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Article

Safety and Efficacy of Second-Generation Cryoballoon Ablation in Patients Aged over 75 Years

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Abstract

Objective: The use of second-generation cryoballoon (CB2) for pulmonary vein isolation (PVI) in atrial fibrillation (AF) ablation therapy is common. This study aimed to compare the safety and efficacy of CB2 ablation for PVI in AF patients aged 75 years and older to those under 75 years old. **Methods**: A retrospective, observational study was conducted, including AF patients who underwent CB2 for PVI between January 2018 and December 2020 at our center. The patients were divided into two groups based on age: those aged 75 years and older (elderly group) and those under 75 years (control group). Procedural characteristics, complications, and one-year follow-up outcomes were compared between the two groups using Student's *t*-test or the chi-square test for univariate analysis. **Results**: A total of 156 AF patients treated with CB2 for PVI were included in the study, with 78 patients aged 75 years and older (elderly group, mean age = 78 years) and 78 patients aged under 75 years (control group, mean age = 66 years). The PVI procedure duration was 86.2 $\pm$ 25.8 minutes for the elderly group and 83.2 $\pm$ 20.8 minutes for the control group (p = 0.413). The elderly group showed a higher trend of complications (8/78, 10.3%) compared to the control group (2/78, 2.6%) (p = 0.049), although no serious complications were observed. One-year follow-up revealed that approximately 80% of patients in both groups did not experience AF recurrence (p = 0.656). **Conclusion**: CB2 ablation for PVI appears to be safe and effective in AF patients aged 75 years and older, with outcomes comparable to those in younger patients. However, special attention should be given to venous puncture in elderly patients.

Keywords

atrial fibrillation; second-generation cryoballoon; elderly

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia, with an increasing prevalence in the aging population [1]. Catheter ablation, particularly pulmonary vein isolation (PVI), has become a well-established treatment for symptomatic AF [2]. The second-generation cryoballoon (CB2) has demonstrated high safety and efficacy in PVI, offering advantages such as shorter procedure times and a faster learning curve compared to radiofrequency ablation [3–5]. Recent studies have shown that cryoballoon ablation may be an effective initial therapy for AF, with lower rates of AF recurrence compared to antiarrhythmic drugs [6–8]. However, limited data are available on the safety and efficacy of CB2 in elderly patients, as most trials have not included patients aged 75 years and older [9–11].

As the prevalence of AF increases with age, it is crucial to evaluate the outcomes of CB2 ablation in elderly patients. Some studies have suggested that cryoballoon ablation may be particularly advantageous for older patients due to shorter procedure times and reduced exposure to prolonged supine positioning [12,13]. However, there is a need for more comprehensive comparisons of procedural characteristics, complications, and long-term outcomes between elderly and younger patients undergoing CB2 ablation. This study aimed to compare the safety and efficacy of CB2 ablation for PVI in AF patients aged 75 years and older to those under 75 years old, focusing on procedural characteristics, complications, and one-year follow-up outcomes.

Methods

Study Population

Seventy-eight patients over 75 years of age who underwent cryoballoon ablation for atrial fibrillation treatment at our center between January 2018 and December 2020 were enrolled in this single-center observational study and clinically followed. Seventy-eight patients aged less than 75 years were selected as the control group, matched for

Table 1. Baseline demographic characteristics of patients in the elderly and control groups.

Variables	Elderly (n = 78)	Control (n = 78)	$T/\chi^2/Z$	*p value*
Age, years, (IQR)	78 (76, 81)	66 (58, 70)	2.153	0.023
Female sex, n (%)	39 (50%)	39 (50%)	0.000	1.000
BMI (kg/m^2, mean ± SD)	25.5 ± 3.4	25.7 ± 3.9	0.450	0.653
PerAF, n (%)	19 (24.4%)	19 (24.4%)	0.000	1.000
LA diameter (mm, mean ± SD)	40.1 ± 4.2	39.5 ± 3.6	0.906	0.366
LVEF (%, mean ± SD)	63.5 ± 5.8	62.4 ± 7.5	0.980	0.329
Hypertension, n (%)	54 (69.2%)	42 (53.8%)	3.900	0.048
Diabetes, n (%)	19 (24.4%)	12 (15.4%)	1.973	0.160
Coronary artery disease, n (%)	4 (5.1%)	6 (7.7%)	-	0.746
History of stroke, n (%)	11 (14.1%)	5 (6.4%)	2.507	0.113
CHA_2DS_2-VASc score (mean ± SD)	3.8 ± 1.2	2.0 ± 1.4	8.686	0.000
HAS-BLED score (mean ± SD)	1.7 ± 0.6	0.8 ± 0.8	8.161	0.000

