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*Article*

# Risk Factors for Recurrence of Atrial Fibrillation within 3 Years after Radiofrequency Ablation

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## Abstract

**Background**: Atrial fibrillation is chronic cardiovascular disease, particularly in older patients. Radiofrequency ablation can successfully treat this condition and restore sinus rhythm. However, the postoperative recurrence rate is relatively high. This investigation aimed to address the factors that might increase the risk of recurrence after radiofrequency ablation. **Methods**: We studied patients who had a successful radiofrequency ablation in our center between 2017 and 2020. We collected information about these patients before the procedure, including their age, sex, obesity, medical history, preoperative laboratory test results, and cardiac ultrasound findings. We divided patients into two groups: those who had atrial fibrillation again within three years and those who did not. We compared the information we collected about these two groups to see if there were any differences to explain why some people had atrial fibrillation again and others did not. We used a statistical method called multivariate logistic regression to analyze these data. **Results**: After reviewing the patients based on specific criteria, we included 297 patients in our final analysis. Within three years after surgery, 109 patients (36.7%) had a recurrence, whereas 188 (63.3%) did not. When we compared the two groups, we found that older patients, those with obesity, a longer history of atrial fibrillation, a larger left atrium, persistent atrial fibrillation, and higher levels of C-reactive protein before surgery were likely to have atrial fibrillation again within three years ($p < 0.05$). Our statistical analysis revealed that these factors were independent predictors of atrial fibrillation recurrence. **Conclusions**: Age, obesity, duration of atrial fibrillation, the size of left atrium, the type of atrial fibrillation, and C-reactive protein (CRP) levels before surgery are closely related to atrial fibrillation recurrence within 3 years after radiofrequency ablation.

## Keywords

atrial fibrillation; radiofrequency ablation; recurrence; risk factors

## Introduction

Atrial fibrillation (AF) is the most prevalent arrhythmia in clinical settings. Its morbidity, mortality rate, and socioeconomic burden resulting from its complications are increasing annually. A study showed that the number of people with AF has increased by 30% in the past 50 years [1]. Another study found that in 2019, about 59.70 million patients had AF/atrial flutter (AFL) worldwide, of which 4.72 million were new cases [2]. AF also poses a heavy burden in China. The number of AF cases has increased from 3533 to 8744 between 1990 and 2016, and the age-standardized incidence rate increased from 549.4 cases per 100,000 people to 604.5 [3]. AF is the result of multiple factors, including alterations in the structure of the atrium and electrophysiological disruption [4,5]. Patients with AF often seek medical attention because of symptoms such as palpitations and chest tightness [6]. The main goal of AF treatment is to improve the quality of life of patients. The key to AF treatment is to restore and maintain a normal heart rhythm [7,8]. Another approach is to control the heart rate, but it increases the bleeding risk and long-term problems for patients [9]. With the development and maturity of technology, radiofrequency ablation is more advantageous in multiple aspects compared with traditional drug therapy [10,11]. One of the biggest challenges with radiofrequency ablation for atrial fibrillation is the difficulty in completely treating the problem and the high rate of recurrence. The early postoperative recurrence (within 3 months after ablation) rate is between 25% and 40%, the late postoperative recurrence (over 3 months after ablation) rate after single ablation is 11%–29%, and the late postoperative recurrence rate after repeated ablation varies from 7% to 33.4% [12–16]. However, current research on the long-term recurrence rates and related risk factors after surgery (1–5 years) is relatively limited. This study aimed to provide a preliminary understanding of the recurrence rate and related factors of patients with AF in China within 3 years after successful radiofrequency ablation through a retrospective study.

