

Significance of Clinical and Biochemical Markers in Predicting Atrial Fibrillation Recurrence after Catheter Ablation

Khasan I. Uralov^{1*}, Nodir U. Zakirov¹, Baxtiyor Dj. Amirkulov¹, Ravshanbek D. Kurbanov¹

¹Republican Specialized Cardiology Scientific Practical Medicine Center, Tashkent, Uzbekistan

Abstract

Background: Pulmonary vein isolation, particularly via radiofrequency ablation (RFA), is a well-established and effective treatment strategy recommended in international clinical guidelines for patients with symptomatic, drug-resistant atrial fibrillation (AF). This study aimed to investigate the incidence and risk factors of early and late recurrence of AF following RFA.

Methods and Results: This prospective, randomized, open-label study included 67 patients (70.1% male) diagnosed with recurrent AF. Any atrial tachyarrhythmia episode lasting more than 30 seconds was defined as a recurrence. All patients underwent RFA of the pulmonary veins (without the CARTO system) between 2022 and 2025. Clinical and laboratory parameters were analyzed before ablation for their association with recurrence.

Early recurrence (ER) was observed in 30 (44.8%) patients, while late recurrence (LR) occurred in 32 (47.8%) patients. Multivariate logistic regression revealed that diabetes mellitus and C-reactive protein (CRP) level at the end of the blanking period remained the only independent predictors of ER. CRP levels demonstrated strong predictive value for early recurrences (AUC = 0.93), with a cutoff point of 1.95 mg/L, a sensitivity of 90%, and a specificity of 85.7% ($P < 0.001$). In ROC analysis for CRP and diabetes combined, the AUC reached 0.957, demonstrating a very high discriminative capacity. The sensitivity was 96.7%, and the specificity was 90.9%, confirming the high accuracy and reliability of the prognostic model ($P < 0.001$).

For late recurrence, multivariate logistic regression revealed that CRP, AF duration, left atrial volume index (LAVI), and erythrocyte sedimentation rate (ESR) were identified as independent predictors of the outcome. In the ROC analysis of 12-month recurrence predictors, the model demonstrated strong statistical significance ($P = 0.000$), with an AUC of 0.83. Although ER was not identified as an independent predictor in the logistic regression model, the ROC analysis demonstrated the predictive relevance of CRP, AF duration, LAVI, ESR, and ER rate, with sensitivity exceeding 75% and specificity above 80%.

Conclusion: Elevated CRP levels and diabetes are strong independent predictors of early AF recurrence after catheter ablation. Longer AF duration, larger left atrial size, increased ESR, and early recurrence rate also contribute to late recurrence. Combined clinical and biochemical evaluation may enhance individualized risk stratification and post-ablation management. (International Journal of Biomedicine. 2025;15(4):653-659.)

Keywords: atrial fibrillation • radiofrequency ablation • recurrence • C-reactive protein • diabetes mellitus

For citation: Uralov KhI, Zakirov NU, Amirkulov BDj, Kurbanov RD. Significance of Clinical and Biochemical Markers in Predicting Atrial Fibrillation Recurrence after Catheter Ablation. International Journal of Biomedicine. 2025;15(4):653-659. doi:10.21103/Article15(4)_OA1

Abbreviations

AH, arterial hypertension; **AF**, atrial fibrillation; **AI**, atherogenic index; **CRP**, C-reactive protein; **DM**, diabetes mellitus; **ESR**, erythrocyte sedimentation rate; **ER**, early recurrence; **eGFR**, estimated glomerular filtration rate; **ESR**, erythrocyte sedimentation rate; **HDL-C**, high-density lipoprotein cholesterol; **IHD**, ischemic heart disease; **IVS**, interventricular septum; **LA**, left atrium; **LVEF**, left ventricular ejection fraction; **LVEDD**, left ventricular end-diastolic diameter; **LVESD**, left ventricular end-systolic diameter; **LVMI**, left ventricular mass index; **LR**, late recurrence; **LAVI**, left atrial volume index; **LDL-C**, low-density lipoprotein cholesterol; **PW**, posterior wall; **PVI**, pulmonary vein isolation; **RBC**, red blood cells; **RFA**, radiofrequency ablation; **RA**, right atrium; **TSH**, thyroid-stimulating hormone; **TC**, total cholesterol; **TG**, triglycerides; **WBC**, white blood cells.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia encountered in clinical practice, and its global prevalence continues to rise each year. In 2021, approximately 52.5 million people worldwide were reported to have AF or atrial flutter, representing a 137% increase over 1990. The age-standardized global prevalence rate was estimated at 620.5 cases per 100,000 population.¹ According to other sources, the number of AF cases globally increased from 33.5 million in 2010 to nearly 59 million in 2019.² The presence of AF increases the risk of stroke by at least fivefold, with more than 20% of cardioembolic strokes being directly related to AF. Moreover, AF is characterized by its recurrent nature, reduced quality of life, and substantial healthcare costs.³

