

# Risk factors for late recurrence in patients with nonvalvular atrial fibrillation after radiofrequency catheter ablation

Zhang Peng MD<sup>1</sup>  | Liu Wen-Heng PhD<sup>1</sup> | Zhao Qing MD<sup>1</sup> | Sun Pin PhD<sup>2</sup> | Cai Shang-Lang MD<sup>1</sup> | Wang Mao-Jing PhD<sup>1</sup> | Pan Ya-Qi MD<sup>1</sup>

<sup>1</sup>Department of Cardiology, The Affiliated Hospital of Qingdao University, Qingdao, China

<sup>2</sup>Department of Cardiac Ultrasound, The Affiliated Hospital of Qingdao University, Qingdao, China

## Correspondence

Wang Mao-Jing, Department of Cardiology, The Affiliated Hospital of Qingdao University, 16 Jiangsu Road, Qingdao, 266000 Shandong, China.  
Email: wangmaojing@sina.com

## Funding information

None.

## Abstract

**Objective:** To identify the risk factors for postoperative atrial fibrillation (AF) recurrence in nonvalvular AF patients undergoing radiofrequency catheter ablation (CA).

**Methods:** We retrospectively reviewed the data from 426 of 450 AF patients who underwent CA. Patients were divided into two groups according to recurrence after the operation; the risk factors for AF recurrence were analyzed. A stratification system for lesions was created based on the cutoff of the risk factors; the associations among the subgroups and the AF recurrence rate were analyzed.

**Results:** AF recurrence occurred in 98 (23.0%) patients. Univariate analysis demonstrated that AF type, hypertrophic cardiomyopathy, left atrial diameter (LAD), left ventricular ejection fraction (LVEF), serum albumin, and D-dimer concentrations were associated with AF recurrence. AF type (OR = 2.907,  $p < .001$ ), serum albumin concentration (OR = 1.112,  $p < .05$ ), and LAD (OR = 1.115,  $p < .001$ ) were independent risk factors for AF recurrence. The area under the ROC curve of LAD for the prediction of AF recurrence was 0.722 (95% CI: 0.664~0.779) and that of serum albumin for the prediction of AF recurrence was 0.608 (95% CI: 0.545~0.672). Further stratification revealed that patients with persistent or paroxysmal AF with LAD  $\geq 43.5$  mm and serum albumin concentration  $\geq 42.2$  g/L had a higher rate of AF recurrence than the reference group.

**Conclusion:** Atrial fibrillation type, LAD, and serum albumin concentration are risk factors for AF recurrence after CA in patients with nonvalvular AF. Patients with persistent AF with LAD  $\geq 43.5$  mm and serum albumin concentration  $\geq 42.2$  g/L have a higher risk of late AF recurrence after surgery.

## KEYWORDS

albumin, atrial fibrillation, left atrial diameter, recurrence, types of atrial fibrillation

## 1 | INTRODUCTION

Atrial fibrillation (AF) is defined as supraventricular tachycardia in which rapid and inconsistent electrical activity of the atria leads to ineffective

atrial contractions. The current prevalence in adults is 2%–4% (Hindricks et al., 2021). AF is the most serious disorder of atrial electrical activity. The main risks associated with AF are stroke and heart failure, which can significantly increase all-cause mortality (Lee et al., 2020; Vinter

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2021 The Authors. *Annals of Noninvasive Electrocardiology* published by Wiley Periodicals LLC.

et al., 2020). Radiofrequency catheter ablation (CA) is mainly performed by electrically isolating the pulmonary veins completely to convert and maintain sinus rhythm. Studies have shown that CA is superior to drug therapy in relieving symptoms related to AF, reducing the burden of AF, and improving the quality of life in patients with AF (Cappato et al., 2010; Poole et al., 2020). The 2020 European Society for Cardiology (ESC)/European Association for Cardio-Thoracic Surgery (EACTS) suggested that CA can be selected as a preferred treatment in patients with paroxysmal or persistent AF (Hindricks et al., 2021). However, there is still the possibility of AF recurrence after CA. The recurrence rate of persistent AF after CA can even reach 75% within 7 years (Rottner et al., 2020). Studies have found that the type of AF, the course of AF, alcohol consumption, and diseases such as hypertension, diabetes, and renal insufficiency will affect the therapeutic effect of CA (Anselmino et al., 2015; Pranata et al., 2020; Steinberg et al., 2014; Voskoboinik et al., 2020; Wang et al., 2014; Zheng et al., 2021). Potential modifiable risk factors, such as serum albumin concentration and hypertrophic cardiomyopathy, have yet to be explored.

This study, which involves a relatively large number of paroxysmal and persistent AF patients, aimed to analyze the independent predictors of postoperative recurrence of AF in patients who underwent CA in our center to provide a reference for early identification of AF patients who are prone to recurrence after CA.

## 2 | PATIENTS AND METHODS

### 2.1 | Patients

We retrospectively reviewed all patients diagnosed with AF who underwent CA at the Affiliated Hospital of Qingdao University between June 2018 and June 2020. The selection criteria were (1) non-valvular AF, (2) paroxysmal or persistent AF, (3) CA of AF for the first time, and (4) preoperative transesophageal echocardiography or left atrial CT imaging showing no thrombus in the left atrium. The exclusion criteria were (1) left ventricular ejection fraction (LVEF)  $\leq 35\%$ , (2) severe liver insufficiency (alanine aminotransferase or aspartate aminotransferase greater than 3 times the upper limit of the normal range), (3) severe renal insufficiency (glomerular filtration rate less than 60 ml/(min $\cdot$ 1.73 m (Lee et al., 2020)), (4) cachexia (>5% weight loss in the previous 6 months or 2%–5% weight loss with either body mass index), and (5) life expectancy less than 1 year. A total of 450 eligible patients were included.

