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ORIGINAL RESEARCH

The Predictive Value of the Neutrophil Percentage-to-Albumin Ratio for Early Recurrence of Atrial Fibrillation After Radiofrequency Catheter Ablation

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Purpose: The neutrophil percentage-to-albumin ratio (NPAR) serves as a robust prognostic indicator for adverse cardiovascular events. This pioneering study is the first to examine the relationship between the NPAR and post-ablation atrial fibrillation (AF) recurrence in patients undergoing radiofrequency catheter ablation (RFCA).

Patients and Methods: In this retrospective analysis, 394 treatment-naïve AF patients undergoing initial RFCA were enrolled and stratified into recurrence and non-recurrence cohorts. The study utilized four composite inflammatory indices as biomarkers: neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and NPAR. Cox proportional hazards regression modeling was employed to assess the prognostic significance of post-ablation AF recurrence following RFCA. Receiver operating characteristic (ROC) curve analysis evaluated the discriminative capacity of inflammatory biomarkers, utilizing area under the curve (AUC) quantification as the principal measure for prognostic stratification accuracy.

Results: With a median follow-up duration of 12.00 months, early AF recurrence occurred in 88 cases (22.34%), demonstrating significantly higher incidence rates in patients with elevated NPAR levels. Univariate Cox regression identified significant associations between AF recurrence and inflammatory indices (NLR, PLR, SII, NPAR), persistent AF phenotype, heart failure status, age, serum creatinine levels, left ventricular ejection fraction (LVEF), B-type natriuretic peptide (BNP) levels, and left atrial diameter (LAD) (all $P < 0.05$). Multivariable analysis demonstrated NPAR, persistent AF, and LAD as independent predictors of post-ablation recurrence (adjusted $P < 0.05$). ROC curve analysis demonstrated superior predictive performance of the NPAR for AF recurrence compared to SII, PLR, and NLR, with AUC of 0.706 ($P < 0.01$; 95% CI: 0.642–0.770). Kaplan-Meier survival analysis demonstrated significantly increased 1-year AF recurrence rates among patients with elevated NPAR levels exceeding 15.36 (log-rank $P < 0.01$).

Conclusion: The NPAR represents a promising novel biomarker for risk stratification of post-ablation AF recurrence in patients undergoing RFCA.

Keywords: neutrophil percentage-to-albumin ratio, atrial fibrillation, radiofrequency catheter ablation, recurrence

Introduction

Atrial fibrillation (AF), a prevalent cardiac arrhythmia characterized by chaotic atrial electrical activity and impaired mechanical function, represents a major clinical cardiovascular disorder that significantly increases the risk of stroke, heart failure, and thromboembolic complications.[1] Despite being a well-established therapeutic intervention for AF, RFCA continues to demonstrate suboptimal long-term efficacy, with persistently elevated recurrence rates posing significant clinical challenges. Following catheter ablation, the 1-year recurrence rates were 10–30% for paroxysmal atrial fibrillation (PAF) and 25–35% for non-paroxysmal atrial fibrillation (NPAF), respectively.[2] Therefore, elucidating

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and modulating the determinants of post-ablation AF recurrence holds critical clinical relevance for formulating targeted therapeutic approaches to mitigate arrhythmia recurrence in this patient population.

Inflammatory pathways serve as a pivotal driver in the pathophysiological continuum of AF, primarily mediated through maladaptive electrophysiological derangements and fibrotic tissue alterations within the atrial substrate.[3] Previous studies have identified the performance of increased levels of C-reactive protein (CRP) and other systemic inflammatory markers for predicting new-onset,[4] recurrence,[5] and left atrial thrombus (LAT)[6] in patients with AF. Emerging clinical evidence highlights the SII as a robust independent predictor of postprocedural atrial fibrillation recurrence, demonstrating superior risk stratification capability in contemporary interventional cardiology practice.[7] Therefore, evaluating the circulating levels of inflammatory and oxidative stress biomarkers and their possible applications in AF diagnosis and management has been the focus of many efforts.

The NPAR, an emerging multidimensional inflammatory biomarker incorporating neutrophil dynamics and albumin homeostasis, has demonstrated high-fidelity correlation with systemic inflammatory burden quantification in translational research. Elevated neutrophil counts portend adverse prognostic significance as a predictor of adverse clinical outcomes by virtue of their pivotal role as mediators of maladaptive inflammatory cascades in the pathophysiological processes underlying tissue injury.[8,9] Albumin had many functions, including osmoregulation, antioxidation and antiinflammation.[10,11] Accumulating evidence from methodologically rigorous investigations has validated the NPAR as a robust prognostic utility across the cardiovascular disease spectrum, spanning acute coronary syndromes (ACS), chronic coronary syndromes (CCS), acute decompensated heart failure (ADHF), cardiogenic shock (CS), and AF phenotypes.[9,11–14]

Notwithstanding the limited evidence elucidating the prognostic significance of the NPAR in AF outcomes, this prospective cohort study was specifically designed to assess the predictive performance of NPAR for post-ablation early AF recurrence following RFCA.

