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The predictive value of pan-immune inflammatory index for early recurrence of atrial fibrillation after cryoablation

Pengyang Gu^{1,2}, Peng Xu³, Yiqun Chen², Jingyu Li^{1,2}, Hanrui Sun^{1,2}, Haixia Xu^{1,2*} and Qi Lu^{1,2*}

Abstract

Objective The pan-immune inflammatory (PIV) index holds prognostic value for cardiovascular diseases. This study aimed to investigate the predictive value of the PIV index regarding recurrence of atrial fibrillation (AF) after cryoballoon ablation (CBA).

Methods The study included 307 patients with AF. Four inflammatory markers, namely, the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune inflammation (SII) index, and PIV index, were used as indicators. COX regression analysis was conducted to evaluate the predictive value of AF recurrence after CBA. A receiver operating characteristic (ROC) curve was plotted, and the area under the curve (AUC) was calculated to evaluate the discriminative power of the indicators.

Result The PIV index [94.9 (168.9,504.9) vs. 143.2 (98.2,210.6), $P < 0.01$] and SII index [366.3 (256.6,491.9) vs. 569.9 (658.1,438.4), $P < 0.01$] were significantly higher in the recurrence group. Univariable COX regression analysis showed that these four indices, persistent AF, and left atrial diameter (LAD) were all associated with AF recurrence. In multivariable regression analysis, the PIV index, persistent AF, and LAD (all $P < 0.05$) were independent predictors of postoperative AF recurrence. The ROC curve analysis showed that the PIV index had a higher predictive value for AF recurrence (AUC = 0.768, $P < 0.01$, 95% CI: 0.696–0.840) than the SII index and NLR. Kaplan–Meier analysis showed that patients with a PIV index > 260.7 had a higher recurrence rate at 1-year follow-up ($P < 0.01$). Subgroup analysis indicated that PIV had a predictive value in patients with different types of AF.

Conclusion PIV index may be a potential biomarker for predicting relapse in patients with AF after CBA.

Keywords Pan-immune inflammatory index, Systemic immune index, Atrial fibrillation, Cryoballoon ablation

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Introduction

Atrial fibrillation (AF) is a prevalent heart rhythm disorder in the health sector, carrying a significant risk of cardiovascular disease. Given its association with an increased stroke risk, disability, and mortality, AF has emerged as an important public health concern worldwide [1]. One of the essential treatment goals for AF is maintaining sinus rhythm. Cryoballoon ablation (CBA) is a novel treatment method that can effectively reduce AF symptoms and maintain sinus rhythm [2]. However, it has been observed that a specific subset of patients continues to experience recurrence following CBA [3]. Identifying and controlling the risk factors for recurrent AF is of great clinical significance for developing a promising strategy to reduce AF recurrence.

Previous research has established a correlation between inflammation and various medical conditions such as hypertension [4], chronic obstructive pulmonary disease [5], atherosclerosis [6], and chronic heart failure [7]. In recent years, an increasing body of research has demonstrated the significant involvement of inflammation in the initiation and perpetuation of left atrial fibrosis and AF [8]. Atrial fibrosis, a pathological alteration, not only impacts the structural integrity of the atrium but also disrupts its electrophysiological function, which could initiate or exacerbate arrhythmias including AF. Prolonged episodes of AF may further contribute to the progression of atrial fibrosis, creating a vicious cycle known as atrial cardiomyopathy [9]. Inflammation plays a vital role in the progression of AF, with C-reactive protein (CRP) emerging as the most extensively utilized inflammatory marker [10]. The findings of a recent clinical study demonstrated the efficacy of the systemic immune inflammation (SII) index [11] in predicting AF recurrence after a cardiovascular procedure. In investigating the factors associated with early recurrence after CBA in patients with AF, a robust association was observed between a novel parameter, the pan-immune inflammatory (PIV) index and clinical outcomes in patients with AF.

