The right atrial diameter as a risk factor predicting recurrence of atrial fibrillation after catheter ablation at mid-term follow-up

Wang Xiaofei
First Affiliated Hospital of Soochow University https://orcid.org/0000-0003-2603-7007
Wang Wenli
First Affiliated Hospital of Soochow University
Zou Cao (nkzc75@163.com)
https://orcid.org/0000-0003-2339-7285

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Abstract

Background

Left atrial diameter (LAD) has been confirmed to predict recurrence of atrial fibrillation (AF) after catheter ablation (CA). The influence of right atrium (RA) size on the prognosis after CA was relatively unclear and lack of research. The objective of the present study was to investigate the relationship between right atrial diameter (RAD) and the mid-term outcome of AF after CA.

Methods

This study retrospectively examined 121 patients who underwent initial CA for symptomatic AF. Cox regression model was used to find risk factors of recurrence. Receiver operating characteristic (ROC) curve was used to evaluate predictive power and determine clinic cutoff value. Kaplan-Meier survival curve and log-rank test were used to analyze success rate.

Results

There were 94 (77.7%) patients of freedom from AF after 24.2 ± 4.5 months' follow-up. Multivariate Cox regression analysis showed both hypertension and RAD were independent risk factors of arrhythmia recurrence after ablation regardless of AF type (HR: 4.915; 95% CI: 1.370-17.635; P = 0.015 and HR: 1.059; 95% CI: 1.001–1.120; P = 0.045, respectively). However, in patients with paroxysmal AF (par-AF), Multivariate analysis showed RAD become the only independent risk factor (HR: 1.031; 95% CI: 1.016–1.340; P = 0.029). ROC curve demonstrated the cutoff value of RAD was 35.5 mm with an area under the curve (AUC) of 0.715 (95% CI: 0.586–0.843, P = 0.009), sensitivity of 81.3% and specificity of 54.2%. Kaplan-Meier survival curve showed significant difference of freedom from par-AF (67.5 vs. 91.4%, log-rank, P = 0.015) between patients with RAD ≥ 35.5 mm and < 35.5 mm in this subgroup. Nevertheless, in patients with persistent AF (per-AF), no risk factor of arrhythmia recurrence was found. In addition, Kaplan-Meier survival curve showed no significant difference of freedom from per-AF (69.7 vs. 87.5%, log-rank, P = 0.31) between patients with RAD ≥ 35.5 mm and < 35.5 mm.

Conclusions

RAD was the independent risk factor predicting recurrence of AF after CA only in patients with par-AF. In patients with RAD < 35.5 mm, there was a significantly higher freedom from par-AF recurrence compared with RAD ≥ 35.5 mm after a mid-term follow-up.

Background

Atrial fibrillation (AF), responsible for stroke and heart failure, is the most common sustained arrhythmia with the prevalence increasing with age. The overall prevalence of AF is in the range of 1–2% of the general population [1]. Catheter ablation (CA) based on pulmonary vein isolation (PVI) has been an effective therapy for patients with AF refractory to antiarrhythmic drugs [2, 3]. However, AF recurs in approximately 30% of patients with paroxysmal AF (par-AF) and in even more patients with persistent AF (per-AF) after CA and repeat procedures are required in these patients [4]. Therefore, it's significantly important to find the powerful risk factors predicting recurrence of AF after CA so that we could intervene it in advance for patients with high risk to reduce recurrence.

Numerous studies have confirmed that atrial enlargement was closely related to outcome of AF after CA, whereas these studies mainly focused on left atrium (LA), which is generally thought to play a leading role in the pathophysiology of AF [5–7]. Although several studies have suggested that right atrium (RA) size could also predict the recurrence [8–10], indicating that RA remodeling was also associated with the AF outcome, the influence of RA size on the prognosis after CA was relatively unclear and lack of research. In this study, our aim was to evaluate the predictive value of right atrial diameter (RAD) and investigate the relationship between RAD and the mid-term outcome in patients with AF after CA.

Methods

Study Population

From November 2016 to June 2018, 121 patients with AF undergoing initial radiofrequency catheter ablation (RFCA) in our hospital were consecutively enrolled in this study approved by the Ethics Committee of Soochow university, including 79 paroxysmal AF (par-AF) patients and 42 persistent AF (per-AF) patients. Patients were aged between 18 and 80 years with documented symptomatic AF episodes refractory to at least one antiarrhythmic drug (Class I or III drugs). We excluded patients with overt pulmonary disease such as chronic obstructive pulmonary disease and moderate to severe pulmonary hypertension and structural cardiac diseases which might cause the enlargement of RA such as severe tricuspid regurgitation. All patients signed the informed consent for the AF ablation procedure and the use of their clinical data in a retrospective study.

Echocardiography

Each patient was performed an examination of transthoracic echocardiography using a Sonos 5500 ultrasound machine (Philips) with a 2.5-Hz transducer before and after 3 months. Echocardiographic techniques and calculations of cardiac dimensions were made in accordance with recommendations of the American Society of Echocardiography [11]. Standard M-mode, 2-dimensional, and color Doppler imaging were performed in the standard parasternal and apical views. Anteroposterior left atrial diameter (LAD) were measured in the parasternal long-axis views and horizontal RAD in the apical 4-chamber view during end-systolic phase. LAD and RAD were defines as distance between the posterior aortic root wall and the posterior LA wall and distance between the center of the mitral annulus and the left atrial roof, respectively. The left ventricular end-diastolic dimension (LVD) and left ventricular end-systolic dimension

(LVS) were measure in the parasternal left ventricular long axis view. The left ventricular ejection fraction (LVEF) was calculated from 2-dimensional recordings using the modified Simpson method. The measurements were averaged over at least 5 cardiac cycles and reviewed by 2 experienced echocardiographers.

