

Predictors of Atrial Fibrillation Late Recurrence and Major Adverse Cardiovascular Events After Radiofrequency Catheter Ablation: A Clinical Nomogram Model

Yan-Xiang Zhou, Yu-Gang Hu, Sheng Cao, Jia-Rui Lei, Fen-Fen Xu, Tuan-Tuan Tan, Qing Zhou

Department of Ultrasonography, Renmin Hospital of Wuhan University, Wuhan, Hubei, People's Republic of China

Correspondence: Qing Zhou, Department of Ultrasonography, Renmin Hospital of Wuhan University, 238 Jiefang Road, Wuhan, Hubei, 430060, People's Republic of China, Tel + 86 027 88041911 x88037, Fax +86 027 88040334, Email qingzhou.wh.edu@hotmail.com

Purpose: This study sought to investigate the predictive factors for atrial fibrillation late recurrence (AFLR) and major adverse cardiovascular events (MACEs) in atrial fibrillation (AF) patients after radiofrequency catheter ablation (RFCA) and construct a nomogram prediction model for providing precious information of screening the high risk patients and giving appropriate preventive interventions.

Patients and Methods: A total of 128 patients with atrial fibrillation (AF) who underwent RFCA were enrolled. Univariate and multivariate Cox regression were used to screen the predictors of AFLR and MACEs (including rehospitalization due to AF recurrence, heart failure, myocardial infarction, coronary revascularization, stroke and all-cause mortality). The nomogram model was constructed to predict AFLR after RFCA. Risk stratification based on the nomogram further predicted AFLR and MACEs after RFCA. Subgroup analysis and survival analysis of high and low risk groups in individuals with AF after RFCA were performed.

Results: During median follow-up of 76.50 (5.75) months, 71 (55.47%) patients experienced AFLR, while 56 (43.75%) suffered from MACEs. Early recurrence, maximum left atrial volume index (LAVImax) and E/Vp were the independent risk factors for predicting AFLR after RFCA. And AFLR was the only independent predictor for MACEs. Accordingly, a nomogram prediction model based on early recurrence, LAVImax and E/Vp was constructed, the 1-year, 3-year and 5-year AUC of AFLR were 0.904, 0.826 and 0.793, respectively. Risk stratification based on the nomogram had high predictive value for AFLR and MACEs. The Kaplan–Meier survival curves showed great discrimination between the low and high risk groups in the probability of free from AFLR and MACEs.

Conclusion: The nomogram model based on early recurrence, LAVImax and E/Vp can be used to predict the AFLR and MACEs after RFCA accurately and individually, in order to provide scientific and effective patient management basis for AF patients after RFCA.

Keywords: atrial fibrillation, radiofrequency catheter ablation, late recurrence, major adverse cardiovascular events

Introduction

Atrial fibrillation (AF) is one of the most common clinical arrhythmias. With the gradual in-depth study of the electrophysiological mechanism of AF, radiofrequency catheter ablation (RFCA) has been widely used in clinical practice to restore sinus rhythm and improve life quality.^{1,2} Although the methodology, such as RFCA, cryoablation and laser balloon ablation, continues to improve and the success rate continues to increase, there is still a different proportion of recurrence.^{3–9} Previous clinical researches^{3–5,7,9} have shown that the recurrence of AF after single RFCA varied from 11% to 29% and 7% to 24% after repeated RFCA in paroxysmal AF during 5 years follow-up, while up to 70% in persistent AF. A total of 61.9% of patients were free of AF recurrence when redo cryoablation procedures were performed.⁶ Long-term freedom from AF was 78.8% for paroxysmal AF and 65.3% for persistent AF, performing laser balloon ablation only.⁸ AF recurrence is closely related to the patient's major adverse cardiovascular events (MACEs) such as re-hospitalization, heart failure, stroke and death.¹⁰ Thus, it is very significant to recognize valid indicators to

predict AF recurrence after RFCA, which will help to improve the successful rate of RFCA, guide clinical practice, even reduce MACEs.

At present, many factors relevant to AF recurrence have been studied, and the predictive value of these factors of various studies are often inconsistent.¹¹ Meanwhile, previous studies have focused on emphasizing the predictive value of a single indicator and came to a conclusion based on a short-term follow-up.^{12–14} There are few relevant researches focusing on the construction of the prediction model for AF late recurrence (AFLR) and MACEs after RFCA according to a long-term follow-up. In this study, we aimed to establish a personalized nomogram prediction model by screening risk factors of AFLR after RFCA and carry out risk stratification to predict AFLR and MACEs on the basis of a long-term follow-up, in order to scientifically and effectively manage the risk of AFLR and MACEs of AF patients after RFCA.

Materials and Methods

Study Population

The study was a retrospective observational cohort study. This study analyzed 150 patients with AF who underwent echocardiography before RFCA in the Department of Ultrasound Imaging at the Renmin Hospital of Wuhan University during August 2015 and November 2016. According to the 2024 expert consensus statement,² paroxysmal AF was defined as self-terminating AF within a 7-day period, persistent AF was defined as lasting longer than 7 days with termination typically requiring pharmacological or electrical cardioversion. Patients who had previous ablation treatment were excluded. Patients with left ventricular (LV) wall-motion abnormalities, valvular heart disease, congenital heart disease, cardiomyopathy, presence of LA thrombus were also excluded. All patients meeting eligibility requirements underwent assessment of demographics, AF characteristics, clinical comorbidities, medications after 3 months post RFCA, and echocardiographic parameters. Our study complies with the Declaration of Helsinki. Approval was obtained from the Ethics Committee of Renmin Hospital of Wuhan University (WDRY2022-K189). As this study is a retrospective study with extremely low research risks, the patients' informed consent was waived by Renmin Hospital of Wuhan University. During the process of using the data, we respect the privacy of patients and ensure the security of the data.

Echocardiography

Transthoracic echocardiography (TTE) was performed on the day before RFCA. An echocardiographic examination was carried out with the Aloka ProSound F75 ultrasound diagnostic system (Hitachi-Aloka Medical Co. Ltd., Tokyo, Japan) equipped with a 1–5 MHz probe. The left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), left atrial anterior-posterior dimension (LAD), and right atrial left-right dimension (RAD) were measured from the 2-dimensional echocardiogram. The left ventricular ejection fraction (LVEF) was calculated with biplane Simpson's method using 2-dimensional images. The minimum and maximum left atrial volume (LAVmax and LAVmin) and the maximum right atrial volume (RAV) were calculated with the biplane area-length method using 2-dimensional images. The electrocardiographic image before the start of the P wave was used to calculate the LA pre-systolic volume (LAVpreA). From these volumes, total, passive, and active emptying volumes and fractions were derived.¹⁵ The formulas for calculating the LA indices are as follows: expansion index (EI) = (LAVmax – LAVmin)/LAVmin, dilated emptying index (DEI) = (LAVmax – LAVmin)/LAVmax, active emptying percentage (AE) = (LAVmax – LAVpreA)/LAVmax, active emptying percentage index (AEI) = AE/body surface area (BSA), passive emptying percentage (PE) = (LAVpreA – LAVmin)/LAVpreA, passive emptying percentage index (PEI) = PE/BSA, LAVImax = LAVmax/BSA, LAVImin = LAVmin/BSA, LAVIpreA = LAVpreA/BSA. Simultaneous recordings of early transmitral flow peak velocity (E) and mitral annular peak velocity in early diastolic at the interventricular septal annulus (e') were performed using the dual Doppler mode. Simultaneous recordings of E/Vp were performed using the M/PW mode. Placed the M-mode cursor with the pulsed sample volume in the center of the mitral valve, avoiding the surrounding area and in the same direction as the flow stream. The pulse doppler sampling volume was placed at the tips of the mitral valve to obtain E velocity. The slope of the first aliasing velocity during early filling was measured as

