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RESEARCH ARTICLE

Long-Term Clinical Outcomes Following Cryoballoon Ablation in Patients with Paroxysmal Atrial Fibrillation: Single-Center Experience

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ABSTRACT

Objective: Atrial fibrillation (AF) is a prevalent arrhythmia, often managed with pulmonary vein isolation (PVI) using cryoballoon ablation, particularly in symptomatic patients. This retrospective single-center study aimed to evaluate the long-term outcomes and influencing factors of cryoballoon-based PVIs.

Materials and Methods: Seventy-four patients diagnosed with paroxysmal AF, symptomatic despite medical therapy, underwent successful cryoballoon PVI between January 2012 and August 2022. Patients were monitored for AF recurrence via ECG and Holter follow-ups. Recurrence rates were compared between groups based on various demographic, echocardiographic, biochemical, and procedural parameters.

Results: A median follow-up of 27 (14.5) months revealed AF recurrence in 50% of patients. Recurrence rates at 1, 3, and 5 years were 23%, 44%, and 51.4%, respectively. Factors significantly associated with recurrence included low hemoglobin and potassium levels, enlarged left atrial diameter, mitral valve abnormalities, and elevated estimated pulmonary artery pressure. Multivariate Cox regression analysis identified left atrial diameter as an independent predictor of recurrence (HR=1.130, 95% CI: 1.010-1.285, p=0.034). A receiver operating characteristic curve was drawn and a cut-off value of 39.5 mm was determined for the left atrium using the Youden index (AUC: 0.747, 95% CI: 0.636-0.859, p<0.001). This cut-off value predicted AF recurrence with 64.9% sensitivity, 70.3% specification.

Conclusion: This study confirms existing literature on cryoballoon PVI outcomes. Left atrial diameter emerges as a significant independent predictor of AF recurrence, highlighting its importance in assessing patient and procedural parameters.

Keywords: Ablation, atrial fibrillation, cryoballoon, pulmonary vein isolation

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INTRODUCTION

Atrial fibrillation (AF) is a significant arrhythmia associated with increased morbidity and mortality in cardiovascular diseases.[1] Although the prevalence of AF in the general population is around 1–2%, this figure can reach 10–12% in individuals aged 80 and older.[2] In patients with AF, coagulation cascade components are found at higher levels in the blood independent of embolic events and are known to be associated with a significantly higher risk of ischemic events compared to those in sinus rhythm.[3,4] The main symptoms of AF include palpitations, exertional dyspnea, and are associated with significant burdens on both patients and the healthcare system, leading to outcomes such as death, stroke, and heart failure, which adversely affect quality of life. Risk factors for the development of AF include age, hypertension, valvular heart disease, heart failure, coronary artery disease, diabetes, chronic kidney disease, inflammatory conditions, surgery, chronic obstructive pulmonary disease (COPD), obstructive sleep apnea syndrome, obesity, physical inactivity, and smoking-alcohol use.[5]

The treatment of AF consists of three main components: rate control, rhythm control, and anticoagulation.[6] Although

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medical antiarrhythmic drugs used for rhythm control may be effective, they often lead to adverse clinical outcomes due to serious side effects. Particularly in patients with paroxysmal atrial fibrillation (PAF), after the discovery that the arrhythmia focus resides in the myocardial cells of the pulmonary veins, catheter ablation therapy has emerged as a treatment option for rhythm control.[7] Radiofrequency (RF) energy-based pulmonary vein isolation has yielded successful results in symptomatic AF patients resistant to medical therapy for rhythm control. However, due to technical complexity, the need for specialized expertise, prolonged procedure duration, and potential side effects associated with RF energy, cryoballoon catheter technology has been developed. In comparative studies, cryoballoon ablation has shown similar efficacy to RF ablation in terms of rhythm control.[8]

In our study, we aimed to evaluate the long-term follow-up and outcomes of cryoballoon-based pulmonary vein isolation in symptomatic PAF patients resistant to medical therapy at our tertiary care center. Patients were examined for AF recurrence, and the relationship between recurrence and various clinical, demographic, echocardiographic, laboratory, and procedural parameters was assessed.