## Methods

### Study Population

This study looked back at patients who had a successful radiofrequency ablation procedure for atrial fibrillation in the first affiliated hospital of Dalian Medical University from 2017 to 2020. All patients were followed up annually. The inclusion criteria include adult patients (age over 18 years); for the first time, the patients received radiofrequency ablation to treat atrial fibrillation and successfully converted to sinus rhythm; follow up time $\geq$3 years; clinical and follow-up data were complete. Exclusion criteria include: concomitant valvular heart disease; previously received surgical or interventional treatment for atrial fibrillation; AF refractory to electrical cardioversion; uncontrolled hyperthyroidism; the recurrence of atrial fibrillation was secondary to acute coronary syndrome or acute stroke. The study followed ethical guidelines and was approved by the Ethic committee of The First Affiliated Hospital of Dalian Medical University, Dalian, China and waived off signed informed consent.

### Electrophysiological Examination and Catheter Ablation

All patients underwent regular anticoagulant therapy for at least 3 weeks, and left atrial and left atrial appendage thrombi were excluded by transesophageal echocardiography before surgery. They also stopped taking antiarrhythmic drugs for a certain period before operation. The procedure was performed under general or local anesthesia and a special mapping system was used to guide the ablation. The femoral veins were punctured on both sides, and coronary sinus electrodes were inserted. Pulmonary vein angiography was conducted in the left atrium. Catheters were inserted through the femoral vein, and the left atrium was mapped. Both pulmonary veins were isolated, and the power values for the anterior and posterior walls were set at 40–45 W and 35–40 W, respectively. Ablation was stopped after 20–30 s or an 80% decrease in the A-wave amplitude. Linear ablations of the top of the left atrium and isthmus of the tricuspid valve were performed in patients with persistent AF (PersAF) and AFL, respectively. If the patient had sustained AF after surgery, external electrical cardioversion can be used to restore the sinus rhythm. In the absence of major bleeding, cardiac tamponade, and other symptoms after surgery, anticoagulant treatment can be resumed and maintained for three months. Later, the need to continue anticoagulation treatment was determined according to CHA2DS2-VASc score. Within three months after the operation, antiarrhythmic drugs were administered for paroxysmal AF and amiodarone or propafenone for PersAF. After three months, the need to use antiarrhythmic drugs was determined based on whether AF recurred and the status of the patient.

### Follow-up

Patients were monitored closely after surgery. Follow-up examinations included routine surface electrocardiogram or 24-h Holter monitoring to evaluate AF recurrence. If the patient had palpitations or other clinical manifestations indicating arrhythmia at the non-scheduled follow-up time, the Holter monitor of the ordinary electrocardiogram was rechecked in time. AF recurrence refers to the occurrence of AF, AFL, and atrial tachycardia from three months after successful AF ablation to the end of three years of follow-up. Duration of $\geq$30 s indicated postoperative AF recurrence [16].

### Data Collection

Information about the patients was collected before the procedure. This included their age, sex, weight gain, basic medical history, preoperative laboratory test results, and cardiac ultrasound results. Follow-up was conducted in outpatient clinics, and all outcomes were recorded in the system.

### Statistical Analysis

Continuous variables were normally distributed confirmed by Kolmogorow-Smironov test and reported as means $\pm$ standard deviations and compared using Student's *t*-test. Categorical variables were compared using a chi-square test. A more complex statistical method called multivariate logistic regression was used to identify the risk factors of AF recurrence and calculate their importance. A $p < 0.05$ was considered statistically significant.

## Results

### Baseline Characteristics

After reviewing the patients based on specific criteria, 297 patients ultimately enrolled in the final analysis, with 109 (36.7%) experiencing recurrence (Fig. 1). According to whether AF relapses within 3 years after successful radiofrequency ablation, two groups were established: recurrence group with 109 cases, and non-recurrence group with 188 cases. We found that older patients, those with obesity, a longer history of AF, a larger left atrium (LAD), persistent AF, and higher levels of C-reactive protein before surgery were more likely to have atrial fibrillation again within three years ($p < 0.05$) (Table 1).