Vp, extending 4 cm from the mitral valve into the left ventricle. Isovolumic relaxation time (IVRT) was measured from the end of aortic flow to the beginning of mitral flow. E deceleration time (EDT) was also measured.

Ablation Procedure

Double trans-septal punctures were performed after placing quadripolar, decapolar, and duo-decapolar catheters at the right ventricle, high right atrium, and coronary sinus, respectively. Three-dimensional mapping of the LA was performed with CARTO (Biosense Webster, Irvine, California) system. Wide antral pulmonary vein isolation was performed. In patients with paroxysmal AF, the endpoint of the procedure was the elimination of trigger focus. If nonpulmonary vein trigger was present, additional ablation was performed to eliminate the nonpulmonary vein trigger.^{16–18} Additional substrate modifications were also allowed if the operator determined that substrate modifications were more important than elimination of trigger points. Non-paroxysmal AF was induced by rapid atrial pacing after pulmonary vein isolation. If no sustained AF was induced (lasting more than 5 minutes), the procedure was terminated. If sustained AF was induced after pulmonary vein isolation, additional ablation, such as complex fractionated atrial electrograph-guided ablation, linear ablation, or low-pressure zone ablation, may be performed as appropriate. Computed tomography was performed to assess the anatomy of the pulmonary veins, and 3D reconstruction maps were created in conjunction with the CARTO systems.

Follow-Up

Postoperative regimens included oral anti-arrhythmic drugs and simultaneous anticoagulation therapy for three months. After RFCA, all patients were followed for 5 to 7 years for AF recurrence and major adverse cardiovascular events (MACEs) by periodic phone interviews, outpatient records and hospitalization records until July 2022. They were seen or telephoned within the first week and then at 3, 6, 12 months and every 6 months after 1 year, as well as at any time they complained of palpitations or other symptoms. At each examination, standard 12-lead electrocardiography or 24-hour Holter recording was performed based on the patient's symptoms, and whether there was any AF recurrence was inquired. Early and late recurrence was defined as an episode lasting more than 30s including AF, atrial flutter and atrial tachycardia after RFCA ≤ 90 days and >90 days after RFCA, respectively.² The primary study outcome was AFLR. The secondary study outcome was MACEs, which included rehospitalization due to AF recurrence, heart failure, myocardial infarction, coronary revascularization, stroke and all-cause mortality. The reasons for hospitalizations were evaluated by the cardiologist who blinded to outcomes.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (version 21.0, SPSS, Inc., Chicago, US) and R program (version 4.0.3). The Kolmogorov–Smirnov test was used to confirm the normal distribution of the data. Normally distributed continuous variables were expressed as the mean $\pm$ standard deviation and assessed by the independent-samples *t*-test. Skew-distributed continuous variables were reported as the median (interquartile range) and compared using a Mann–Whitney *U*-test. Categorical variables were presented as the frequency (percentage) and analyzed using a χ^2 test. Univariate and multivariate Cox regression models with the forward LR method were used to identify predictors of AFLR and MACEs, and to adjust for known confounders and for variables that were significant on the univariate model. Multivariable Cox regression analysis informed the construction of a nomogram. The discriminating ability of the nomogram was evaluated using calibration curves and decision curve analysis (DCA). The time-dependent receiver operator characteristic (ROC) curves were performed to further understand the prediction capabilities. Waterfall plots were performed to further show the risk stratification based on the nomogram. The forest plot and Kaplan–Meier survival curves were performed to reveal the results of subgroup analysis and survival analysis of high and low risk groups. All *P* values were two-sided, and *P*-values <0.05 were considered statistically significant.

Results

We excluded 6 AF patients because of a poor acoustic window in the echocardiogram, 8 AF patients who failed to undergo RFCA, and 8 AF patients who were lost to follow up. As a result, 128 AF patients (80 males, 48 females; aged

59.63 ± 9.90 years) were included in the final study, as shown in Table 1. The median follow-up time for all patients was 76.50 months, and the interquartile range was 5.75 months. During the follow-up, 71 (55.47%) patients experienced AFLR, and 57 (44.53%) maintained sinus rhythm. Seventy-two (56.25%) patients were free from MACEs, while 56

Table 1 Comparisons of Demographic, Clinical, and Echocardiographic Characteristics