### 2.2 | Methods

#### 2.2.1 | Preoperative preparation

All patients were treated with warfarin or new oral anticoagulants (NOACs), such as rivaroxaban and dabigatran, for at least 1 month before CA. Echocardiography was performed to evaluate the structure and function of the cardiac tissue, and transesophageal

echocardiography or left atrial CT imaging was performed within 48 hours before the operation to exclude left atrial thrombus.

#### 2.2.2 | Radiofrequency catheter ablation methods

All operations were performed by the same doctor. After puncturing the right femoral vein, a 10-grade coronary sinus electrode was sent into the coronary sinus, and then the 8.5 F Swartz long sheath was sent to the right atrium. The atrial–septal puncture needle was sent along the sheath to the fossa ovale to puncture the interatrial septum. After a successful puncture, an intravenous injection of 100 IU/kg unfractionated heparin sodium was performed, and 1000 IU unfractionated heparin sodium was added every hour during the operation. During the operation, the activated whole blood-clotting time (ACT) was monitored every 0.5 h, and the ACT value was stable at 250–350 s. The Swartz long sheath was inserted into the left atrium, the star-mapping electrode was placed along with the sheath to the left atrium, and the left atrium model was built under the guidance of the Carto system. A 3.5-mm ablation catheter (Smart Touch, Johnson & Johnson) was used for CA, the discharge energy was 35–40 W, the ablation index (AI) was 350–500, the limited ablation temperature was 43°C, the ablation time was 20–30 s, and the flow rate of saline perfusion was 23 ml/min. The ablation strategy for paroxysmal AF was pulmonary vein isolation (PVI) combined with shattered potential ablation. The ablation strategy for persistent AF was PVI combined with left atrium top line, bottom line, mitral-valve isthmus line, and tricuspid-valve isthmus line ablation and shattered potential ablation. Ablation was successful when both pulmonary veins reached bidirectional electrical isolation, and the patients with AF were subjected to direct current synchronous electrical cardioversion after linear ablation.

#### 2.2.3 | Postoperative sinus rhythm maintenance and anticoagulation methods

All patients were given standardized anticoagulant therapy with warfarin or NOAC for at least 3 months after the operation. Patients with normal thyroid function were given oral propafenone or amiodarone to maintain sinus rhythm. The dosage of propafenone was 150 mg three times a day, and the dosage of amiodarone was 200 mg three times a day for the first 10 days and was adjusted to 200 mg once a day after the first 10 days. Patients with a history of pulmonary fibrosis or thyroid dysfunction, including hypothyroidism, subclinical hypothyroidism, and hyperthyroidism, were administered dronedarone to maintain sinus rhythm, the dosage of that was 400 mg twice a day. The treatment course of antiarrhythmic drugs was 3 months after CA.

#### 2.2.4 | Postoperative follow-up

All patients were advised to return for follow-up at the outpatient clinic 1, 3, 6, and 12 months after the operation. The main content of

**TABLE 1** Comparison of baseline data between the recurrence group and the nonrecurrence group

	Nonrecurrence group (n = 328) N (%)	Recurrence group (n = 98) N (%)	$\chi^2$	p Value
Age (years)				
≥60	218 (66.5)	60 (61.2)	0.91	.339
<60	110 (33.5)	38 (38.8)		
Sex				
Male	193 (58.8)	61 (62.2)	0.55	.560
Female	135 (41.2)	37 (37.8)		
Postoperative antiarrhythmic drugs				
Amiodarone	248 (75.6)	78 (79.6)	0.67	.414
Propafenone	49 (14.9)	11 (11.2)	0.86	.354
Dronedarone	16 (4.9)	3 (3.1)	0.59	.445
None	15 (4.6)	6 (6.1)	0.39	.534

the follow-up was the symptoms related to AF, signs of AF, and 24-h Holter examination results. Patients were informed to promptly perform a 24-h Holter examination and record the recurrence of AF if they felt dizziness, palpitations, chest tightness, suffocation, or other symptoms related to AF.

The first 3 months after the first ablation was a window period during which any atrial arrhythmia occurrence was not counted as AF recurrence.

Late recurrence of AF is defined as atrial arrhythmias, including atrial fibrillation, atrial flutter, and atrial tachycardia that lasts more than 30 s after 3 months of CA. According to the late recurrence of AF after CA, the patients were divided into a recurrence group and a nonrecurrence group.

### 2.2.5 | Data collection

Clinical data, echocardiography data, and serological indicators of the included patients were collected from the hospital information system of the Affiliated Hospital of Qingdao University. (1) Clinical data: age, sex, type of AF, course of AF, body mass index (BMI), hypertension, hypertrophic cardiomyopathy, coronary atherosclerotic heart disease, diabetes, cerebrovascular disease, and left atrial appendage occlusion; (2) Echocardiography data (preoperatively): left atrial diameter (LAD), LVEF, and pulmonary artery pressure; (3) Serological indicators (preoperatively): neutrophil-to-lymphocyte ratio (N/L), D-dimer, albumin, globulin, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol.

### 2.3 | Statistical analysis

Categorical variables are presented as frequencies and percentages, and the comparison of categorical variables between groups was performed by the  $\chi$  (Lee et al., 2020) test. The continuous variables are presented as  $\bar{x} \pm s$ . Two independent sample t-tests (for normally

distributed data) or the Mann-Whitney U tests (for non-normally distributed data) were used for continuous variables. The risk factors considered significant in univariate analysis were subsequently included in multivariate logistic regression analyses to identify the independent variables associated with AF recurrence. The Cox proportional hazards model was used to estimate the hazard ratio (HR) with its 95% confidence interval (CI). Independent risk factors that met the characteristics of the continuous variables were applied to the receiver operating characteristic curve (ROC curve) to obtain the Youden index (sensitivity + specificity-1), and the best cutoff value of the independent risk factors was determined to evaluate its sensitivity and specificity for predicting the recurrence of AF. The patients were divided into several subgroups according to the cutoff point of each risk factor. Setting the subgroup with the lowest risk as the reference group, the difference in AF recurrence rate between other subgroups and the reference group was evaluated by Fisher's exact test. Survival curves for the incidence of AF recurrence in each subgroup were calculated with the Kaplan-Meier method.  $p < .05$  (two-sided) was considered statistically significant in all statistical analyses. All analyses were performed by SPSS software (SPSS, version 23.0).

