (9.1%) patients had permanent pacemaker (PPM) implanted and the proportion of patients with

PPM remained comparable between the study groups (7.1 vs. 12.2%, $p = 0.24$). The mean LA diameter for the total cohort was 4.34 ± 0.74 cm, while the median left ventricular ejection fraction (LVEF) was 60 (55–64) %. Patients undergoing CB ablation had higher LVEF [60 (55–65) vs. 60 (50–60), $p < 0.01$] as compared to

the RF cohort. There was no significant difference in LA size between the RF vs. CB cohorts.

3.2. Procedural data

All the included patients achieved acute procedural success with complete isolation of PVs. One patient in CB group required touch up RF ablation to achieve complete PVI. Out of 112 patients undergoing RF ablation, a total of 74 (66%) patients also received non-PV ablation (Table 2). Similarly, in the CB group, a total of 14 (18.9%) patients underwent non-PV ablation by RF energy. CTI ablation was the most common non-PV ablation performed in 33(17.7%) patients, followed by roof ablation performed in 23 (12.4%) patients. The proportions of patients requiring roof, posterior wall, mitral isthmus line, and CTI ablations were higher in the RF cohort as compared to the CB cohort. The median procedure time was higher in RF group [226.5 (194.7–286.7) vs. 197 (172.7–233), $p < 0.01$] as compared to CB group (Table 3). There was no significant difference in recurrence rate at 1- year of follow up between RF and CB groups (36.6 vs 31.1%, $p = 0.43$).

3.3. Safety and efficacy outcomes

The incidence of overall complications was comparable between the RF and CB cohort (1.8% vs. 2.7%, $p = 0.67$) (Table 4). Pericardial effusion and cardiac tamponade occurred in one patient each in the RF group as compared to one patient developing pericardial effusion in the CB group. One patient in the CB group developed transient acute kidney injury. Two patients in each group required extended hospitalization (>48 h). No access site or vascular complications were observed. No incidence of PNP were recorded. There was no significant difference between the arrhythmia-free survival rate at 1-year follow-up between patients receiving RF vs. CB ablation (63.4 vs. 68.9%, $p = 0.33$) (Fig. 2). A total of 64 (34.4%) patients were on AAD. Among RF group, 40 (35.7%) patients continued AAD, similarly, 24 (32.4%) patients continued AAD in the CB group. The arrhythmia free survival off AAD at 1-year follow up was 47.3% and 55.4% in the RF and CB groups respectively. All the included patients continued anticoagulation at 1 year of follow-up. A total of 19 (10.2%) patients underwent repeat ablation.

4. Discussion

Given the rising proportion of elderly patients with AF, the utilization of CA in elderly patients is growing. Numerous studies have investigated the outcomes of CA of AF in elderly patients, and the mean age of the included patients is variable [4–15]. Previously published randomized controlled trials such as CABANA included 14% of the patients older than 75 years undergoing CA for AF, similarly EAST AFNET trial included 30% of the patient with age >75 years [14,15]. Santangeli et al., reported comparable safety and efficacy outcomes of CA of AF in octogenarians as compared to a younger patient cohort (<80 years) [16]. Peri-procedural CVE has theoretically remained an important concern with CA of AF in

elderly patients. Guiot et al., in their study reported a comparable peri-procedural CVE rate between patient cohorts ≥ 65 and < 65 years old [17]. While there is substantial data regarding the outcomes of CA for AF in elderly patients, the data comparing the outcomes of the RF vs CB AF ablation in the elderly patients remains limited. To the best of our knowledge, ours is the only study from the US providing real-world evidence of safety and efficacy outcomes of CB vs. RF AF ablation in patients older than 75 years. The main findings of our study are: (1) The safety and efficacy of index CB vs. RF AF ablation in the elderly patients appears to be comparable; (2) CB AF ablation is associated with a shorter procedure time.

Our findings are in line with the previous studies from Asia, which also reported comparable safety and efficacy of CB vs. RF ablation of AF in elderly patients [4,5]. The mean age of included patients was 78 years in these studies, similar to our study. However, our success rate at one-year follow-up is lower as compared to the previous studies. This may be due to a greater proportion of PsAF patients, higher average LA diameter, and higher BMI in our cohort, as these factors have been reported to be associated with a lower success rate of an ablation procedure [4,18–20]. Our results suggest that CB AF ablation is associated with a shorter procedure time as compared to RF AF ablation in patients older than 75 years. Similar findings have been reported in the previous studies [4,5]. The shorter procedure time with CB ablation could probably be due to a single transseptal puncture and single circumferential ablation with large cooling surface area available in second generation CB [21]. Shorter procedure time of ablation can be beneficial in the elderly patients since it can minimize the duration of anesthesia and can translate into decreased peri-procedural complications.