The PIV is a comprehensive inflammation index that could serve as a reliable and convenient alternative factor for assessing inflammation in clinical practice. It also serves as a strong prognostic indicator for adverse outcomes in various chronic diseases [12–15]. However, the relationship between the PIV index and clinical outcomes in patients with AF remains unclear. Thus, this study was designed to investigate the predictive value of the PIV index for the early recurrence of AF after CBA.

Materials & methods

Study population

This single-center, nonrandomized study was conducted at the Department of Cardiology, Affiliated Hospital of Nantong University from January 2019 to December

2021. A total of 307 consecutive patients with AF who underwent CBA were included; among whom 65 patients relapsed within one year.

The inclusion criteria were as follows: (1) symptomatic AF; (2) administration of standard anticoagulation therapy for at least 3 weeks before surgery or confirmation through transesophageal echocardiography (TEE) of the absence of thrombus in the left atrial appendage (LAA); and (3) patients with paroxysmal or persistent AF who successfully underwent cryoballoon ablation for the first time. Paroxysmal AF was defined as AF that terminates spontaneously or with intervention within 7 days of onset. Persistent AF was defined as AF that is continuously sustained beyond 7 days, including episodes terminated by cardioversion (drugs or electrical cardioversion) after >7 days.

The exclusion criteria were as follows: (1) age < 18 years; (2) myocardial infarction; (3) congenital heart disease; (4) cardiomyopathy; (5) valvular heart disease; (6) hepatic and renal insufficiency; (7) active malignant tumor; (8) anticoagulant taboos; (9) pregnant women; (10) systemic inflammatory and/or autoimmune diseases; and (11) patients who refused, were lost to follow-up, or dropped out. This study was approved by the ethics committee of the Affiliated Hospital of Nantong University (2022-K088). Post-hoc analysis variable definitions: PIV was defined as $\text{platelet (P)} \times \text{neutrophil (N)} \times \text{monocyte (M)} / \text{lymphocyte (L)}$, and SII was defined as $(\text{P} \times \text{N}) / \text{L}$. The neutrophil-lymphocyte ratio (NLR) was defined as (N / L) , and the platelet-lymphocyte ratio (PLR) was defined as (P / L) .

CBA procedure and post-procedural follow-up

All patients received standard anticoagulation therapy for at least 3 weeks before the procedure. Thrombi in the left atrium and LAA were excluded using TEE before surgery. CBA was performed by two experienced interventional cardiologists, and the activated thrombin time was continuously monitored during the operation to maintain it at 300 to 350 s. The complete disappearance of the pulmonary vein potential was confirmed as the endpoint of the operation.

Anticoagulation and anti-arrhythmic drugs should be administered for at least 2 to 3 months postoperatively. Twenty-four-hour Holter monitoring was performed 1, 3, 6, and 12 months after ablation to detect AF recurrence. Early recurrence of AF was defined as any electrical evidence of AF, atrial flutter, or atrial tachycardia lasting more than 30 s within one year after the 3-month blank period.

Statistical analysis

Continuous variables were presented as the mean \pm standard deviations (SD) or median (interquartile ranges).

Categorical variables were described as frequencies and percentages. The independent Student's *t*-test and Mann-Whitney *U* test were used to compare the differences between the two groups. The chi-squared test or Fisher's exact test was used to analyze categorical variables. COX regression analysis was employed to assess the association between the inflammation index and early recurrence, followed by multivariable adjustments. Persistent AF, New York Heart Association (NYHA), left atrial diameter (LAD), and exhibit higher creatinine (Cr), PIV, SII, NLR and PLR were taken into account in multivariable logistic regression analysis. Receiver operating characteristic (ROC) curves were plotted to identify the cutoff values of the inflammation index that could be used to predict early recurrence. The point with the largest Joden index (sensitivity+specificity-1) was chosen as the best cut-off point. The area under the ROC curve (AUC) was calculated and pair-wise comparison was made. To eliminate the effect of AF type on the study results, subgroup analyses were performed according to AF type. COX regression analysis was used to evaluate the association between inflammatory index and early recurrence. ROC curve was used to evaluate the value of PIV index in predicting early recurrence of AF after CBA. Statistical significance was set at $P < 0.05$. Statistical analyses were performed using SPSS Statistics software (version 26.0; SPSS, Chicago, IL, USA).