## 3 | RESULTS

### 3.1 | Comparison of baseline data between the recurrence group and the nonrecurrence group

A total of 450 patients who met the inclusion and exclusion criteria were included in this study. Among them, 208 had persistent AF, and 242 had paroxysmal AF. A total of 24 (5.3%) patients were lost to follow-up. Overall, the average follow-up time was 18.2 months. Late recurrence of AF was observed in 23% (98/426) of patients, the recurrence rate of persistent AF was 38.1% (74/194), and the recurrence rate of paroxysmal AF was 10.3% (24/232). In the recurrence group, there were 37 (37.8%) men and 61 (62.2%) women, and the average age was  $60.7 \pm 9.6$  years. A total of 79.6% (78/98) of patients

took amiodarone, 11.2% (11/98) of patients took propafenone, 3.1% (3/98) of patients took dronedarone after CA, and 6.1% (6/98) of patients did not take antiarrhythmic drugs to maintain sinus rhythm as prescribed by the doctor. There were 328 people in the nonrecurrence group; 193 (58.8%) patients were male, 135 (41.2%) patients were female, and the mean age was  $62.0 \pm 9.6$  years old. A total of 75.6% (248/328) of patients took amiodarone, 14.9% (49/328) of patients took prophylaxis, and 4.9% (16/328) of patients took dronedarone to maintain sinus rhythm after CA. In the nonrecurrence group, 4.6% (15/328) of patients did not take antiarrhythmic drugs to maintain sinus rhythm after surgery. All the detailed clinical data of the two groups of patients are shown in Table 1.

### 3.2 | Univariate analysis of atrial fibrillation recurrence

As shown in Table 2, AF recurrence was associated with the types of AF, hypertrophic cardiomyopathy, LAD, LVEF, serum D-dimer concentration, and serum albumin concentration in univariate analysis ( $p < .05$ ). In terms of clinical data, the proportion of persistent atrial fibrillation in the recurrence group was higher than that in the nonrecurrence group (74.5% vs. 36.6%,  $p < .001$ ), and the proportion of hypertrophic cardiomyopathy was also higher in the recurrence group (5.1% vs. 1.2%,  $p = .019$ ). Regarding echocardiography data, the recurrence group had a larger LAD ( $45.0 \pm 5.5$  mm vs.  $40.5 \pm 5.2$  mm,  $p < .001$ ) and a lower LVEF ( $56.7\% \pm 6.3\%$  vs.  $59.3\% \pm 4.1\%$ ) than the nonrecurrence group ( $p < .001$ ). Taking into account the serological indicators, the concentration of serum D-dimer in the recurrence group was lower than that in the nonrecurrence group ( $274.27 \pm 114.34$  mmol/L vs.  $314.98 \pm 114.34$ ,  $p = .03$ ), and the serum albumin concentration was higher than that in the nonrecurrence group ( $43.0 \pm 3.6$  g/L vs.  $41.4 \pm 3.9$  g/L,  $p = .002$ ).

### 3.3 | Multivariate analysis of atrial fibrillation recurrence

Multivariate analysis showed that the types of AF (OR = 2.907,  $p < .001$ ), serum albumin concentration (OR = 1.112,  $p < .05$ ), and LAD (OR = 1.115,  $p < .001$ ) were independent risk factors for AF recurrence. Details of the independent risk factors are presented in Table 3.

### 3.4 | ROC curve of risk factors related to recurrence of AF

As shown in Figure 1, the area under the ROC curve of LAD for the prediction of AF recurrence was 0.722 (95% CI: 0.664–0.779). When the LAD was 43.5 cm, the Youden index reached the maximum (0.356), and the sensitivity and specificity to predict AF recurrence were 63.3% and 72.3%, respectively. The area under the ROC curve

for serum albumin to predict atrial fibrillation recurrence was 0.608 (95% CI: 0.545–0.672), and the Youden index was the highest (0.207) when the serum albumin concentration was 42.2 g/L, for which the sensitivity and specificity were 62.2% and 58.5%, respectively.

### 3.5 | Statistical analysis and survival analyses of stratification related to cutoff points of risk factors

We divided all patients into a persistent AF group (Group A) and a paroxysmal AF group (Group B) according to the type of AF. Group A was divided into 4 subgroups in terms of the cutoff point of LAD and serum albumin: Group A1 (LAD < 43.5 mm and serum albumin concentration < 42.2 g/L), Group A2 (LAD  $\geq$  43.5 mm and serum albumin concentration < 42.2 g/L), Group A3 (LAD < 43.5 mm and serum albumin concentration  $\geq$  42.2 g/L) and Group A4 (LAD  $\geq$  43.5 mm and serum albumin concentration  $\geq$  42.2 g/L). Similarly, Group B was divided into 4 subgroups: Group B1 (LAD < 43.5 mm and serum albumin concentration < 42.2 g/L), Group B2 (LAD  $\geq$  43.5 mm and serum albumin concentration < 42.2 g/L), Group B3 (LAD < 43.5 mm and serum albumin concentration  $\geq$  42.2 g/L) and Group B4 (LAD  $\geq$  43.5 mm and serum albumin concentration  $\geq$  42.2 g/L). During an average follow-up of 18.2 months, the postoperative recurrence rates of AF in Group A1, Group A2, Group A3, and Group A4 were 27.1%, 37.3%, 22.2%, and 64.0%, respectively (Figure 2). Group A1 was regarded as the reference group, and only Group A4 had a significantly higher recurrence rate of AF than the reference group (64.0% vs. 27.1%,  $p < .05$ ). Furthermore, the recurrence rates in Groups B1, B2, B3, and B4 were 4.0%, 3.4%, 11.4%, and 43.5%, respectively (Figure 3). Taking Group B1 as the reference group, the recurrence rate in Group B4 was significantly different compared with that in the reference group (43.5% vs. 4.0%,  $p < .05$ ). Details of the recurrence rate of AF in subgroups are presented in Table 4, as are other details.

