Cryoballoon Ablation of Atrial Fibrillation in Octogenarians

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Abstract

A significant proportion of AF patients with advanced age are being treated in clinical practice. Cryoballoon ablation of AF given its shorter procedure time and comparable efficacy to radiofrequency ablation, has rapidly become a commonly used tool for AF ablation. Data regarding the outcomes of cryoballoon ablation of AF in octogenarians are limited because of the exclusion of this age group in the previous studies. The authors report outcomes of 15 octogenarian AF patients undergoing index cryoballoon ablation at a single centre. The mean age of the included patients was 83 ± 3 years. In total, 13 patients (87%) presented with paroxysmal AF, and two (13%) had long-standing persistent AF. At 6 and 12 months of follow-up, freedom from AF was 80% and 70%, respectively. None of the patients suffered any procedure-related complications. Cryoballoon ablation appears to be a safe and effective approach for treating symptomatic AF refractory to antiarrhythmic drug therapy in octogenarian patients, based on outcomes in this cohort. These findings require further validation in prospective randomised studies with larger sample sizes.

Keywords

AF, cryoballoon ablation, octogenarians, radiofrequency ablation, pulmonary vein isolation, elderly, transient phrenic nerve palsy

Methods

We describe the safety and efficacy outcomes of 15 octogenarian patients undergoing index AF ablation using the second-generation cryoballoon at the Johns Hopkins Hospital between 2012 and 2019.

The study participants were non-consecutively included and derived from an institutional review board-approved, prospectively populated clinical database of AF ablation patients. Demographics, clinical history, procedural data, complications, and outcomes were recorded for each case. Patients were excluded if they had prior catheter ablation of AF, left atrial thrombus detected on pre-procedural transthoracic echocardiography (TTE) or CT scan, and advanced comorbidities and frailty precluding catheter ablation. Arrhythmia recurrence and peri-procedural complications were ascertained based on monitoring strategies described in the 2017 Heart Rhythm Society consensus document. Arrhythmia recurrence was defined as any AF or atrial tachyarrhythmia sustained for >30 seconds recorded by a surface ECG or rhythm-monitoring device after a 90-day blanking period. Procedure-related complications, such as major bleeding, minor bleeding, phrenic nerve palsy, cerebral embolism, pericardial effusion/tamponade, atriooesophageal fistula or extended hospitalisation, were assessed.

Pre-procedural Management

AAD management was left to the discretion of the operator. Pre-procedure TOE was performed only for the patients presenting in AF at...
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The time of ablation, as per the institutional practice. All patients underwent a preprocedural 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) underwent cessation of 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 ablation procedure for all patients unless contraindicated.

Ablation Strategy
All ablation procedures were performed under general anaesthesia. Femoral site access was obtained and intravenous heparin administered to maintain activated clotting times >350 seconds. After a trans-septal puncture at the fossa ovalis, a long deflectable sheath (FlexCath Advance sheath, Medtronic) 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 the CARTO-Biosense system (Carto 3, Biosense Webster or Ensite NavX, St Jude Medical). 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 second-generation cryoballoon 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 the demonstration of balloon occlusion with contrast injection. Goal temperatures were between −35°C and −55°C. Freezes were aborted if the oesophageal temperature fell below 28°C or if phrenic nerve 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 mm or 23 mm second-generation cryoballoon. Additional cavo-tricuspid isthmus (CTI) ablation using radiofrequency energy was performed at the discretion of the operator in patients with history of clinically documented typical atrial flutter. An endocardial map of the right atrium was created. His bundle position was identified and marked. Radiofrequency energy was delivered to create a line of electrical block along the CTI, which was verified by bidirectional, differential atrial pacing. Intracardiac electrograms and conduction were measured at rest and after ablation.