MATERIALS and METHODS

Study Population

Our study is a single-center, observational, retrospective cohort study. Ninety-nine consecutive patients who underwent successful cryoballoon pulmonary vein isolation for PAF between January 2012 and August 2022 were included in the study. Inclusion criteria were as follows: age 18 years and older and patients who underwent cryoballoon pulmonary vein isolation for AF rhythm control. Exclusion criteria included patients who underwent RF ablation during the same session (n=18), those with insufficient clinical and preoperative parameters (n=3), and those without postoperative follow-up (n=4). After applying inclusion and exclusion criteria, a total of 74 patients were included in the study. Clinical, demographic, and angiographic data were extracted from the hospital's electronic database. The study protocol was approved by the local ethics committee on 04.04.2023 with decision number 2023.03-31, and all procedures were conducted in accordance with the principles of the Helsinki Declaration.

Definitions

The clinical definition of AF was defined as AF rhythm lasting longer than 30 seconds on a single-lead ECG recording or persisting throughout the entire ECG recording on a 12-lead recording. PAF was defined as AF that spontaneously or with intervention terminates within 7 days of symptom onset. Persistent AF refers to AF that has been present for more than 7 days from onset, which terminates with cardioversion after 7 days.[9] Comorbidity definitions included diabetes mellitus, defined by a fasting blood glucose level ≥126 mg/dL and/or HbA1c ≥6.5%, and/or recent use of insulin or antidiabetic drugs; hypertension, defined by systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg and/or use of antihypertensive drugs; heart failure, defined by left ventricular ejection fraction (LVEF) <50% on echocardiography; COPD, defined by chronic bronchitis or emphysema.

Routine biochemical tests and echocardiography were performed preoperatively for each patient. Pulmonary veins were evaluated using contrast-enhanced computed tomography in each patient. Routine transesophageal echocardiography (TEE) was performed preoperatively for atrial thrombus assessment. First-generation cryoballoon catheters (Arctic Front 2AF281, Medtronic, USA) were used in 9 patients, while second-generation cryoballoon catheters (Arctic Front 2AF283, Medtronic, USA) were used in 65 patients for the procedure. Patients who underwent successful cryoballoon pulmonary vein isolation were followed annually in outpatient clinics and emergency services to investigate the occurrence of AF recurrence. For AF recurrence, patients' ECG and Holter recordings were reviewed annually. Patients with complete ECG recordings showing AF and those with AF lasting more than 30 seconds on Holter monitoring were considered to have recurrence.

Ablation Procedure

Before the cryoballoon procedure, all patients were evaluated with detailed medical history and physical examination. Transthoracic echocardiography (TTE) and TEE were performed for all patients to assess accompanying structural diseases and thrombus. Additionally, computed tomography was used for anatomical evaluation of the left atrium and pulmonary veins before the procedure. After admission to the laboratory, under local anesthesia, a sheath was inserted into the right femoral vein, left femoral vein, and left femoral artery after puncture. A pigtail catheter was directed to the aortic root from the left femoral artery, and pressure recording was performed. The coronary sinus catheter was directed from the left femoral vein to the coronary sinus. IV Heparin was administered to the patient during the procedure, and activated clotting time was maintained at 300–350 seconds during the cryoballoon procedure. The transeptal catheter was directed from the right femoral vein to the superior vena cava. After reaching the atrial septum, septostomy was performed with a Brockenbrough needle, and the left atrium was accessed. Then, the cryoballoon catheter was advanced into the left atrium. When the cryoballoon catheter approached the ostium of the pulmonary vein, a soft circular mapping catheter was advanced into the pulmonary vein, and pulmonary vein potentials were recorded. Subsequently, the balloon was initially inflated inside the left atrium with a normal gas. The inflated balloon was advanced to the ostium of the pulmonary vein, and a contrast agent was given through the catheter to ensure complete occlusion of the pulmonary vein. Liquid nitrogen gas was sent into the balloon via CryoConsol, and the cooling process was started, generally achieving pulmonary vein isolation with a procedure lasting 180–240 seconds and not exceeding –60°C. The mapping catheter was used to monitor the isolation of the pulmonary veins. After all pulmonary veins were isolated and pulmonary vein potentials were checked with the mapping catheter, the balloon was deflated inside the left atrium, and the catheter was withdrawn to complete the procedure.