### Factors Associated with AF Recurrence

A more complex statistical analysis showed that (Table 2) several factors were independently associated with atrial fibrillation recurrence. These factors included old

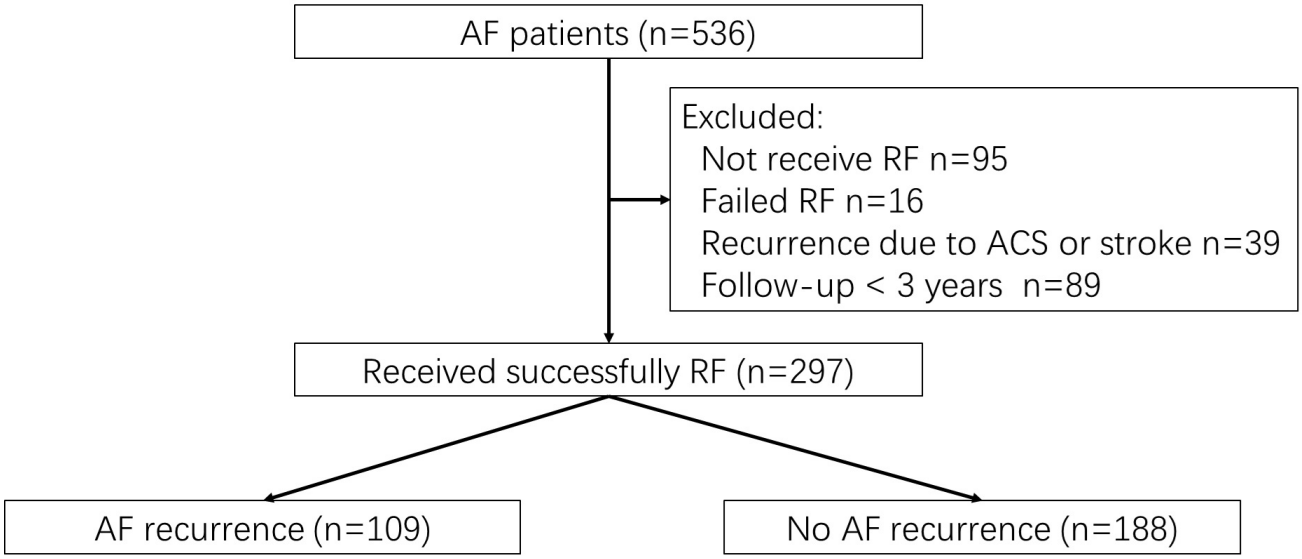


**Fig. 1. Flowchart of patients' enrollment.** AF, atrial fibrillation; RF, radiofrequency ablation; ACS, acute coronary syndrome.

age, obesity, AF duration, LAD, PersAF, and high levels of C-reactive protein before surgery.

### *Recurrence Rates in Different Groups*

The recurrence rates of AF during different follow-up periods after grouping were calculated according to different factors identified in multivariate analysis (Table 3, Fig. 2). Older patients were more likely to have atrial fibrillation again after three years, but there was no significant difference in the first two years. People with obesity were more likely to have atrial fibrillation again starting from the second year after radiofrequency ablation ($p < 0.05$). People with chronic atrial fibrillation were more likely to have atrial fibrillation again starting from the first year after surgery ($p < 0.05$). The effects of LAD, PersAF, and preoperative elevated C-reactive protein (CRP) (Fig. 2) on the recurrence rate and disease course were comparable, with significant differences starting from the first year after surgery ($p < 0.05$).

## Discussion

AF recurrence after radiofrequency ablation can lead to recurrent palpitations, palpitations, and even blood pressure drops and shock caused by rapid ventricular rate. Conversely, it can undermine patients' confidence in treatment and even lead to doctor–patient disputes. Therefore, it is important to assess the risk of recurrence before the procedure. Moreover, sufficient preoperative communication, adequate intraoperative ablation, rigorous postoperative monitoring, and appropriate drug intervention are necessary. In this study, patients with AF that was successfully ablated were followed up for a long term. Three-year follow-up data were collected. The total recurrence rate within 3 years after successful AF ablation was 36.7%, whereas the 1- and 2-year recurrence rates were 11.1% and 22.6%, respectively. Statistical analysis identified several factors that were associated with atrial fibrillation recurrence. These included old age, obesity (BMI $\geq$27 kg/m$^2$), AF duration, LAD, PersAF, and high preoperative C-reactive protein levels. Further analysis showed that different factors had different impacts on the rate of recurrence; however, most of the negative effects of these factors were already evident during the follow-up period in the first year after surgery.