Materials and Methods

Study Population

This single-center retrospective cohort study enrolled consecutive patients with de novo non-valvular atrial fibrillation (NVAF) who underwent initial RFCA at Weifang People's Hospital during the December 2022 to December 2023 study period. Eligible patients met all criteria: (1) NVAF or paroxysmal/non-paroxysmal AF diagnosis; (2) age >18 years; (3) candidates for de novo AF ablation; (4) written informed consent; and (5) preprocedural anticoagulation ≥3 weeks or TEE-confirmed LAA thrombus exclusion. Exclusion criteria comprised: (1) systemic inflammatory/autoimmune diseases; (2) hepatic/renal dysfunction; (3) severe valvulopathy; (4) active malignancy with <1-year prognosis; (5) incomplete clinical/imaging data; and (6) follow-up discontinuation.

Data Collection and Definitions

Participant data—including sociodemographics, medical history, smoking status, laboratory results, and procedural details—were extracted from electronic health records. Demographic/clinical parameters comprised age, sex, Body mass index (BMI), smoking/alcohol status, Diabetes mellitus (DM), hypertension, Coronary heart disease (CHD), stroke/Transient Ischemic Attack (TIA) history, heart failure, and AF phenotypes (paroxysmal/non-paroxysmal). Fasting peripheral venous phlebotomy was performed preprocedurally following ≥8-hour overnight fasting during index hospitalization. Laboratory analyses quantified key hematologic/biochemical parameters: complete blood count (white cells, lymphocytes, monocytes, neutrophils, platelets), neutrophil percentage (NE%), uric acid, blood urea nitrogen, creatinine, fasting glucose, lipid profile (total cholesterol, triglycerides, LDL-C, HDL-C), BNP, and albumin. Echocardiographic evaluation included LAD, LVEDD, and LVEF. The CHA_2DS_2-VASc score components comprised: hypertension, heart failure, diabetes, vascular disease, age 65–74 years, and female sex (1 point each); prior stroke/TIA or age ≥75 years (2 points each).[15] This research received ethical approval from Weifang People's Hospital Institutional Review Board (KYLL20250425-2) and complied strictly with Helsinki Declaration protocols. Variable definitions: NPAR = (Neutrophil% in WBC)×100/Albumin (g/dL); SII = (Platelets × Neutrophils)/Lymphocytes; NLR = Neutrophils/Lymphocytes; PLR = Platelets/Lymphocytes. BMI = Weight (kg)/Height (m^2). DM = Oral hypoglycemics/

insulin use or admission HbA1c ≥ 6.5%. CHD diagnosis required ≥50% stenosis in ≥1 major coronary artery. AF classification: PAF (<7 days, typically <48 h); NPAF (>7 days). Duration was calculated from first AF symptom/diagnosis to RFCA date. AF duration was dichotomized using the median cutoff (24 months). AF classification: Paroxysmal (self-terminating/terminated within 7 days); Persistent (sustained >7 days, including cardioversion-terminated episodes). Early AF recurrence comprised documented AF/atrial flutter/tachycardia episodes >30 seconds occurring 3–12 months post-ablation.

Ablation Protocol and Periprocedural Management

Preprocedural transthoracic echocardiography evaluated cardiac structure and function. Preprocedural transesophageal echocardiography or cardiac computed tomography angiography (CTA) ruled out left atrial thrombus. Preablation cardiac CTA evaluated pulmonary vein and left atrial anatomy in all patients. All interventional procedures were conducted under fentanyl-induced analgesia. Femoral venous access was obtained via Seldinger technique, with coronary sinus cannulation using a standard 10-pole catheter. Fluoroscopy-guided single transseptal puncture followed. Following single transseptal puncture, a pentaray catheter (Biosense Webster) was advanced for anatomical modeling. Following anatomical modeling, the pentaray catheter was exchanged for an ablation catheter to perform the procedure. Intravenous unfractionated heparin was initiated peri-transseptally, maintaining ACT 250–300s throughout. Radiofrequency ablation was performed using the CARTO3 3D electroanatomic mapping system (Biosense Webster). All ablation procedures utilized pressure-sensing catheters (ThermoCool SmartTouch SF). The radiofrequency energy was delivered at a power of 40–45 W with a target temperature of 25–30°C, and the saline irrigation rate was maintained at 15–20 mL/min. Lesion quality was guided by the Ablation Index (AI), with the following site-specific target values: 500–550 for the anterior wall, 350–400 for the posterior wall, 450–500 for the cavotricuspid isthmus and roof line, and 550–600 for the mitral isthmus. Circumferential pulmonary vein isolation (CPVI) was universally implemented as the standard therapeutic intervention for all patients with AF. For non-paroxysmal AF, operators performed adjunctive linear ablation at their discretion (left atrial roof, floor, posterior wall, mitral/tricuspid isthmus). Following ablation, electrical cardioversion was performed to restore sinus rhythm in cases of persistent AF. The procedural endpoint was the complete electrical isolation of all pulmonary veins, which was rigorously verified by confirming both entrance block and exit block. The verification method involved differential pacing from the coronary sinus and from within the pulmonary veins. Per ESC guidelines, all eligible patients received postprocedural oral anticoagulation and amiodarone for ≥3 months.[16] Refractory to oral amiodarone, patients underwent electrical cardioversion for rhythm maintenance.