Pulmonary vein isolation (PVI), particularly via radiofrequency ablation (RFA), is a well-established and effective treatment strategy recommended in international clinical guidelines for patients with symptomatic, drug-resistant AF. In some cases, especially for paroxysmal AF, ablation is also considered as a first-line rhythm control strategy. Compared with pharmacological therapy, catheter ablation has demonstrated superior efficacy in maintaining sinus rhythm, improving quality of life, reducing hospitalizations due to heart failure, and lowering the risk of stroke and cardiovascular mortality.⁴

Despite these benefits, AF recurrence after PVI remains a significant clinical challenge. Long-term rhythm control after a single ablation procedure is achieved in only about half of patients, with most recurrences occurring within the first year—the period considered to be the most vulnerable.⁵ Early recurrence (ER) (within 3 months after RFA) is reported in 20%–40% of patients, depending on the type of AF (paroxysmal or persistent), the patient population, and the monitoring method. Although these arrhythmias were previously regarded as clinically insignificant, growing evidence now supports ER as a strong predictor of subsequent relapse and long-term procedural failure. In other words, the presence of ER markedly increases the likelihood of late recurrence (LR) (between 3 and 12 months after RFA).⁶

The one-year recurrence rate varies among studies. Meta-analyses have reported that 25%–40% of patients experience recurrence within a year after a single ablation procedure, depending on the monitoring methods, AF type, and recurrence definition criteria. Continuous or implantable monitoring devices often detect asymptomatic paroxysms, leading to higher reported recurrence rates.⁶

Various predictors of AF recurrence have been proposed in the literature, including clinical, social, and lifestyle characteristics, as well as procedural parameters, laboratory findings, and echocardiographic markers. However, methodological and clinical heterogeneity among studies has led to inconsistent results. Therefore, identifying reliable clinical and biochemical predictors of AF recurrence after PVI is crucial for optimizing patient selection, tailoring post-procedural management, and improving long-term outcomes.

This study aimed to investigate the incidence and risk factors of early and late AF recurrence following RFA.

Materials and Methods

This prospective, randomized, open-label study included 67 patients (70.1% male) diagnosed with recurrent AF. Among them, 46 had paroxysmal and 21 had persistent AF. All patients underwent RFA of the pulmonary veins (without the CARTO system) between 2022 and 2025.

Before RFA, all patients underwent the standard examination: 12-lead ECG, transthoracic echocardiography, transesophageal echocardiography to exclude left atrial appendage thrombus, 24-hour Holter monitoring, complete blood count, biochemical tests (ALT, AST, urea, creatinine, glucose, lipid profile, and CRP). In patients over 50 years of age, coronary angiography was performed to diagnose coronary artery disease. All patients received anticoagulant therapy before surgery in accordance with current guidelines.⁷ Patients who had previously taken amiodarone discontinued it at least 40 days before the procedure. To assess the presence of inflammation at the end of the blanking period, CRP levels were re-measured. Clinical and laboratory parameters were analyzed before ablation for their association with recurrence.

Electrophysiological Study and RFA

The procedure was performed under fluoroscopic guidance (C-arm Siemens) and local anesthesia (0.5% novocaine or lidocaine). The right jugular and bilateral femoral veins were punctured, and transseptal access to the left atrium was achieved via PREFACE introducers (Biosense Webster). Pulmonary vein anatomy and size were assessed using an angiographic catheter, then replaced with a Lasso catheter. Circular mapping of the pulmonary veins was performed to evaluate the size and electrical activity of the muscular sleeves. During sinus rhythm, double or multicomponent potentials were recorded along the pulmonary vein ostia—low-frequency components representing the left atrium and high-frequency components representing pulmonary vein activity. In complex cases, coronary sinus pacing was used to differentiate them. Electrical isolation was achieved by circumferential ablation around the venous ostia, starting from the earliest activation site, divided into 12 segments (Biosense Webster Stockert 70 Ablation System). Ablation parameters: temperature 40–44 °C, power 30–35 W, irrigation rate 17–30 mL/min. Post-procedural assessments of pulmonary vein refractoriness, AF inducibility, fragmented activity, and conduction times were performed.

After the procedure, patients received class IC antiarrhythmic drugs (propafenone, n=33; lappaconitine hydrobromide, n=34) for three months, anticoagulant therapy, and additional symptomatic management as indicated. Outpatient follow-up lasted 12 months after ablation.