Variable	AFLR		p	MACEs		p
	Yes (n=71)	No (n=57)		Yes (n=56)	No (n=72)	
Demographics						
Age (y)	61.51±8.39	57.28±11.14	0.016	61.89±8.38	57.86±10.66	0.022
Gender, female (n,%)	24 (33.8%)	24 (42.1%)	0.335	20 (35.7%)	28 (38.9%)	0.713
Body mass index (kg/m ²)	25.40±2.99	24.12±2.67	0.013	25.52±3.12	24.29±2.64	0.018
AF characteristics						
Persistent (n, %)	30 (42.3%)	10 (17.5%)	0.003	23 (41.1%)	17 (23.6%)	0.034
AF Duration (months)	24 (100.5)	36 (43)	0.328	24 (45)	24 (52.75)	0.214
CHA2DS2-VASc score	1.62±1.17	1.39±1.31	0.134	1.75±1.22	1.33±1.23	0.007
Early recurrence	27 (37.5%)	5 (8.8%)	0.000	17 (30.4%)	15 (20.8%)	0.217
Comorbidities (n, %)						
Hypertension	44 (62.0%)	28 (49.1%)	0.145	40 (71.4%)	32 (44.4%)	0.002
Diabetes	7 (9.9%)	6 (10.2%)	0.901	3 (5.4%)	10 (13.9%)	0.113
Coronary artery disease	11 (15.5%)	7 (12.3%)	0.603	10 (17.9%)	8 (11.1%)	0.276
Heart failure	1 (1.4%)	1 (1.8%)	1.000	2 (3.6%)	0 (0.0%)	0.369
Hyperlipemia	11 (15.5%)	9 (15.8%)	0.462	8 (14.3%)	12 (16.7%)	0.713
Smoke	15 (21.1%)	12 (21.1%)	0.992	12 (21.4%)	15 (20.8%)	0.935
Drink	12 (16.9%)	10 (17.5%)	0.924	6 (10.7%)	16 (22.2%)	0.087
Medications (n, %)						
Amiodarone	3 (4.2%)	4 (7.0%)	0.765	1 (1.8%)	6 (8.3%)	0.221
β-blockers	19 (26.8%)	14 (24.6%)	0.777	13 (23.2%)	20 (27.8%)	0.558
ACEI or ARBs	6 (8.5%)	7 (12.3%)	0.476	5 (8.9%)	8 (11.1%)	0.685
Anticoagulants	12 (16.9%)	1 (1.8%)	0.005	9 (16.1%)	4 (5.6%)	0.051
Antiplatelet	10 (14.1%)	10 (17.5%)	0.592	7 (12.5%)	13 (18.1%)	0.390
Antihyperlipidemic	11 (15.5%)	4 (7.0%)	0.138	9 (16.1%)	6 (8.3%)	0.177
Echocardiographic						
LVEDD (mm)	46.56±3.26	45.79±3.24	0.183	46.27±3.18	46.18±3.35	0.881
LVESD (mm)	33.42±4.61	32.21±4.55	0.140	33.02±4.46	32.77±4.74	0.771
LVEF (%)	60.07±6.13	60.00±6.91	0.951	59.16±6.15	60.76±6.68	0.169
LAD (mm)	42.30±5.58	37.63±5.60	0.000	42.73±5.67	38.26±5.60	0.000
LAVImax (mL/m ²)	34.73±12.05	26.82±9.68	0.000	35.18±12.83	28.11±9.75	0.001
LAVIpreA (mL/m ²)	24.10±11.27	18.13±8.25	0.001	24.24±12.16	19.27±8.32	0.010
LAVImin (mL/m ²)	18.43±10.44	12.63±6.78	0.000	18.39±11.15	13.87±7.31	0.010
DEI	0.49±0.16	0.54±0.13	0.039	0.50±0.17	0.52±0.14	0.521
AEI	0.18±0.08	0.19±0.08	0.409	0.19±0.09	0.18±0.08	0.760
PEI	0.14±0.09	0.19±0.08	0.004	0.15±0.09	0.17±0.08	0.168
RAD (mm)	38.65±4.52	36.35±4.41	0.005	38.37±4.45	37.04±4.65	0.104
RAV (mL)	49.35±14.99	40.71±15.16	0.002	48.38±15.55	43.26±15.40	0.066
E/e'	10.55±2.92	9.43±2.82	0.030	10.65±2.92	9.58±2.85	0.038
IVRT (ms)	57.86±20.08	60.56±14.16	0.398	58.89±22.98	59.16±12.17	0.938
EDT (ms)	137.54±28.70	144.06±34.69	0.251	140.66±30.59	140.16±32.41	0.929
E/Vp	1.62±0.69	1.29±0.42	0.003	1.52±0.49	1.44±0.70	0.474

Abbreviations: AF, atrial fibrillation; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; LVEF, left ventricular ejection fraction; LAD, left atrial anterior-posterior dimension; LAVImax, maximum LA volume index; LAVIpreA, pre-systolic LA volume index; LAVImin, minimum LA volume index; DEI, dilated emptying index; AEI, active emptying percentage index; PEI, passive emptying percentage index; RAD, right atrial left-right dimension; RAV, right atrial volume; E, blood flow velocity of mitral valve at early diastolic; e', velocity of the initial wave of the septal mitral annulus; IVRT, isovolumic relaxation time; EDT, E deceleration time.

(43.75%) patients experienced MACEs: 26 patients were rehospitalized due to AF recurrence, 10 patients had heart failure, 11 patients had stroke, 6 patients experienced coronary revascularization and 3 patients died.

Comparisons Between Patients with and Without AFLR and MACEs

The baseline demographic, clinical, and echocardiographic characteristics overall and between patients who experienced AFLR and those who did not are summarized in [Table 1](#). Patients who experienced AFLR were more likely to have AF early recurrence and persistent AF ($P < 0.01$), higher age and BMI ($P < 0.01$), and greater use of anticoagulants ($P < 0.01$). Of interest, there were no differences in gender, AF duration, CHA2DS2-VASc scores and comorbidities such as hypertension, diabetes mellitus, hyperlipemia ($P > 0.05$ for all). With respect to echocardiographic variables, patients who experienced AFLR had larger LAD, LAVImax, LAVIpreA, LAImmin, RAD, RAV ($P < 0.01$ for all) and lower DEI ($P < 0.05$), PEI ($P < 0.01$). Patients who experienced AFLR had greater E/e' ($P < 0.05$) and E/Vp ($P < 0.01$) compared with those who did not ($P < 0.05$ for both). Parameters of LV dimensions, LVEF, AEI, IVRT and EDT did not show a significant association with the primary outcome ($P > 0.05$ for all).

Differences between patients who did and did not experience the secondary outcome are presented in [Table 1](#). Patients who suffered MACEs were older ($P < 0.05$) with higher BMI ($P < 0.05$), higher CHA2DS2-VASc score ($P < 0.01$), and higher rates of persistent AF ($P < 0.05$) and hypertension ($P < 0.01$). Although the use of anticoagulants was slightly higher in the patients with MACEs, the difference was not statistically significant ($P = 0.051$). And there were no differences in residual clinical characteristics between patients who experienced MACEs and those who did not ($P > 0.05$ for all). With respect to echocardiographic variables, patients with MACEs had greater LAD, LAVImax, LAVIpreA, LAVImin ($P \leq 0.01$ for all), and higher E/e' ratio ($P < 0.05$). No differences in LA function parameters were noted between patients with and without MACEs. Other parameters such as LV dimensions, LVEF, RAD, RAV, IVRT, EDT and E/Vp also did not achieve statistical significance between the two groups ($P > 0.05$ for all).

Univariate and Multivariate Cox Regression Analysis of AFLR and MACEs

As shown in [Table 2](#), early recurrence, LAVImax and E/Vp were the independent risk factors for AFLR after RFCA. The hazard ratio (HR) and 95% confidence interval (CI) of early recurrence were 5.951 and (4.025, 8.800). While 1.032 and (1.020, 1.045) were of LAVImax, 1.691 and (1.208, 2.170) were of E/Vp. With regard to MACEs after RFCA, AFLR was the only independent risk factor (HR 5.944, 95 CI: 2.906–12.157), presented in [Table 3](#).