Previous studies have mainly focused on short-term recurrence of atrial fibrillation after radiofrequency ablation. One study found that nearly half of patients (46.77%) experienced recurrence within the first three months [17]. Another study of a larger group of patients found that 38% recurred within 90 days [13]. A third study reported a recurrence rate of 28% within the first 90 days [18]. A more recent study showed that 78.9% of patients were free from symptomatic recurrence for at least 12 months [19]. Therefore, the overall AF recurrence rate after 3 months to 1 year shows a decreasing trend. The study found a lower rate of atrial fibrillation recurrence at one year compared to previous studies. This improvement may be due to advancements in ablation technology, equipment upgrades, and optimization of drug treatment in recent years. A few studies have analyzed the recurrence rate and related factors of late-stage AF. Long-term follow-up studies have shown that the recurrence rate can increase over time. One study found that the rate increased from 5.8% at two years to 25.5% at five years [20]. Another study found that the rate of arrhythmia-free survival decreased over time, with most recurrences happening within six months after ablation [21]. A large-sample study compared patients with persistent atrial fib-

**Table 1. Comparison of the baseline characteristics between the recurrence and non-recurrence groups.**

| Characteristics | Recurrence | Non-recurrence | t/$X^2$ value | *p*-value |
|---|---|---|---|---|
| | n = 109 | n = 188 | | |
| Age (years) | 67.4 ± 5.7 | 65.9 ± 5.1 | 2.339 | 0.020 |
| Male (n, %) | 76 (69.7) | 125 (66.5) | 0.330 | 0.566 |
| History (n, %) | | | | |
| Smoking | 21 (19.3) | 43 (22.9) | 0.531 | 0.466 |
| Alcohol | 34 (31.2) | 47 (25.0) | 1.334 | 0.248 |
| Hypertension | 32 (29.4) | 67 (35.6) | 1.225 | 0.268 |
| CAD | 25 (22.9) | 48 (25.5) | 0.251 | 0.616 |
| Stroke | 11 (10.1) | 26 (13.8) | 0.884 | 0.347 |
| Diabetes | 10 (9.2) | 24 (12.8) | 0.878 | 0.349 |
| AF | | | | |
| AF duration (years) | 4.1 ± 0.8 | 3.7 ± 0.6 | 4.886 | <0.001 |
| LAD (mm) | 39.9 ± 3.6 | 38.5 ± 3.2 | 3.469 | 0.001 |
| PersAF (n, %) | 45.0 (47.9) | 49.0 (52.1) | 7.389 | 0.007 |
| BMI (kg/$m^2$) | 24.9 ± 2.8 | 24.2 ± 2.3 | 2.331 | 0.020 |
| SBP (mmHg) | 132.8 ± 12.5 | 134.6 ± 12.9 | 1.172 | 0.242 |
| Fast glucose (mmol/L) | 6.4 ± 1.3 | 6.6 ± 1.2 | 1.342 | 0.180 |
| TC (mmol/L) | 5.8 ± 0.6 | 5.9 ± 0.5 | 1.542 | 0.124 |
| TG (mmol/L) | 2.6 ± 0.7 | 2.7 ± 0.7 | 1.187 | 0.236 |
| ALT (U/L) | 28.7 ± 4.2 | 28.0 ± 3.8 | 1.472 | 0.142 |
| Creatine (μmol/L) | 81.3 ± 7.9 | 80.4 ± 7.1 | 1.010 | 0.313 |
| CRP (μg/L) | 642.0 ± 93.0 | 615 ± 76 | 2.714 | 0.007 |
| WBC (×$10^9$/L) | 8.1 ± 1.7 | 7.8 ± 1.4 | 1.643 | 0.102 |
| Hemoglobin (g/L) | 150.8 ± 6.4 | 149.5 ± 5.8 | 1.240 | 0.216 |
| Platelet (×$10^9$/L) | 192.4 ± 20.8 | 195.3 ± 21.7 | 1.127 | 0.261 |
| Follow-up medication (n, %) | | | | |
| Statins | 37.0 (33.9) | 51.0 (27.1) | 1.538 | 0.215 |
| ACEI/ARB | 26.0 (23.9) | 43.0 (22.9) | 0.037 | 0.847 |
| Aspirin | 63.0 (57.8) | 118.0 (62.8) | 0.715 | 0.398 |

