Safety and Efficacy of Cryoballoon versus Radiofrequency Ablation for Atrial Fibrillation in Elderly Patients and Predictors of Arrhythmia Recurrence

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Abstract

Introduction: There are limited data describing the experience of index 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 AF ablation between January 2010 and March 2019 at our center. Major complications and efficacy, defined as freedom from any atrial tachyarrhythmia (ATA) lasting [?]30 seconds after one year of follow-up, were assessed in patients with index RF vs. CB ablation. Predictors of ATA recurrence at 1 year follow-up were also evaluated. Results: In our cohort of 194 patients, the mean age was 78 $\pm$ 3.1 years, 58.2% were men, and 39.4% had persistent AF. The mean left atrial (LA) diameter was 4.5 $\pm$ 0.7, while the mean CHA2DS2-VASc score was 3.5 $\pm$ 1.2. The majority (n=149, 76.8%) underwent RF ablation. The incidence of complications was similar in the two sub-groups (RF: 1.3% vs. CB: 2.2%, p=0.67). No significant difference in success rate at 1-year follow-up was found between patients receiving RF vs. CB ablation (59.7% vs. 66.7%, p=0.68). In a multivariable model adjusting for the relevant covariates only LA size [HR=1.64, CI: 1.15-2.34, p$<$0.01] was independently associated with ATA recurrence at 1year follow-up. Conclusion: In our cohort of elderly patients undergoing index CA for AF, RF ablation was the predominant modality with similar safety and efficacy relative to CB ablation. LA size was a significant predictor of ATA recurrence at 1year independent of index ablation modality.

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Abstract

Introduction:

There are limited data describing the experience of index 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 AF ablation between January 2010 and March 2019 at our center. Major complications and efficacy, defined as freedom from any atrial tachyarrhythmia (ATA) lasting [?]30 seconds after one year of follow-up, were assessed in patients with index RF vs. CB ablation. Predictors of ATA recurrence at 1 year follow-up were also evaluated.

Results:

In our cohort of 194 patients, the mean age was 78 + 3.1 years, 58.2% were men, and 39.4% had persistent AF. The mean left atrial (LA) diameter was 4.5 + 0.7, while the mean CHA_2DS_2-VASc score was 3.5 + 1.2. The majority (n=149, 76.8%) underwent RF ablation. The incidence of complications was similar in the two sub-groups (RF: 1.3% vs. CB: 2.2%, p=0.67). No significant difference in success rate at 1-year follow-up was found between patients receiving RF vs. CB ablation (59.7% vs. 66.7%, p=0.68). In a multivariable model adjusting for the relevant covariates only LA size [HR=1.64, CI: 1.15-2.34, p<0.01] was independently associated with ATA recurrence at 1year follow-up.

Conclusion:

In our cohort of elderly patients undergoing index CA for AF, RF ablation was the predominant modality with similar safety and efficacy relative to CB ablation. LA size was a significant predictor of ATA recurrence at 1year independent of index ablation modality.

Keywords:

Atrial fibrillation, Radiofrequency ablation, Cryoballoon ablation, Left atrium, Transient phrenic nerve palsy,

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 compare the safety and efficacy of CB vs. RF ablation

in elderly patients and to determine the predictor of arrhythmia recurrence in a contemporary cohort of patients at our center.

Methods:

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 2010 and March 2019. The demographics, 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.

Peri-procedural management

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 hours prior to the ablation procedure, with resumption 4 hours post-procedure. Anticoagulation was continued for a minimum of 3 months following the ablation procedure for all patients unless contraindicated.

RF ablation

All ablation procedures were performed under general anesthesia. Femoral site access was

obtained, and intravenous heparin administered to maintain activated clotting times >350 s.

After performing a double transseptal puncture, 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 pre-acquired CT scan. A 4-mm open-tip irrigated RF catheter (Thermocool or Thermocool SmartTouch, Biosense-Webster) was then positioned in the left atrium: PV isolation (PVI) was performed using real-time automated display of RF application points (Visitag, Biosense-Webster) with predefined catheter stability settings. Starting energy delivery parameters were 25 to 40 W on the posterior wall and 35 to 45 W at other sites. Target contact force was between 5 and 20 g for cases performed after 2014 with the Thermocool Smart Touch catheter. 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.

CB ablation

After a trans-septal puncture at the fossa ovalis, a long deflectable sheath (FlexCath Advance sheath; Medtronic, Inc, Minneapolis, MN) was introduced into the LA using intracardiac

echocardiographic guidance. Pulmonary venous angiograms were obtained for each of the four

PVs to serve as a fluoroscopic reference. An endocardial map of the LA was created via a

CARTO-Biosense (Carto [R] 3; Biosense Webster, Inc, Diamond Bar, CA) or Ensite system

(NavX, St. Jude Medical, Inc, St. Paul, MN). Right-sided phrenic nerve (PN) pacing was

performed during ablation of the right PVs. A second generation CB catheter with a 23- or 28

mm balloon (Arctic Front Advance, Medtronic) and a PV mapping catheter were passed into the

LA via the long sheath. Cryo lesions were targeted to the PVs after demonstration of balloon occlusion with contrast injection. Goal temperatures were between -35 to -55C. Freezes were aborted if the esophageal temperature fell below 28 $^{\circ}$C or if PN pacing showed diminution of diaphragmatic excursion during right-sided PV lesion delivery. Following the delivery of at least two lesion sets per vein, electrical isolation of each PV was reassessed, and additional applications of cryotherapy delivered with either a 28 or 23 mm second-generation CB as necessary.