IQR, interquartile range; BMI, body mass index; SD, standard deviation; LA, left atrial; PerAF, persistent atrial fibrillation; LVEF, left ventricular ejection fraction.

gender and atrial fibrillation type. Matching was performed through the selection of patients equally into the categories. The matching results were determined by Chi-square test to show that there was no significant difference in gender or atrial fibrillation type between these two groups (Table 1). Atrial fibrillation history was defined as the time from first diagnosis to ablation. Patients with atrial fibrillation episodes lasting longer than 7 days requiring external electrical cardioversion or chemical cardioversion to restore sinus rhythm were defined as having persistent atrial fibrillation. Patients with persistent atrial fibrillation for longer than 1 year were also included and classified as longstanding persistent atrial fibrillation. All patients had a clear diagnosis of atrial fibrillation and met indications for catheter ablation. Exclusion criteria were the presence of an intracavitary thrombus, uncontrolled heart failure, moderate or severe valvular disease, prior valve replacements, left atrial diameter exceeding 50 mm on transthoracic echocardiography, and previous atrial fibrillation ablation procedures. This study was reviewed and approved by the local ethics committee (Ethical approval number: 2022-0429-6).

Cryoballoon Ablation Procedure

All patients underwent pre-procedural left atrial computed tomography angiography to delineate pulmonary vein anatomy and exclude thrombus [7]. Not all patients underwent pre-procedural transesophageal echocardiography. Periprocedural anticoagulation was managed per individual physician discretion. Patients received conscious analgesia with fentanyl citrate during the procedure. Femoral vein puncture was performed using the modified Seldinger technique, and a guidewire was advanced into the femoral vein after successful puncture. Major groin complications were defined as a hemoglobin decrease of at least 2 g/dL due to groin pseudoaneurysm, hematoma larger than 3 cm, arteriovenous fistula, retroperitoneal bleeding, or death from groin bleeding. Minor bleeding complications included minor groin issues not requiring invasive treatment, such as arteriovenous fistulae, pseudoaneurysms, hematomas, hematuria, epistaxis, or hemoptysis.

The procedures were performed under fluoroscopic guidance. After transseptal puncture and left atrial access, a decapolar catheter and quadripolar catheter were positioned in the coronary sinus and right ventricle via the left femoral vein, respectively. Heparin was administered to maintain an activated clotting time between 300–350 seconds. The transseptal sheath was exchanged for a 15-Fr steerable sheath, and a 20-mm spiral mapping catheter was used to advance the 28-mm cryoballoon into the pulmonary veins for mapping and support. Pulmonary vein occlusion was confirmed by contrast injection demonstrating total contrast retention without atrial backflow. Cryoenergy applications were delivered for 180 seconds once occlusion was achieved. If pulmonary vein potentials were visible, the time to isolation was recorded. No additional applications were performed after isolation if the temperature reached $\leq$–40 °C within 60 seconds, with a minimum temperature limit of –55 °C. Phrenic nerve pacing was performed during right-sided pulmonary vein ablation to monitor for phrenic nerve injury. The application sequence was left superior, left inferior, right superior, and right inferior pulmonary veins. Additional touch-up radiofrequency ablation was performed if complete isolation was not achieved after a maximum of 4 cryoapplications.

Follow-up and Data Collection

Patients were scheduled for follow-up visits at 3, 6, and 12 months post-procedure, including 24-hour Holter monitoring. Additional telephone interviews were conducted regularly. Basic patient characteristics, procedural characteristics including time to pulmonary vein isolation, application times, and fluoroscopy times were collected.

Atrial fibrillation recurrence was defined as a documented atrial fibrillation or atrial tachycardia episode lasting longer than 30 seconds on Holter or 12-lead electrocardiogram (ECG), irrespective of symptoms. Procedure-related complications such as pericardial effusion, cerebral or peripheral embolism, venous hematoma, or pseudoaneurysm were also recorded.