Statistical Analysis

The statistical analysis of the study utilized the Statistical Package for the Social Sciences version 26.0 (SPSS Inc., Chicago, Illinois, USA). Various methods were employed to assess the distribution of variables, including visual techniques such as histograms and probability curves, as well as analytical methods like the Kolmogorov-Smirnov test. Numerical variables were presented as mean±standard deviation if normally distributed, while non-normally distributed variables were represented as median (interquartile range). Categorical variables were expressed as percentages (%). Numerical variables were compared between two groups using the unpaired Student's t-test and Mann-Whitney U test based on the distribution, while categorical variables were compared using the Chi-square or Fisher's exact test. Event-free survival analyses were performed using the Kaplan-Meier method and compared using the log-rank test. Hazard ratios (HRs) and 95% confidence intervals (95% CI) for clinical endpoints were calculated using univariate and multivariate Cox proportional hazard models. A significance level of $p<0.05$ was considered statistically significant throughout the study.

RESULTS

A total of 74 patients were included in the study, with a mean age of 53.8±10.9 years, of which 36 (48.6%) were female. The median follow-up duration was 27 (14.52) months, during which a total of 50% of patients experienced AF recurrence. According to the follow-up duration, AF recurrence was observed in 23% of patients at 1-year follow-up, 44% of patients who completed 3-year follow-up, and 51.4% of patients who completed 5-year follow-up. Patients were divided into two groups based on the occurrence of AF recurrence.

The basic demographic, clinical, and medical treatment data of the study group are presented in Table 1. There were no statistically significant differences between the two groups in terms of demographic, clinical, and medical treatment characteristics. Pre-procedural laboratory data for the study group are presented in Table 2. Similarly, there were no statistically significant differences between the two groups in terms of demographic, clinical, and medical treatment characteristics. While both groups showed similarities in laboratory characteristics, lower values of hemoglobin ($p=0.028$) and potassium ($p=0.008$) were observed in the group with AF recurrence. Other laboratory parameters were similar between the two groups.

The echocardiographic and procedural data of the study group are presented in Table 3. While both groups showed similarities in echocardiographic parameters, higher values of left atrium diameter ($p<0.021$), mitral regurgitation severity ($p=0.046$), and estimated pulmonary artery pressure ($p=0.001$) were observed in the group with AF recurrence. Other echocardiographic parameters were similar between the two groups. Additionally, there were no statistically significant differences in procedural data between the two groups.

Univariate Cox regression analyses were performed with all parameters to determine the predictors of long-term AF recurrence development, and the results are shown in Table 4. Hemoglobin ($p=0.09$), potassium ($p=0.007$), mitral regurgitation ($p=0.004$), elevated pulmonary artery pressure ($p<0.001$), and left atrium diameter ($p<0.001$) were significant predictors for the development of AF recurrence in long-term follow-up. In the multivariate Cox regression analysis with these parameters, left atrium diameter ($p=0.034$) was identified as an independent predictor for the development of AF recurrence in long-term follow-up.

A ROC curve was drawn to determine the optimal cutoff value for left atrium diameter, which best detects AF recurrence in long-term follow-up (Fig. 1), and a cutoff value of 39.5 mm was determined using the Youden index (AUC: 0.747, 95% CI: 0.636–0.859, $p<0.001$). This cutoff value can detect AF recurrence with 64.9% sensitivity and 70.3% specificity.

Kaplan-Meier survival analysis revealed that higher left atrium diameter significantly increased the risk of long-term AF recurrence in patients (Log-rank: $p<0.001$) (Fig. 2).

Table 1. Demographic, clinical, and medical terapy characteristics of the study group

	All patients (n=74)		AF group (n=37)		Non-AF group (n=37)		p
	n	%	n	%	n	%	
Age, years	53.8±10.9		53.2±9.5		54.4±12.3		0.627
BMI, (kg/m²)	29.8±6.7		28.1±3.8		31.3±8.4		0.119
Gender (female)	36	48.6	16	43.2	20	54.1	0.352
Smoking	15	20.5	7	19.4	8	21.6	0.818
CHF	1	1.4	1	2.7	0	0	0.314
HT	36	48.6	16	43.2	20	54.1	0.352
DM	6	8.1	4	10.8	2	5.4	0.394
CAD	3	4.1	1	2.7	2	5.4	0.556
Hyperthyroidism	13	17.6	5	13.5	8	21.6	0.359
COPD	5	6.8	2	5.4	3	8.1	0.643
Medical treatment							
Beta Bloker	65	87.8	31	83.8	34	91.9	0.286
CCB	8	10.8	6	16.2	2	5.4	0.134
Sotalol	6	8.1	2	5.4	4	10.8	0.394
Amiodarone	30	40.5	15	40.5	15	40.5	1
Propafenone	31	41.9	16	43.2	15	40.5	0.814