Preparation of procedure

Before the procedure, adequate oral anticoagulation was discontinued and replaced by low molecular weight heparin for bridging 3–5 days whereas all anti-arrhythmic drugs (AADs) such as amiodarone or propafenone were not stopped. All patients underwent transesophageal echocardiography (Vivid7 color Doppler ultrasound system, probe frequency 1.7–3.4 MHZ) 24 h prior to the procedure to exclude LA thrombus and multi-slice computed tomography performed with a 320-detector row, dynamic volume scanner (Aquilon ONE; Toshiba Medical Systems, Tokyo, Japan) for three dimension (3D) reconstruction of the LA and pulmonary veins (PVs) before the procedure.

Radiofrequency catheter ablation

All patients underwent ablation in deep sedation applying a continuous intravenous infusion of fentanyl, while no esophageal temperature monitoring was performed. A decapolar catheter was advanced into the coronary sinus through the right internal jugular vein. After double transseptal punctures, two SL1 sheaths (St. Jude Medical Inc., Little Canada, MN) were advanced into the LA. Then, intravenous heparin (100 IU/kg) was administered immediately and 1000 units of heparin were given every hour. The decapolar Lasso mapping catheter (Biosense Webster, USA) was sent to pulmonary veins through one of the SL1 long sheath; the other SL1 was performed for pulmonary venography.

The 3D geometric image of the LA and PVs was reconstructed by a tip-integrated contact force (CF) sensor catheter (Thermocool Smart Touch; Biosense-Webster, Inc, Diamond Bar, CA) with a CARTO3 mapping system. Before mapping and ablation, calibration of CF catheter and respiratory gating were performed. The ablation was guided by an automated ablation lesion tagging module (VisiTag module of the CARTO3 system) and the optimum VisiTag settings comprised a maximum distance of 2.5 mm, minimum time period of 5 s and a force over time (FOT) > 5 g for 40% of the ablation time. The energy was delivered at a maximum power output of 25–35 W depending on the ablation sites (25 W for the posterior aspects of the PVs and 30–35 W for the anterior aspects) and the upper temperature limit was set to 43℃. The catheter tip was irrigated with saline at a flow rate of 2 mL/min during mapping and 17 mL/min during ablation (CoolFlow Pump; Biosense Webster).

All patients underwent pulmonary vein isolation (PVI) around ipsilateral pulmonary vein antrum (0.5-1 cm outside the pulmonary vein ostia) and atrial linear ablation using point-by-point quantitative ablation with the distance between lesions less than 6 mm under the guidance of VisiTag. The patients with par-AF and per-AF whose duration were less than 1 year just underwent PVI. Per-AF patients with duration longer than 1 year or LAD greater than 45 mm had additional ablation line such as left atrial top line, anterior wall line or mitral valve isthmus line. Cavotricuspid isthmus ablation line was performed when typical atrial flutter

was induced by burst atrial pacing or observed clinically. After PVI or additional ablation line, cardioversion was performed when atrial fibrillation still didn't terminate.

Procedural endpoint was PVI confirmed by demonstration of entrance and exit block, plus complete block of the lines in per-AF cases. Entrance PVs block was defined as the complete absence of PV potentials, and exit block was defined as the absence of LA conduction by pacing from sequential bipolar electrodes of a Lasso catheter positioned at the right or left PVs. In case of reconnection during waiting for 20 minutes, touch-up ablation at the putative site of reconnection was continued until PVI was resistant to subsequent waiting.

Follow-up

After ablation, anticoagulation with warfarin or a novel oral anticoagulant (NOAC) was required for at least 3 months, while in some cases longer according to the thromboembolic risk. AADs such as amiodarone or propafenone were continued up to the 3-month follow-up. All patients underwent routine follow-up examination at our outpatient clinic 3 months after ablation and at 3-month intervals thereafter tested pulse rate three times a day. A standard 12-lead ECG was mandatory and 24 h-Holter monitoring was strongly encouraged during each clinical visit. The recurrence of AF was defined as any documented atrial tachyarrhythmia (AF, atrial flutter, or atrial tachycardia) lasting ≥ 30 s after the post-ablation blank period.

Statistical Analysis

All statistical analyses were performed in SPSS Statistics 23.0. Results are presented as a mean ± standard deviation, median with 25-75th percentile, or frequencies and percentage (%) of patients. Continuous variables were evaluated using unpaired or paired samples t test. Pearson's or continuity correction chi-square test was used for the categorical variables. To find risk factors of recurrence, variables that showed a univariate relationship with outcome ($P < 0.1$) were entered into multivariate Cox proportional-hazards regression model using an "enter" method to determine whether they remained significant. Receiver operating characteristic (ROC) curve was used to evaluate the predictive power and determine the clinic cutoff value. Kaplan-Meier survival curve and log-rank test were used to analyze the success rate of ablation. The statistical significance was set at $P < 0.05$.

Results

Patient Characteristics

Patient characteristics at baseline were listed in Table 1. In all 121 patients including 94 (77.7%) patients of freedom from AF and 27 (22.3%) patients of recurrence (no-AF group and AF group, respectively) after 24.2 ± 4.5 months' follow-up (range 18.0 to 37.5 months), the mean age was 62.2 ± 9.3 years, 61 patients (50.4%) were male and 79 patients (65.3%) had par-AF. Compared to the patients in no-AF group, RAD and hypertension were significantly higher in patients of AF group (40 ± 4.6 vs. 37.4 ± 6.1 mm and 88.9%

vs. 53.2%, respectively), while there was no significant difference in other characteristics between the two groups.