Statistical Analysis

Basic patient information and clinical laboratory test results were subjected to descriptive analysis. Continuous variables are presented as mean ± standard deviation (SD) or median (interquartile range [IQR]), while categorical variables are expressed as frequencies and percentages. Univariate analysis was performed using Student's *t*-test for continuous variables and the chi-square test for categorical variables. A *p*-value of less than 0.05 was considered statistically significant.

Results

Patient Characteristics

A total of 156 individuals were included in the study, with 78 participants in each of the elderly and control groups. The composition of gender and AF type (paroxysmal or persistent) showed no variation between the groups. Significant differences were not observed in variables such as body mass index (BMI), left atrial diameter, or left ventricular ejection fraction (LVEF) ($p < 0.05$). Concerning comorbid conditions, more patients in the elderly group were diagnosed with hypertension ($p = 0.048$), while there were no significant variances in the occurrences of diabetes, coronary heart disease, and stroke between the two groups ($p > 0.05$) (Table 1).

Procedural Data

The procedure time median was 86.2 ± 25.8 minutes for the elderly group and 83.2 ± 20.8 minutes for the control group, with a non-significant *p*-value of 0.413. Additionally, the fluoroscopic time was 22.9 ± 8.2 minutes for the elderly group and 23.4 ± 7.3 minutes for the control group, with a *p*-value of 0.672. The elderly group had a higher real-time recording rate of pulmonary vein potentials (PVPs) (70.8% *vs*. 61.2%, $p = 0.011$). The time to isolation (TTI) was significantly longer in the elderly group (39.3 ± 13.2 s *vs*. 36.5 ± 13.4 s, $p = 0.031$), and the mean temperature at 60 seconds was lower in the elderly group (–40.9 ± 4.5 ℃ *vs*. –39.6 ± 5.5 ℃, $p = 0.001$). There was no notable difference in the nadir temperature between the two groups (–48.0 ± 5.6 ℃ *vs*. –48.7 ± 5.8 ℃, $p = 0.130$). Additionally, freezing behavior was examined individually for each pulmonary vein (PV), showing that the TTI of right inferior pulmonary vein (RIPV) (41.0 ± 11.9 s *vs*. 34.2 ± 12.6 s, $p = 0.019$) and the temperature of left inferior pulmonary vein (LIPV) at 60 seconds (–38.3 ± 3.4 ℃ *vs*. –34.7 ± 5.9 ℃, $p = 0.001$) were significantly different between the two groups, with no other notable differences in the parameters mentioned in Table 2.

Complications

In the elderly group, there were 8 procedural complications, while the control group had 2 complications (10.3% *vs*. 2.6%, $p = 0.049$). Within the elderly group, complications related to femoral vein puncture accounted for 5 cases, with 3 femoral vein hematomas, 1 femoral artery pseudoaneurysm, and 1 femoral arteriovenous fistula reported. Two patients experienced transient phrenic nerve palsy (PNP) during ablation in the elderly group, which resolved completely by the end of the procedure. A pericardial effusion was noted during transseptal puncture, with no adverse outcomes requiring additional therapy. There were no serious complications such as symptomatic stroke, atrial esophageal fistulas, or death in either group (see Table 2).

Follow-up Results

Following the 12-month observation period, 16 individuals (20.5%) in the older population and 14 subjects (17.9%) in the comparison group experienced AF relapse. Both groups exhibited similar rates of ablation success at the 12-month follow-up (79.5% *vs*. 82.1%, $p = 0.656$). There were no instances of delayed or unforeseen complications throughout the entire monitoring period.

Discussion

Our study evaluated the safety and efficacy of CB2 for PVI in elderly AF patients aged 75 years and older. Our study revealed the following key findings: (1) Elderly patients experienced a notable increase in complications related to femoral vein puncture compared to those under 75 years old, with no significant variance in other complications like phrenic nerve paralysis (PNP) and pericardial tamponade; (2) Procedural times, fluoroscopy durations, and X-ray doses required by elderly patients were comparable to those of younger patients when receiving CB2 treatment; (3) The clinical success rate among the elderly patients was akin to that of the younger cohort following a one-year monitoring period.