## 4 | DISCUSSION

The 2 main findings of the present retrospective, single-center study are as follows: 1. The type of atrial fibrillation, preoperative LAD, and preoperative serum albumin concentration were independent risk factors for recurrence of nonvalvular AF after initial CA. 2. Patients with paroxysmal atrial fibrillation with LAD  $\geq$  43.5 mm and serum albumin concentration  $\geq$  42.2 g/L and patients with persistent atrial fibrillation with LAD  $\geq$  43.5 mm and serum albumin concentration  $\geq$  42.2 g/L had a higher recurrence rate of AF after surgery.

Catheter ablation is the preferred treatment strategy for AF and can effectively convert and maintain sinus rhythm, relieve symptoms related to AF, and significantly improve quality of life (Packer et al., 2019; Pluymaekers et al., 2019). The 2020 ESC/EACT guidelines for the management of atrial fibrillation suggested that the risk of postoperative recurrence should be considered when evaluating the indications for CA in patients with AF (Hindricks et al., 2021).

**TABLE 2** Comparison of indicators between the recurrence group and the nonrecurrence group

	Nonrecurrence group (n = 328) N (%)	Recurrence group (n = 98) N (%)	$\chi^2/t/U$	p Value
BMI (kg/m <sup>2</sup> )	26.3 ± 3.1	25.7 ± 3.5	1.38 <sup>#</sup>	.170
Type of AF				
Persistent	120 (36.6)	74 (74.5)	46.10*	<.001
Paroxysmal	208 (63.4)	24 (25.5)		
Course of AF				
≥1 year	210 (64.0)	64 (65.3)	0.05*	.816
<1 year	118 (36.0)	34 (34.7)		
Hypertension				
Presence	196 (59.8)	60 (61.2)	0.07*	.795
Absence	132 (40.2)	38 (38.8)		
Type 2 diabetes				
Presence	58 (17.7)	23 (23.5)	1.64*	.200
Absence	270 (82.3)	75 (76.5)		
Coronary atherosclerotic heart disease				
Presence	119 (36.3)	43 (43.9)	1.85*	.174
Absence	209 (63.7)	55 (56.1)		
Cerebrovascular disease				
Presence	42 (12.8)	13 (13.3)	0.01*	.905
Absence	286 (87.2)	85 (86.7)		
Hypertrophic cardiomyopathy				
Presence	4 (1.2)	5 (5.1)	5.50*	.019
Absence	324 (98.8)	93 (94.9)		
Combined left atrial appendage closure				
Presence	26 (7.9)	7 (7.1)	0.07*	.799
Absence	302 (92.1)	91 (92.9)		
LAD (mm)	45.0 ± 5.5	40.5 ± 5.2	7.25 <sup>#</sup>	<.001
LVEF (%)	56.7 ± 6.3	59.3 ± 4.1	-4.70 <sup>Δ</sup>	<.001
Pulmonary artery pressure (mmHg)	32.1 ± 8.2	30.7 ± 7.3	1.51 <sup>Δ</sup>	.132
N/L	2.03 ± 1.01	2.09 ± 1.20	0.51 <sup>#</sup>	.610
D-dimer (ug/L)	314.98 ± 114.34	274.27 ± 114.34	-2.17 <sup>#</sup>	.030
Albumin (g/L)	41.64 ± 3.90	43.02 ± 3.62	3.12 <sup>#</sup>	.002
Globulin (g/L)	24.08 ± 3.80	24.85 ± 4.47	1.69 <sup>#</sup>	.092
HDL-C (mmol/L)	1.31 ± 0.45	1.30 ± 0.38	-0.31 <sup>#</sup>	.755
LDL-C (mmol/L)	2.52 ± 0.95	2.44 ± 0.81	-0.75 <sup>#</sup>	.453

Abbreviations: AF, atrial fibrillation; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; N/L, neutrophil-to-lymphocyte ratio.

\* $\chi^2$ -test.

<sup>#</sup>t-test.

<sup>Δ</sup>U-test.

Studies have found that actively controlling risk factors for recurrence of AF before surgery can effectively improve the success rate of CA (Hindricks et al., 2018).

In this study, it was found that the type of AF was an independent risk factor for the recurrence of AF after CA, and persistent AF was prone to recurrence compared with paroxysmal AF, which was

consistent with previous findings (Pranata et al., 2020). The occurrence of AF is related to abnormal electrical activity of the pulmonary vein, and the maintenance of AF is related to electrical remodeling and structural remodeling of the left atrium. The maintenance of AF further aggravates the electrical remodeling and structural remodeling of the left atrium, making it difficult for AF to reverse into sinus

rhythm. Patients with persistent AF should be more alert to the risk of recurrence of AF after CA.

In our study, LAD was found to be the strongest risk factor for AF recurrence, which is consistent with previous studies (Lee et al., 2018; Teh et al., 2012). As the frequency and duration of atrial fibrillation increase, the left atrial cardiomyocytes decrease and are gradually replaced by fibrous tissue. Then, the left atrium continues

TABLE 3 Multivariate analysis of recurrence of AF

Risk factors	OR (95%CI)	p Value
Type of AF	2.907 (1.633–5.175)	<.001
Albumin	1.112 (1.036–1.193)	.003
LAD	1.115 (1.058–1.175)	<.001

Abbreviations: AF, Atrial fibrillation; LAD, Left atrium diameter.

to expand, and the structural and electrical remodeling of the left atrium progresses gradually. Finally, AF is easier to trigger and maintain, resulting in further expansion of the left atrium and forming a vicious cycle. Previous studies found that LAD >50 mm is a strong predictor of AF recurrence after CA (D'Ascenzo et al., 2013). We found that LAD >43.5 mm has high specificity and sensitivity for predicting the recurrence of AF. Therefore, LAD should be carefully evaluated before CA. Patients with LAD >43.5 mm should be aware of the risk of AF recurrence.