Outcomes and Follow-Up

Postdischarge follow-up occurred at 1, 3, 6, and 12 months, comprising clinical evaluation, 12-lead ECG, and 24-hour Holter monitoring. Symptomatic AF patients underwent supplemental outpatient evaluation. If the patients had any AF-related symptoms, we performed further ECGs and Holter ECG examinations. Atrial arrhythmias (AF, atrial flutter, or atrial tachycardia) during the 90-day post-ablation blanking period were excluded from recurrence analysis. Early recurrence of AF was defined as documented episodes of AF, atrial flutter, or atrial tachycardia lasting ≥30 seconds occurring between 3 months and 1 year post-procedure.

Statistical Analysis

Continuous variables were presented as mean ± SD or median with interquartile range guided by distribution normality assessed via Shapiro–Wilk testing. Continuous variables were analyzed using Student's *t*-test or Mann–Whitney *U*-test according to data distribution normality, while categorical variables were reported as frequency counts with corresponding percentages. Categorical variables were analyzed using chi-square or Fisher's exact tests, with the selection contingent upon expected cell frequencies. To assess the interrelationship between the inflammatory markers (NPAR, NLR, PLR, and SII), Spearman's rank correlation coefficients were calculated. Univariate Cox proportional hazards regression analysis was used to identify potential predictors of AF recurrence, and variables with a p-value < 0.10 were considered for inclusion in the multivariate models. Due to significant multicollinearity observed among the inflammatory markers, we constructed four separate multivariate Cox regression models to prevent biased estimates. Each model

included a single inflammatory marker (NPAR, NLR, PLR, or SII) along with other significant covariates from the univariate analysis to independently evaluate its prognostic value. The proportional hazards (PH) assumption for all final multivariate models was formally tested using the Schoenfeld residuals test, with a p-value > 0.05 indicating the assumption was met. To compare the relative performance and goodness-of-fit of the four parallel models, the Akaike Information Criterion (AIC) was calculated for each. A lower AIC value signifies a better balance between model fit and parsimony. ROC curves were also constructed to determine the optimal cutoff values of the inflammatory indices for predicting early recurrence, with diagnostic accuracy assessed through AUC analysis using the Youden index. Statistical significance was defined as a two-tailed P value < 0.05. All statistical analyses were conducted using IBM SPSS Statistics (version 25.0; IBM Corp, Armonk, NY, USA).

Results

Baseline Characteristics

The study flowchart (Figure 1) details the enrollment process, wherein 394 of 418 consecutive AF patients undergoing first-time RFCA met predefined inclusion criteria and were retained for final analysis. Over the 12-month follow-up period, 88 cases of AF recurrence (cumulative incidence 22.34%) were recorded, with event rates calculated per Kaplan-Meier methodology. Baseline characteristics of patients stratified by AF recurrence status were systematically compared using standardized group-wise analyses, with comprehensive statistical evaluations detailed in Table 1. Patients with AF recurrence were older and had higher rates of smoking, heart failure, and persistent AF versus non-recurrent cases. They also had higher levels of BNP, creatinine, Neutrophil percentage, LVEDD, and LA diameter (P < 0.05). AF recurrence was associated with lower albumin, lymphocyte counts, and LVEF versus non-recurrent cases (all P < 0.05). AF recurrence was associated with elevated NPAR, SII, NLR, and PLR versus non-recurrent cases (all P < 0.05).

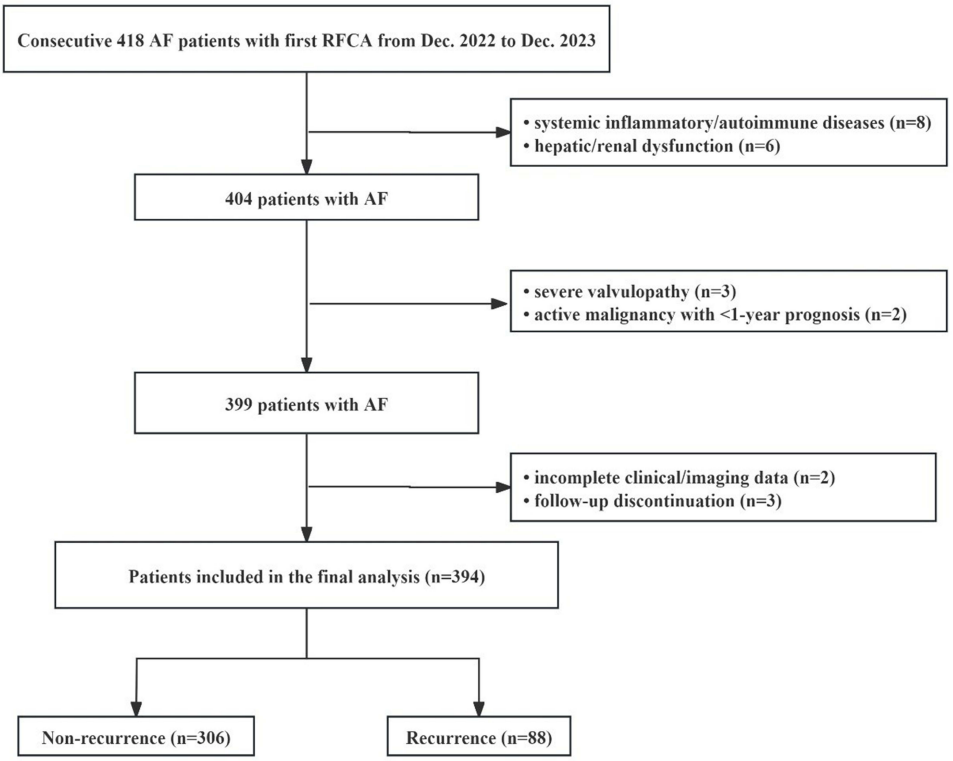

Figure 1 Flow diagram of patient's selection.