Previous studies have reported favorable outcomes with cryoballoon ablation in elderly AF patients, but most included a relatively small sample size or defined elderly as over 65–70 years old [14,15]. Our study specifically focused on those 75 years and above, an important population given the increasing prevalence of AF with advanced age [16]. The approximately 80% freedom from AF recurrence

Table 2. Procedural parameters in the elderly and control groups.

Variables	Elderly (n = 78)	Control (n = 78)	$T/\chi^2/Z$	*p* value
Procedure time (min, mean ± SD)	86.2 ± 25.8	83.2 ± 20.8	0.821	0.413
Fluoroscopy time, (min, mean ± SD)	22.9 ± 8.2	23.4 ± 7.3	0.424	0.672
Fluoroscopy radiation dosage (mGy, mean ± SD)	149.9 ± 166.1	145.4 ± 93.2	0.207	0.837
RTR of PVP, n (%)	221 (70.8%)	191 (61.2%)	6.429	0.011
TTI (s, mean ± SD)	39.3 ± 13.2	36.5 ± 13.4	2.169	0.031
LSPV	44.0 ± 12.8	43.9 ± 12.2	0.031	0.975
LIPV	36.6 ± 14.3	34.1 ± 13.6	0.910	0.365
RSPV	34.9 ± 11.7	33.1 ± 12.2	0.803	0.424
RIPV	41.0 ± 11.9	34.2 ± 12.6	2.389	0.019
T60 (°C, mean ± SD)	–40.9 ± 4.5	–39.6 ± 5.5	3.294	0.001
LSPV	–41.6 ± 4.3	–40.7 ± 3.8	1.344	0.181
LIPV	–38.3 ± 3.4	–34.7 ± 5.9	4.736	0.000
RSPV	–43.1 ± 4.1	–43.0 ± 3.7	0.123	0.902
RIPV	–40.7 ± 4.8	–39.9 ± 4.9	0.976	0.330
Nadir temperature (°C, mean ± SD)	–48.0 ± 5.6	–48.7 ± 5.8	0.626	0.130
LSPV	–49.3 ± 4.6	–49.4 ± 4.6	0.226	0.822
LIPV	–44.3 ± 4.5	–44.8 ± 5.4	0.609	0.543
RSPV	–50.9 ± 4.8	–52.4 ± 4.5	1.918	0.057
RIPV	–47.7 ± 6.0	–48.3 ± 6.0	0.704	0.482
Touch-up ablation, n (% of all PVs)	1 (0.3%)	2 (0.6%)	-	1.000
Complications, n (%)	8 (10.3%)	2 (2.6%)	-	0.049

PV, pulmonary vein; PVP, pulmonary vein potential; TTI, time to isolation; LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein; RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein; SD, standard deviation; RTR, real-time recording; T60, Temperature at 60 seconds.

at 1 year in both the elderly and younger groups aligns with recent randomized trials and meta-analyses evaluating CB2 efficacy [17,18].

While the overall complication rate was higher in the elderly group (10.3% *vs*. 2.6%), this was primarily driven by issues related to venous access, with no significant differences in serious procedural complications like phrenic nerve palsy or pericardial effusion. Vascular access challenges are an expected finding in older patients with fragile veins and impaired healing [19]. Careful ultrasound-guided venous puncture and meticulous hemostasis may help mitigate this risk. Notably, we did not observe any strokes, atrio-esophageal fistulas, or procedural deaths in either group.

Procedure times and fluoroscopy exposure were similar between the two cohorts. While the time to pulmonary vein isolation was slightly longer in the elderly, this short delay is unlikely to be clinically meaningful. Prior studies suggest a benefit to achieving faster time to isolation [20], but both groups met the conventional target of less than 40 seconds on average. Real-time pulmonary vein potential monitoring was more frequently employed in the elderly group, allowing for confirmation of durable isolation [21].

Age-related changes in cardiac electrophysiology may explain some of the procedural differences observed between the elderly and younger groups. Advanced age is associated with fibrotic remodeling of the atria, slowing of conduction, and altered electrogram characteristics, which could impact cryoablation parameters like time to isolation [22]. The lower mean temperature at 60 seconds in the elderly group may reflect increased atrial scarring and impaired lesion formation with cryotherapy [23]. It is also important to consider the heightened risk profile of elderly AF patients, who have a higher burden of comorbidities like hypertension, diabetes, and stroke as seen in our study population. While catheter ablation is generally well-tolerated, these comorbid conditions could potentially increase susceptibility to periprocedural complications [24]. Careful pre-procedural evaluation and optimization of comorbidities is warranted in this higher risk elderly population.