In our study, it was found that patients with higher serum albumin levels before surgery had a higher risk of postoperative recurrence of AF. However, the causal relationship between serum albumin levels and recurrence of AF is still controversial. A large-scale prospective cohort study showed that the serum albumin level was independently inversely associated with incident AF but did not find a

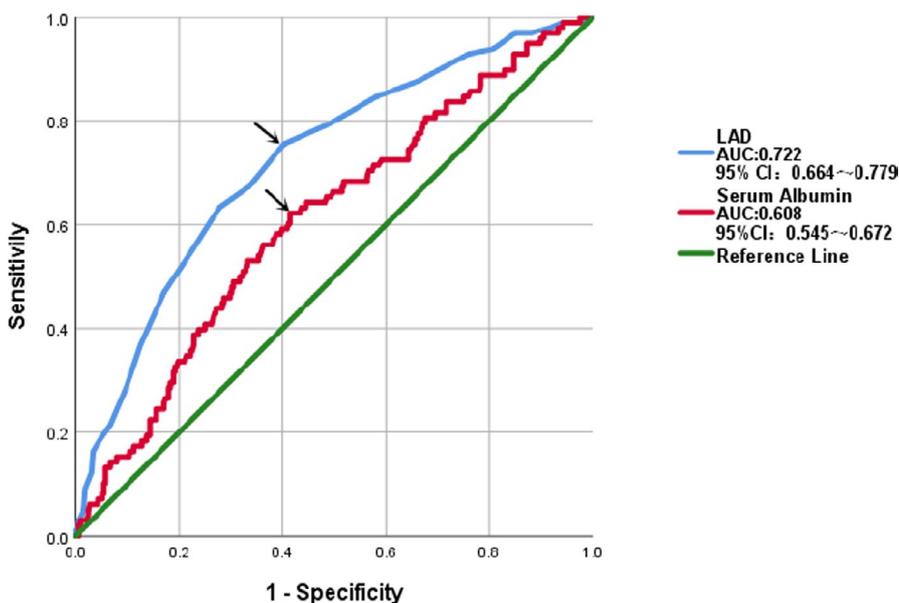


FIGURE 1 ROC curve of LAD and serum albumin for recurrence of atrial fibrillation. Note: The arrows indicate the cutoff point of LAD (blue line) and serum albumin (red line) corresponding to the best sensitivity and specificity. LAD =43.5 cm and serum albumin =42.2 g/L. LAD: The anteroposterior diameter of the left atrium

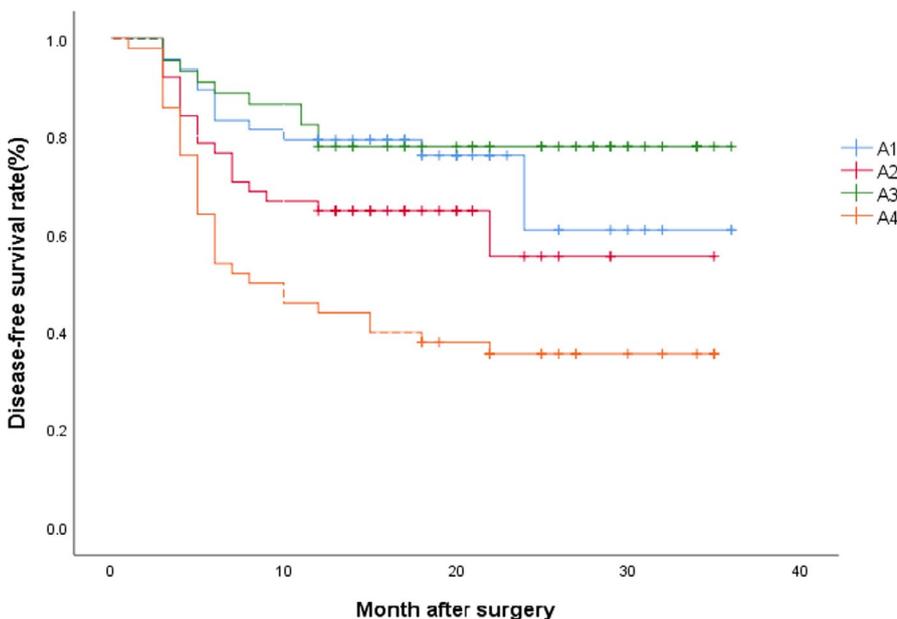
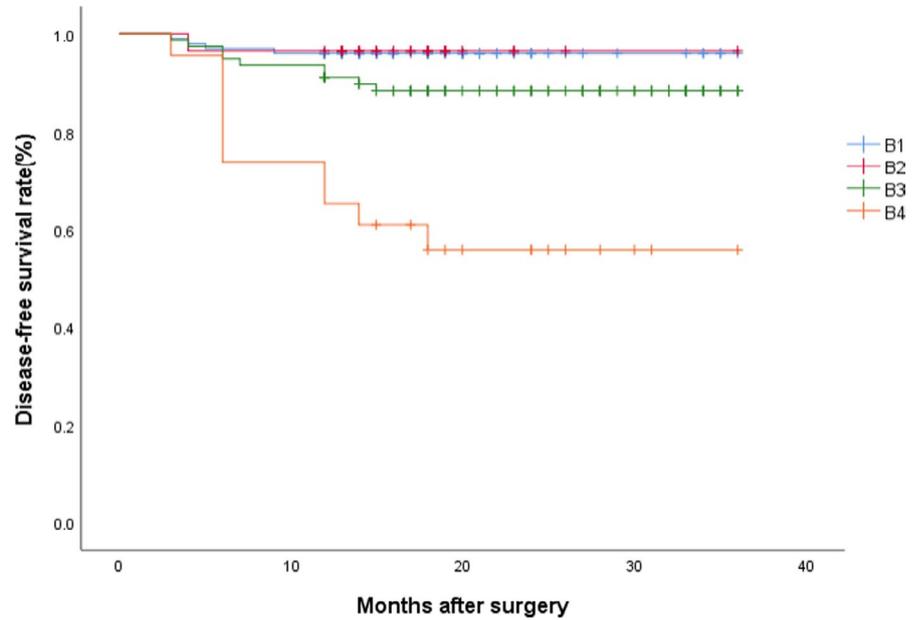