Table 2 Univariate and Multivariate Cox Regression Modeling for Predicting AFLR

	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age	1.030 (1.012–1.049)	0.001	–	–
Body mass index	1.101 (1.040–1.165)	0.001	–	–
AF duration	1.002 (1.000–1.005)	0.051	–	–
CHA2DS2-VASc	1.102 (0.968–1.254)	0.151	–	–
Persistent AF	2.012 (1.439–2.813)	0.000	–	–
Early recurrence	4.984 (3.500–7.096)	0.000	5.951 (4.025–8.800)	0.000
LAVImax	1.028 (1.017–1.039)	0.000	1.032 (1.020–1.045)	0.000
LAVIpreA	1.027 (1.014–1.040)	0.000	–	–
LAVImin	1.034 (1.019–1.048)	0.000	–	–
DEI	0.246 (0.080–0.758)	0.015	–	–
PEI	0.017 (0.002–0.132)	0.000	–	–
RAV	1.021 (1.012–1.031)	0.000	–	–
E/e	1.070 (1.016–1.128)	0.010	–	–
E/Vp	1.797 (1.426–2.265)	0.000	1.619 (1.208–2.170)	0.001

Abbreviation: AFLR, atrial fibrillation late recurrence.

Table 3 Univariate and Multivariate Cox Regression Modeling for Predicting MACEs

	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age	1.035 (1.005–1.066)	0.022	–	–
Body mass index	1.116 (1.020–1.222)	0.017	–	–
AF duration	0.998 (0.994–1.003)	0.432	Not selected	–
CHA2DS2-VASc	1.241 (1.014–1.519)	0.036	–	–
Persistent AF	1.708 (1.002–2.910)	0.049	–	–
Early recurrence	1.754 (0.991–3.103)	0.054	–	–
LAVImax	1.029 (1.011–1.047)	0.002	–	–
LAVIpreA	1.026 (1.011–1.042)	0.017	–	–
LAVImin	1.031 (1.006–1.056)	0.014	–	–
PEI	0.126 (0.005–3.133)	0.207	Not selected	–
RAV	1.015 (0.999–1.031)	0.072	–	–
E/e	1.078 (0.990–1.172)	0.014	–	–
AFLR	5.944 (2.906–12.157)	0.000	5.944 (2.906–12.157)	0.000

Abbreviation: MACEs, major adverse cardiovascular events.

Construction and Verification of a Nomogram Model for Predicting AFLR After RFCA

Accordingly, a nomogram model based on early recurrence, LAVImax and E/Vp was constructed to predict the AFLR risk after RFCA. As shown in the nomogram model (Figure 1A), with the extension of early recurrence, LAVImax and E/Vp, the nomogram score gradually increased and the risk degree increased accordingly, which indicated that the probability of free from AF gradually decreased. The total score obtained by calculating all risk factors could be used to estimate the risk of 1-year, 3-year and 5-year AFLR after RFCA.

The calibration curves of the nomogram showed high consistencies between the predicted and observed survival probability (Figure 1B). The decision curve analysis (DCA) showed that the nomogram could better predict the 1-year, 3-year and 5-year AFLR after RFCA (Figure 1C). The time-dependent ROC showed the AUCs for predicting 1-year, 3-year and 5-year AFLR after RFCA were 0.904, 0.826 and 0.793, which indicated that the model had good accuracy and differentiation (Figure 1D).

Risk Stratification, Subgroup Analysis and Survival Analysis Predicting AFLR and MACEs

We finally made a risk stratification based on total points calculated using the nomogram. Patients with AF were divided into two risk groups: low risk (total points < 4.45) and high risk (total points ≥ 4.45). As shown in Figures 2 and 3, risk stratification based on the nomogram and subgroup analysis had high predictive value for AFLR and MACEs. The Kaplan–Meier survival curves showed great discrimination among the two groups in the probability of free from AFLR and MACEs (all Log Rank P<0.01).

Discussion

Nowadays, RFCA is the most effective treatment method for AF. AF recurrence is heterogeneous, with some people having a relapse early, while others can be cured from AF for years. In this study, we found that the recurrence rate of AF patients after RFCA was not optimistic. During the mean follow-up of 76.50 (5.75) months, the overall late recurrence rate of AF was about 55.47%, including 75% in 40 persistent AF patients while 46.59% in 88 paroxysmal AF patients. The relatively high recurrence rate after RFCA has affected the clinical prognosis of patients. We found 43.75% of the AF patients after RFCA experienced MACEs. And AFLR was an independent risk factor for MACEs. Therefore, we may effectively identify the risk factors of AFLR after RFCA and conduct risk stratification predicting MACEs, so as to intervene in time to ensure the therapeutic effect of surgery and improve prognosis of patients. Our study revealed that