Data are presented as percentage, mean standard deviation or median (interquartile range). AF: Atrial fibrillation; BMI: Body mass index; CHF: Congestive heart failure; HT: Hypertension; DM: Diabetes mellitus; CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease; CCB: Calcium channel blocker

Table 2. Pre-procedural laboratory data for the study group

	All patients (n=74)	AF group (n=37)	Non-AF group (n=37)	p
WBC, 10^6/L	7.5±1.6	7.4±1.5	7.5±1.6	0.742
Hemoglobin, g/dL	13.5±1.7	14.7±1.5	13.1±1.8	**0.028**
Platelet, 10^3/mL	246.8±54.9	245.9±52.9	247.9±58	0.880
Neutrophil, 10^3/mL	4.5±1.4	4.2±1.2	4.7±1.5	0.125
Lymphocyte, 10^3/mL	2.24±0.69	2.4±0.7	2.1±0.6	0.069
Monocyte (10*9/L)	0.58±0.18	0.59±0.20	0.56±0.15	0.629
Albumin (g/L)	4.1±0.4	4.0±0.47	4.16±0.34	0.400
ALT (U/L)	18 (14.5–24.5)	16 (15–22)	18 (14–28)	0.539
AST (U/L)	18 (14–23)	17 (14–21)	19 (15–37.5)	0.122
Creatinine, mg/dL	0.82±1.8	0.80±0.13	0.84±0.21	0.317
Sodium (mmol/L)	137.4±15.4	140.1±1.8	134.7±21.6	0.144
Potassium (mmol/L)	4.3±0.5	4.47±0.36	4.01±0.57	**0.008**
Calcium (mmol/L)	9.1±0.6	9.17±0.46	9.1±0.64	0.618
Magnesium (mmol/L)	1.97±0.22	1.98±0.25	1.97±0.19	0.913

Data are presented as percentage, mean±standard deviation or median (interquartile range). WBC: White blood cells; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase

DISCUSSION

We present the results of a retrospective cohort study evaluating the clinical characteristics and outcomes of adult patients undergoing cryoablation for Paroxysmal AF at our tertiary cardiovascular center. The median follow-up duration of our study was 27 (14.52) months.

Table 3. The echocardiographic and procedural data of the study group

	All patients (n=74)		AF group (n=37)		Non-AF group (n=37)		p
	n	%	n	%	n	%	
LVEF (%)	59.4±5.5		60.2±3.9		58.6±6.7		0.214
Left atrium diameter, (mm)	37.8±4.5		36.5±3.7		40.9±3.9		**<0.001**
Interventricular septum, (mm)	10.1±1.3		9.9±1.3		10.4±1.2		0.098
LVDD							0.077
Grade 0	32	43.8	19	51.4	13	36.1	
Grade 1	37	50.7	18	48.6	19	52.8	
Grade 2	4	5.5	0	0	4	11.1	
Grade 3	1	1.4	0	0	1	2.8	
Mitral regurgitation							**0.046**
None	20	27	12	32.4	8	21.6	
Mild	47	63.5	25	67.6	22	59.5	
Moderate	6	8.1	0	0	6	16.2	
Severe	1	1.4	0	0	1	2.7	
PASP							**0.001**
<35 mm/Hg	61	82.4	36	97.3	25	67.6	
>35 mm/Hg	13	17.8	1	2.7	12	32.4	
Procedural variable							
Processing time, minute	144.2±28.1		143.1±30.6		145.3±25.8		0.744
Cryoballoon catheter type							0.286
1st Generation cryoballoon catheter	9	12.2	3	8.1	6	16.2	
2nd Generation cryoballoon catheter	65	87.8	34	91.9	31	83.8	
Balloon cooling degree, °C	−43.9±5.3		−44.6±5.2		−43.2±5.3		0.282
Balloon duration, seconds	255.4±28.2		253±25		257.8±31.2		0.462
Extra balloon application	9	12.2	3	8.1	6	16.2	0.286

Data are presented as percentage, mean standard deviation or median (interquartile range). AF: Atrial fibrillation; LVEF: Left ventricular ejection fraction; LVDD: Left ventricle diastolic functions; PASP: Pulmonary arterial systolic pressure.