Table 1
Baseline Patient Characteristics

Variable	Total	No-AF group (n = 94)	AF group (n = 27)	P-value
Age (years)	62.2 ± 9.3	62.2 ± 9.9	62.1 ± 7.0	0.973
Male (n,%)	61 (50.4)	45 (47.9)	16 (59.3)	0.297
Type of AF (n,%)				
Paroxysmal	79 (65.3)	63 (67.0)	16 (59.3)	0.455
Persistent	42 (34.7)	31 (33.0)	11 (40.7)	0.455
AF duration (months)	24.8 ± 36.7	27.1 ± 38.7	16.5 ± 27.7	0.116
BMI (kg/m^2)	24.8 ± 2.9	24.7 ± 3.1	25.2 ± 2.1	0.391
CHA2DS2-VASc score	1.8 ± 1.3	1.7 ± 1.2	2.1 ± 1.3	0.081
Clinical diseases (n, %)				
Hypertension	74 (61.2)	50 (53.2)	24 (88.9)	**0.001**
Diabetes mellitus	14 (11.6)	9 (9.6)	5 (18.5)	0.348
Coronary artery disease	15 (12.4)	10 (10.6)	5 (18.5)	0.445
Anticoagulants (n, %)				
Warfarin	18 (14.9)	14 (14.9)	4 (14.8)	1.000
NOAC	103 (85.1)	80 (85.1)	23 (85.2)	1.000
Antiarrhythmic drugs (n, %)				
Amiodarone	96(80.7)	76 (82.6)	20 (74.1)	0.323
Propafenone	23(19.3)	16 (17.4)	7 (25.9)	0.323
LAD (mm)	43.0 ± 6.1	42.8 ± 6.2	43.7 ± 5.6	0.481
RAD (mm)	38.0 ± 5.8	37.4 ± 6.1	40.0 ± 4.6	**0.044**
LVD (mm)	49.5 ± 5.0	49.4 ± 5.0	49.6 ± 5.2	0.872
LVS (mm)	32.5 ± 5.7	32.5 ± 5.9	32.4 ± 5.0	0.945
LVEF (%)	62.6 ± 8.0	62.1 ± 8.2	62.6 ± 7.5	0.982

NO-AF group, freedom from atrial fibrillation, BMI body mass index, NOAC novel oral anticoagulants, LAD left atrial diameter, RAD right atrial diameter, LVD left ventricular end-diastolic dimension, LVS left ventricular end-systolic dimension, LVEF left ventricular ejection fraction

Reversible atrial structural remodeling

The improvement of echocardiographic parameters was listed in Table 2. after a follow-up of 3 months. In patients with par-AF, only RAD significantly decreased between preoperative and postoperative group. In contrast, in patients with per-AF, both LAD and RAD significantly decreased. In addition, LVEF was improved significantly in both type of AF.

Table 2
The change of echocardiographic parameters

Variable	Par-AF group (n = 79)			Per-AF group (n = 42)		P-value
	Pre-CA	Post-CA	P-value	Pre-CA	Post-CA	
LAD (mm)	41.2 ± 5.6	40.5 ± 35.3	0.266	45.5 ± 4.1	42.6 ± 3.3	**0.001**
RAD (mm)	35.8 ± 3.6	33.8 ± 4.2	**0.001**	41.6 ± 6.9	36.8 ± 5.0	**0.001**
LVD (mm)	48.2 ± 4.5	48.9 ± 3.9	0.239	50.7 ± 5.9	50.7 ± 5.6	1.000
LVS (mm)	30.8 ± 4.0	31.3 ± 3.3	0.329	34.7 ± 6.8	33.0 ± 5.5	0.046
LVEF (%)	63.9 ± 6.5	65.9 ± 4.8	0.043	58.4 ± 11.8	63.6 ± 7.8	0.010

LAD left atrial diameter, RAD right atrial diameter, LVD left ventricular end-diastolic dimension, LVS left ventricular end-systolic dimension, LVEF left ventricular ejection fraction

Analysis of risk factors in patients with both par-AF and per-AF

The variables that were consider clinically relevant to the procedural outcome based on prior knowledge or expected clinical relevance and that showed significant difference in above-mentioned RAD and hypertension were entered into a Cox proportional-hazards regression model to adjust for potential confounders (Table 3). In the univariate analysis, hypertension (HR: 5.627; 95% CI: 1.694–18.695; P = 0.005) and RAD (HR: 1.060; 95% CI: 1.002–1.121; P = 0.041) were found to influence AF recurrence after ablation. The multivariate analysis showed that both hypertension (HR: 4.915; 95%CI: 1.370-17.635; P = 0.015) and RAD (HR: 1.059; 95% CI: 1.001–1.120; P = 0.045) were the independent risk factors of arrhythmia recurrence after ablation regardless of AF type.

Table 3
The univariate and multivariate analysis of risk factors predicting recurrence of AF

Predictive factor	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (years)	1.001 (0.962–1.042)	0.947	-	-
Sex (female)	0.661 (0.306–1.425)	0.291	-	-
Per-AF	1.413 (0.655–3.050)	0.378	-	-
AF duration (months)	0.991 (0.978–1.005)	0.213	-	-
CHA2DS2-VASc score	1.310 (0.968–1.773)	0.080	1.097 (0.774–1.553)	0.604
BMI (kg/m^2)	1.049 (0.924–1.192)	0.457	-	-
Hypertension	5.627 (1.694–18.695)	0.005	4.915 (1.370-17.635)	**0.015**
Diabetes mellitus	1.924 (0.728–5.085)	0.187	-	-
Coronary artery disease	1.895 (0.717–5.009)	0.197	-	-
LAD (mm)	1.030 (0.968–1.096)	0.349	-	-
RAD (mm)	1.060 (1.002–1.121)	0.041	1.059 (1.001–1.120)	**0.045**
LVD (mm)	1.010 (0.937–1.090)	0.791	-	-
LVS (mm)	1.000 (0.938–1.066)	0.993	-	-
LVEF (%)	0.997 (0.952–1.045)	0.914	-	-