During follow-up, patients were evaluated at 3, 6, 9, and 12 months with 24-hour Holter monitoring and echocardiography. Unscheduled visits were performed in cases of recurrent arrhythmia, hospital admission, or emergency service contact, with reasons for hospitalization verified via phone interviews. Any atrial tachyarrhythmia episode lasting more than 30 seconds (AF, atrial flutter, or atrial tachycardia) was defined as a recurrence. Patients were categorized into two groups based on recurrence timing: the ER group and the LR group.

Statistical analysis was conducted using IBM SPSS Statistics, version 27. Quantitative variables with normal distribution were expressed as mean \pm standard deviation ($M \pm SD$); non-normally distributed variables—as median (interquartile range); categorical variables—as absolute numbers and percentages. Comparisons between two independent groups were made using the Student's t-test (for normally distributed data) or the Mann–Whitney U test (for non-normal data). Categorical variables were analyzed using Fisher's exact test or Pearson's χ^2 test, as appropriate. Predictors of AF recurrence were assessed using ROC curve analysis and logistic regression. ROC analysis was used to evaluate the predictive performance of key variables and to determine the optimal cut-off points, along with their corresponding sensitivity and specificity. Logistic regression was performed to identify independent predictors of recurrence; variables with $P < 0.25$ in univariate analysis were entered into the multivariate model. Statistical significance was set at $P < 0.05$.

Results

Baseline clinical characteristics of the study patients are presented in Table 1. Early recurrence was observed in 30 (44.8%) patients, while late recurrence occurred in 32 (47.8%) patients.

The median number of AF-free days was 142 days (range: 17.5–600 days). Among patients with recurrence, the proportion of males was 60% in the ER group and 56.3% in the LR group. The mean age of the cohort was 51.5 ± 11.9 years. Patients with recurrence tended to be older: 54.43 ± 9.1 vs. 49.1 ± 13.4 years ($P=0.06$) at 3 months and 54.78 ± 9.9 vs. 48.5 ± 12.8 years ($P=0.029$) at 12 months (Table 1).

A history of COVID-19 infection was present in 61% of patients, with no significant difference between groups. Among patients with recurrence, the duration of AF was significantly longer at 12 months (5 [3–8] years vs. 2 [1–6] years, $P=0.008$). Arterial hypertension and ischemic heart disease were observed in 74.6% of all patients and were more frequent in those with recurrence, though without statistical significance. Myocarditis and idiopathic AF were reported in 15% and 10.4% of cases, respectively.

Diabetes mellitus was significantly more prevalent in the recurrence groups at 3 months (26.7% vs. 5.4%, $P=0.034$) and at 12 months (25% vs. 5.7%, $P=0.039$). Echocardiographic evaluation revealed that patients with recurrence had larger LA diameters and LAVI at 3 months (4.45 (4.15–4.7) cm vs. 41.5 (3.85–4.35) mm, $P=0.004$; 27 (24–32.7 vs. 23 (21–28) mL/m², $P=0.004$). These differences remained more pronounced at 12 months ($P<0.001$ in both cases). IVS and PW thickness tended to be greater in the recurrence groups, though not statistically significant. LVEF was preserved in both groups.

Table 1.

Baseline clinical characteristics of the study patients.

Characteristics	Total n=67	3 months		P-value	12 months		P-value
		Recurrence n= 30	No recurrence n= 37		Recurrence n=32	No recurrence n=35	
Men, n (%)	47 (70.1%)	18 (60%)	29 (78.37%)	0.11	18 (56.3%)	29 (82.9%)	0.03
Women, n (%)	20 (29.9%)	12 (40%)	8 (21.63%)		14 (43.8%)	6 (17.1%)	
Mean age, years	51.52 \pm 11.88	54.43 \pm 9.1	49.1 \pm 13.4	0.06	54.78 \pm 9.9	48.5 \pm 12.8	0.029
COVID 19, n (%)	41 (61%)	16 (53.3%)	25 (67.6%)	0.23	19 (59.4%)	22 (62.9%)	0.77
Rural residence, n (%)	36 (53.7%)	16 (53.3%)	20 (54%)	1.0	18 (56.2%)	18 (51.4%)	0.7
Follow-up duration, month Me [IQR]	22 (19–31)	20 (19–25)	27 (18–32)	0.196	21 (19–28)	23 (15–31)	0.8
AF duration, month Me [IQR]	4 (2–7)	4 (3–6)	2 (1–8)	0.64	5 (3–8)	2 (1–6)	0.008
Paroxysmal, n (%)	46 (68.7%)	20 (66.7%)	26 (70.3%)	0.79	19 (59.4%)	27 (77.1%)	0.18
Persistent, n (%)	21 (31.3%)	10 (33.3%)	11 (29.7%)		13 (40.6%)	8 (22.9%)	
CHA2DS2VASc score, Me [IQR]	2 (0–3)	2 (1–4)	1 (0–2)	0.011	2 (1–4)	1 (0–2)	0.014
HASBLED score, Me [IQR]	1 (0.5–2)	2 (1–2)	1 (0–2)	0.011	2 (1–2)	1 (0–2)	0.004
AH/IHD, n (%)	50 (74.6%)	26 (86.7%)	24 (64.9)	0.1	27 (84.4%)	23 (65.7%)	0.15
Myocarditis, n (%)	10 (15%)	3 (10%)	7 (18.9%)		2 (6.3%)	8 (22.9%)	
Idiopathic AF, n (%)	7 (10.4%)	6 (16.2%)	1 (3.3%)		3 (9.4%)	4 (11.4%)	
DM, n (%)	10 (14.9%)	8 (26.7%)	2 (5.4%)	0.034	8 (25%)	2 (5.7%)	0.039
BMI, Me [IQR]	29.2 (27.5–31.24)	28.9 (27.6–31.6)	29.4 (27.5–31.4)	0.73	29.3 (26.7–32.3)	29.3 (27.6–30.9)	0.4
Obesity, n (%)	27 (40.3%)	11 (36.7%)	16 (43.2%)	0.58	15 (46.9%)	12 (34.3%)	0.29