Results

Baseline characteristics

A total of 307 patients who underwent CBA were included in this study. The recurrence group comprised 65 (21.1%) patients. Compared to the sinus rhythm (SR) group, patients in the recurrence group were more likely to be male, have persistent AF, possess a larger left atrial diameter (LAD), and exhibit higher creatinine (Cr) levels (Table 1). All four inflammation indices were significantly higher in the recurrence group than in the control group.

COX regression analysis of the association between inflammation index and early AF recurrence

Univariable COX regression analysis showed that persistent AF, cardiac function class II and III, creatinine, PIV, SII, and other indicators were risk factors for early AF recurrence. In multivariable COX analysis, persistent AF (hazard ratio (HR): 1.844, 95% confidence interval (CI): 1.013–3.356, $P = 0.045$), PIV (HR: 1.004, 95% CI: 1.003–1.006, $P < 0.001$), and LAD (HR: 1.061, 95% CI: 1.002–1.125, $P = 0.044$) remained independent predictors of early AF recurrence (Table 2).

Discriminative ability of inflammation index

Comparisons of various inflammatory indices for predicting early AF recurrence are summarized in Table 3.

PIV had the highest AUC (0.768 [95% CI 0.695–0.841]). The ROC curves for the inflammation indices are presented in Fig. 1. According to the pair-wise comparison of the AUCs, the PIV appeared to perform better than the other three indices (Table 4). Kaplan–Meier survival curve analysis showed that patients with a PIV index > 260.7 had a higher recurrence rate of AF (log-rank $P < 0.01$) (Fig. 2).

Subgroup analysis

To ensure the accuracy and reliability of the study results, detailed subgroup analyses were performed to eliminate the influence of AF type on the outcomes. Patients with persistent AF who underwent CBA were found to have a significantly higher recurrence rate than those with paroxysmal AF ($P < 0.001$) (Fig. 3). In the paroxysmal AF group, PIV was an independent predictor of early AF recurrence in the multivariable COX regression analysis (Table 5). In the persistent AF group, both PIV and the LAD were independent predictors of early AF recurrence. The ROC analysis of the two groups showed no significant difference between PIV and the predictive value for early AF recurrence after CBA (AUC: 0.772 vs. 0.771, $P = 0.99$) (Fig. 4). These data further confirm the importance of PIV in predicting early AF recurrence and this conclusion is applicable to patients with different types of AF.

Discussion

This study investigated the association between a novel inflammatory marker, PIV index, and AF recurrence following CBA. These findings suggest that not only does the PIV index serve as a valuable predictor of early AF recurrence after CBA, but it also surpasses other inflammatory markers in terms of its predictive ability. Additionally, the PIV index showed significant potential for predicting recurrence among patients with various subtypes of AF. Considering their wide availability in laboratory and clinical settings, inflammatory markers, such as the PIV index, offer promise as cost-effective and efficient predictors. Therefore, it is reasonable to recommend these indicators as predictive tools for assessing AF recurrence after CBA, allowing clinicians and patients to perform more comprehensive and accurate risk assessments, while offering improved treatment options.