HR hazard ratio, Per-AF persistent atrial fibrillation, BMI body mass index, LAD left atrial diameter, RAD right atrial diameter, LVD left ventricular end-diastolic dimension, LVS left ventricular end-systolic dimension, LVEF left ventricular ejection fraction

Subgroup analysis in patients with Par-AF

The characteristics of patients with par-AF were listed in Table 4. In patients with Par-AF, 16 (20.3%) patients experienced recurrence after 24.5 ± 4.5 months' follow-up. Similarly, compared to the patients in no-AF group, RAD and hypertension were significantly higher in patients of AF group (38.3 ± 3.4 vs. 35.4 ± 3.8 mm and 87.5% vs. 50.8%, respectively), while there was no significant difference in other characteristics between the two groups. Interestingly, the multivariate Cox regression analysis showed RAD become the only independent risk factor of arrhythmia recurrence after ablation in par-AF (HR: 1.031; 95% CI: 1.016–1.340; P = 0.029) (Table 5).

Subsequently, the ROC curve was used to determine the cutoff point of RAD with the greatest sensitivity and specificity to predict recurrence of AF. The cutoff value of RAD was 35.5 mm with an area under the curve (AUC) of 0.715 (95% CI: 0.586–0.843, P = 0.009), sensitivity of 81.3% and specificity of 54.2%

(Fig. 1). Kaplan-Meier survival curve showed significant difference of freedom from par-AF (67.5% vs. 91.4%, log-rank, P = 0.015) between patients with RAD ≥ 35.5 mm and < 35.5 mm (Fig. 2).

Table 4
Comparison of Subgroup Patient Characteristics

Variable	Par-AF (n = 79)		P	Per-AF (n = 42)		P
	Non-AF group (n = 63)	AF group (n = 16)	value	Non-AF group (n = 31)	AF group (n = 11)	value
Age (years)	62.2 ± 10.5	60.4 ± 8	0.449	62.1 ± 8.6	64.6 ± 4.4	0.364
Male (n, %)	29 (46)	9 (56.3)	0.465	16 (51.6)	7 (63.6)	0.737
AF duration (months)	26.5 ± 39.1	15.6 ± 22.1	0.148	28.3 ± 38.6	17.8 ± 35.4	0.433
BMI (kg/m^2)	24.2 ± 3.3	25 ± 1.8	0.338	25.6 ± 2.5	25.3 ± 6.4	0.905
CHA2DS2-VASc score	1.6 ± 1.2	2 ± 1.3	0.288	1.7 ± 1.3	2.4 ± 1.4	0.183
Clinical diseases (n, %)						
Hypertension	32 (50.8)	14 (87.5)	**0.008**	18 (58.1)	10 (90.9)	0.107
Diabetes mellitus	6 (9.5)	3 (18.5)	0.551	3 (9.7)	2 (18.2)	0.836
Coronary artery disease	7 (11.1)	2 (12.5)	1.000	3 (9.7)	3 (27.3)	0.352
Anticoagulants (n, %)						
Warfarin	7 (11.1)	3 (18.8)	0.689	7 (22.6)	1 (9.1)	0.595
NOAC	56 (88.9)	13 (81.3)	0.689	24 (77.4)	10 (90.9)	0.595
Antiarrhythmic drugs (n, %)						
Amiodarone	49 (80.3)	12 (75.0)	0.903	27 (87.1)	8 (72.7)	0.530
Propafenone	12 (19.7)	4 (25.0)	0.903	4 (12.9)	3 (27.3)	0.530
LAD (mm)	40.9 ± 5.7	42.4 ± 5.5	0.366	46.5 ± 5.5	45.6 ± 5.5	0.664

BMI body mass index, NOAC novel oral anticoagulants, LAD left atrial diameter, RAD right atrial diameter, LVD left ventricular end-diastolic dimension, LVS left ventricular end-systolic dimension, LVEF left ventricular ejection fraction

Variable	Par-AF (n = 79)		P	Per-AF (n = 42)		P
RAD (mm)	35.4 ± 3.8	38.3 ± 3.4	**0.009**	41.3 ± 7.6	42.6 ± 5.2	0.629
LVD (mm)	48.4 ± 4.8	49.3 ± 4.6	0.509	51.4 ± 4.9	50.0 ± 6.1	0.442
LVS (mm)	31.4 ± 5.5	31.7 ± 5.1	0.874	34.7 ± 6.2	33.6 ± 4.9	0.566
LVEF (%)	64.2 ± 5.1	63.6 ± 9.2	0.816	59.2 ± 11.6	61.1 ± 3.9	0.441

BMI body mass index, NOAC novel oral anticoagulants, LAD left atrial diameter, RAD right atrial diameter, LVD left ventricular end-diastolic dimension, LVS left ventricular end-systolic dimension, LVEF left ventricular ejection fraction

Table 5
Analysis of risk factors predicting recurrence of patients with Par-AF

Predictive factor	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (years)	0.988 (0.946–1.033)	0.606	-	-
Sex (female)	0.656 (0.244–1.763)	0.404	-	-
AF duration (months)	0.991 (0.974–1.009)	0.335	-	-
CHA2DS2-VASc score	1.239 (0.826–1.861)	0.300	-	-
BMI (kg/m^2)	1.066 (0.915–1.242)	0.415	-	-
Hypertension	5.373 (1.221–23.651)	0.026	4.326 (0.968–19.335)	0.055
Diabetes mellitus	1.929 (0.548–6.796)	0.307	-	-
Coronary artery disease	1.210 (0.275–5.325)	0.801	-	-
LAD (mm)	1.055 (0.964–1.154)	0.242	-	-
RAD (mm)	1.204 (1.046–1.385)	0.009	1.031 (1.016–1.340)	**0.029**
LVD (mm)	1.039 (0.937–1.152)	0.464	-	-
LVS (mm)	1.008 (0.929–1.093)	0.851	-	-
LVEF (%)	0.978 (0.901–1.061)	0.588	-	-