FIGURE 2 Survival curve of postoperative atrial fibrillation recurrence in Group A. During an average of 18.2 months of follow-up, postoperative atrial fibrillation recurrence rates in Group A1, Group A2, Group A3, and Group A4 were 27.1%, 37.3%, 22.2%, and 64.0%, respectively

**FIGURE 3** Survival curve of postoperative atrial fibrillation recurrence in Group B. Postoperative atrial fibrillation recurrence rates in Group B1, Group B2, Group B3, and Group B4 were 4.0%, 3.4%, 11.4%, and 43.5%, respectively



**TABLE 4** Subgroup analysis of recurrence of AF

Types of AF LAD (mm)	Paroxysmal		Persistent	
	<43.5	≥43.5	<43.5	≥43.5
Albumin (g/L)				
<42.2	4/101 (4.0%)	1/29 (3.4%)	13/48 (27.1%)	19/51 (37.3%)
≥42.2	9/79 (11.4%)	<b>10/23 (43.5%)</b>	10/45 (22.2%)	<b>32/50 (64.0%)</b>

Note: Italics indicate the reference group. Bold indicates the significant difference in AF recurrence compared with the reference group.

Abbreviation: AF, atrial fibrillation.

causal role of serum albumin in the etiology of AF (Liao et al., 2019). A recently published meta-analysis reported that a low serum albumin level is associated with an increased risk of AF, and they found that 10 g/L serum albumin decreased the risk of AF by 36% (Wang et al., 2021), which is different from our findings. In our study, we excluded patients with severe liver insufficiency and malnutrition that may lead to severe hypoproteinemia. The different criteria for the inclusion of patients may be an important reason for the different results of the study. As far as we are concerned, the main physiologic properties of serum albumin include colloid osmotic effects and anti-inflammatory and antioxidant activity (Wang et al., 2021). We propose that the anti-inflammatory and antioxidant abilities of patients with hypoalbuminemia are impaired, making AF prone to relapse. But the anti-inflammatory and antioxidant characteristics of patients with higher serum albumin concentrations may have reached a limit. We speculate that patients with higher serum albumin levels have increased effective circulating blood volume because of increased plasma colloid osmotic pressure, which may aggravate cardiac remodeling and make AF prone to recurrence. Furthermore, albumin supplements for patients with hypoalbuminemia might be a therapeutic target for reducing the risk of AF according to some other studies (Arques, 2018), but the role of albumin in the prevention of AF is uncertain, as well as the underlying mechanism. However, higher serum albumin levels may also make atrial fibrillation prone to

recurrence according to our study. Regardless, the measurement of serum albumin is simple, inexpensive, and widely available and would be of immense clinical benefit if serum albumin is shown to play a role in the prediction of AF. A larger multicenter trial should be performed to confirm our conclusion.

We found that taking 43.5 mm of LAD and 42.2 g/L of serum albumin concentration as the cutoff points, for both paroxysmal AF and persistent AF, the recurrence rate of postoperative AF was significantly higher in patients whose preoperative LAD and serum albumin concentrations were both greater than the respective cutoff points. The recurrence rate of AF was significantly different from that of the corresponding reference group. Patients with LAD ≥43.5 mm and serum albumin concentration ≥42.2 g/L had the highest postoperative recurrence rate, with an average recurrence rate of 64% during the follow-up period of 18.2 months. LAD and serum albumin levels are readily available clinical indicators. The preoperative application of LAD and serum albumin levels to assess the risk of postoperative recurrence of AF is clinically practical. For persistent AF patients with a higher LAD and higher serum albumin levels, the benefits of CA and the risk of postoperative AF recurrence should be evaluated comprehensively.

A study found that in AF patients with LVEF ≤35% who underwent CA, the success rate of the first operation was only 40% after 23 months of follow-up (Dagres et al., 2011). Patients whose LVEF

was less than 35% were not included in this study, but the LVEF in the recurrence group was still lower than that in the nonrecurrence group. Therefore, patients with AF should actively improve their cardiac function before undergoing CA.

A study found that among 531 AF patients complicated with hypertrophic cardiomyopathy who underwent CA, the success rates of an operation and multiple operations were only 32.9% and 50.4%, respectively (Zhao et al., 2016). A total of 9 patients were complicated with hypertrophic cardiomyopathy in this study, and 5 patients had AF recurrence despite the use of antiarrhythmic agents after surgery. The success rate was only 44.4%. For patients with AF complicated with hypertrophic cardiomyopathy, the risk of recurrence of AF should be monitored when undergoing CA.

The study has the following limitations. First, the determination of postoperative recurrence of AF was based on the results of 24-h Holter examination. However, this does not rule out the possibility that asymptomatic patients with recurrence of AF did not undergo 24-h Holter examination in time and were included in the nonrecurring group. Additionally, we only found that patients with higher preoperative serum albumin concentrations had a higher postoperative AF recurrence rate, but we did not detect the serum albumin level after surgery and did not elucidate the pathophysiological mechanism.

## 5 | CONCLUSION

The type of AF, LAD, and serum albumin concentration are risk factors for recurrence of AF after CA in patients with nonvalvular AF. Patients with persistent AF with LAD  $\geq 43.5$  mm and serum albumin concentration  $\geq 42.2$  g/L have a higher risk of late recurrence of AF after surgery.