Table 4. Univariate and multivariate Cox regression analyses to identify predictors of long-term AF recurrence development

	Univariate analyses			Multivariate analyses		
	HR	95%CI (lower–upper)	p	HR	95%CI (lower–upper)	p
Hemoglobin	0.746	0.604–0.921	**0.009**	0.864	0.678–1.101	0.237
Potassium	0.382	0.190–0.769	**0.007**	0.682	0.263–1.764	0.430
Left atrium diameter	1.186	1.085–1.297	**<0.001**	1.139	1.010–1.285	**0.034**
Mitral regurgitation	2.522	1.355–4.693	**0.004**	1.705	0.772–3.765	0.187
PASP	3.924	1.941–7.933	**<0.001**	1.816	0.645–5.109	0.259

HR: Hazard ratio; CI: Confidence interval; PASP: Pulmonary arterial systolic pressure

The main findings of our study are summarized below:

1. During the follow-up period, a total of 37 patients (50%) experienced AF recurrence.
2. When looked at annually: In the 1-year follow-up period, AF recurrence was detected in 17 out of 74 patients (23%), in the 3-year follow-up period, it was observed in 22 out

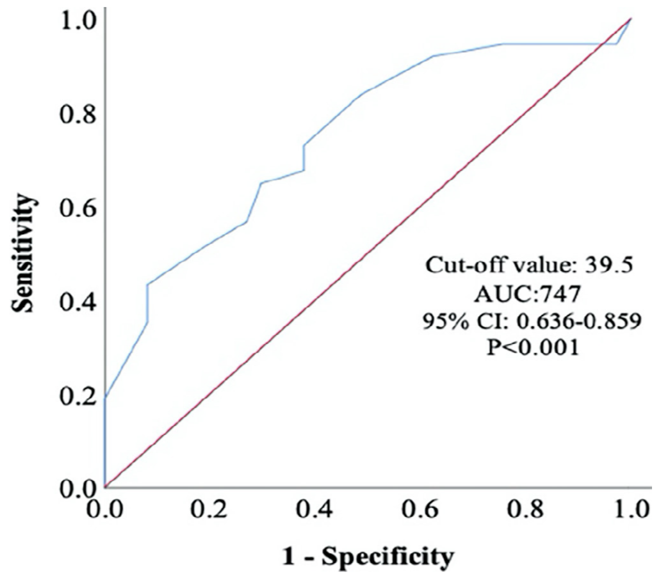

Figure 1. ROC curve for left atrial diameter, as a predictor of AF recurrence

AUC: Area under curve; ROC: Receiver operating characteristic; AF: Atrial fibrillation

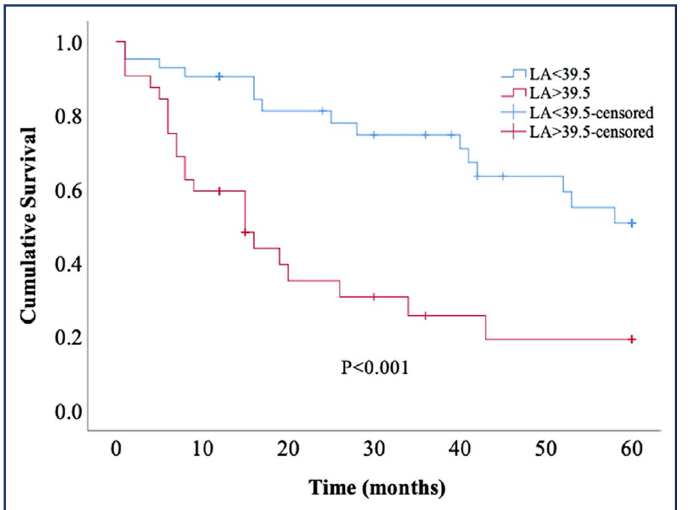

Figure 2. Kaplan–Meier survival curves for left atrial diameter in AF recurrence

LA: Left atrium

of 50 patients (44%), and in the 5-year follow-up period, it was found in 19 out of 37 patients (51.4%).