HR hazard ratio, BMI body mass index, LAD left atrial diameter, RAD right atrial diameter, LVD left ventricular end-diastolic dimension, LVS left ventricular end-systolic dimension, LVEF left ventricular ejection fraction

Subgroup analysis in patients with Per-AF

The characteristics of patients with per-AF were listed in Table 4. In patients with Per-AF, 11 (26.2%) patients experienced recurrence after 23.5 ± 4.5 months' follow-up. There was no significant difference in all characteristics between the two groups in this type of AF. In addition, the Cox regression analysis showed that no risk factor of arrhythmia recurrence after ablation was found in per-AF (Table 6). Kaplan-Meier survival curve showed no significant difference of freedom from AF (69.7% vs. 87.5%, log-rank, P = 0.31) between patients with RAD ≥ 35.5 mm and < 35.5 mm in this subgroup, though the former showed the trend of lower success rate. (Fig. 3).

Table 6
Analysis of risk factors predicting recurrence of patients with Per-AF

Predictive factor	**Univariate analysis**		**Multivariate analysis**	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (years)	1.037 (0.959–1.121)	0.366	-	-
Sex (female)	0.723 (0.211–2.470)	0.605	-	-
AF duration (months)	0.992 (0.970–1.014)	0.477	-	-
CHA2DS2-VASc score	1.364 (0.865–2.150)	0.181	-	-
BMI (kg/m^2)	0.987 (0.777–1.253)	0.912	-	-
Hypertension	5.659 (0.724–44.247)	0.099	6.284 (0.800-49.363)	0.080
Diabetes mellitus	1.684 (0.363–7.802)	0.505	-	-
Coronary artery disease	2.740 (0.725–10.360)	0.137	-	-
LAD (mm)	0.971 (0.870–1.083)	0.596	-	-
RAD (mm)	1.021 (0.939–1.111)	0.626	1.031 (0.953–1.116)	0.448
LVD (mm)	0.950 (0.842–1.072)	0.403	-	-
LVS (mm)	0.967 (0.866–1.079)	0.546	-	-
LVEF (%)	1.016 (0.955–1.081)	0.607	-	-

HR hazard ratio, BMI body mass index, LAD left atrial diameter, RAD right atrial diameter, LVD left ventricular end-diastolic dimension, LVS left ventricular end-systolic dimension, LVEF left ventricular ejection fraction

Discussion

Main Findings

In this study, we investigated the relationship between RAD and the mid-term outcome of AF after CA. We mainly found RAD was the independent risk factor predicting recurrence of AF after CA only in patients with par-AF. In these patients, RA enlargement is significantly associated with the recurrence after a mid-term follow-up. However, in patients with per-AF, the predictive value of RAD is relatively limited and there was no significantly higher freedom from AF in patients with increased RAD.

Atrial Remodeling as a Predictor of AF Recurrence

The predictive value of RAD might be due to an association between RA anatomical remodeling and outcome of AF after CA. Increased RAD involving RA remodeling may provide the substrate for AF to be sustained. Contributing to atrial enlargement, atrial structural remodeling, particularly fibrosis related to cell death, fibroblast proliferation, and excess extracellular matrix production, is important in many forms of AF [12].Atrial remodeling causes AF progression to permanent forms, so remodeling development is potentially a predictor of treatment response [13].Since Haïssaguerre et al. [14] found the PVs was an important source of ectopic beats initiating frequent paroxysms of AF, many studies focusing on LA has found LA remodeling can predict the recurrence [15, 16].Increased RAD is likely a reflection of RA tissue fibrosis and structural remodeling and atrial remodeling has been found in RA [17, 18].In addition, there is muscular bridge providing interatrial connection between the muscular sleeves of the right PVs and the RA [19]. Thus, it’s reasonable to identify RA remodeling as a predictor of AF, though few studies evaluating the determinants of AF recurrence focused on RA. In patients with per-AF underwent electrical cardioversion, RA size including RA diameter, RA areas, right atrial volume index (RAVI) has been confirmed to predict the recurrence [20, 21], but in patients underwent CA, little is known about the importance of the degree of dilation of the RA on prediction of AF recurrence.

RA Remodeling as a Predictor of AF Recurrence

Moon’s study [9] for the first time to investigated the RA anatomic remodeling assessed with multidetector computed tomography in AF patients found that RA anatomical remodeling, measure as RAVI, might affect the early recurrence after ablation. Houltz et al. [10] reported that RA areas may be important variables in prediction of long-term rhythm outcome after intraoperative ablation for AF. But their study may be limited in that they did not fully distinguish between par-AF and per-AF. As a common sense, AF, as a progressive disease of which the natural history involves evolution from paroxysmal to persistent to permanent forms, has generally more complicated triggering or maintaining mechanisms for the type of per-AF, implicating a more diffuse abnormality of the atrial substrate, which more likely contributed to the recurrence after ablation [12]. Unlike these study including both par-AF and per-AF, our research found RA structural remodeling, measured as RAD which is more clinically available parameter, might affect the outcome only in patients with par-AF at a mid-term follow-up. In patients with per-AF, RAD failed to predict the maintenance of sinus rhythm, though the increased RAD showed the trend of lower success rate. We hypothesized that the phenomenon simultaneously indicated RA remodeling played a more important role only in the pathophysiology of AF at early stage.