Inflammation is closely associated with the onset and persistence of AF [16, 17]. The inflammatory response can result in alterations in atrial tissue, such as fibrosis, leukocyte infiltration, and oxidative damage. These changes contribute to electrical and structural remodeling [18, 19], thereby increasing the risk of developing AF. Inflammation plays a pivotal role in both initiation and perpetuation of AF. Through inducing the release of inflammatory cells and factors, inflammation can

Table 1 Baseline clinical characteristics of the study patients

	SR group (n = 242)	Recurrent group(n = 65)	P
Age	65.3 ± 10.2	65.5 ± 8.2	0.938
Sex	122(50.4)	41(63.1)	0.093
BMI(kg·m ⁻²)	25.2 ± 3.0	24.8 ± 3.3	0.438
Persistent AF	94(38.8)	41(63.1)	0.001
Previous History			
Hypertension	145(59.9)	43(66.2)	0.392
Diabetes mellitus	48(19.8)	9(13.8)	0.369
Hyperlipidemia	39(16.1)	7(10.8)	0.333
Coronary arteries disease	79(32.6)	22(33.8)	0.882
Stroke	31(12.8)	8(12.3)	0.552
NYHA			0.107
I	115(47.5)	29(44.6)	
II	96(39.7)	21(32.3)	
III	25(10.3)	14(21.5)	
CHA ₂ DS ₂ -VASc	2.9 ± 1.7	2.7 ± 1.7	0.452
HAS-BLED	1.2 ± 0.9	1.4 ± 1.1	0.318
HB (g·L ⁻¹)	136.1 ± 17.9	139.8 ± 18.3	0.149
Neutrophil (×10 ⁹ ·L ⁻¹)	3.5 ± 1.1	4.4 ± 1.6	<0.001
Lymphocyte (×10 ⁹ ·L ⁻¹)	1.7 ± 0.6	1.5 ± 0.6	<0.019
Monocyte (×10 ⁹ ·L ⁻¹)	0.4 ± 0.1	0.6 ± 0.2	<0.001
Platelets (×10 ⁹ ·L ⁻¹)	181.2 ± 53.5	188.4 ± 47.0	0.325
Cr (μmol·L ⁻¹)	69.9 ± 17.8	75.8 ± 19.3	0.021
eGFR	94.4 ± 22.9	89.4 ± 21.6	0.120
Nt-pro BNP (pg·mL ⁻¹)	621.1 ± 676.1	7378 ± 681.7	0.218
Total cholesterol (mmol·L ⁻¹)	4.2 ± 1.0	4.1 ± 1.0	0.279
Triglyceride (mmol·L ⁻¹)	1.6 ± 0.9	1.4 ± 0.7	0.092
HDL (mmol·L ⁻¹)	1.1 ± 0.3	1.1 ± 0.2	0.654
LDH (mmol·L ⁻¹)	2.7 ± 0.8	2.6 ± 0.8	0.350
Total bilirubin (μmol·L ⁻¹)	14.3 ± 7.6	16.4 ± 8.3	0.054
T3 (pmol·L ⁻¹)	4.7 ± 0.6	4.7 ± 0.7	0.544
T4 (pmol·L ⁻¹)	12.2 ± 2.2	12.7 ± 2.3	0.114
TSH (mIU·L ⁻¹)	2.5 ± 1.6	2.5 ± 1.5	0.683
PIV	143.2(98.2,210.6)	294.9(168.9,504.9)	<0.001
SII	366.3(256.6,491.9)	569.9(658.1,438.4)	<0.001
NLR	2.0(1.6,2.7)	3.0(2.0,4.0)	<0.001
PLR	105.9(84.0,137.0)	122.2(101.1,188.0)	<0.001
Echocardiographic			
LAD (mm)	42.8 ± 4.9	45.1 ± 5.2	<0.001
LVESD (mm)	32.4 ± 4.7	33.4 ± 5.1	0.112
LVEDD (mm)	47.9 ± 4.5	49.0 ± 4.7	0.106
LVEF (%)	60.6 ± 6.6	59.5 ± 7.1	0.229