Table 1 Baseline Characteristics

Variables	All (n = 394)	Non-Recurrence (n = 306)	Recurrence (n = 88)	P Value
Demographics				
Age, years	64.30±9.60	63.70±9.50	66.20±8.10	0.044
Female,n (%)	170(43.10)	138(45.10)	32(36.40)	0.145
BMI, kg/m2	25.85±3.57	25.87±3.54	25.83±3.73	0.940
Medical history				
Smoking,n (%)	52(13.20)	33(10.80)	19(21.60)	0.008
Drinking,n (%)	21(5.30)	15(4.90)	6(6.80)	0.481
Comorbidities				
Heart failure,n (%)	62(15.70)	38(12.40)	24(27.30)	0.001
Hypertension, n (%)	216(54.80)	170(55.60)	46(52.30)	0.586
DM,n (%)	60(15.20)	42(13.70)	18(20.50)	0.122
CHD,n (%)	127(32.20)	95(31.00)	32(36.40)	0.347
Stroke,n (%)	54(13.10)	41(13.40)	13(14.80)	0.741
NPAF, n (%)	162(41.10)	109(35.60)	53(60.20)	0.000
Laboratory data				
BNP, pg/mL	112(50.70,227.00)	89(41.80,194)	159.80(93.80,357.80)	<0.001
Blood urea, mmol/L	5.70(4.78,6.93)	5.60(4.80,6.90)	6.15(4.53,7.08)	0.268
UA, (μmol/L)	327.00(267.75,393.00)	327.00(269.75,385.00)	327.50(261.75,415.00)	0.311
Creatinine, (μmol/l)	64.00(54.00,75.00)	63.0(53.00,74.00)	78.75(67.50,78.50)	0.023
TC, mmol/L	4.10(3.40,4.90)	4.20(3.50,4.90)	3.90(3.10,4.70)	0.055
TG, mmol/L	1.27(0.96,1.81)	1.28(0.96,1.84)	1.25(0.93,1.66)	0.523
LDL-C, mmol/L	2.61(1.98,3.19)	2.63(2.02,3.22)	2.40(1.74,3.09)	0.054
HDL-C, mmol/L	1.16(0.99,1.41)	1.17(1.01,1.40)	1.15(0.98,1.43)	0.932
Albumin, g/L	41.95(39.37,44.53)	42.10(39.70,45.03)	41.00(38.73,43.58)	0.009
Glucose (mmol/L)	5.40(4.80,6.60)	5.30(4.80,6.40)	5.50(4.83,7.60)	0.085
WBC count ($\times10^9$/L)	5.89(4.99,6.94)	5.91(5.08,6.96)	5.65(4.80,6.87)	0.344
Neutrophils ($\times10^9$/L)	3.57(2.95,4.38)	3.53(2.89,4.36)	3.71(3.05,4.85)	0.092
Lymphocyte ($\times10^9$/L)	1.68(1.36,2.11)	1.77(1.44,2.60)	1.43(1.11,1.89)	<0.001
Monocytes ($\times10^9$/L)	0.36(0.29,0.46)	0.36(0.29,0.46)	0.36(0.28,0.46)	0.888
Platelet count ($\times10^9$/L)	211.00(179.00,253.00)	214.00(181.00,257.5)	202.00(177.25,244.50)	0.108
Neutrophil, %	61.70±9.42	60.37±9.01	66.32±9.42	<0.001
Imaging				
LAD,mm	39.10±5.98	38.27±5.79	41.96±5.78	<0.001
LVEDD,mm	49.40±4.67	49.13±4.59	50.33±4.84	0.023
LVEF, %	62.44±8.37	63.08±8.00	60.19±9.22	0.03
Scoring system				
CHA_2DS_2-VASc score	2.52±1.55	2.50±1.56	2.57±1.48	0.701
Compound biomarkers				
NPAR	14.51(12.92,16.65)	14.24(12.64,16.05)	16.45(13.92,18.16)	<0.001
SII	437.61(319.85,662.47)	415.53(309.88,604.25)	575.77(388.92,744.39)	<0.001
NLR	2.11(1.55,2.99)	1.99(1.47,2.73)	2.79(1.84,3.62)	<0.001
PLR	125.64(99.58,158.99)	121.22(96.61,151.72)	140.61(116.06,174.19)	<0.001

Abbreviations: BMI, Body mass index; NPAF, nonparoxysmal atrial fibrillation; DM, Diabetes mellitus; CHD, Coronary heart disease BNP, B-type natriuretic peptide; UA, uric acid; TC, Total cholesterol; TG, Total glyceride; LDL, Low density lipoprotein cholesterol; HDL, High-density lipoprotein cholesterol; LAD, Left atrial diameter; LVEDD, Left ventricular end-diastolic diameter; LVEF, Left ventricular ejection fraction; NPAR, neutrophil percentage-to-albumin ratio; SII, Systemic immune inflammation; NLR, Neutrophil-lymphocyte ratio; PLR, Platelet-lymphocyte ratio.