Actually, both Akutsu et al. [22] and Wen et al [8] also found that RA remodeling is associated with post-CA recurrence in par-AF. Akutsu et al. found a large RA volume was associated with the recurrence at short-term follow-up of within 6 months. Wen et al found increased RAD was an independent predictor for recurrence only in par-AF patients with LA dilation, indicating that RAD < 35.5 mm is associated with a better recurrence-free survival at over 2-year follow-up. Differently, our study suggested RAD can predict recurrence in patients with par-AF regardless of the LA size, maybe an earlier pathophysical stage of AF than Wen's study population, at mid-term follow-up, which might complement the Wen's finding. Similarly, our study found the risk of recurrence increased significantly for RAD above 35.5 mm with 81.3% sensitivity and 54.2% specificity after a mid-term follow-up. Interestingly, this is quite the same clinic cutoff value reported by Wen's studies with 85.4% sensitivity and 29.2% specificity. Imperfectly, both Akutsu and Wen's study failed to evaluate the reversible atrial remodeling for the patients without AF recurrence after CA. We found only RAD significantly decreased in patients with par-AF, whereas both LAD and RAD decreased in per-AF. Our research showed that the RAD could decrease significantly after restoring sinus rhythm by ablation after three months, which simultaneously confirmed the important role of RA remodeling in par-AF, as the early stage of AF. Further, as several studies demonstrated [9, 10, 21], although the univariate regression adjusted for several clinical and demographic risk factors, LA size was not identified as a significant predictor of AF recurrence, which is not in accordance with the results from the previous study. This might result from some unmeasured confounders and different study population, ablation strategy or follow-up time.

Clinical implications

Our findings provided additional insights to the understanding of predictor of AF recurrence. In addition to LA remodeling, RA remodeling was also associated with the AF recurrence. The RA size ought to be taken into account in rhythm outcome prediction of ablation treatment. RA remodeling might be a more important factor than left atrial remodeling in the pathophysiology of AF at early stage. Preventing atrial remodeling (so-called upstream therapy) [12] at this stage, intervened in advance for patients with high risk, might suppress the recurrence of the AF, especially in patients of RAD ≥ 35.5 mm. Since the majority of studies mainly focused on LA, the importance of the RA on the outcome of AF after CA might have been seriously ignored. The measurement of preprocedural RA size, combined with the LA size, might provide more reliable prognostic information for patients of AF ready for undergoing ablation. In addition, RA substrate mapping or RA triggers examination during ablation procedure might be beneficial to the outcome in patients with large RA.

Study Limitations

This study was a retrospective and observational study at single center with relatively limited amount of patients and potential selection bias. Thus, what kind of population will show the predictive value of RAD remains unclear. Larger prospective studies are needed to establish predictive utility of RAD in recurrence of AF after CA. In addition, the limited intensity of arrhythmia monitoring on follow-up could have overestimated the chronic success rate. Further, our study used two-dimensional echocardiography to evaluate RA size, which is clinically the most common used method. However, cardiac magnetic

resonance is currently considered as the “gold-standard” technique for investigation of the RA and the best approach for accurate RA evaluation is using at least two different imaging techniques [23].

Conclusion

The current study mainly revealed that large RAD was the independent risk factor predicting recurrence of AF after CA only in patients with par-AF. In these patients, there was a significantly higher freedom from AF recurrence in patients with RAD < 35.5 mm compared with RAD ≥ 35.5 mm after a mid-term follow-up, indicating that both LA and RA size ought to be taken into account in prediction of rhythm outcome after especially in par-AF.

Abbreviations

Par-AF: paroxysmal atrial fibrillation; Per-AF: persistent atrial fibrillation; CA: catheter ablation; PVI: pulmonary vein isolation; PVs: pulmonary veins; CF: contact force; LA: left atrium; RA: right atrial; AADs: anti-arrhythmic drugs; BMI: body mass index; NOAC: novel oral anticoagulants; HR: hazard ratio; CI: confidence interval; LAD: left atrial diameter; RAD: right atrial diameter; LVD: left ventricular end-diastolic dimension; LVS: left ventricular end-systolic dimension; LVEF: left ventricular ejection fraction; ROC: Receiver operating characteristic; AUC: area under the curve; RAVI: right atrial volume index.

Declarations

Acknowledgments

Not applicable

Authors’ contributions

XF Wang and WL Wang have contributed equally to this work. XF Wang acquired, analyzed and interpreted data as a major contributor in writing the manuscript. WL Wang helped with initial data collection, statistical analysis and critical revision. MS Hu and SK Sun helped with data collection and proofreading of data and manuscript. QK Xuan, J Meng and X Li helped with data collection and interpretation. Professor C Zou is responsible for the whole study, made substantial contributions to design and conduction of the study and revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available due to a further study of this area but are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Soochow university. All patients gave written informed consent for the use of their clinical data in the study.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Department of Cardiology, The First Affiliated Hospital of Soochow University, Suzhou 215000, Jiangsu, China