Table 1: Baseline Patient Characteristics

| Demographics | Study Population (n=15), n (%)* |
|--------------|--------------------------------|
| Age (years)  | 83 ± 3                         |
| Male         | 9 (60)                         |
| Former smoker| 5 (33)                         |
| AF duration (years) | 8.9 ± 8.2            |
| Paroxysmal/long-standing persistent | 13 (87) / 2 (13)          |
| BMI (kg/m²)  | 26.8 ± 5.2                     |
| CHF          | 2 (13)                         |
| Hypertension | 12 (80)                        |
| Diabetes     | 3 (20)                         |
| Stroke/TIA   | 4 (27)                         |
| CAD          | 6 (40)                         |
| CHA₂DS₂,VASc score | 4.2 ± 1.7                  |
| HASBLED score| 2.4 ± 0.8                      |
| Previous atrial flutter ablation | 4 (27)                   |
| OSA          | 2 (13)                         |
| CKD          | 3 (20)                         |
| Hyperlipidaemia | 8 (53)                    |
| Pacemaker implantation | 2 (13)                   |

| Echocardiographic Parameters | Study Population |
|-----------------------------|------------------|
| Left atrial diameter (cm)   | 4.5 ± 1.2        |
| Left ventricular ejection fraction (%) | 63.7 ± 3.5   |

| Drugs | Study Population (n=15) |
|-------|-------------------------|
| Class I | 0 (0)                  |
| Class III | 7 (47)                |
| Beta-blocker | 11 (73)               |
| Ca²⁺ channel blocker | 6 (40)             |

*Unless otherwise specified. CAD = coronary artery disease; CHF = congestive heart failure; CKD = chronic kidney disease; OSA = obstructive sleep apnoea; TIA = transient ischaemic attack.

Table 2: Procedural Characteristics

| Procedure/Characteristic | Study Population (n=15) |
|-------------------------|-------------------------|
| Additional CTI ablation n (%) | 2 (13)              |
| Number of PVs isolated  | 61                      |
| Mean number of PV isolated per patient | 4.07 ± 0.458        |
| Anatomical variant of PV, n (%) | 3 (20)              |
| LSPV diameter (mm)      | 17.7 ± 4.6             |
| LIPV diameter (mm)      | 15.5 ± 3.3             |
| RSPV diameter (mm)      | 16.9 ± 7.2             |
| RIPV diameter (mm)      | 17.1 ± 3.6             |
| Mean number of freezes per patient | 10.8 ± 2.1         |
| Ablation duration per patient (s) | 1,530 ± 411.6    |
| Nadir temperature (°C)  | 40 ± 2.8               |

CTI = cavo-tricuspid isthmus; PV = pulmonary vein; LSPV = left superior pulmonary vein; LIPV = left inferior pulmonary vein; RSPV = right superior pulmonary vein; RIPV = right inferior pulmonary vein.

Figure 1: Freedom From AF During Follow-up Following Cryoballoon Ablation

Kaplan-Meier survival curve showing the percentage of the included 15 patients free from AF after a 3-month blanking period.

Follow-up duration (months)

Freedom from AF

0 3 6 9 12 15

Blanking period

100%

80%

60%

40%

20%

0%
Clinical Follow-up
All patients were observed in the hospital for a minimum of one night post-ablation. Routine follow-up (history, exam, and electrocardiography or Holter) was performed at the outpatient clinic or by a local cardiologist at 3, 6 and 12 months and additionally, if prompted by symptoms. Status of symptoms, including AF burden and effect of ablation on quality of life, was assessed in each patient at follow-up visit. Event monitors were arranged for patients in whom symptoms suggestive of AF developed in the post-blanking phase of follow-up. AAD 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 telephone interviews.

Statistical Analysis
Quantitative variables were described with measures of central tendency and dispersion (mean and standard deviation). Qualitative variables were described as frequencies. All analysis was done using SPSS Statistics Software for Windows version 23.0 (IBM).