### ACKNOWLEDGEMENT

The authors thank Qingdao University for the assistance with statistical analysis. Graphical abstract image was modified from Servier Medical Art (<http://smart.servier.com/>).

### CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

### AUTHOR CONTRIBUTIONS

Peng Zhang, Mao-Jing Wang: Conceptualization. Peng Zhang: Formal analysis, software, validation, and writing—original draft. Pin Sun, Qing Zhao: Data curation. Pin Sun, Qing Zhao, Shang-Lang Cai: Investigation. Pin Sun: Methodology. Wen-Heng Liu, Ya-Qi Pan: Writing—review & editing. Shang-Lang Cai: Supervision.

### ETHICAL APPROVAL

The research followed rules for the protection of human subjects. This study was approved by the Ethical Committee of The Affiliated Hospital of Qingdao University (No. QYFYWZLL 26465). Informed consent was obtained from the patients and their families.

### OPEN ACCESS

All data are provided in full in the results section of this paper.

### DATA AVAILABILITY STATEMENT

Data available on request from the authors.

### ORCID

Zhang Peng  <https://orcid.org/0000-0002-4682-4385>

### REFERENCES

- Anselmino, M., Matta, M., D'ascenzo, F., Pappone, C., Santinelli, V., Bunch, T. J., Neumann, T., Schilling, R. J., Hunter, R. J., Noelker, G., Fiala, M., Frontera, A., Thomas, G., Katritsis, D., Jais, P., Weerasooriya, R., Kalman, J. M., & Gaita, F. (2015). Catheter ablation of atrial fibrillation in patients with diabetes mellitus: A systematic review and meta-analysis. *Ep Europace*, 17(10), 1518–1525. <https://doi.org/10.1093/europace/euv214>
- Arques, S. (2018). Human serum albumin in cardiovascular diseases. *European Journal of Internal Medicine*, 52, 8–12. <https://doi.org/10.1016/j.ejim.2018.04.014>
- Cappato, R., Calkins, H., Chen, S. A., Davies, W., Lesaka, Y., Kalman, J., Kim, Y. H., Klein, G., Natale, A., Packer, D., & Skanes, A. (2010). Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circulation: Arrhythmia and Electrophysiology*, 3(1), 32–38.
- Dagres, N., Varounis, C., Gaspar, T., Piorkowski, C., Eitel, C., Iliodromitis, E. K., Lekakis, J. P., Flevari, P., Simeonidou, E., Rallidis, L. S., Tsougos, E., Hindricks, G., Sommer, P., & Anastasiou-Nana, M. (2011). Catheter ablation for atrial fibrillation in patients with left ventricular systolic dysfunction. A systematic review and meta-analysis. *Journal of Cardiac Failure*, 17(11), 964–970. <https://doi.org/10.1016/j.cardfail.2011.07.009>
- D'Ascenzo, F., Corleto, A., Biondi-Zoccai, G., Anselmino, M., Ferraris, F., di Biase, L., Natale, A., Hunter, R. J., Schilling, R. J., Miyazaki, S., Tada, H., Aonuma, K., Yenn-Jiang, L., Tao, H., Ma, C., Packer, D., Hammill, S., & Gaita, F. (2013). Which are the most reliable predictors of recurrence of atrial fibrillation after transcatheter ablation?: A meta-analysis. *International Journal of Cardiology*, 167(5), 1984–1989. <https://doi.org/10.1016/j.ijcard.2012.05.008>
- Hindricks, G., Sepehri Shamloo, A., Lenarczyk, R., Kalarus, Z., Arya, A., Kircher, S., Dharma, A., & Dagres, N. (2018). Catheter ablation of atrial fibrillation: Current status, techniques, outcomes and challenges. *Kardiologia Polska (Polish Heart Journal)*, 76(12), 1680–1686.
- Lee, H. L., Hwang, Y. T., Chang, P. C., Wen, M. S., & Chou, C. C. (2018). A three-year longitudinal study of the relation between left atrial diameter remodeling and atrial fibrillation ablation outcome. *Journal of Geriatric Cardiology: JGC*, 15(7), 486.
- Lee, K. J., Kim, B. J., Han, M. K., Kim, J. T., Choi, K. H., Shin, D. I., Yeo, M. J., Cha, J. K., Kim, D. H., Nah, H. W., Kim, D. E., Ryu, W. S., Park, J. M., Kang, K., Lee, S. J., Kim, J. G., Oh, M. S., Yu, K. H., Lee, B. C., ... & Bae, H. J. (2020). Effect of heart rate on stroke recurrence and mortality in acute ischemic stroke with atrial fibrillation. *Stroke*, 51(1), 162–169. <https://doi.org/10.1161/STROKEAHA.119.026847>
- Liao, L. Z., Zhang, S. Z., Li, W. D., Liu, Y., Li, J. P., Zhuang, X. D., & Liao, X. X. (2019). Serum albumin and atrial fibrillation: Insights from epidemiological and mendelian randomization studies. *European Journal of Epidemiology*, 35, 113–122.
- Packer, D. L., Mark, D. B., Robb, R. A., Monahan, K. H., Bahnson, T. D., Poole, J. E., Noseworthy, P. A., Rosenberg, Y. D., Jeffries, N., Mitchell, L. B., Flaker, G. C., Pokushalov, E., Romanov, A., Bunch, T. J., Noelker, G., Ardashev, A., Revishvili, A., Wilber, D. J., Cappato, R., ... & Lee, K. L. (2019). Effect of catheter ablation vs antiarrhythmic drug therapy on mortality, stroke, bleeding, and cardiac arrest