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Figures

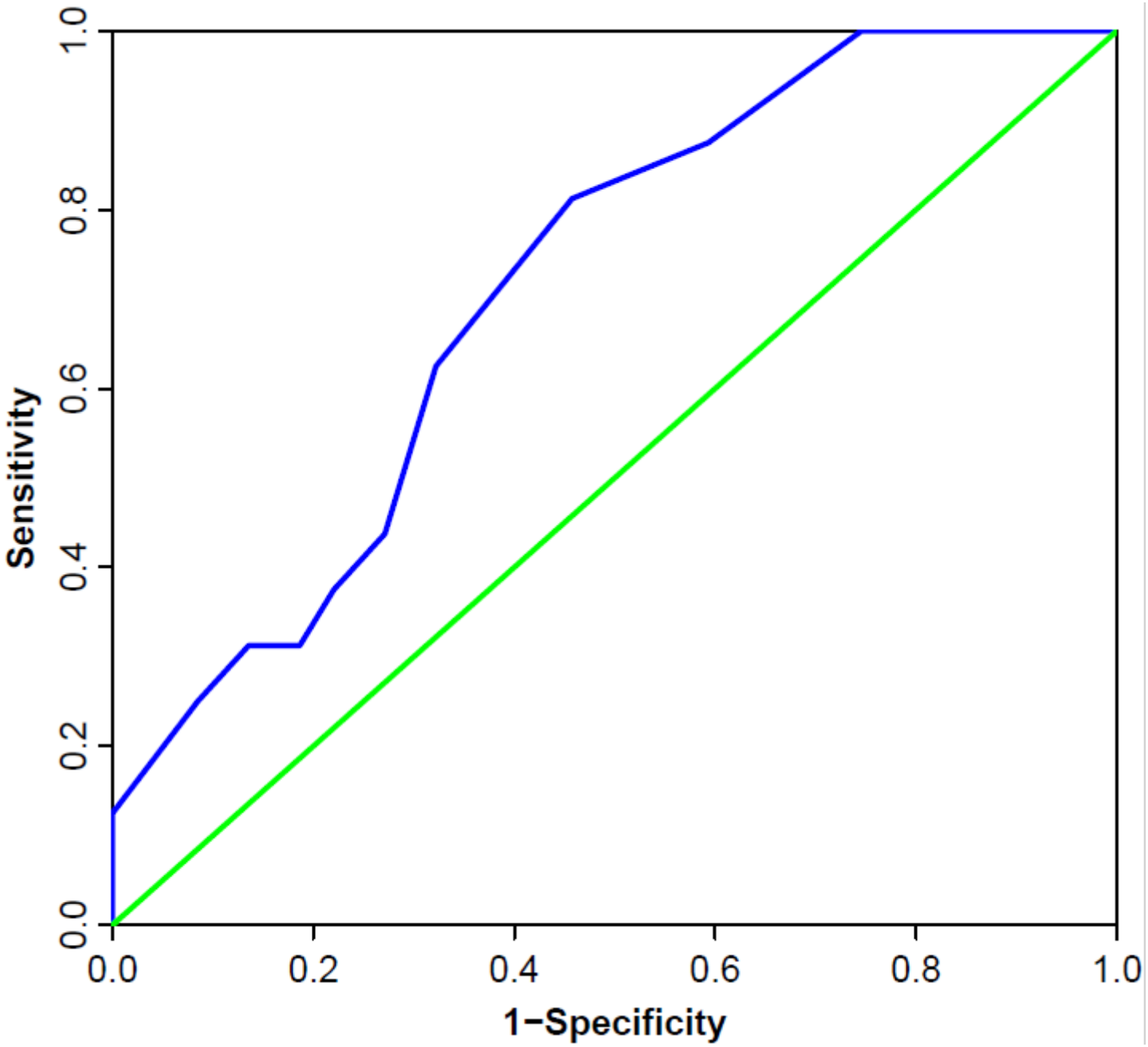

Figure 1

ROC curve showed the predictive power of recurrence of patients with par-AF after ablation. The cutoff value of RAD was 35.5 mm with an area under the curve (AUC) of 0.715(95%CI:0.586-0.843, P=0.009), sensitivity of 81.3% and specificity of 54.2%.