Results
Patient Population
The cohort comprised 15 patients between 80 and 88 years of age who underwent cryoballoon AF ablation between 2012 and 2019. The clinical characteristics of our patient cohort are shown in Table 1. The mean patient age was 83 ± 3 years and 60% of the patients were men. Of the 15 patients, 13 (87%) presented with paroxysmal AF (PAF) and two (13%) had long-standing persistent AF (PsAF). The mean time since AF was first diagnosed was 8.9 ± 8.2 years. Mean CHA2DS2-VASc score and HASBLED scores were 4.2 ± 1.7 and 2.4 ± 0.8, respectively. Mean LA diameter was 4.5 ± 1.2 cm.

Ablation Procedure and Acute Outcomes
Of the 15 patients, five (33%) had catheter ablation performed on continuous anticoagulation with warfarin and the remaining 10 (67%) underwent ablation on minimally interrupted DOAC anticoagulation. Four patients (27%) presented in AF at the time of ablation and underwent preprocedural TOE to rule out left atrial appendage thrombi before cryoballoon ablation. Table 2 describes the procedural characteristics. In all the patients, 100% of PVs were successfully isolated at the end of the procedure. Three patients had variant PV anatomy (one patient each with left common, left middle, and right middle PVs). Two patients underwent additional CTI ablation. None of the patients suffered any procedure-related complications.

Efficacy of Ablation with Follow-up
During a mean follow-up duration of 15.8 months (range 6–60 months), AF recurred in three patients. The freedom from AF recurrence was 80% and 70% at 6 and 12 months of follow-up, respectively (Figure 1). Thirteen of the 15 patients reported significant reduction in symptoms and AF burden associated with improvement in quality of life following catheter ablation. Anticoagulation following catheter ablation was continued in all the patients at 3 months follow-up visit except in one patient who developed occult gastrointestinal bleeding secondary to gastritis. Table 3 provides patient specific safety and efficacy outcome data for all patients included in this report.

Discussion
This case series describes the outcomes of cryoballoon ablation for AF in octogenarian patients. Our report reveals that second-generation cryoballoon ablation was a safe and effective procedure in this cohort.
The success rate was 70% at 1 year of follow-up, and there were no complications. Our results serve to extend and confirm the findings of a number of prior publications that have reported the outcomes of cryoballoon ablation in elderly patients with AF. The definition of ‘elderly’ in these series included patients aged as young as 70 years, and the reported success rates range from 62 to 87%. In the aggregate, these studies have investigated safety and efficacy rates at 1 year in a total of 2,235 patients. In all the studies, no significant differences were seen in either efficacy or safety rates when comparing outcomes with non-elderly patients. The most commonly reported complication was transient phrenic nerve palsy. The reported incidence of phrenic nerve palsy with cryoballoon ablation ranges from 4 to 14%. Phrenic nerve palsy is described to occur more commonly with right superior PV (RSPV) ablation because of the proximity of the right phrenic nerve to the RSPV. Several risk factors for phrenic nerve palsy during cryoballoon ablation have been identified, including shorter distance between the RSPV and right phrenic nerve, larger ostial vein size, circular shape of pulmonary vein ostium and greater obtuse angle between the RSPV and LA.

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Clinical Perspective

- Given the association of AF with increasing age, a significant proportion of AF patients with advanced age are being treated in clinical practice.

- Cryoballoon AF is associated with a shorter procedure time and comparable efficacy to radiofrequency ablation and has become the commonly used tool for AF ablation.

- Data related to the outcomes of cryoballoon ablation of AF in octogenarian patients are limited because of the exclusion of this age group in previous studies.

- Cryoballoon ablation appears to be a safe and effective approach for treating symptomatic AF refractory to antiarrhythmic drug therapy in octogenarian patients.

Conclusion

The findings of our report should be interpreted with attention to the associated limitations. These include the single-centre, retrospective and observational nature of the study and lack of a comparator group, the small sample and the lack of continuous ECG monitoring.