Correlation Among Inflammatory Markers

Spearman correlation analysis confirmed strong, significant positive correlations among the four inflammatory markers (Figure S1). For instance, NPAR was strongly correlated with NLR (r = 0.811, p < 0.001), and SII was strongly

Table 2 Discriminatory Performance of the Inflammatory Index

	Cutoff Value	Sensitivity (%)	Specificity (%)	AUC (95% CI)	P Value
NPAR	15.36	0.659	0.68	0.706 (0.642–0.770)	<0.001
NLR	2.34	0.682	0.66	0.693 (0.630–0.756)	<0.001
SII	507.21	0.625	0.647	0.654 (0.589–0.719)	<0.001
PLR	125.44	0.716	0.556	0.634 (0.569–0.700)	<0.001

Abbreviations: NPAR, neutrophil percentage-to-albumin ratio; SII, Systemic immune inflammation; NLR, Neutrophil-lymphocyte ratio; PLR, Platelet-lymphocyte ratio; AUC, area under curve; CI, confidence interval.

correlated with PLR (r = 0.760, p < 0.001). These results underscored the issue of multicollinearity, justifying our analytical strategy of constructing separate multivariate models.

Discriminatory Performance of the Inflammatory Index

ROC analysis assessed the predictive performance of risk factors for AF recurrence post-RFCA. Table 2 compares inflammatory indices predicting early AF recurrence. The NPAR had the highest AUC (0.706 [95% CI 0.642–0.770]). Figure 2 illustrates ROC curves of inflammatory indices with comparative AUC metrics. Kaplan-Meier analysis demonstrated significantly elevated AF recurrence rates in patients with NPAR > 15.36 (log-rank P < 0.01; Figure 3A). Kaplan-Meier analyses using Youden-optimized cutoff thresholds demonstrated significantly increased early AF recurrence rates in patients with elevated SII, PLR, and NLR (log-rank P < 0.01 for all; Figure 3).

Independent Predictive Value of Inflammatory Markers in Multivariate Analysis

Univariate Cox regression analysis identified several potential predictors of early AF recurrence, including all four inflammatory markers (Table 3, *univariate results not shown in final table*). To assess their independent predictive power while avoiding multicollinearity, we built four separate multivariate models, with results detailed in Table 3. The proportional hazards assumption was met for all models (all global p > 0.05).

After adjusting for core covariates (Age, Serum creatinine, NPAF, Heart Failure, LAD, LVEF, BNP), each inflammatory marker remained a significant independent predictor of AF recurrence: NPAR (HR: 1.173, 95% CI: 1.104–1.247, p < 0.001, in Model 1), NLR (HR: 1.112, 95% CI: 1.042–1.185, p < 0.001, in Model 2), PLR (HR: 1.007, 95% CI: 1.003–1.011, p < 0.001, in Model 3), SII (HR: 1.001, 95% CI: 1.000–1.002, p = 0.001, in Model 4). In all models, NPAF and LAD were also consistent independent predictors. To determine the optimal model, we compared their Akaike Information Criterion (AIC) values. The model including NPAR (Model 1) achieved the lowest AIC of

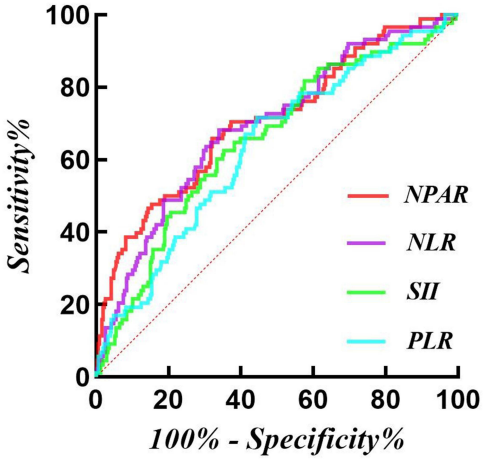

Figure 2 Receiver operating characteristic (ROC) curve analysis of the NPAR, NLR, SII, and PLR to predict AF recurrence.