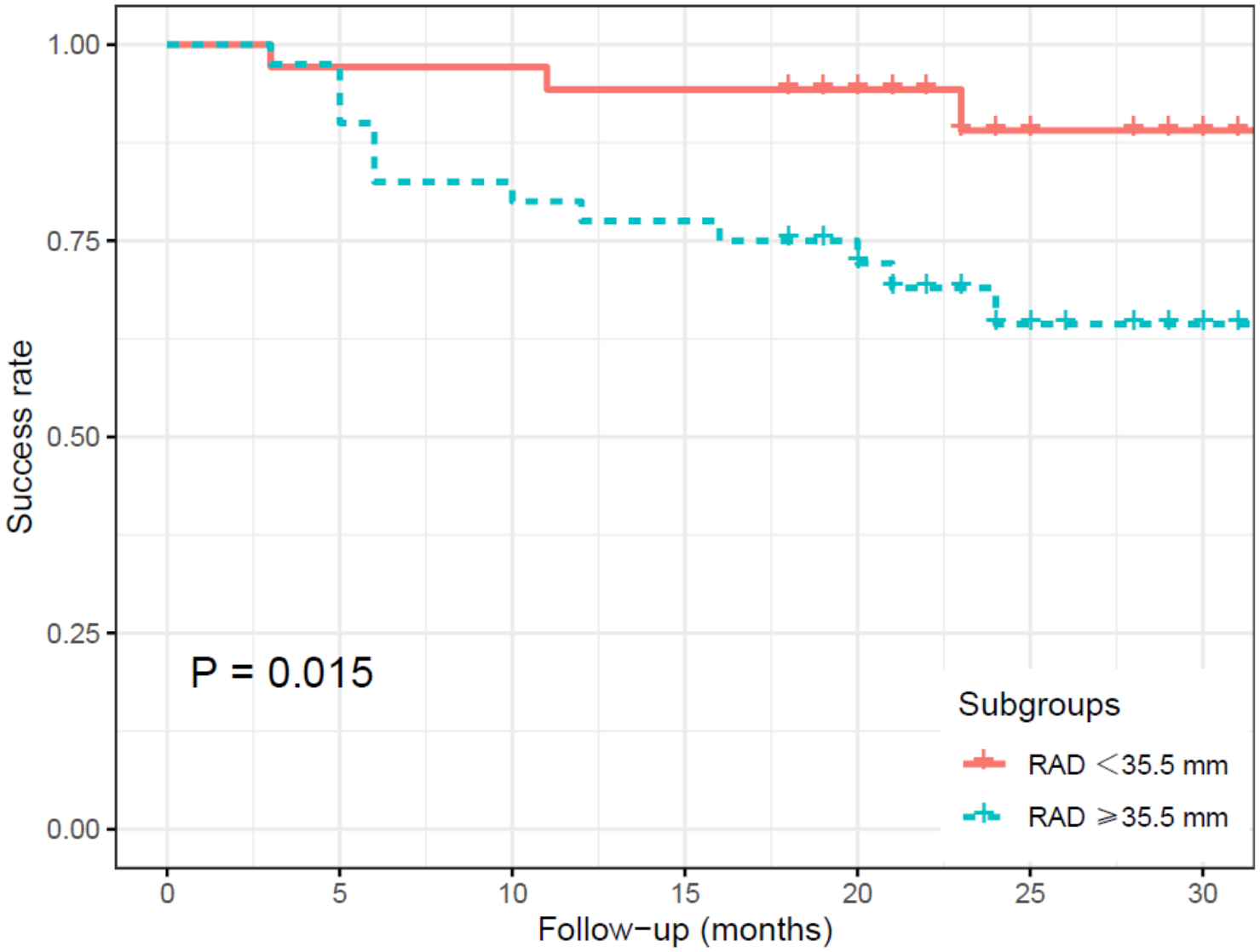

Figure 2

Kaplan-Meier survival curve showed significant difference of freedom from par-AF (91.4 vs.67.5%, log-rank, P = 0.015) between patients with RAD ≥35.5 mm and <35.5 mm.

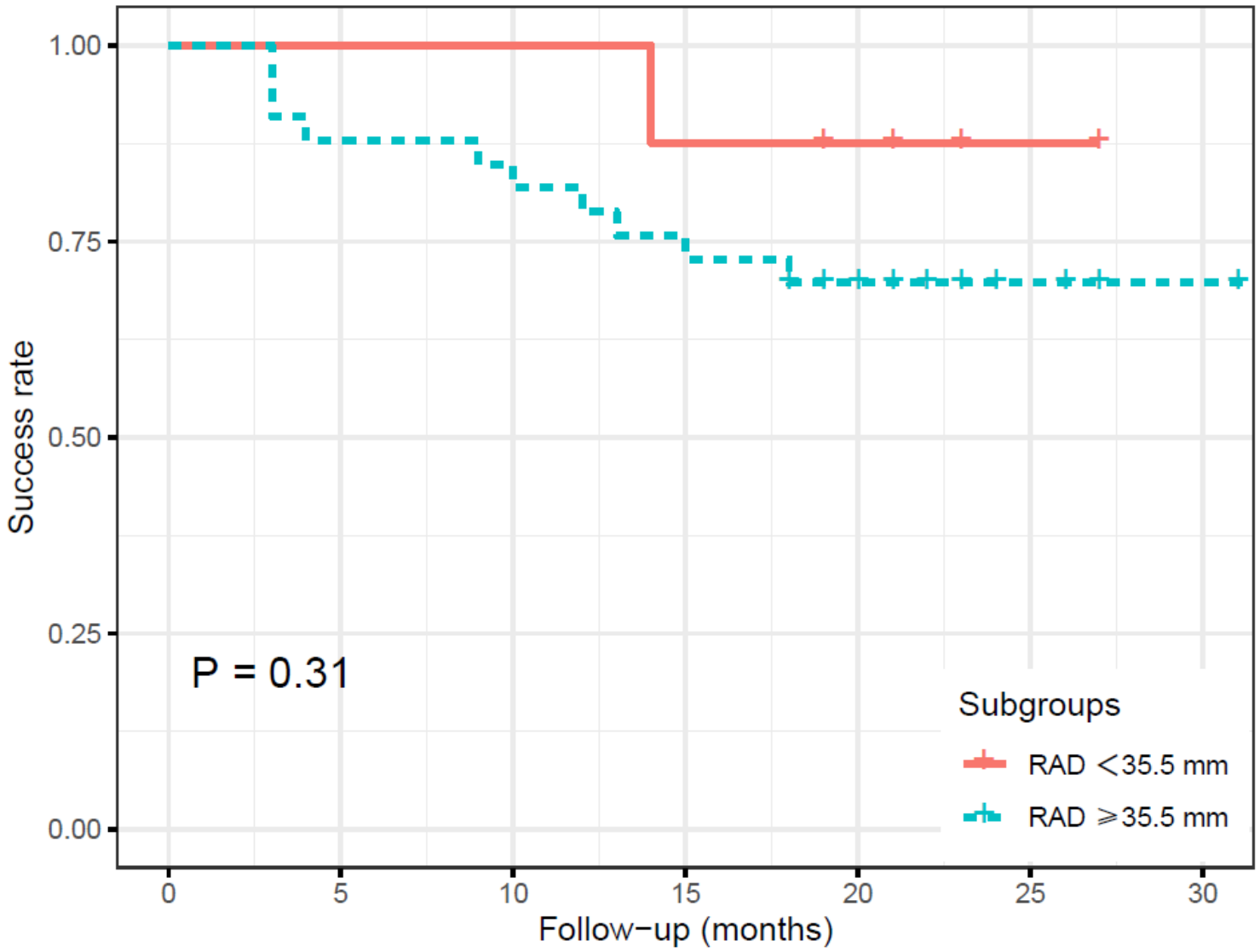

Figure 3

Kaplan-Meier survival curve showed no significant difference of freedom from per-AF (69.7 vs.87.5%, log-rank, P = 0.31) between patients with RAD ≥35.5 mm and <35.5 mm.