AF: Atrial fibrillation; NYHA: New York Heart Association; BMI: Body mass index; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol; TSH: Thyroid-stimulating hormone; SII: Systemic immune inflammation; LVEDD: Left ventricular end-diastolic diameter; LVEF: Left ventricular ejection fraction; LVESD: Left ventricular end-systolic diameter; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; LAD: left atrial diameter

exacerbate and expedite the electrical and structural remodeling of the atrium, thereby promoting fibrosis associated with AF. This reciprocal relationship between inflammation and AF establishes a detrimental cycle, wherein they mutually reinforce each other. Upon sensing tissue damage, neutrophils promptly secrete inflammatory mediators (such as interleukin (IL)-1, IL-8, TNF-α), which infiltrate into the site of myocardial injury. Simultaneously, it stimulates the production of hematopoietic factors and facilitates neutrophil differentiation in the bone marrow, resulting in an elevated neutrophil count. However, chronic inflammation leads to a reduction in lymphocyte count due to stress-induced responses in vivo, increased apoptosis rates, downregulation of proliferation and differentiation processes, and redistribution during lymphogenesis. Moreover, platelets can also contribute to the initiation and maintenance of AF through their reliance on transforming growth factor-β1 [20].

Inflammation also plays a crucial role in the regulation of calcium stabilization and connexins, both of which have been implicated in the initiation of AF and heterogeneous atrial conduction. Inflammatory pathways mediate cardiomyocyte apoptosis, which is closely associated with the occurrence and maintenance of AF. In summary, inflammation, through various mechanisms, significantly affects atrial electrophysiological and structural changes that may influence immune system function and subsequently contribute to the onset and persistence of AF [21]. Thus, a significant correlation exists between systemic inflammatory diseases and AF, where the exacerbation of the inflammatory condition is linked to an elevated risk of AF. The elucidation of these associations offers a novel avenue for investigating the underlying mechanisms governing AF.

Emerging evidence underscores the pivotal role of inflammation in precipitating bleeding episodes among AF patients, hinting that the activation of a systemic inflammatory state could be a strong predictor of subsequent bleeding occurrences. In a recent cohort of AF patients undergoing direct oral anticoagulant (DOAC) therapy, both the HAS-BLED and DOAC scores exhibited only a moderate capacity in forecasting major bleeding events [22]. Notably, a prior investigation introduced the novel ORBIT-i score, which incorporates the systemic inflammatory status alongside traditional bleeding risk factors, demonstrating superior discriminatory power over the ORBIT and HAS-BLED scores in the same cohort [23]. Herein, the PIV index could emerge as a promising tool for predicting major bleeding complications during DOAC treatment in AF patients.

Studies have shown that inflammatory markers such as hs-CRP, white blood cell count, and IL-6 are closely related to the recurrence of AF after CBA [24]. Increased levels of these inflammatory markers may be related to

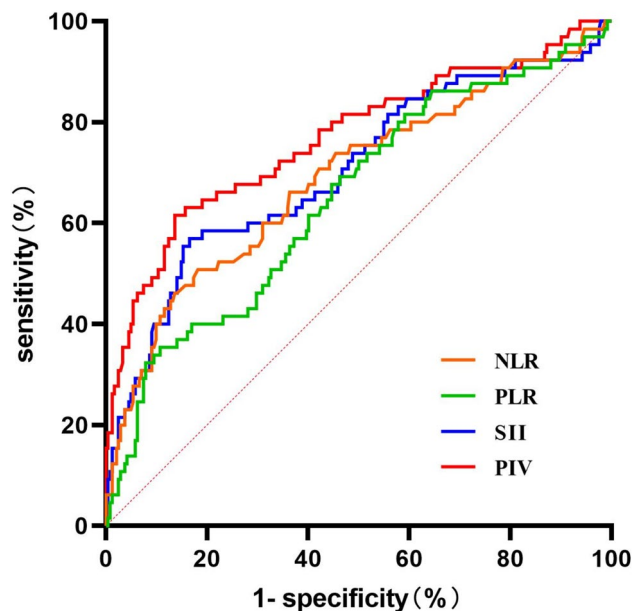
Table 2 Univariable and Multivariable logistic regression analysis