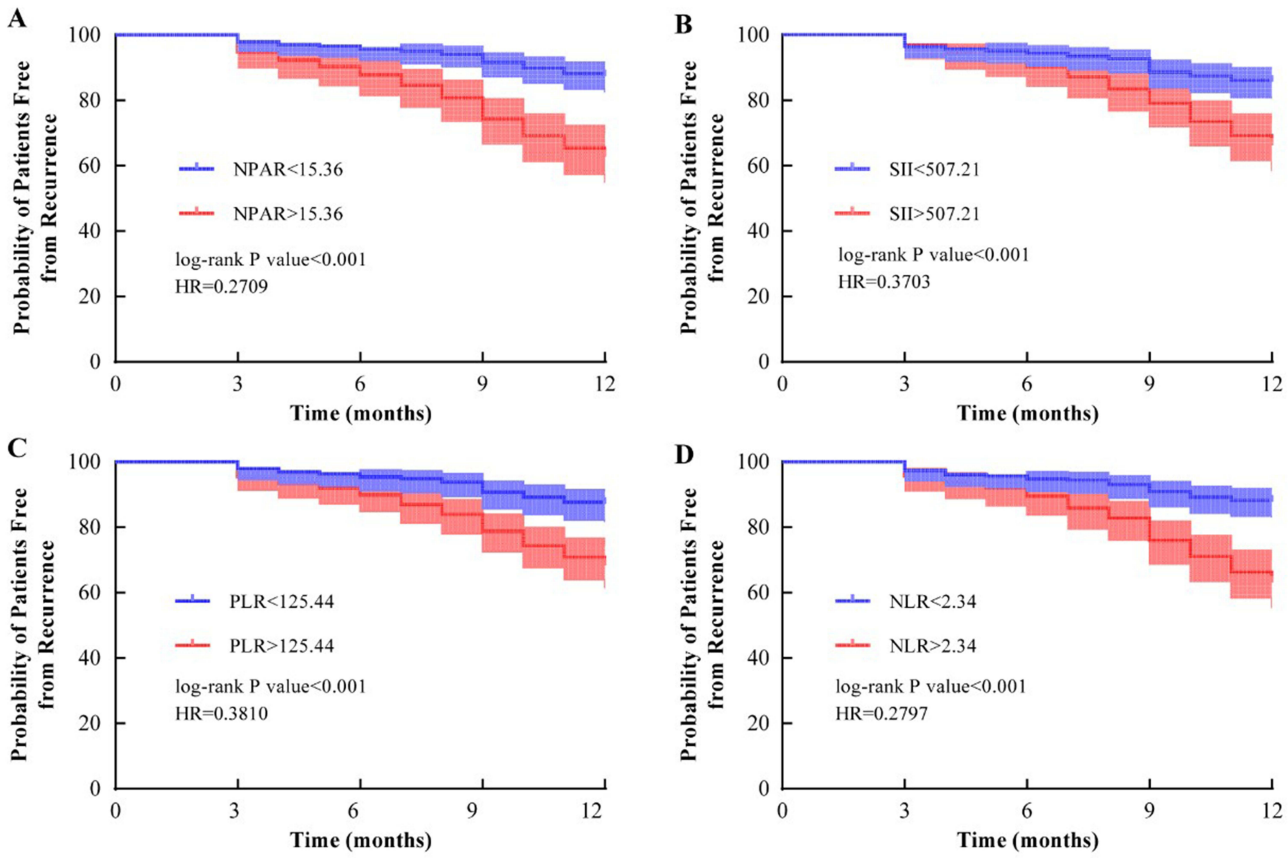

Figure 3 Kaplan–Meier survival estimates of atrial fibrillation recurrence in patients with atrial fibrillation undergoing stratified by radiofrequency catheter ablation the (**A**) NPAR, (**B**) SII, (**C**) PLR, and (**D**) NLR.

993.441, indicating it provided the best balance of model fit and parsimony. This was superior to the models for NLR (AIC = 1000.910), PLR (AIC = 1001.133), and SII (AIC = 1004.589), statistically reinforcing NPAR as the most robust inflammatory predictor in our cohort.

Table 3 Separate Multivariate Cox Proportional Hazards Models Evaluating the Independent Predictive Value of Four Inflammatory Markers for Atrial Fibrillation Recurrence

Variable	Model 1 (NPAR)		Model 2 (NLR)		Model 3 (PLR)		Model 4 (SII)	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Inflammatory Marker								
NPAR	1.173 (1.104–1.247)	<0.001						
NLR			1.112 (1.042–1.185)	<0.001				
PLR					1.007 (1.003–1.011)	<0.001		
SII							1.001 (1.000–1.002)	0.001
Core Covariates								
Age	1.004 (0.980–1.029)	0.745	1.013 (0.990–1.038)	0.269	1.012 (0.988–1.036)	0.327	1.017 (0.994–1.042)	0.149
Serum creatinine	1.003 (0.992–1.014)	0.614	1.003 (0.992–1.015)	0.563	1.009 (0.998–1.019)	0.118	1.006 (0.995–1.017)	0.312
NPAF	1.715 (1.053–2.794)	0.030	1.609 (0.991–2.613)	0.054	1.646 (1.015–2.668)	0.043	1.619 (1.002–2.616)	0.049
Heart Failure	1.507 (0.839–2.708)	0.170	1.483 (0.833–2.639)	0.180	1.340 (0.748–2.401)	0.326	1.396 (0.764–2.551)	0.277
LAD	1.059 (1.016–1.105)	0.007	1.062 (1.018–1.108)	0.005	1.062 (1.019–1.108)	0.005	1.064 (1.020–1.110)	0.004

(*Continued*)

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Table 3 (Continued).