Table 1 (continued).

Baseline clinical characteristics of the study patients.

Characteristics	Total n=67	3 months		P-value	12 months		P-value
		Recurrence n= 30	No recurrence n= 37		Recurrence n=32	No recurrence n=35	
Echocardiographic Parameters							
IVS, cm Me [IQR]	1 (0.9-1.15)	1.07 (0.95-1.2)	1 (0.89-1.12)	0.06	1.07 (0.95-1.2)	1 (0.9-1.11)	0.158
PW, cm Me [IQR]	0.95 (0.9-1.05)	0.97 (0.91-1.1)	0.93 (0.9-1.0)	0.09	0.95 (0.9-1.1)	0.93 (0.9-1.0)	0.316 0.13
LAD, cm Me [IQR]	4.3 (3.95-4.55)	4.45 (4.15-4.7)	4.15 (3.85-4.35)	0.004	4.45 (4.2-4.6)	4.0 (3.8-4.35)	<0.001
LAVI, mL/m ² Me [IQR]	25.9 (22-30.4)	27 (24-32.7)	23 (21-28)	0.004	28 (25.3-34.6)	22.1 (20.5-26.7)	<0.001
LVEDD, cm Me [IQR]	4.9 (4.8-5.2)	4.9 (4.8-5.3)	4.9 (4.7-5.2)	0.62	4.9 (4.75-5.3)	4.9 (4.8-5.1)	0.626
LVESD, cm Me [IQR]	3.4 (3.2-3.6)	3.4 (3.3-3.6)	3.4 (3.2-3.7)	0.86	3.45 (3.25-3.6)	3.4 (3.2-3.5)	0.4
LVEF, % Me [IQR]	60.45 (58.8-62.5)	60.3 (56.4-62.2)	61.5 (59.3-62.8)	0.177	60.3 (56.3-62.2)	62 (59.3-62.7)	0.1
RA med, cm Me [IQR]	4 (3.85-4.2)	4 (3.9-4.25)	4 (3.8-4.1)	0.7	4.05 (3.95-4.25)	3.95 (3.7-4.1)	0.056
LVMI, g/m ² Me [IQR]	86 (75-102)	95 (82.3-102.8)	81.2 (66.1-90.2)	0.03	97.4 (81.2-102.7)	80.9 (72.7-89.1)	0.01
Biochemical Parameters							
CRP, mg/L Me [IQR]	0.5 (0.5-5)	5 (5-5)	0.5 (0.5-0.5)	<0.001	5 (1.95-5)	0.5 (0.5-0.5)	<0.001
TSH, mIU/mL (M±SD)	2.31±1.11	2.48±1.32	2.16±0.91	0.265	2.59±0.99	2.05±1.17	0.05
Free T4, pmol/mL (M±SD)	17.84±2.7	18.9±2.9	16.9±2.17	0.002	18.7±3.1	17±1.95	0.008
TC, mg/dL (M±SD)	192.4±42.1	198.6±26.2	187.8±51.47	0.28	195.9±32.3	189.2±49.6	0.5
TG, mg/dL Me [IQR]	139 (97-202)	148 (104-178)	131 (97-202)	0.6	139 (92-170.5)	131 (98-204)	0.37
HDL-C, mg/dl (M±SD)	44.7±10.7	44.7±12.5	44.7±9.1	0.98	45.2±12.8	44.2±8.5	0.7
VLDL-C, mg/dL Me [IQR]	31 (20-40)	29.5 (21-36)	31 (20-41)	0.57	28 (18.5-34.5)	33 (20.5-44)	0.13
LDL-C, mg/dL (M±SD)	115.37±42	121.73±31	110.2±49	0.27	119.3±33.83	111.8±48.6	0.46
AI (M±SD)	3.4 (2.3-4.2)	3.67±1.13	3.35±1.3	0.3	3.6±1.25	3.4±1.22	0.5
Glucose, mmol/L Me [IQR]	5.1 (4.8-5.8)	5 (4.4-5.5)	5.3 (4.9-5.8)	0.48	5 (4.5-5.65)	5.3 (4.8-5.8)	0.51
Urea, mmol/L (M±SD)	6±1.39	6.4±1.36	5.66±1.35	0.027	6.44±1.3	5.6±1.37	0.013
Creatinine, μmol/L (M±SD)	90.7±21.5	98.5±18.6	84.38±21.8	0.007	98.97±21.1	83.14±19.1	0.002
eGFR, mL/min/1.73m ² Me [IQR]	79 (65-100)	71 (64-79)	98 (73-110)	<0.001	67.5 (54.5-79)	88 (76.5-106)	<0.001
Uric acid, mg/dL, Me [IQR]	5 (4.3-5.7)	5.6 (4.5-6.9)	4.9 (4.3-5.2)	0.01	5.2 (4.4-5.8)	5.0 (4.3-5.6)	0.27
Complete Blood Count							
Platelets, ×10 ⁹ /L Me [IQR]	255 (228-308)	255 (232-296)	242 (221-343)	0.96	255 (227-293)	242 (228-342)	0.67
WBC, ×10 ⁹ /L (M±SD)	6.4±1.40	6.3±1.52	6.5±1.32	0.6	6.4±1.52	6.4±1.32	0.9
RBC, ×10 ¹² /L (M±SD)	4.83±0.55	4.78±0.58	4.87±0.52	0.5	4.7±0.56	4.95±0.52	0.059
ESR, mm/60min Me [IQR]	3 (2-15)	2 (2-18)	3 (2-11)	0.8	4 (2-23)	3 (2-11)	0.014