3. Regarding AF recurrence, left atrium diameter was identified as an independent predictor in multivariate Cox regression analysis with a p-value of 0.034.
4. In the ROC curve, a cut-off value of 39.5 mm for the left atrium diameter can detect AF recurrence with 64.9% sensitivity and 70.3% specificity.

Our observed rates of AF recurrence in the study are comparable to those reported in the current literature. When looking at large-scale studies in this regard, for instance, in the multicenter, prospective Freeze-AF study involving 2329 patients in the cryoballoon arm with a follow-up duration of 441 days, an atrial arrhythmia recurrence rate of 30.7% was reported.[10] In another meta-analysis that included 3 randomized controlled trials and 8 retrospective studies with a mean follow-up duration of 16.5 months, the recurrence rate was found to be 33.1%.[11] In a prospective study that examined 5-year follow-ups after cryoballoon ablation, the recurrence rate of AF was found to be 41%.[12] Our study also reveals a similar pattern, with higher rates of recurrence observed in the initial years, yet the 5-year follow-up numbers are consistent with recent studies.

Left atrial enlargement is both a precursor and a result of AF structurally. The enlargement of the left atrium creates a new substrate for AF by inducing structural and electrical heterogeneity. Furthermore, the irregular contractions seen in AF raise left atrial pressure, which in turn promotes left atrial enlargement and remodeling. Consequently, this perpetuates the development of a new substrate for AF.[13] In the catheter ablation guidelines published by the European Heart Rhythm Association (EHRA) in 2017, it is mentioned that studies conducted after AF ablation procedures have examined the main factors in terms of recurrence. These factors include non-paroxysmal AF types, increased left atrial diameter, age, hypertension, and the presence of left atrial fibrosis in MR.[14] In a meta-analysis involving 7217 patients who underwent ablation procedures, serious left atrial enlargement (>50 mm) was identified as a significant predictor when examining recurrence predictors.[15] In a meta-analysis involving 2825 patients, it was found that left atrial enlargement is associated with recurrence and is a better predictor than EF value.[16] Our study has demonstrated that left atrial diameter is one of the most valuable parameters in terms of the development and recurrence of atrial fibrillation.

Anemia and iron deficiency seem to be prevalent among individuals with AF. It is well-documented that the coexistence of anemia in AF patients correlates with an elevated risk of bleeding, cardiac events, and overall mortality.[17] Recent cohort studies have also shown that low hemoglobin levels and anemia may be associated with the development of new-onset AF.[18,19] Furthermore, in a recent study by Kim et al.,[20] the association between hemoglobin levels post atrial fibrillation catheter ablation (AFCA) and rhythm outcomes was investigated for the first time. Anemia was found to be independently associated with clinical recurrence following AFCA. This phenomenon can be explained by several mechanisms, including neurohormonal, hemodynamic, and renal changes, through which anemia may contribute to cardiovascular diseases.[21] However, it is unclear whether anemia has a causal relationship with adverse cardiovascular outcomes or if it simply serves as a marker of more advanced disease. In our study, we also observed lower hemoglobin levels in the group experiencing AF recurrence. However, while it was a significant parameter in univariate analysis, it was not an independent predictor in multivariate analysis. This may be attributed to the relatively small scale of our study cohort.

Potassium, a vital intracellular cation, is crucial for preserving cell membrane sensitivity to stimuli. Reduced serum potassium levels escalate transmembrane electrochemical gradients, inducing cellular hyperpolarization. This alteration adversely impacts depolarization and contraction mechanisms. Hypokalemia, a prevalent electrolyte imbalance encountered in medical settings, affects roughly 20% of hospitalized patients. Moreover, it correlates with the occurrence of AF and ventricular fibrillation (VF).[22] In a study conducted on elderly adults, the frequency of hypokalemia in individuals with AF was found to be 30.98%, and this condition was strongly associated with cardiovascular death.[23] Additionally, Farah et al.[24] have demonstrated that low serum potassium levels increase the risk of AF. However, in a recent study by Filipovic et al.,[25] no difference was found in the initial serum potassium levels between patients undergoing ablation, regardless of AF recurrence. In our study, although lower serum potassium levels were observed in the group experiencing AF recurrence, potassium levels were not identified as an independent determinant of AF recurrence.