One limitation of this study is the retrospective, single-center design which may impact generalizability. Additionally, our AF recurrence surveillance relied primarily on ambulatory ECG monitoring which could potentially miss asymptomatic episodes. Larger multi-center randomized trials with continuous ECG monitoring would help validate these findings.

Conclusion

In summary, this study adds to the growing evidence that second-generation cryoballoon ablation can be safely and effectively performed in elderly AF patients over 75

years old, with reasonable periprocedural safety and 1-year clinical efficacy comparable to younger individuals. Careful attention to vascular access is warranted in this population. As the AF epidemic continues to grow along with an aging population, cryoballoon ablation represents an important treatment option for elderly patients.

Availability of Data and Materials

The datasets used during the present study are available from the corresponding author upon reasonable request.

Author Contributions

RJ and KZ performed the experiment, collected the data and wrote the manuscript; TC performed the intervention procedure and participated the discussion; HL contributed significantly to statistics and analysis; YL directed the conception and design of the study, and review the whole manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The study were approved by the Ethics Committee of Clinical School of Cardiovascular Disease, Tianjin Medical University. Informed consent was obtained from the paticipatant. This study was reviewed and approved by the local ethics committee (Ethical approval number: 2022-0429-6).

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Conflict of Interest

The authors declare no conflict of interest.

References

[1] Lippi G, Sanchis-Gomar F, Cervellin G. Global epidemiology of atrial fibrillation: An increasing epidemic and public health challenge. International Journal of Stroke: Official Journal of the International Stroke Society. 2021; 16: 217–221.

[2] Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, *et al*. 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. European Heart Journal. 2021; 42: 373–498.

[3] Jimenez-Candil J, Hernandez Hernandez J, Cruz Galban A, Blanco F, Moriñigo JL, Sanchez García M, *et al*. Clinical and economic outcomes of a systematic same-day discharge programme after pulmonary vein isolation: comparison between cryoballoon vs. radiofrequency ablation. Europace: European Pacing, Arrhythmias, and Cardiac Electrophysiology: Journal of the Working Groups on Cardiac Pacing, Arrhythmias, and Cardiac Cellular Electrophysiology of the European Society of Cardiology. 2023; 25: euad265.

[4] Aryana A, Heist EK, Pitha JV, Fan R, Park JK. Pulmonary Vein Isolation Using Visually Guided Second-Generation Cryoballoon: A Multicenter, Prospective, Real-World Experience. The Journal of Innovations in Cardiac Rhythm Management. 2021; 12: 4600–4610.

[5] Maltoni S, Negro A, Camerlingo MD, Pecoraro V, Sassone B, Biffi M, *et al*. Comparison of cryoballoon and radiofrequency ablation techniques for atrial fibrillation: a meta-analysis. Journal of Cardiovascular Electrophysiology. 2021; 32: 1365–1376.

[6] Wazni OM, Dandamudi G, Sood N, Hoyt R, Tyler J, Durrani S, *et al*. Cryoballoon Ablation as Initial Therapy for Atrial Fibrillation. The New England Journal of Medicine. 2021; 384: 316–324.

[7] Kuniss M, Pavlovic N, Velagic V, Hermida JS, Healey S, Arena G, *et al*. Cryoballoon ablation vs. antiarrhythmic drugs: first-line therapy for patients with paroxysmal atrial fibrillation. Europace: European Pacing, Arrhythmias, and Cardiac Electrophysiology: Journal of the Working Groups on Cardiac Pacing, Arrhythmias, and Cardiac Cellular Electrophysiology of the European Society of Cardiology. 2021; 23: 1033–1041.

[8] Andrade JG, Wells GA, Deyell MW, Bennett M, Essebag V, Champagne J, *et al*. Cryoablation or Drug Therapy for Initial Treatment of Atrial Fibrillation. The New England Journal of Medicine. 2021; 384: 305–315.

[9] Chun KRJ, Okumura Y, Scazzuso F, Frontera A, Magnani S. Safety and efficacy of cryoballoon ablation for the treatment of atrial fibrillation in elderly patients: A collaborative analysis. Pacing and Clinical Electrophysiology. 2021; 44: 360–368.