Characteristic	Univariable			Multivariable		
	HR	95% CI	p	HR	95% CI	p
Age, years	1.001	0.977–1.025	0.963			
Sex	0.621	0.375–1.028	0.064			
Hypertension	1.293	0.773–2.161	0.327			
Diabetes	1.479	0.731–2.989	0.276			
Hyperlipidemia	1.526	0.697–3.343	0.291			
Coronary artery disease	0.946	0.566–1.582	0.833			
Stroke	1.011	0.482–2.118	0.978			
Persistent AF	2.690	1.527–4.738	0.001	1.844	1.013–3.356	0.045
NYHA II	0.524	0.277–0.991	0.047	1.400	0.647–3.032	0.393
NTHA III	0.459	0.233–0.903	0.024	1.957	0.907–4.20	0.803
Cr	1.013	1.013–1.024	0.022	1.016	1.003–0.990	0.656
PIV	1.004	1.003–1.004	<0.001	1.004	1.003–1.006	<0.001
SII	1.002	1.001–1.002	<0.001	0.999	0.997–1.001	0.273
NLR	1.231	1.151–1.318	<0.001	1.088	0.913–1.298	0.347
PLR	1.008	1.004–1.012	<0.001	1.001	0.993–1.008	0.852
LAD	1.082	1.031–1.136	<0.001	1.061	1.002–1.125	0.044

AF: Atrial fibrillation; SII: Systemic immune inflammation; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; LAD: left atrial diameter; HR: hazard ratio; CI: confidence interval

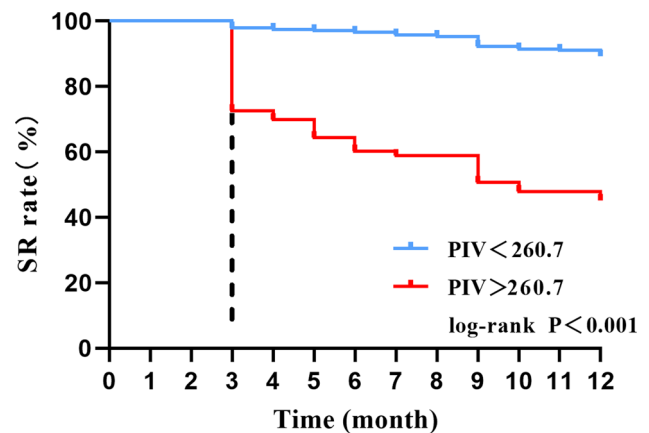
Table 3 Discrimination ability of inflammatory indices

	PIV	SII	NLR	PLR
Cutoff value	260.6	544.1	2.9	162.1
Sensitivity (%)	0.62	0.57	0.51	0.35
Specificity (%)	0.86	0.84	0.83	0.89
AUC (95% CI)	0.768 (0.695–0.841)	0.705 (0.627–0.783)	0.691 (0.612–0.769)	0.649 (0.572–0.727)

**Fig. 1** Receiver operating characteristic (ROC) curve analysis of the PIV, SII, NLR, and PLR to predict AF recurrence**Table 4** Pair-wise comparison of ROC curves

	PIV	SII	NLR	PLR
PIV	-	$P=0.001$	$P=0.004$	$P=0.001$
SII		-	$P=0.437$	$P=0.05$
NLR			-	$P=0.203$
PLR				-

SII: Systemic immune inflammation; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; ROC curve: Receiver operating characteristic curve

**Fig. 2** Kaplan–Meier survival estimates of atrial fibrillation recurrence in patients with atrial fibrillation undergoing cryoablation stratified by the pan-immune inflammatory index

the postoperative inflammatory response, which in turn affects the recurrence rate of AF. In a study on the relationship between subclinical inflammation and recurrence of AF after CBA [25], it was observed that elevated levels of inflammatory markers such as CRP reduced the success rate of ablation. This suggests that the inflammatory response plays an important role in the occurrence