In our investigation, we found that AF recurrence was significantly more common among patients whose estimated pulmonary artery pressure exceeded 35 mmHg, as calculated via the tricuspid valve. Elevated pulmonary artery pressure induces hemodynamic alterations in the right ventricle and atrium, leading to long-term volume overload, dilation of these chambers, compromised systolic and diastolic functions, and myocardial remodeling. Patients with pulmonary hypertension (PH) are known to be at a heightened risk of atrial arrhythmias due to increased right atrial pressure and pulmonary wedge pressure. Moreover, these atrial arrhythmias are associated with higher mortality rates, underscoring the importance of restoring sinus rhythm in managing such patients with atrial arrhythmias.[26] Additionally, in another study, elevated estimated pulmonary artery pressure was identified as a predictor of AF recurrence after RF ablation.[27] Elevated estimated pulmonary artery pressure may predict AF recurrence in patients scheduled for cryoballoon ablation. However, in our patient cohort, estimated pulmonary artery pressure was determined via echocardiography. Nevertheless, assessing patients' pulmonary artery pressures invasively could provide more precise clinical decisions.

A significant level of mitral regurgitation (MR) accompanies AF in 7.4% to 29% of patients.[28] In our study, similarly, moderate MR was present in 6 patients (8.1%), and severe MR was present in 1 patient (1.4%). As known, MR increases preload in the left atrium (LA) and left ventricle (LV), dilates LA and LV, and this leads to increased regurgitation, creating a vicious cycle.[29] The severity of MR is associated with the rate of recurrent atrial tachyarrhythmias; a more severe degree of MR indicates a higher rate of recurrent atrial tachyarrhythmias.[30] Studies investigating the association between the degree of MR and the prediction of AF recurrence post-ablation have shown that when 95 patients with moderate or higher baseline MR were compared one-to-one with 95 patients with mild MR, those with MR had a higher rate of AF recurrence compared to controls.[31] On the contrary, in a smaller-scale study, MR was not found to be an independent determinant of post-ablation AF recurrence in patients undergoing catheter ablation for PAF.[32] In our study, similarly, higher degrees of MR were observed in the group experiencing recurrence, but it was not identified as an independent variable in Cox regression analysis. This finding is consistent with the study conducted by Ke et al.,[32] which initially appeared to have similar high MR degrees.

Limitation

This study possesses several limitations that warrant acknowledgment. Firstly, its single-center retrospective design may constrain the generalizability of the findings, potentially influenced by the characteristics of a particular population. Secondly, the sample was drawn exclusively from a single hospital within a specified timeframe, potentially limiting the applicability of the results to broader populations. Moreover, the sample size may impact the statistical power of subgroup analyses. Thirdly, the presence of missing or incomplete demographic and clinical data hinders a comprehensive evaluation of all potential effects. Specifically, the absence of clinical assessments during long-term follow-ups may introduce bias into the results. Lastly, the study exclusively focused on cryoballoon ablation therapy, warranting a more expansive analysis to assess the long-term outcomes of alternative treatment modalities (such as radiofrequency ablation or surgical ablation). Acknowledging these limitations is crucial for interpreting the research findings and assessing their applicability. Future studies may adopt different methodological approaches to address these limitations and yield more robust and comprehensive results.

CONCLUSION

This study highlights the importance of considering clinical factors and technical aspects in predicting recurrences in long-term follow-ups after cryoballoon ablation in patients with symptomatic PAF resistant to medical therapy. In patients with enlarged LA, more careful monitoring and specific management strategies may be needed to reduce the risk of recurrence post-ablation.

Disclosures

Ethics Committee Approval: The study was approved by the Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Clinical Research Ethics Committee (No: 2023.03-31, Date: 04/04/2023).

Authorship Contributions: Concept: C.C., A.E.; Design: C.C., A.E.; Supervision: C.C., A.E.; Materials: M.A.; Data Collection or Processing: C.C., M.A.; Analysis or Interpretation: C.C., M.A.; Literature Search: C.C., M.A.; Writing: C.C.; Critical review: C.C., M.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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