- among patients with atrial fibrillation: The CABANA randomized clinical trial. *JAMA*, 321(13), 1261–1274. <https://doi.org/10.1001/jama.2019.0693>
- Pluymaekers, N. A. H. A., Dudink, E. A. M. P., Luermans, J. G. L. M., Meeder, J. G., Lenderink, T., Widdershoven, J., Bucx, J. J. J., Rienstra, M., Kamp, O., Van Opstal, J. M., Alings, M., Oomen, A., Kirchhof, C. J., Van Dijk, V. F., Ramanna, H., Liem, A., Dekker, L. R., Essers, B. A. B., & Crijns, H. J. G. M. (2019). Early or delayed cardioversion in recent-onset atrial fibrillation. *New England Journal of Medicine*, 380(16), 1499–1508. <https://doi.org/10.1056/NEJMoa1900353>
- Poole, J. E., Bahnson, T. D., Monahan, K. H., Johnson, G., Rostami, H., Silverstein, A. P., Al-Khalidi, H. R., Rosenberg, Y., Mark, D. B., Lee, K. L., & Packer, D. L. (2020). Recurrence of atrial fibrillation after catheter ablation or antiarrhythmic drug therapy in the CABANA trial. *Journal of the American College of Cardiology*, 75(25), 3105–3118.
- Potpara, T., Dages, N., Arbelo, E., Bax, J. J., Blomström-Lundqvist, C., Boriani, G., Castella, M., Dan, G. A., Dilaveris, P. E., Fauchier, L., Filippatos, G., Kalman, J. M., La Meir, M., Lane, D. A., Lebeau, J. P., Lettino, M., Lip, G. Y. H., Pinto, F. J., & Zakirov, N. U. (2021). 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*, 42(5), 373–498. <https://doi.org/10.1093/eurheartj/ehaa612>
- Pranata, R., Chintya, V., Raharjo, S. B., Yamin, M., & Yuniadi, Y. (2020). Longer diagnosis-to-ablation time is associated with recurrence of atrial fibrillation after catheter ablation—Systematic review and meta-analysis. *Journal of Arrhythmia*, 36(2), 289–294. <https://doi.org/10.1002/joa3.12294>
- Rottner, L., Bellmann, B., Lin, T., Reissmann, B., Tönnis, T., Schleberger, R., Nies, M., Jungen, C., Dinshaw, L., Klatt, N., Dickow, J., Münkler, P., Meyer, C., Metzner, A., & Rillig, A. (2020). Catheter ablation of atrial fibrillation: State of the art and future perspectives. *Cardiology and Therapy*, 9(1), 45–58. <https://doi.org/10.1007/s40119-019-00158-2>
- Steinberg, J. S., Palekar, R., Sichrovsky, T. et al (2014). Very long-term outcome after initially successful catheter ablation of atrial fibrillation[J]. *Heart Rhythm: the Official Journal of the Heart Rhythm Society*, 11(5), 771–776. <https://doi.org/10.1016/j.hrthm.2014.02.003>
- Teh, A. W., Kistler, P. M., Lee, G., Medi, C., Heck, P. M., Spence, S. J., Sparks, P. B., Morton, J. B., & Kalman, J. M. (2012). Electroanatomic remodeling of the left atrium in paroxysmal and persistent atrial fibrillation patients without structural heart disease. *Journal of Cardiovascular Electrophysiology*, 23(3), 232–238. <https://doi.org/10.1111/j.1540-8167.2011.02178.x>
- Vinter, N., Huang, Q., Fenger-Grøn, M., Frost, L., Benjamin, E. J., & Trinquart, L. (2020). Trends in excess mortality associated with atrial fibrillation over 45 years (Framingham Heart Study): Community based cohort study. *BMJ*, 370, m2724. <https://doi.org/10.1136/bmj.m2724>
- Voskoboinik, A., Kalman, J. M., De Silva, A., Nicholls, T., Costello, B., Nanayakkara, S., Prabhu, S., Stub, D., Azzopardi, S., Vizi, D., Wong, G., Nalliah, C., Sugumar, H., Wong, M., Kotschet, E., Kaye, D., Taylor, A. J., & Kistler, P. M. (2020). Alcohol abstinence in drinkers with atrial fibrillation. *New England Journal of Medicine*, 382(1), 20–28. <https://doi.org/10.1056/NEJMoa1817591>
- Wang, T., Xia, Y. L., Zhang, S. L., Gao, L. J., Xie, Z. Z., Yang, Y. Z., & Zhao, J. (2014). The impact of hypertension on the electromechanical properties and outcome of catheter ablation in atrial fibrillation patients. *Journal of Thoracic Disease*, 6(7), 913.
- Wang, Y., Du, P., Xiao, Q., Li, J., Liu, X., Tan, J., & Zhang, X. (2021). Relationship between serum albumin and risk of atrial fibrillation: A dose-response meta-analysis. *Frontiers in Nutrition*, 8, 546. <https://doi.org/10.3389/fnut.2021.728353>
- Zhao, D. S., Shen, Y., Zhang, Q., Lin, G., Lu, Y. H., Chen, B. T., Shi, L. S., Huang, J. F., & Lu, H. H. (2016). Outcomes of catheter ablation of atrial fibrillation in patients with hypertrophic cardiomyopathy: A systematic review and meta-analysis. *Europace*, 18(4), 508–520. <https://doi.org/10.1093/europace/euv339>
- Zheng, J., Zu, D. L., Cheng, K. Y., Xia, Y. L., Dong, Y. X., & Gao, Z. Y. (2021). Decreased eGFR predicts long-term recurrence after catheter ablation of atrial fibrillation in mild to moderate renal insufficiency. *BMC Cardiovascular Disorders*, 21, 508.

**How to cite this article:** Peng, Z., Wen-Heng, L., Qing, Z., Pin, S., Shang-Lang, C., Mao-Jing, W., & Ya-Qi, P. (2022). Risk factors for late recurrence in patients with nonvalvular atrial fibrillation after radiofrequency catheter ablation. *Annals of Noninvasive Electrocardiology*, 27, e12924. <https://doi.org/10.1111/anec.12924>