Variable	Model 1 (NPAR)		Model 2 (NLR)		Model 3 (PLR)		Model 4 (SII)	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
LVEF BNP Model Fit	1.009 (0.984–1.034) 1.000 (0.999–1.001)	0.497 0.989	1.008 (0.983–1.033) 1.000 (0.999–1.001)	0.538 0.786	1.001 (0.976–1.026) 1.001 (0.989–1.011)	0.959 0.814	1.007 (0.983–1.033) 1.000 (0.999–1.001)	0.558 0.995
AIC	993.441		1000.910		1001.133		1004.589	

Notes: Each model (Model 1–4) includes a single inflammatory marker plus the same set of core covariates (Age, Serum creatinine, NPAF, Heart Failure, LAD, LVEF, and BNP). The proportional hazards assumption was met for all models ($p > 0.05$).

Abbreviations: HR, hazard ratio; CI, confidence interval; NPAR, neutrophil percentage-to-albumin ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; NPAF, non-paroxysmal atrial fibrillation; LAD, left atrial diameter; LVEF, left ventricular ejection fraction; BNP, B-type natriuretic peptide; AIC, Akaike Information Criterion.

Discussion

Inflammation plays a crucial role in the occurrence and development of AF. Inflammatory mediators induce modifications in atrial electrophysiological characteristics and tissue architecture, thereby promoting susceptibility to AF. These pathophysiological changes are clinically termed electrical remodeling and structural remodeling of the atria, correspondingly. The electrical remodeling in AF traditionally encompasses three hallmark features: abbreviated action potential duration, impaired intercellular electrical coupling, and dysregulated calcium (Ca2+) homeostasis. Notably, connexin proteins (particularly Cx40 and Cx43), which constitute the gap junctions responsible for cardiomyocyte electrotonic coupling, exhibit both quantitative and spatial redistribution under inflammatory conditions - a pathophysiological alteration directly linked to AF progression.[17] The inflammatory state can lead to the recruitment and activation of neutrophils, T cells, platelets, and macrophages. Activated platelets release TGF-β1 into the blood and local tissue to induce atrial fibrosis and structural remodeling, while activated macrophages and neutrophils release pro-inflammatory factors (eg TNF-α, IL-1β, IL-6, and galectin-3) that drive both atrial structural and electrical remodeling.[18] As evidenced by the above discussion, inflammation significantly impacts atrial electrophysiological properties and structural remodeling through multiple mechanisms.

Anti-inflammatory agents have been explored as potential treatment options for AF. Evidence indicates steroids reduce AF incidence in septic patients.[19] Kim et al demonstrated short-term steroid therapy reduces early AF recurrence post-catheter ablation.[20] Despite evidence from multiple studies indicating the beneficial effects of corticosteroids in AF, their clinical utility is limited by the associated adverse effects. Emerging evidence indicates that low-dose colchicine mitigates atrial electrical remodeling and reduces AF recurrence rates, substantiating its antiarrhythmic potential through inflammatory pathway modulation.[21] Although studies have suggested that colchicine may prevent AF recurrence after catheter ablation,[22] its role in preventing the occurrence of AF remains controversial.[23] Nevertheless, this evidence collectively provides further support for the hypothesis that inflammatory processes may drive the pathogenesis and progression of AF. Thus, future research efforts focused on elucidating the inflammatory mechanisms underlying AF and developing novel anti-inflammatory therapeutics are expected to lead to breakthroughs in AF management.

Neutrophils, as key cellular mediators of inflammation, represent an essential leukocyte subpopulation that plays a pivotal role in orchestrating innate immune responses.[24] Studies have demonstrated that in cases of myocardial ischemia, the release of NADPH oxidase, myeloperoxidase, and lipoxygenase from neutrophils contributes to exacerbated oxidative stress and endothelial dysfunction.[25] Neutrophil extracellular traps (NETs), composed of DNA-protein complexes extruded from activated neutrophils, have been implicated in the pathogenesis of multiple cardiovascular disorders. Li et al[26] elucidate NETs formation mechanisms in AF, revealing their cardiotoxic effects via mitochondrial dysfunction and autophagic activation in cardiomyocytes. This work delineates a self-perpetuating cycle where NETs and cardiomyocyte-derived inflammatory mediators synergistically drive AF progression and fibrotic remodeling. These findings implicate neutrophil-mediated inflammation in the pathogenesis of adverse clinical outcomes, suggesting actionable therapeutic targets for mitigating disease progression.[27]

Serum albumin not only serves as an indicator of nutritional status but emerging evidence has revealed its anti-inflammatory,[28] antioxidant,[29] anticoagulant, and antiplatelet aggregation properties,[30] demonstrating its multifaceted involvement in various cardiovascular diseases. Serum albumin demonstrates protective effects against sepsis-induced endothelial dysfunction by attenuating inflammatory and oxidative stress pathways, while hypoalbuminemia potentiates these detrimental mechanisms.[31] A recent retrospective case-control study involving 950 patients with AF and 963 age- and sex-matched non-AF controls in sinus rhythm demonstrated that low serum albumin levels were significantly associated with AF in male patients.[32]