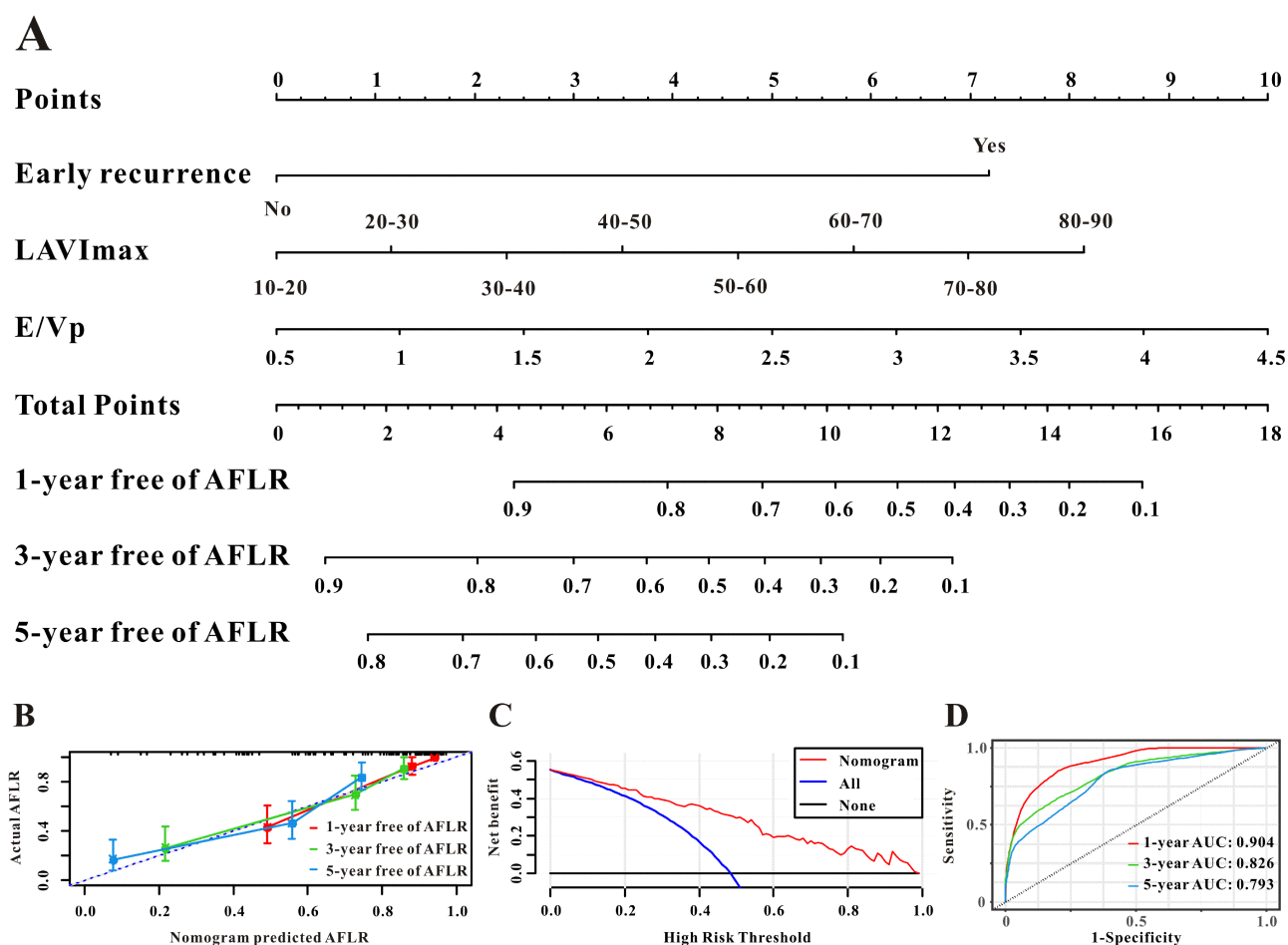


Figure 1 Construction and verification of a nomogram model for predicting the risk of AFLR after RFCA. **(A)** Nomogram model of late recurrence risk after RFCA for AF patients. **(B)** The calibration curve of nomogram model for 1-year, 3-year, and 5-year free of AFLR. **(C)** Decision curve analysis (DCA) of nomogram using training set. **(D)** Time-dependent ROC curves of nomogram model predicting 1-year, 3-year and 5-year AFLR after RFCA.

Abbreviations: AFLR, atrial fibrillation late recurrence; RFCA, radiofrequency catheter ablation; AF, atrial fibrillation; ROC, receiver operating characteristic.

early recurrence, LAVImax and E/Vp were independent predictors for AFLR. Early recurrence is generally not considered to be actual clinical recurrence, and up to 90 days after RFCA is known as the blanking period. The reason is that AF or AT recurrences immediately after RFCA are due to transient inflammation related to ablation, and most early recurrences will fade away as time goes on.¹⁹ However, there are reports suggesting that early recurrence should not be considered insignificant.^{20,21} Recent studies^{22–24} reported that patients who experienced early recurrence presented a significantly increased risk of late recurrence. A study reported by Mujovic et al²⁵ showed that a significantly higher incidence of pulmonary vein reconnection at 3-months after the initial RFCA in patients with early recurrence as compared to those without early recurrence (88.2% vs 41.7%). The study suggested that early recurrence should not be considered as a transient phenomenon but the result of pulmonary vein reconnection. Kim et al²³ revealed that patients with early recurrence experienced a 4.3- and 3.6-fold increased risk of late recurrence after single and multiple procedures, respectively. So, early recurrence may be a form of late recurrence occurring earlier.

Enlargement of the LA is a common finding in patients with AF with an impact on the success of their rhythm control therapy. Enlargement of the LA can affect left atrial bipolar voltage and cause myocardial interstitial fibrosis, endocardium remodeling, and hypertrophy of myocardial cells, leading to electrophysiological changes of ion channels, with subsequent improvement in the myocardial excitability and self-discipline, inducing AF.^{26,27} LAVI predicted AF recurrence much more accurately compared to the LA diameter, indicating that LAVI is a more accurate approach for determining the LA size and predicting AF recurrences, as previously described.²⁸ Numerous studies have shown that

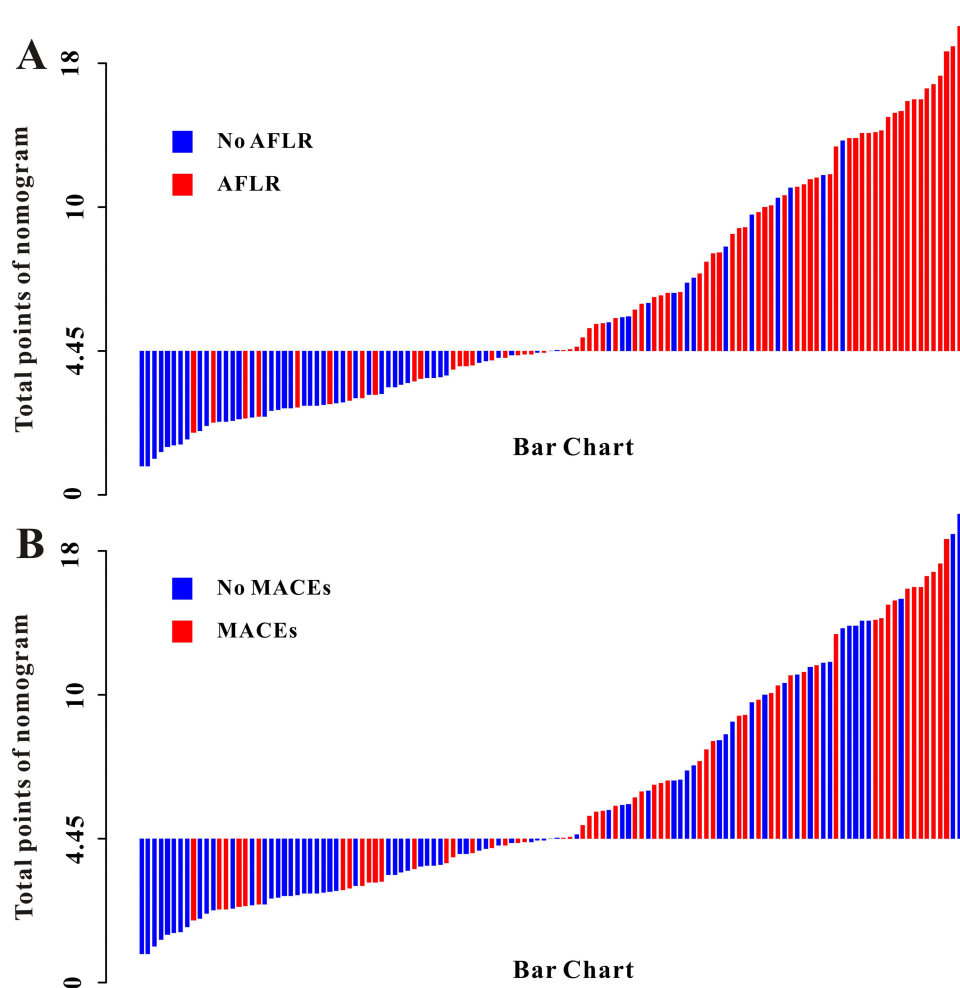


Figure 2 Waterfall plots showed risk stratification based on the nomogram model predicting AFLR (A) and MACEs (B) in patients with AF after RFCA. **Abbreviation:** MACEs, major adverse cardiovascular events.