Among laboratory parameters, CRP levels were significantly higher in the recurrence groups at both 3 and 12

months ($P<0.001$ in both cases). Baseline urea and creatinine were also higher in patients with recurrence at 3 months

(6.4 ± 1.36 vs. 5.66 ± 1.35 mmol/L, $P=0.027$; 98.5 ± 18.6 vs. 84.38 ± 21.8 μ mol/L, $P=0.007$) and 12 months (6.44 ± 1.3 vs. 5.6 ± 1.37 mmol/L, $P=0.013$; 98.97 ± 21.1 vs. 83.14 ± 19.1 μ mol/L; $P=0.002$). eGFR was significantly lower in patients with recurrence at 3 months (71 (64-79) vs. 98 (73-110) mL/min/1.73m², $P<0.001$). This difference remained significant at 12 months ($P<0.001$). Serum uric acid levels were elevated only in the recurrence group at 3 months (5.6 (4.5-6.9) vs. 4.9 (4.3-5.2) mg/dL; $P=0.01$). Lipid profile parameters did not differ significantly between groups.

Thyroid hormones showed notable variation: free T4 levels were higher in the recurrence group at 3 months (18.9 ± 2.9 vs. 16.9 ± 2.17 pmol/mL; $P=0.002$) and 12 months (18.7 ± 3.1 vs. 17 ± 1.95 pmol/mL; $P=0.008$). Complete blood count parameters were comparable between groups. However, at 12 months, the recurrence group showed a trend toward a lower erythrocyte count (4.7 ± 0.56 vs. $4.95 \pm 0.52 \times 10^{12}$ /L; $P=0.059$) and a significantly higher ESR (4 (2-23) vs. 3 (2-11) mm/60min; $P=0.014$).

Overall, analysis of the blanking period and the subsequent 12-month follow-up after RFA identified several clinical, echocardiographic, and biochemical variables associated with AF recurrence. Notably, higher CHA₂DS₂-VASc and HAS-BLED scores, presence of DM, left atrial enlargement and remodeling, and elevated left ventricular mass index were found to be important recurrence predictors.

Among biochemical markers, elevated CRP levels at the end of the ER period, increased free T4, and renal dysfunction parameters were significantly associated with recurrence. Additionally, elevated serum uric acid levels were associated with the end of the ER period. At 12 months, recurrence was more frequent among older and female patients, and those with longer AF duration, higher TSH levels, and elevated ESR values.