Our complication rates are lower in comparison to the rate reported in previous studies [4,5]. Transient PNP has been reported to be the most commonly associated complication with CB ablation [22,23]. Ikenouchi et al., in their study of patients >75 years old, reported transient PNP as the most common complication following CB ablation [5]. However, we did not observe any incidence of PNP in our study. This could be due to effective phrenic nerve monitoring; however, it could also reflect the small size of the CB cohort in our study. We also observed a lower incidence of cardiac tamponade as compared to previous studies. Overall, the safety data from our small study suggest that CA of AF is a relatively safe procedure in patients >75 years old with appropriate patient selection.

5. Limitations

Our study has several limitations, including those inherent to a single-center, non-randomized, retrospective study with small sample size. Given the retrospective nature of the study, there could be a possibility of selection bias. Nevertheless, our study provides valuable real-world data from the US related to the AF ablation outcomes in the elderly population who are generally considered at high risk for ablation procedure and provide impetus for further prospective large-scale randomized studies. Finally, the

Table 2

Extra pulmonary ablation lesions, for all patients and by RF ablation vs. CB ablation.

Variables	Total (n = 186)	RF ablation (n = 112)	CB ablation (n = 74)	p-value
Roof ablation, n (%)	23 (12.4)	19 (17)	4 (5.4)	0.01
Floor ablation, n (%)	5 (2.7)	4 (3.6)	1 (1.4)	0.65
Posterior wall ablation, n (%)	12 (6.5)	12 (10.7)	0 (0)	<0.01
Mitral isthmus line ablation, n (%)	14 (7.5)	12 (10.7)	2 (2.7)	0.04
CTI ablation, n (%)	33 (17.7)	26 (23.2)	7 (9.5)	0.01
Other, n (%)	1 (0.5)	1 (0.9)	0 (0)	1.00

Table 3
Procedural characteristics, for all patients and by RF ablation vs. CB ablation.

Variables	Total (n = 186)	RF ablation (n = 112)	CB ablation (n = 74)	p-value
Pulmonary vein isolation rate, n (%)	186 (100)	112 (100)	74 (100)	
Procedure duration (minutes)	213.5 (185.2–259.0)	226.5 (194.7–286.7)	197 (172.7–233)	<0.01
Recurrence at 1-year of F/up, n (%)	64 (34.4)	41 (36.6)	23 (31.1)	0.43

Table 4
Procedural complications, for all patients and by RF ablation vs. CB ablation.

Complications	Total (n = 186)	RF ablation (n = 112)	CB ablation (n = 74)	p-value
Overall, n (%)	4 (2.2)	2 (1.8)	2 (2.7)	0.67
Cardiac tamponade, n (%)	1 (0.5)	1 (0.9)	0	0.51
Acute kidney injury, n (%)	1 (0.5)	0	1 (0.4)	0.51
Pericardial effusion, n (%)	2 (1.1)	1 (0.9)	1 (1.4)	0.51
Extended hospitalization (>48 h), n (%)	4 (2.2)	2 (1.8)	2 (2.7)	0.65

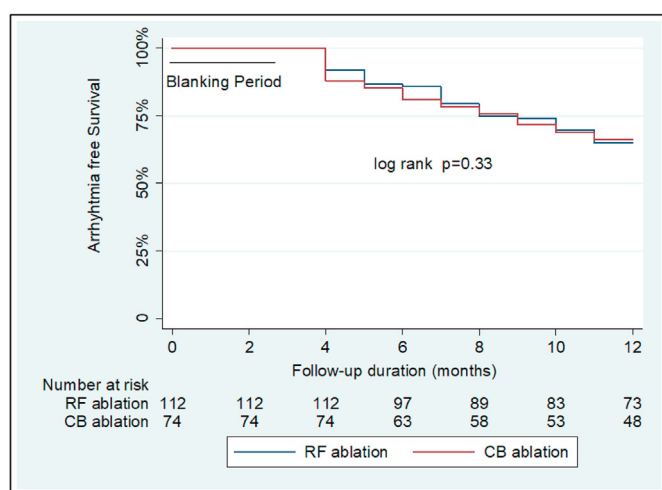


Fig. 2. Kaplan-Meier survival curve of patients free of arrhythmia at 1 year.

lack of continuous ECG monitoring after ablation could have resulted in the underestimation of arrhythmia recurrence.

6. Conclusion

In conclusion, our study suggested that the safety and efficacy of index CB vs. RF AF ablation in patients >75 years of age might be comparable. CB AF ablation may offer the advantage of a shorter procedure time. Further prospective randomized studies with a large sample size are required to confirm our findings and to guide the selection of appropriate ablation modality in the elderly age group to achieve optimal outcomes.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authors have no conflicts to disclose

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