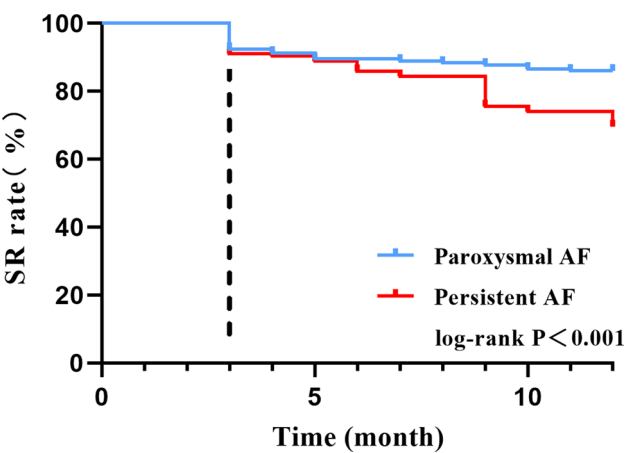


Fig. 3 Kaplan–Meier survival estimates of recurrent atrial fibrillation in patients undergoing cryoablation stratified by AF type before ablation

and recurrence of AF. Furthermore, Framingham et al. [26] observed that white blood cell count was related to the incidence and recurrence of AF, confirming the association between inflammation and AF. Inflammatory indices such as SII, NLR, and PLR have also been widely used in recent years to predict the recurrence of AF after different treatment strategies [27–29]. These inflammatory indices reflect the inflammatory status of the body and provide a valuable reference for predicting the recurrence of AF.

In a retrospective study [30], NLR predicted the recurrence of AF in patients with a successful sinus conversion rate after catheter ablation. This suggests that NLR, as an inflammatory marker, can reflect the risk of AF recurrence. Moreover, Kus et al. [11] also showed that the SII index was an independent predictor of AF recurrence after direct current cardioversion with a higher predictive value than NLR. This suggests that the SII index may have a higher accuracy in predicting AF recurrence. Clarifying this relationship will offer novel insights and approaches to assess treatment options for patients with AF. Through a deeper understanding of the relationship between inflammation and AF, we can better

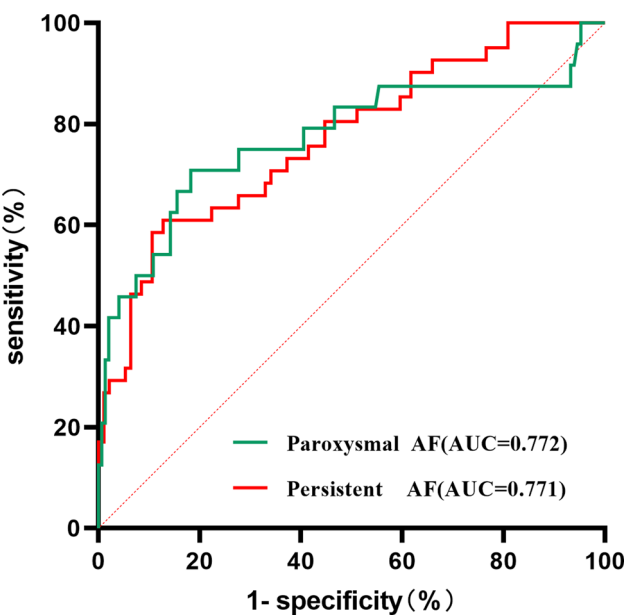


Fig. 4 Receiver operating characteristic (ROC) curve of pan-immune inflammatory index (PIV) for the recurrence of different types of atrial fibrillation

comprehend the pathogenesis of AF and provide new strategies and programs for its prevention and treatment. Additional support for the link between inflammation and AF comes from recognizing that inhibiting inflammation achieves anti-arrhythmic effects. The anti-inflammatory effects of glucocorticoids have demonstrated a reduction in both AF recurrence after ablation [31] and new-onset AF after cardiac surgery [32], providing strong evidence for the importance of suppressing inflammation in the prevention and treatment of AF. However, the multitude of complex side effects associated with steroids makes them less than ideal treatment for AF. Colchicine, with its anti-inflammatory effects, has been shown to reduce early recurrence of AF after catheter ablation for a short period [32], providing further evidence that reinforces the association between inflammation and AF. Another promising agent is a sodium-glucose