Logistic regression analysis was performed to identify independent predictors of AF recurrence after RFA. While several factors showed significance in univariate analysis, multivariate logistic regression revealed that DM and CRP level at the end of the blanking period remained the only independent predictors of ER. The obtained logistic regression model was found to be statistically significant ($P<0.001$). The Nagelkerke pseudo-R² value was 0.81, indicating that the model has a strong explanatory power for the outcome variable. According to the regression coefficient analysis, the presence of DM and elevated CRP levels during the blanking period were identified as factors directly associated with an increased likelihood of AF recurrence. Specifically, the presence of DM increased the odds of recurrence by 26-fold (95% CI: 1.93–351.8), while each 1mg/L rise in CRP level increased the risk of recurrence by 3.58 times (95% CI: 2.1–6.1) (Figure 1a). The model demonstrated strong predictive performance: sensitivity - 96.7%, specificity - 89.2%, and overall accuracy - 92.5%.

For late recurrence, CRP, AF duration, LAVI, and ESR were identified as independent predictors of the outcome. The obtained logistic regression model was found to be statistically significant ($P<0.001$), with a Nagelkerke pseudo-R² value of 0.71.

- Each 1 mg/L rise in CRP level increased the recurrence risk by 2.14 times (95% CI: 1.4–3.2; $P<0.01$)
- Each additional year of AF duration increased the recurrence risk by 1.26 times (95% CI: 1.05–1.52; $P<0.05$)
- Each 1 mL rise in LAVI increased the recurrence risk by 1.18 times (95% CI: 1.04–1.35; $P<0.05$)
- Each 1 mm/h rise in ESR increased the recurrence risk by 1.10 times (95% CI: 1.01–1.20; $P<0.05$) (Figure 1b).

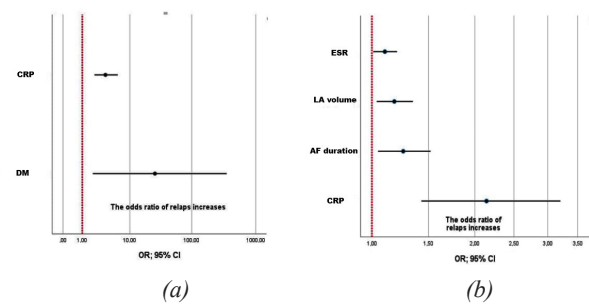


Fig. 1. Logistic regression analysis: (a) ER and (b) LR.

The model demonstrated strong predictive performance: sensitivity – 84.4%, specificity – 80.0%, and overall accuracy – 82.1%.

The area under the ROC curve (AUC) reflecting the relationship between 3-month AF recurrence and CRP level was 0.93, indicating excellent discriminative ability. The obtained model was statistically significant ($P=0.000$). The cutoff value for CRP was 1.95mg/L; thus, patients with CRP ≥ 1.95 mg/L were predicted to have a high risk of recurrence. At this threshold, the sensitivity and specificity were 90% and 85.7%, respectively (Figure 2A). When ROC analysis was performed for CRP and DM combined, the AUC reached 0.957, demonstrating a very high discriminative capacity. The sensitivity was 96.7%, and the specificity was 90.9%, confirming the high accuracy and reliability of the prognostic model ($P<0.001$) (Figure 2b).

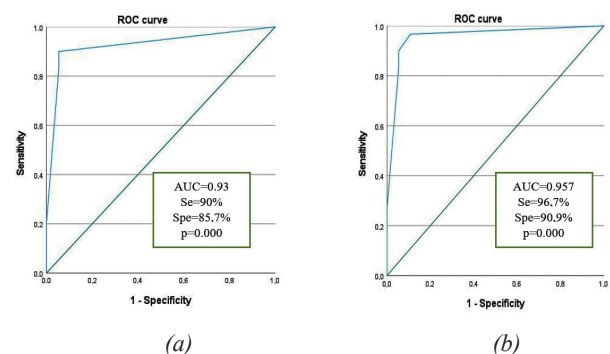


Fig. 2. ROC analysis of 3-month recurrence predictors: (a) CRP and (b) CRP+DM.

In the ROC analysis of 12-month recurrence predictors, the model demonstrated strong statistical significance ($P=0.000$), with an AUC of 0.83. Although ER was not

identified as an independent predictor in the logistic regression model, the ROC analysis demonstrated the predictive relevance of CRP, AF duration, LAVI, ESR, and ER rate, with sensitivity exceeding 75% and specificity above 80% (Figure 3).