ALT, alanine aminotransferase; BMI, body mass index; CAD, coronary artery disease; LAD, left atrial diameter; PersAF, persistent atrial fibrillation; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; WBC, white blood cell; ACEI, angiotensin conversion enzyme inhibitor; ARB, angiotensin receptor blocker; CRP, C-reactive protein.

**Table 2. Multivariate logistic regression analysis of factors associated with AF recurrence.**

| Factors | *p*-value | OR | 95% CI |
|---|---|---|---|
| Age ≥65 years | 0.009 | 1.94 | 1.19–3.30 |
| Obesity | 0.017 | 2.18 | 1.13–4.19 |
| AF duration | 0.028 | 1.77 | 1.05–2.96 |
| Left atrial diameter | 0.045 | 1.60 | 1.01–2.62 |
| PersAF | 0.011 | 1.92 | 1.17–3.21 |
| Elevated CRP | 0.006 | 2.65 | 1.43–4.75 |

AF, atrial fibrillation; PersAF, persistent atrial fibrillation.

rillation (PersAF) to those with paroxysmal atrial fibrillation (PAF). It found that the recurrence rate increased more quickly in the PersAF group [22]. In this study, the 3-year recurrence rate was 36.7%, which is relatively low.

This study found several factors that were linked to atrial fibrillation recurrence within three years after radiofrequency ablation. These factors were identified using both simple and more complex statistical methods. As people get older, they are more likely to experience health problems and other negative outcomes. In this study, the recurrence risk of older patients within 3 years after radiofrequency ablation was significantly increased, which may be because older patients have different complications, longer duration, and more pronounced myocardial remodeling, which are closely related to AF and its recurrence [23]. Obesity also increases the recurrence risk after radiofrequency ablation for AF, which is consistent with some previous reported [24,25]. A review of multiple studies found that obesity was associated with a higher risk of atrial fibrillation recurrence after radiofrequency ablation. However, it did not increase the risk of other complications. The researchers also found that this effect was stronger in older patients. Another review of multiple studies found that people with the highest body mass index were more likely to have