The superior prognostic performance of NPAR over other inflammatory markers like NLR and PLR likely resides in its unique ability to capture two synergistic pathophysiological pathways central to AF recurrence. On one hand, an elevated neutrophil count (the numerator of NPAR) signifies a heightened state of acute inflammation. Neutrophils are key drivers of oxidative stress and release pro-inflammatory cytokines, directly promoting atrial fibrosis and adverse electrical remodeling, which creates a vulnerable substrate for arrhythmia. On the other hand, a low serum albumin level (the denominator) reflects a compromised systemic state. Albumin is not only a major antioxidant and anti-inflammatory protein but also a crucial indicator of nutritional status. Thus, hypoalbuminemia indicates a diminished systemic defense capacity and nutritional reserve, rendering the atrial substrate less resilient to inflammatory insults. Therefore, NPAR functions as a more holistic biomarker. It simultaneously quantifies the degree of inflammatory "attack" (neutrophils) and the body's "defense" and repair capacity (albumin). This "two-hit" perspective explains why it may outperform markers that only capture the cellular inflammatory component. This concept is supported by evidence from other cardiovascular conditions, such as heart failure and acute myocardial infarction, where NPAR has also been shown to be a potent predictor of adverse outcomes, reflecting its role as a robust marker of systemic inflammation and physiological stress.[33,34] Furthermore, a study by Cai et al demonstrated that elevated NPAR values were independently associated with increased 28-day all-cause and cardiovascular mortality rates in octogenarian patients with AF.[35]

NLR, PLR, and SII are composite inflammatory markers that can predict recurrence after catheter ablation in patients with AF. Bazoukis et al[36] showed that postablation NLR was significantly higher in patients with the late AF recurrence and a post-ablation NLR > 3.9 can predict the late AF recurrence with 70% of sensitivity and 38% of specificity. A retrospective cohort study demonstrated that elevated NLR independently predicted adverse AF outcomes, serving as a clinically actionable biomarker for AF prognosis in multivariable-adjusted models.[37] Seçkin Dereli et al demonstrated that elevated PLR independently predicts AF recurrence post-successful electrical cardioversion (ECV) in non-valvular persistent AF patients.[38] A study by Elmas Kaplan et al demonstrated that higher SII index levels are an independent predictor of AF recurrence after cryoablation.[39] Moreover, a recent study also found that the SII index serves as a valuable biomarker for predicting AF recurrence after ablation in hypertensive patients, demonstrating superior predictive performance compared to C-reactive protein (CRP) and high-sensitivity CRP (hsCRP).[40] In conclusion, these inflammatory indices serve as markers of systemic inflammation and offer a reliable tool for assessing the risk of AF recurrence.

To our knowledge, this novel investigation not only pioneers the evaluation of the NPAR for predicting AF recurrence post-radiofrequency catheter ablation but also conducts the first head-to-head comparison of NPAR, SII, NLR, and PLR in forecasting post-procedure arrhythmia recurrence. These findings demonstrate that the NPAR not only exhibits superior predictive accuracy for early AF recurrence post-RFCA but also outperforms established inflammatory indices in prognostic stratification. Given the widespread application of these inflammatory markers in both laboratory and clinical settings, they show promise as cost-effective predictive indicators following radiofrequency ablation for atrial fibrillation. This advancement would enable clinicians to conduct more comprehensive and accurate risk assessments while simultaneously providing improved treatment options.

Limitations

This monocentric observational study, conducted exclusively in a Chinese cohort, has inherent limitations including modest sample size and potential selection bias common to single-center designs. The absence of continuous rhythm monitoring via patient-activated devices or implantable loop recorders (ILRs) in this study may have contributed to under detection of asymptomatic AF episodes, thereby potentially underestimating the true AF recurrence rate. Furthermore, a key limitation is the absence of subgroup analyses. We did not stratify our cohort based on different ablation strategies

(eg, pulmonary vein isolation alone versus more extensive linear or substrate-based ablation), age strata, or body mass index. Different procedural approaches may influence the inflammatory response and long-term outcomes, and the predictive power of NPAR may vary across different patient profiles. Therefore, the predictive stability and robustness of NPAR across these clinically relevant subgroups remain to be confirmed. Future prospective, large-scale, multicenter studies are warranted to validate our findings and to explore whether the prognostic utility of NPAR differs among these diverse patient populations and procedural approaches.

Conclusion

In patients with AF, the NPAR emerged as an independent prognostic predictor of AF recurrence following RFCA, establishing its potential clinical utility as a novel biomarker for post-procedural risk stratification. This study establishes a novel prognostic biomarker enabling clinicians to objectively stratify post-procedural recurrence risk and guide personalized therapeutic interventions.

Abbreviations

NPAR, neutrophil percentage-to-albumin ratio; AF, atrial fibrillation; RFCA, radiofrequency catheter ablation; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; ROC, Receiver operating characteristic; AUC, area under the curve; LVEF, left ventricular ejection fraction; BNP, B-type natriuretic peptide; LAD, left atrial diameter, PAF, paroxysmal atrial fibrillation; NPAF, persistent atrial fibrillation; LAT, left atrial thrombus; BMI, Body mass index; TIA, Transient Ischemic Attack; NETs, Neutrophil extracellular traps.

Data Sharing Statement

Data supporting the findings of this study can be obtained from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

The Ethics Committee of The Weifang People's Hospital reviewed and approved all studies involving human participants (KYLL20250425-2). Informed consent was waived due to the retrospective nature of the study. At the same time, patient data was anonymized or maintained with confidentiality, and this study was in line with the Declaration of Helsinki.

Consent for Publication

All authors approved the final manuscript and the submission to this journal.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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