Outcome Assessment

Arrhythmia recurrence and peri-procedural complications were ascertained based on monitoring strategies suggested in the 2017 Heart Rhythm Society[3](HRS) consensus document. 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 major bleeding, phrenic nerve palsy, cerebral embolism, pericardial effusion/tamponade, atrioesophageal fistula, or extended hospitalization (>48 hours) 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. Antiarrhythmic drug therapy, if present at the time of ablation was discontinued at the 3-month follow-up visit. Outcomes were assessed via electronic health record reviews or phone interviews.

Statistical Analysis

Continuous variables were described with measures of central tendency and dispersion (mean and standard deviation). Categorical variables were described as frequencies. Continuous variables were evaluated by$t$ - test, and categorical variables were compared withχ^2 or Fisher's exact test. 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. Multivariable Cox proportional hazards regression analysis was used to assess the impact of variables of interest on the recurrence of atrial arrhythmia, adjusting for relevant covariates known to influence the recurrence rate. Follow-up for all patients was censored at one year after ablation. A p-value of < 0.05 was considered statistically significant. All analyses were performed using SPSS Statistics Software for Windows version 23.0 (IBM Corporation, Armonk, New York).

Results

Patient characteristics

Our study included a total of 194 patients, of whom 149 (76.8%) underwent RF ablation and 45 (23.1%) underwent CB ablation (Table 1). The mean age of the study patients was 78 $\pm$ 3.1 years, and 113 (58.2%) were men. 117 (60.6%) of all patients had PAF, while 76 (39.4%) of the patients had persistent AF (PsAF). The mean body mass index (BMI) was 27.9 $\pm$ 5.1 kg/m^2, and the mean CHA_2DS_2-VASc score was 3.5 $\pm$ 1.2.

A history of hypertension was documented in 132 (68%) patients, diabetes mellitus (DM) and congestive heart failure (CHF) in 25 (12.9%) patients each, stroke/ transient ischemic attack (TIA) in 21 (10.8%) patients, and OSA in 19 (9.8%) patients. Overall, no significant difference was detected in any baseline comorbidities between the groups.

Imaging characteristics

The mean LA diameter for the total cohort was 4.4 ± 0.7 cm, while the mean LVEF was 55.7 ± 10.1 % (Table 2). Patients undergoing RF ablation had higher LA diameter (4.5 vs. 4.1 cm, p=<0.01) as compared to the CB cohort. There was no significant difference in LVEF between the RF vs. CB cohorts.

Safety and efficacy outcomes

The incidence of complications was comparable between the RF and CB cohort (1.3% vs. 2.2%, p=0.67). Pericardial effusion and cardiac tamponade occurred in one patient each in the RF group, and one patient in the CB group developed transient acute kidney injury. There was no significant difference between the success rate of freedom from AF or AT at 1 year follow-up between patients receiving RF vs. CB ablation (59.7% vs. 66.7%, p=0.68) (Figure 1).

Predictors of arrhythmia recurrence

In a multivariable model adjusting for the age, body mass index (BMI), CHA_2DS_2VASc score, AF type and duration, obstructive sleep apnea (OSA), chronic obstructive pulmonary disease (COPD), left ventricular ejection fraction (LVEF), and index RF vs. CB ablation, only LA size was independently associated with ATA recurrence at 1year. Each increment of 1 cm in LA size was associated with a 1.6-fold greater risk of ATA recurrence [HR=1.64, CI: 1.15-2.34, p<0.01] (Table 3).

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[4-13]. To the best of our knowledge, ours is the first study from the US to compare the outcomes of CB vs. RF AF ablation in elderly patients. The main findings of our study are: (1) The safety and efficacy of index CB vs. RF AF ablation in the elderly patients are similar; (2) LA diameter is an independent predictor of arrhythmia recurrence after AF ablation in the elderly patients, regardless of index ablation modality.

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 are lower as compared to the previous studies. This may be due to a greater proportion of PsAF patients and higher average LA diameter in our cohort, as these factors have been reported to be associated with lower success rate of an ablation procedure[4,14,15]. We also demonstrated that higher LA diameter is an independent predictor of arrhythmia recurrence in elderly patients after CA of AF. This finding consolidates the evidence of the pathologic role of dilated LA in initiation and maintenance of AF in elderly patients and suggests that dilated LA has independent poor prognostic value regardless of the ablation modality and presence of other comorbidities such as OSA and PsAF, which contributes to arrhythmia recurrence.

Our complication rates are lower in comparison to the rate reported in previous studies[4,5]. Transient phrenic nerve palsy (PNP) has been reported to be the most commonly associated complication with CB ablation[16,17]. 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. Over-all 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.

Our study has several limitations, including those inherent to a single-center, non-randomized, retrospective study with a small sample size. The choice of ablation technique was left to the discretion of the operator. In addition, only patients enrolled after 2014 were treated with contact force sensing catheters, which are associated with an improved success rate. This could have introduced some bias. Finally, the lack of continuous ECG monitoring after ablation could have resulted in underestimation of arrhythmia recurrence.

In conclusion, based on our study, the safety and efficacy of index CB vs. RF AF ablation in patients > 75 years of age is comparable, and LA diameter is a significant predictor of arrhythmia recurrence independent of index ablation modality. Further prospective randomized studies are required to confirm our findings.

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