$\text{LAVI} \geq 34 \text{ mL/m}^2$ is an independent risk factor for AF recurrence. At the same time, compared to patients without AF recurrence, patients with AF recurrence after RFCA have a higher average LAVI, and LAVI measurements have an independent positive correlation with the AF recurrence rate.^{12–14,23,29,30} And AF patients with $\text{LAVI} \geq 34 \text{ mL/m}^2$ had a higher probability to experience MACEs than those with $\text{LAVI} < 34 \text{ mL/m}^2$.³¹ In our study, patients with AFLR or MACEs had larger LAD and LAVI, but LAVI had higher predictive value. Although atrial systolic function parameters reduced in patients with recurrent AF, they did not provide better prognostic value compared with LAVImax.

Studies^{14,32,33} have shown that left ventricular diastolic dysfunction (LVDD) can increase the risk of AF recurrence after RFCA. LVDD leads to the increase of left ventricular filling pressure, with subsequent damage to the left atrial (LA) substrate and myocardial fibrosis during the long term which accounts for the structural basis for the AF recurrence. Ejima et al³⁴ confirmed by univariate analysis that patients with persistent AF and diastolic dysfunction were more likely to have AF recurrence after radiofrequency ablation. Multivariate analysis confirmed that preoperative diastolic dysfunction was an independent risk factor for AF recurrence. E/e' , IVRT, EDT, E/V_p can reflect left ventricular diastolic dysfunction in patients with AF. In this study, only E/e' and E/V_p were statistically different between recurrent and non-recurrent AF. And in this study, E/e and E/V_p were obtained through the dual Doppler mode. Dual Doppler echocardiography, which enables simultaneous recording of 2 pulsed Doppler waveforms of flow-flow, flow-tissue, and tissue-tissue velocities, has advantages of more timesaving and reliable data for the determination of single-beat E/e' and E/V_p .³⁵ Okamatsu et al³⁶ who examined 24 patients with hypertrophic cardiomyopathy demonstrated that E/e' ratio was the only predictor of AF recurrence following pulmonary veins isolation (PVI). Patients with $E/e' \geq 15$ had a significantly higher

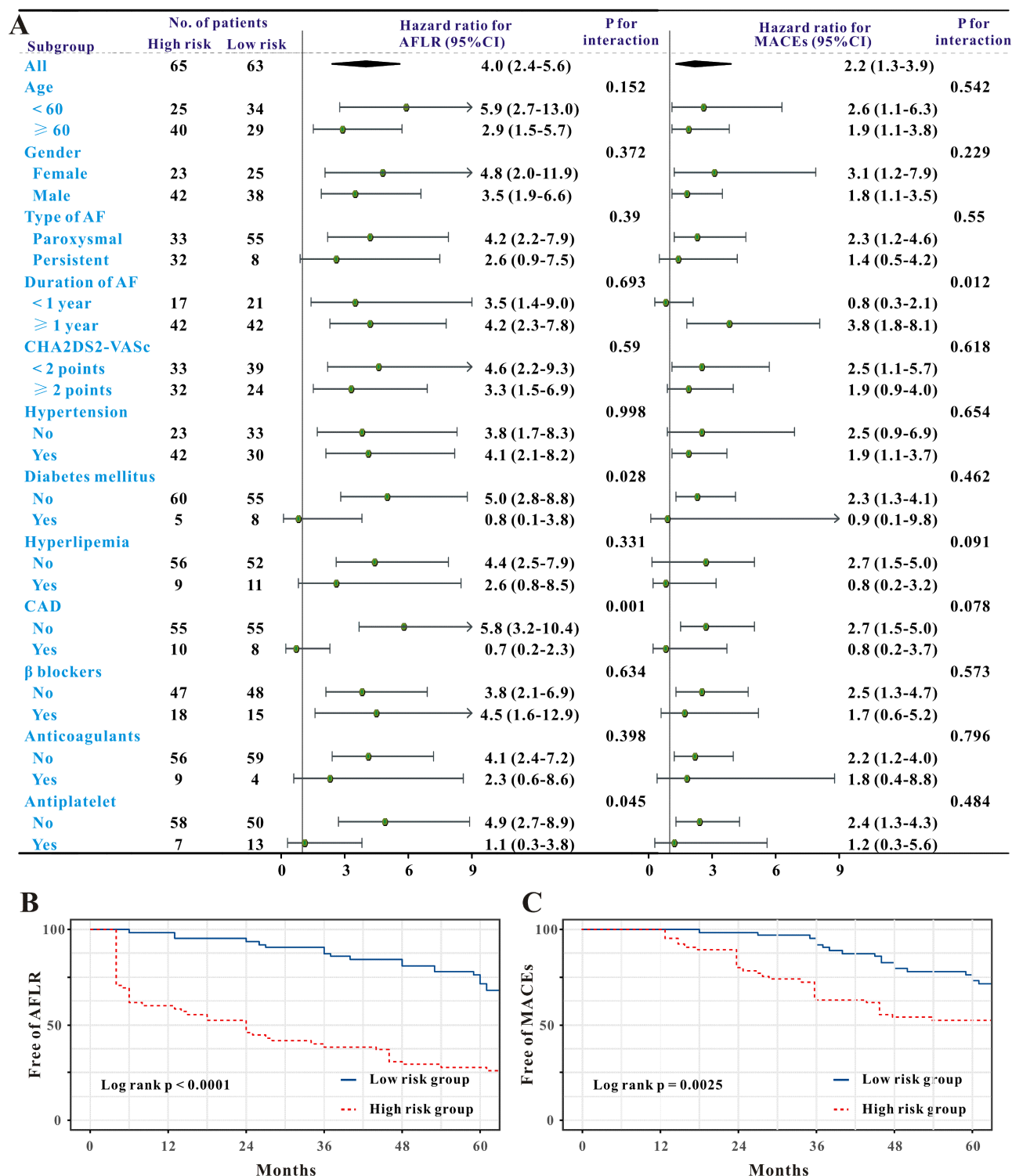


Figure 3 Subgroup analysis and survival analysis of high and low risk groups in individuals with AF after RFCA. The forest plot revealed the results of subgroup analysis for AFLR and MACEs-free survival (**A**). Kaplan-Meier survival curves of AFLR (**B**) and MACEs (**C**) based on low and high risk groups in patients with AF after RFCA.

Abbreviation: CAD, coronary artery disease.

risk of AF recurrence than those with $E/e' < 15$. Hirai et al³⁷ found that the recurrence rate of AF in patients with $E/e' > 13$ increased 12 months after RFCA, which confirmed that E/e' was an effective predictor of AF recurrence. This study found that E/Vp , rather than E/e' , was an independent predictor of AF recurrence, which may be associated with a lower proportion of patients with $E/e' > 13$. Garcia et al³⁸ revealed that E/Vp was the best indicator to estimate pulmonary capillary wedge pressure compared with E , E/A and Vp . Alejandro A Diaz³⁹ showed that stable congestive heart failure and AF patients with $E/Vp \geq 1.5$ experienced much more clinical events. E/Vp index was the only significant predictor of clinical outcome.