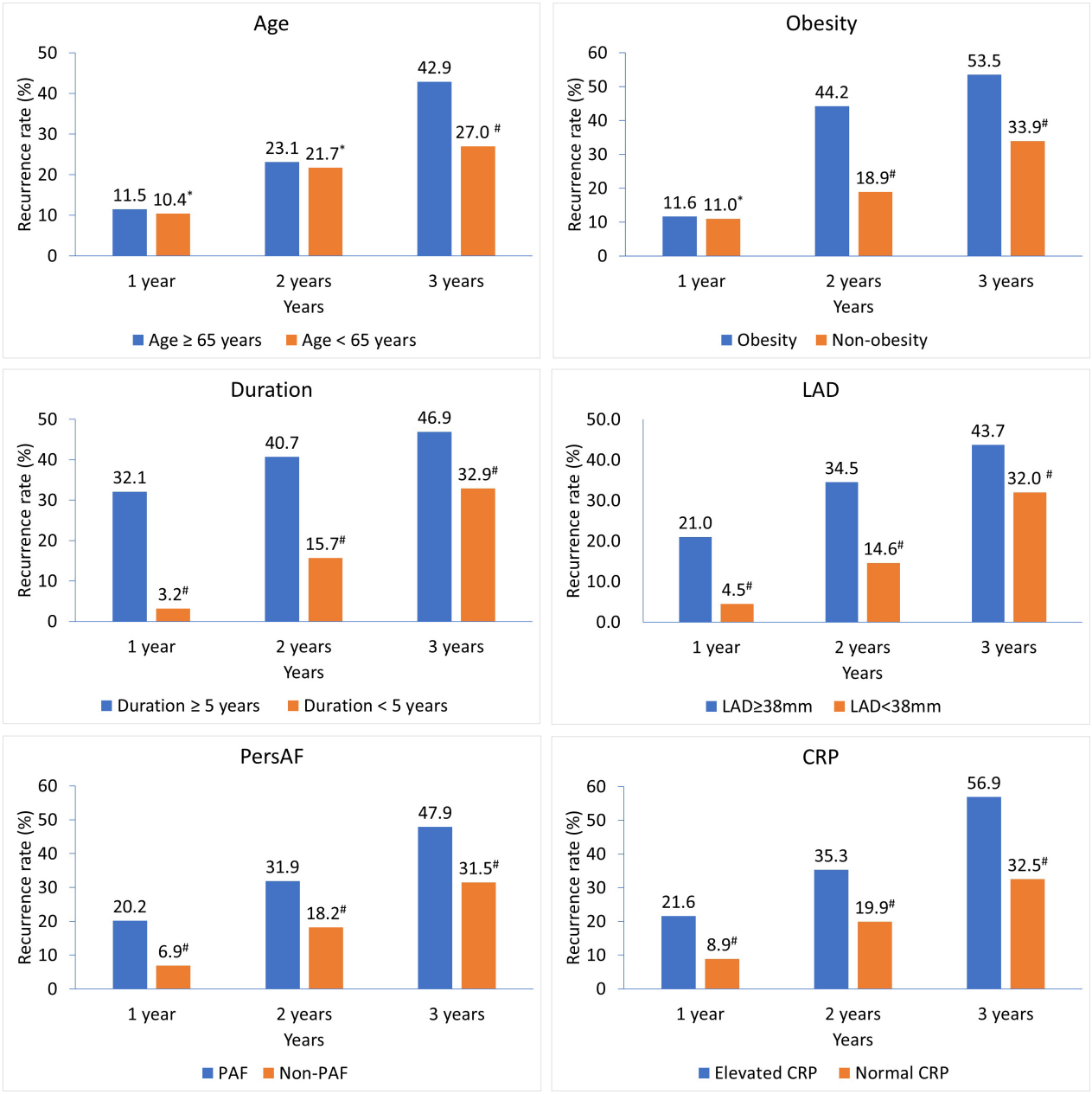


**Fig. 2. Recurrence rate in different groups.** $^{*}p > 0.05$, $^{\#}p < 0.05$. CRP, C-reactive protein; LAD, left atrial diameter; PersAF, persistent atrial fibrillation.

atrial fibrillation recurrence and other complications after radiofrequency ablation compared to those with the lowest body mass index [26]. This study also found that a longer history of atrial fibrillation was associated with a higher risk of recurrence, which is similar to some previous data. Another review included six studies and found that people who had atrial fibrillation for a shorter time before the procedure were less likely to have a recurrence [27]. In a large-sample retrospective cohort study, Li *et al.* [14] included 1763 patients with AF who underwent radiofrequency ablation, and late recurrence was noted in 643 (36.5%) patients at a median follow-up of 35 months. A more complex statistical analysis demonstrated that chronic AF was an independent risk factor for recurrence (HR = 1.80) [14]. The size of the left atrium is also a risk factor [28], as it can lead to changes in the structure of the heart [16,22]. Similarly, in our study, PersAF increased the recurrence risk after AF surgery, which was confirmed in the study by Wokhlu *et al.* and D'Ascenzo *et al.* [22,29]. In recent years, CRP has received widespread attention in clinical practice, and many patients undergo routine CRP testing after admission. In this study, patients with high CRP levels before radiofrequency ablation had higher recurrence rates during follow-up and showed differences from the first year after surgery. CRP is a marker of inflammation in the body. It is associated with an increased risk of heart disease and other health