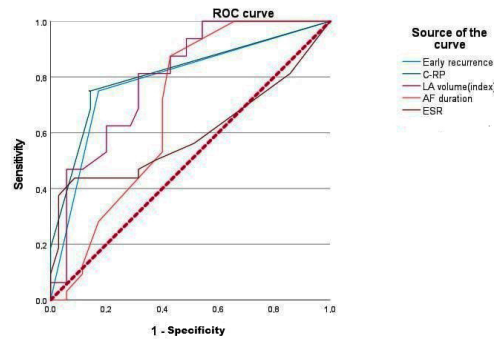


Fig. 3. ROC analysis of 12-month recurrence predictors.

Discussion

The findings of this study provide important insights into the clinical and biochemical factors associated with AF recurrences during both the early post-RFA blanking period and the subsequent 12-month follow-up. Recurrences were observed in nearly half of the patients within the early and late phases, underscoring the clinical relevance of recurrence. The study identified DM and elevated CRP levels as independent predictors of AF recurrence after RFA. Previous research has consistently shown DM to be an independent risk factor for AF development.^{8,9} Chronic hyperglycemia leads to oxidative stress, accumulation of advanced glycation end-products, myocardial fibrosis, and remodeling of ion channels and gap junctions in the atrial myocardium. These changes reduce conduction velocity, impair homogeneity of impulse propagation, and prolong the action potential duration, thereby creating a substrate conducive to AF initiation and maintenance.¹⁰ High CRP levels were also identified as a strong predictor, consistent with prior studies.¹¹ Elevated CRP reflects ongoing myocardial inflammation and fibrotic activity, which promote post-ablation electrical remodeling. In ROC analysis, CRP showed an AUC of 0.93 (95% CI: 0.85–0.99), indicating excellent discriminatory power. The cutoff value of 1.95 mg/L was identified as an optimal threshold; patients with CRP \geq 1.95 mg/L were at a significantly higher risk of recurrence. Additionally, ESR also indicates the inflammation process and is identified as an LR predictor in our study. Among echocardiographic parameters, increased LA size and LAVI were also significantly associated with recurrence, in line with previous literature.⁷ LA enlargement is recognized as a key marker of both electrical and mechanical remodeling. Increased LVMI and impaired renal function were noted, suggesting a multifactorial mechanism of recurrence.¹² During a 12-month follow-up, female sex and older age were associated with a higher recurrence risk, partially consistent with prior studies.^{13,14} Although some discrepancies exist as population, genetic, or structural differences.¹⁵

Conclusion

Analysis of the blanking period and 12-month follow-up after RFA revealed several clinical, echocardiographic, and biochemical parameters associated with AF recurrence. Specifically, higher CHA₂DS₂-VASc and HAS-BLED scores, the presence of DM, LA remodeling, increased LV mass, as well as elevated CRP, free T₄, and markers of renal dysfunction, were found to be significantly correlated with recurrence. According to multivariate logistic regression analysis, DM and CRP levels at the end of the blanking period remained independent predictors of recurrence.

Although several factors influenced LR, only LA enlargement, longer AF history, and elevated levels of CRP, ESR, and ER rate were identified as independent predictors of LR. These findings indicate that the above factors serve as reliable prognostic markers of AF recurrence after RFA and should be considered in clinical practice for patient follow-up and management. Combined clinical and biochemical evaluation may enhance individualized risk stratification and post-ablation management.

Ethical Approval

This study was approved by the Ethics Committee at Republican Specialized Cardiology Scientific Practical Medicine Center; Protocol No. 5 dated June 10, 2025. Written informed consent was obtained from all the participants.

Competing Interests

The authors declare that they have no conflicts of interest.

References

- Li X, Li Z, He H, Wang S, Su H, Kang G. Global burden and health inequality of atrial fibrillation/atrial flutter from 1990 to 2021. *Front Cardiovasc Med*. 2025 May 21;12:1585980. doi: 10.3389/fcvm.2025.1585980. PMID: 40469078; PMCID: PMC12133759.
- Linz D, Gawalko M, Betz K, Hendriks JM, Lip GYH, Vinter N, Guo Y, Johnsen S. Atrial fibrillation: epidemiology, screening and digital health. *Lancet Reg Health Eur*. 2024 Feb 1;37:100786. doi: 10.1016/j.lanepe.2023.100786. PMID: 38362546; PMCID: PMC10866942.
- Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, et al.; ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J*. 2021 Feb 1;42(5):373-498. doi: 10.1093/eurheartj/ehaa612. Erratum in: *Eur Heart J*. 2021 Feb 1;42(5):507. doi: 10.1093/eurheartj/ehaa798. Erratum in: *Eur Heart J*. 2021 Feb 1;42(5):546-547. doi: 10.1093/eurheartj/ehaa945. Erratum in:

- Eur Heart J. 2021 Oct 21;42(40):4194. doi: 10.1093/eurheartj/ehab648. PMID: 32860505.
4. Mark DB, Anstrom KJ, Sheng S, Peterson ED, Poole JE, Piccini JP, et al. Catheter ablation versus medical therapy for atrial fibrillation: long-term follow-up of the CABANA trial. *J Am Coll Cardiol*. 2023;81(5):479–492. doi:10.1016/j.jacc.2022.11.037.
 5. Stauffer N, Knecht S, Badertscher P, Krisai P, Hennings E, Serban T, et al. Repeat catheter ablation after very late recurrence of atrial fibrillation after pulmonary vein isolation. *Europace*. 2024 May 2;26(5):euae096. doi: 10.1093/europace/euae096. PMID: 38607938; PMCID: PMC11068271.
 6. Darby AE, DiMarco JP. Recurrent atrial fibrillation after catheter ablation: incidence and predictors. *Heart Rhythm*. 2016;13(2):281–287. doi:10.1016/j.hrthm.2015.08.024.
 7. Tzeis S, Gerstenfeld EP, Kalman J, Saad EB, Sepehri Shamloo A, Andrade JG, et al. 2024 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. *Europace*. 2024 Mar 30;26(4):euae043. doi: 10.1093/europace/euae043. Corrected and republished in: *Heart Rhythm*. 2024 Sep;21(9):e31–e149. doi: 10.1016/j.hrthm.2024.03.017. PMID: 38587017; PMCID: PMC11000153.
 8. Aune D, Feng T, Schlesinger S, Janszky I, Norat T, Riboli E. Diabetes mellitus, blood glucose and the risk of atrial fibrillation: A systematic review and meta-analysis of cohort studies. *J Diabetes Complications*. 2018 May;32(5):501–511. doi: 10.1016/j.jdiacomp.2018.02.004. Epub 2018 Feb 17. PMID: 29653902.
 9. Creta A, Providência R, Adragão P, de Asmundis C, Chun J, Chierchia G, et al. Impact of Type-2 Diabetes Mellitus on the Outcomes of Catheter Ablation of Atrial Fibrillation (European Observational Multicentre Study). *Am J Cardiol*. 2020 Mar 15;125(6):901–906. doi: 10.1016/j.amjcard.2019.12.037. Epub 2019 Dec 30. PMID: 31973808.
 10. Liu C, Fu H, Li J, Yang W, Cheng L, Liu T, Li G. Hyperglycemia aggravates atrial interstitial fibrosis, ionic remodeling and vulnerability to atrial fibrillation in diabetic rabbits. *Anadolu Kardiyol Derg*. 2012 Nov;12(7):543–50. doi: 10.5152/akd.2012.188. Epub 2012 Aug 8. PMID: 22877897.
 11. Meyre PB, Sticherling C, Spies F, Aeschbacher S, Blum S, Voellmin G, et al. C-reactive protein for prediction of atrial fibrillation recurrence after catheter ablation. *BMC Cardiovasc Disord*. 2020 Sep 29;20(1):427. doi: 10.1186/s12872-020-01711-x. PMID: 32993521; PMCID: PMC7526257.
 12. Boyalla V, Harling L, Snell A, Kralj-Hans I, Barradas-Pires A, Haldar S, et al. Biomarkers as predictors of recurrence of atrial fibrillation post ablation: an updated and expanded systematic review and meta-analysis. *Clin Res Cardiol*. 2022 Jun;111(6):680–691. doi: 10.1007/s00392-021-01978-w.
 13. Wesselink R, Mossink B, Meulendijks ER, van den Berg NWE, Neefs J, Kawasaki M, et al. Women Have More Recurrences of Atrial Fibrillation than Men after Thoracoscopic Ablation and Suffer More from Established Risk Factors. *J Clin Med*. 2023 Apr 2;12(7):2650. doi: 10.3390/jcm12072650.
 14. Kawamura I, Aikawa T, Yokoyama Y, Takagi H, Kuno T. Catheter ablation for atrial fibrillation in elderly patients: Systematic review and a meta-analysis. *Pacing Clin Electrophysiol*. 2022 Jan;45(1):59–71. doi: 10.1111/pace.14413. Epub 2021 Dec 9. PMID: 34816458.
 15. Nielsen J, Kragholm KH, Christensen SB, Johannessen A, Torp-Pedersen C, Kristiansen SB, et al. Periprocedural complications and one-year outcomes after catheter ablation for treatment of atrial fibrillation in elderly patients: a nationwide Danish cohort study. *J Geriatr Cardiol*. 2021 Nov 28;18(11):897–907. doi: 10.11909/j.issn.1671-5411.2021.11.005. PMID: 34908927; PMCID: PMC8648543.

***Corresponding author:** Khasan I. Uralov. E-mail: hasan.uralov0319@gmail.com