The nomogram is a kind of graphical model for estimating specific outcomes or survival in association with certain risk factors. Although RFCA for AF has achieved a certain success rate, postoperative recurrence is still inevitable. The recurrence is closely associated with poor prognosis. Meanwhile, it is difficult to evaluate the risk factors for AFLR and predict MACEs in each AF patient after RFCA. It is also very difficult to identify those patients who are prone to AFLR and experience MACEs in the absence of a prediction model. In this study, a nomogram model of AF recurrence risk was constructed based on the three independent risk factors including early recurrence, LAVImax and E/Vp . The calibration curves of the nomogram showed high consistencies. The verification of the nomogram model of AF recurrence risk showed that the 1-year, 3-year and 5-year AUC were 0.904, 0.826 and 0.793, respectively, which suggested that the nomogram model of AF recurrence had good accuracy and differentiation for screening the recurrence risk in AF patients after RFCA. Meanwhile, our data suggested that patients with early recurrence, larger LAVImax and higher E/Vp had a higher risk of AFLR and MACEs. We can perform a personalized risk assessment, guide the optimal treatment and prevent MACEs for patients with high risk according to the nomogram model.

Limitations of the Study

The present study was a single-center study, and the sample size was small. A multicenter study with larger samples should be conducted to further enhance the results. In addition, results of laboratory tests were lacking in the study's data. Another limitation of our study is the dependence on periodic ECG and 24-hour Holter monitoring rather than continuous long-term monitoring, which may have resulted in underdetection of asymptomatic AF episodes and precluded assessment of AF burden. Furthermore, this nomogram model needs further external validation.

Conclusion

Patients with AF have a high rate of recurrence after RFCA. The nomogram models constructed by early recurrence, LAVImax and E/Vp have good prediction ability for AFLR and MACEs after RFCA, and can provide reference for screening the high risk patients and giving appropriate preventive intervention. As a preliminary retrospective single-center study, these findings require validation through larger multicenter prospective investigations.

Funding

This research was supported by Natural Science Foundation of Hubei Province (Grant No. 2023AFB172), the National Natural Science Foundation of China (Grant No. 82402271), the Natural Science Foundation of Hubei Province (No. 2024AFB883), and the Health and Science Technology Project of Hubei Province (No. WJ2025M122).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Deshpande R, AlKhadra Y, Singanallur P, et al. Outcomes of catheter ablation versus antiarrhythmic therapy in patients with atrial fibrillation: a systematic review and meta-analysis. *J Interv Card Electrophysiol.* 2022;65:773–802. doi:10.1007/s10840-022-01365-z
2. Tzeis S, Gerstenfeld EP, Kalman J, et al. European Heart Rhythm Association/Heart Rhythm Society/Asia Pacific Heart Rhythm Society/Latin American Heart Rhythm Society expert consensus statement on catheter and surgical ablation of atrial fibrillation. *J Interv Card Electrophysiol.* 2024;67(5):921–1072. doi:10.1007/s10840-024-01771-5