**Table 3. Recurrence in different groups (n = 297).**

| Groups | 1 year | 2 years | 3 years |
|---|---|---|---|
| n | 33 (11.1) | 67 (22.6) | 109 (36.7) |
| Age | | | |
| ≥65 years (n = 182) | 21 (11.5) | 42 (23.1) | 78 (42.9) |
| <65 years (n = 115) | 12 (10.4) * | 25 (21.7) * | 31 (27.0) # |
| Obesity | | | |
| Yes (n = 43) | 5 (11.6) | 19 (44.2) | 23 (53.5) |
| No (n = 254) | 28 (11.0) * | 48 (18.9) # | 86 (33.9) # |
| AF duration | | | |
| ≥5 years (n = 81) | 26 (32.1) | 33 (40.7) | 38 (46.9) |
| <5 years (n = 216) | 7 (3.2) # | 34 (15.7) # | 71 (32.9) # |
| Left atrial diameter | | | |
| ≥38 mm (n = 119) | 25 (21.0) | 41 (34.5) | 52 (43.7) |
| <38 mm (n = 178) | 8 (4.5) # | 26 (14.6) # | 57 (32.0) # |
| PersAF | | | |
| Yes (n = 94) | 19 (20.2) | 38 (31.9) | 45 (47.9) |
| No (n = 203) | 14 (6.9) # | 29 (18.2) # | 64 (31.5) # |
| High CRP (>0.5 mg/L) | | | |
| Yes (n = 51) | 11 (21.6) | 18 (35.3) | 29 (56.9) |
| No (n = 246) | 22 (8.9) # | 49 (19.9) # | 80 (32.5) # |

AF, atrial fibrillation; PersAF, persistent atrial fibrillation. Compared with data above, $^{*}p > 0.05$, $^{\#}p < 0.05$.

problems. A study revealed a close relationship between CRP and cardiac remodeling [30]. Watanabe *et al.* [31] reported that there was a relationship between C-reactive protein (CRP) levels and the size of the left atrium. People with paroxysmal atrial fibrillation had a larger left atrium compared to those without ($p < 0.001$). Additionally, a longer AF duration was associated with higher CRP levels and a larger LAD [31].

One of the strengths of this study is that it focused on common clinical factors that are related to AF recurrence after radiofrequency ablation. It did not use indicators from radiofrequency ablation nor used indicators that are currently rare or not actually applied in clinical practice. The obtained risk factors are clear indicators in clinical practice, which facilitate doctors' quick judgment in decision-making. However, this study also has some shortcomings. First, this is a retrospective study, and some patients were not included in the analysis because they were lost during follow-up and had incomplete data, which may lead to case selection bias. Second, it was conducted at only one hospital and involved a relatively small number of patients. To confirm the findings of this study and others, a larger study involving multiple hospitals is needed.

## Conclusions

This retrospective study confirmed that age, obesity, AF duration, LAD, AF type, and preoperative C-reactive protein levels were closely related to AF recurrence within 3 years after radiofrequency ablation. These findings will help clinicians evaluate the risk of AF recurrence and make reasonable follow-up plans.

## Availability of Data and Materials

The datasets used and/or analyzed during the current study were available from the corresponding author on reasonable request.

## Author Contributions

TL and NL had a substantial contributions to the conception and design of the work and acquisition of data for the work. YD, TL and NL had a substantial contribution to the acquisition and interpretation of the data and wrote and revised the manuscript. All authors read and approved the final manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Ethics Approval and Consent to Participate

All procedures involving human participants in this study were conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study received approval from the Ethics Committee of Medical Research Ethics Committee of the First Affiliated Hospital of Jinzhou Medical University (2024-08-20). Individual informed consent was waived by Ethic committee. All procedures were conducted in accordance with the relevant guidelines and regulations outlined in the Declaration of Helsinki.


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## Conflict of Interest

The authors declare no conflict of interest.

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