[10] Wazni O, Moss J, Kuniss M, Andrade J, Chierchia GB, Mealing S, *et al*. An economic evaluation of first-line cryoballoon ablation vs antiarrhythmic drug therapy for the treatment of paroxysmal atrial fibrillation from a U.S. Medicare perspective. Heart Rhythm O2. 2023; 4: 528–537.

[11] Shi LB, Rossvoll O, Tande P, Schuster P, Solheim E, Chen J. Cryoballoon vs. radiofrequency catheter ablation: insights from NOrwegian randomized study of PERSistent Atrial Fibrillation (NO-PERSAF study). Europace: European Pacing, Arrhythmias, and Cardiac Electrophysiology: Journal of the Working Groups on Cardiac Pacing, Arrhythmias, and Cardiac Cellular Electrophysiology of the European Society of Cardiology. 2022; 24: 226–233.

[12] Boho A, Stancik J, Misikova S, Mrazek V, Hatala R. Long-term outcome after cryoballoon ablation of atrial fibrillation in elderly patients. Journal of Geriatric Cardiology. 2021; 18: 114–122.
[13] Matsushita K, Arai K, Fukuzawa K, Imamura K, Okumura Y, Kofune T, *et al*. Efficacy and safety of cryoballoon ablation in elderly patients with atrial fibrillation: A multicenter study. Journal of Arrhythmia. 2020; 36: 917–922.
[14] Kuck KH, Brugada J, Fürnkranz A, Metzner A, Ouyang F, Chun KRJ, *et al*. Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation. The New England Journal of Medicine. 2016; 374: 2235–2245.
[15] Kuniss M, Deisenhofer I, Schmidt B, Sticherling C, Ziackers M, Chun KRJ. Cryoballoon ablation for paroxysmal atrial fibrillation: 5-year outcome after single procedure and predictors of recurrence. Journal of Interventional Cardiac Electrophysiology. 2022; 65: 39–49.
[16] Ruff CT, Giugliano RP, Braunwald E, Murphy SA, Brown K, Jarolim P, *et al*. Peripheral artery disease in patients with acute coronary syndromes. Circulation. 2014; 130: 1568–1576.
[17] Chen S, Schmidt B, Yap SC. Cryoballoon or radiofrequency ablation for atrial fibrillation: an updated meta-analysis. Clinical Research in Cardiology. 2021; 110: 624–638.
[18] Cheng X, Li X, He Y, Liu X, Qiu J, Zhou L. Cryoballoon vs radiofrequency ablation for paroxysmal atrial fibrillation: an updated meta-analysis of randomized and observational studies. Eurointervention. 2021; 16: 1076–1082.
[19] Davis JJ, Svendsen JB, Konyn P, Dalili D, Peterson B, Rajan R, *et al*. Complications of arterial vascular access in interventional radiology. Current Problems in Diagnostic Radiology. 2021; 50: 536–549.
[20] Looi KL, Arora J, Tavizón FP, Kumar N, Han FT, Lim PO, *et al*. Time to pulmonary vein isolation and atrial fibrillation recurrence following cryoballoon ablation: a systematic review and meta-analysis. Journal of the American Heart Association. 2021; 10: e021233.
[21] Rottner L, Mathew S, Snipelisky D, Zaman J, Bowler D, Han J, *et al*. Feasibility, safety, and outcomes of achieving durable single-box pulmonary vein isolation in paroxysmal atrial fibrillation with cryoballoon ablation guided by real-time recordings. Heart Rhythm. 2022; 19: 1203–1211.
[22] Yao Y, Sveniece S, Sedaghat G, Hunter H, Hussain N, Carr K, *et al*. Aging impairs atrial structure and function in humans. Cardiovascular Research. 2021; 117: 787–797.
[23] Takahashi K, Okumura Y, Watanabe I, Kofune M, Kumagai K, Hiroki J, *et al*. Cryoablation time to encircling pulmonary veins is a predictor of atrioesophageal fistula after second-generation cryoballoon ablation. Journal of the American Heart Association. 2020; 9: e015972.
[24] Gersh BJ, Hev EV, Chung MK, Brinker M, Kitzman DW, Rich MW, *et al*. Catheter ablation for atrial fibrillation in the elderly: a systematic review and meta-analysis. Journal of the American Heart Association. 2022; 11: e024267.