3. Di Biase L, Santangeli P, Burkhardt DJ, et al. Endo-epicardial homogenization of the scar versus limited substrate ablation for the treatment of electrical storms in patients with ischemic cardiomyopathy. *J Am Coll Cardiol*. 2012;60:132–141. doi:10.1016/j.jacc.2012.03.044
4. Cappato R, Calkins H, Chen SA, et al. Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circ Arrhythm Electrophysiol*. 2010;3:32–38. doi:10.1161/CIRCEP.109.859116
5. Luik A, Kunzmann K, Hörmann P, et al. Cryoballoon vs. open irrigated radiofrequency ablation for paroxysmal atrial fibrillation: long-term Freeze AF outcomes. *BMC Cardiovasc Disord*. 2017;17:135. doi:10.1186/s12872-017-0566-6
6. Nekić A, Prepolec I, Pašara V, et al. Treatment of atrial fibrillation with second-generation cryoballoon followed by contact-sensing radiofrequency catheter ablation for arrhythmia recurrences-results of a 5-year follow-up. *J Interv Card Electrophysiol*. 2024;67(6):1407–1417. doi:10.1007/s10840-024-01752-8
7. Choi SH, Yu HT, Kim D, et al. Late recurrence of atrial fibrillation 5 years after catheter ablation: predictors and outcome. *Europace*. 2023;25(5):113. doi:10.1093/europace/euad113
8. Koopman P, Bekelaar T, Schurmans J, et al. Pulmonary vein isolation by visually guided laser balloon ablation: single-center 5-year follow-up results. *J Interv Card Electrophysiol*. 2023;66(9):2081–2089. doi:10.1007/s10840-023-01544-6
9. Ngo L, Lee XW, Elwashahy M, et al. Freedom from atrial arrhythmia and other clinical outcomes at 5 years and beyond after catheter ablation of atrial fibrillation: a systematic review and meta-analysis. *Eur Heart J Qual Care Clin Outcomes*. 2023;9(5):447–458. doi:10.1093/ehjqcco/qcad037
10. Kany S, Kuck KH, Brachmann J, et al. Outcomes in patients experiencing complications associated with atrial fibrillation ablation: data from the german ablation registry. *Int J Cardiol*. 2022;363:64–70. doi:10.1016/j.ijcard.2022.06.019
11. D'Ascenzo F, Corleto A, Biondi-Zoccai G, et al. Which are the most reliable predictors of recurrence of atrial fibrillation after transcatheter ablation?: a meta-analysis. *Int J Cardiol*. 2013;167:1984–1989. doi:10.1016/j.ijcard.2012.05.008
12. Guo F, Li C, Yang L, et al. Impact of left atrial geometric remodeling on late atrial fibrillation recurrence after catheter ablation. *J Cardiovasc Med*. 2021;22:909–916. doi:10.2459/JCM.0000000000001255
13. Kranert M, Shchetynska-Marinova T, Liebe V, et al. Recurrence of atrial fibrillation in dependence of left atrial volume index. *Vivo*. 2020;34(2):889–896. doi:10.21873/invivo.11854
14. Onishi N, Kaitani K, Amano M, et al. Relationship between left ventricular diastolic dysfunction and very late recurrences after multiple procedures for atrial fibrillation ablation. *Heart Vessels*. 2018;33:41–48. doi:10.1007/s00380-017-1027-y
15. Miao Y, Xu M, Zhang C, et al. An echocardiographic model for predicting the recurrence of paroxysmal atrial fibrillation after circumferential pulmonary vein ablation. *Clin Cardiol*. 2021;44:1506–1515. doi:10.1002/clc.23712
16. Della Rocca DG, Di Biase L, Mohanty S, et al. Targeting non-pulmonary vein triggers in persistent atrial fibrillation: results from a prospective, multicentre, observational registry. *Europace*. 2021;23(12):1939–1949. doi:10.1093/europace/euab161
17. Yagishita A, Sakama S, Iimura K, et al. Clinical relevance of left atrial structural remodeling and non-pulmonary vein foci in atrial fibrillation. *J Interv Card Electrophysiol*. 2025;68(5):977–983. doi:10.1007/s10840-024-01931-7
18. Oza SR, Hincapie D, Gupta M, et al. Isoproterenol for unmasking dormant conduction and non-pulmonary vein triggers during atrial fibrillation ablation: prospective multicenter study. *J Cardiovasc Electrophysiol*. 2025;36(9):2304–2317. doi:10.1111/jce.70007
19. Onishi N, Kaitani K, Nakagawa Y, et al. The association between late-phase early recurrence within the blanking period after atrial fibrillation catheter ablation and long-term recurrence: insights from a large-scale multicenter study. *Int J Cardiol*. 2021;341:39–45. doi:10.1016/j.ijcard.2021.07.053
20. Hodges G, Bang CN, Torp-Pedersen C, et al. Significance of early recurrence of atrial fibrillation after catheter ablation: a nationwide Danish cohort study. *J Interv Card Electrophysiol*. 2021;60:271–278. doi:10.1007/s10840-020-00741-x
21. Li Z, Wang S, Hidru TH, et al. Long atrial fibrillation duration and early recurrence are reliable predictors of late recurrence after radiofrequency catheter ablation. *Front Cardiovasc Med*. 2022;9:864417. doi:10.3389/fcvm.2022.864417
22. Vaishnav AS, Levine E, Coleman KM, et al. Early recurrence of atrial fibrillation after pulmonary vein isolation: a comparative analysis between cryogenic and contact force radiofrequency ablation. *J Interv Card Electrophysiol*. 2020;57:67–75. doi:10.1007/s10840-019-00639-3
23. Kim YG, Boo KY, Choi JI, et al. Early recurrence is reliable predictor of late recurrence after radiofrequency catheter ablation of atrial fibrillation. *JACC Clin Electrophysiol*. 2021;7:343–351. doi:10.1016/j.jacep.2020.09.029
24. Park CS, Kim H, Lee SR, et al. Prognostic implication of early recurrence after cryoballoon ablation in patients with atrial fibrillation. *J Interv Card Electrophysiol*. 2024;67(2):285–292. doi:10.1007/s10840-023-01555-3
25. Mujovic N, Marinkovic M, Markovic N, et al. The relationship of early recurrence of atrial fibrillation and the 3-month integrity of the ablation lesion set. *Sci Rep*. 2018;8(1):9875. doi:10.1038/s41598-018-28072-y
26. Nattel S, Harada M. Atrial remodeling and atrial fibrillation: recent advances and translational perspectives. *J Am Coll Cardiol*. 2014;63(22):2335–2345. doi:10.1016/j.jacc.2014.02.555
27. Li DL, Hajjar AHE, Ayoub T, et al. Left atrial volume affects the correlation of voltage map with magnetic resonance imaging. *J Interv Card Electrophysiol*. 2024;67(2):263–271. doi:10.1007/s10840-023-01522-y
28. Marchese P, Malavasi V, Rossi L, et al. Indexed left atrial volume is superior to left atrial diameter in predicting nonvalvular atrial fibrillation recurrence after successful cardioversion: a prospective study. *Echocardiography*. 2012;29(3):276–284. doi:10.1111/j.1540-8175.2011.01580.x
29. Marchandise S, Garnir Q, Scavée C, et al. Prediction of left atrial fibrosis and success of catheter ablation by speckle tracking echocardiography in patients imaged in persistent atrial fibrillation. *Front Cardiovasc Med*. 2022;9:856796. doi:10.3389/fcvm.2022.856796
30. Njoku A, Kannabhiran M, Arora R, et al. Left atrial volume predicts atrial fibrillation recurrence after radiofrequency ablation: a meta-analysis. *Europace*. 2018;20(1):33–42. doi:10.1093/europace/eux013
31. Bhat A, Gan GCH, Chen HHL, et al. Association of left atrial metrics with atrial fibrillation rehospitalization and adverse cardiovascular outcomes in patients with nonvalvular atrial fibrillation following index hospitalization. *J Am Soc Echocardiogr*. 2021;34(10):1046–1055.e3. doi:10.1016/j.echo.2021.06.015
32. Chung H, Lee BK, Min PK, et al. Left ventricular filling pressure as assessed by the e/e' ratio is a determinant of atrial fibrillation recurrence after cardioversion. *Yonsei Med J*. 2016;57(1):64–71. doi:10.3349/ymj.2016.57.1.64
33. Evranos B, Kocuyigit D, Gurses KM, et al. Increased left atrial pressure predicts recurrence following successful cryoablation for atrial fibrillation with second-generation cryoballoon. *J Interv Card Electrophysiol*. 2016;46(2):145–151. doi:10.1007/s10840-016-0107-8

34. Ejima K, Shoda M, Arai K, et al. Impact of diastolic dysfunction on the outcome of catheter ablation in patients with atrial fibrillation. *Int J Cardiol.* **2013**;164(1):88–93. doi:10.1016/j.ijcard.2011.06.093
35. Zhou Y, Chen J, Hu B, et al. The predictive value of intra-left atrial mechanical delay for 1-year recurrence of atrial fibrillation after catheter ablation: a clinical follow-up study using dual Doppler echocardiography. *J Clin Ultrasound.* **2018**;46(8):519–526. doi:10.1002/jcu.22629
36. Okamatsu H, Ohara T, Kanzaki H, et al. Impact of left ventricular diastolic dysfunction on outcome of catheter ablation for atrial fibrillation in patients with hypertrophic cardiomyopathy. *Circ J.* **2015**;79(2):419–424. doi:10.1253/circj.CJ-14-0823
37. Hirai T, Coteones G, Makki N, et al. Usefulness of left ventricular diastolic function to predict recurrence of atrial fibrillation in patients with preserved left ventricular systolic function. *Am J Cardiol.* **2014**;114(1):65–69. doi:10.1016/j.amjcard.2014.03.061
38. Garcia MJ, Ares MA, Asher C, et al. An index of early left ventricular filling that combined with pulsed Doppler peak E velocity may estimate capillary wedge pressure. *J Am Coll Cardiol.* **1997**;29(2):448–454. doi:10.1016/S0735-1097(96)00496-2
39. Diaz AA, Rodríguez EM, Escudero E. Is the E/Vp index useful for evaluating prognosis in chronic heart failure with atrial fibrillation? A pilot study. *J Echocardiogr.* **2010**;8(3):80–86. doi:10.1007/s12574-010-0036-y

International Journal of General Medicine

Publish your work in this journal

The International Journal of General Medicine is an international, peer-reviewed open-access journal that focuses on general and internal medicine, pathogenesis, epidemiology, diagnosis, monitoring and treatment protocols. The journal is characterized by the rapid reporting of reviews, original research and clinical studies across all disease areas. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/international-journal-of-general-medicine-journal>

Dovepress
Taylor & Francis Group