Table 5 Multivariable logistic regression analysis

Characteristic	Paroxysmal AF			Persistent AF		
	HR	95% CI	p	HR	95% CI	p
NYHA II	2.849	0.507–16.014	0.235	1.090	0.431–2.759	0.855
NTHA III	1.081	0.153–7.657	0.938	0.945	0.402–2.222	0.897
Cr	1.021	0.993–1.049	0.143	1.001	0.986–1.017	0.871
PIV	1.007	1.004–1.011	<0.001	1.004	1.001–1.007	0.005
SII	0.997	0.992–1.003	0.321	0.999	0.996–1.002	0.607
NLR	1.104	0.456–2.672	0.826	1.027	0.839–1.257	0.796
PLR	0.992	0.979–1.004	0.177	1.007	0.996–1.018	0.238
LAD	1.012	0.922–1.112	0.798	1.096	1.009–1.191	0.029

AF: Atrial fibrillation; SII: Systemic immune inflammation; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; LAD: left atrial diameter; HR: hazard ratio; CI: confidence interval

cotransporter 2 inhibitor [33, 34] which directly targets inflammatory pathways such as the nucleotide-binding domain-like receptor protein-3 inflammasome and reduces NLR levels. These findings provide evidence that moderate suppression of the preoperative inflammatory state may improve the outcomes of AF ablation. However, further studies are needed to evaluate the long-term efficacy and safety of these approaches.

Is this index able to accurately reflect the patient's true condition? Has it taken into account the variability among different populations? Sometimes, the ideal outcomes achieved in clinical studies may differ from the actual results in real-world applications. Although the pan-immune inflammation index has indicated promising value in studies, effectively applying these indicators in real-world clinical scenarios remains a challenge. Further research is needed to validate the role of the pan-immune inflammation index in various diseases and explore how to standardize its measurement and interpretation of results. More large-scale clinical trials are needed to assess its actual effectiveness and suitability in different clinical scenarios.

To our knowledge, this is the first study to explore the use of PIV index in predicting AF recurrence after CBA. The PIV index is an innovative inflammation index [35], which can comprehensively quantify the level of systemic inflammation. It effectively reveals the overall inflammatory response and immune system activation status of patients by calculating four key inflammation-related cell indicators: lymphocytes, neutrophils, platelets, and monocytes. Although the value of this novel biomarker in predicting cardiovascular disease [36] and cancer [37, 38] has been widely recognized, there are still relatively few clinical studies on the use of the PIV index to predict AF recurrence. Additionally, as a novel biomarker, the PIV index holds great potential in clinical practice owing to its low cost, simple calculations, and easy accessibility. Routinely detecting inflammation-related cell markers in patients allows doctors to easily obtain the PIV index data, enabling a more accurate prediction of patient prognosis. This will help improve the quality of care and quality of life for patients.

Limitations

This was a retrospective study. Because 24-hour Holter monitoring was performed only at the follow-up node, recurrent paroxysmal AF in asymptomatic patients may be neglected. Moreover, the sample size was small. In order to further reveal the relationship between the PIV index and AF recurrence, a large sample, prospective, multicenter study is required.

Conclusion

Our findings indicate the predictive value of PIV in patients with AF. This provides a new predictor for clinicians to better evaluate the postoperative recurrence risk in patients and formulate corresponding treatment strategies.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12872-024-04329-5>.

Supplementary Material 1

Acknowledgements

Not applicable.

Author contributions

PYG, PX, YQC, JYL and HRS contributed to the study conception and design. Data collection and statistical analysis were performed by PX, JYL and PYG. The first draft of the manuscript was written by PYG and HRS. Funding was obtained by HXX and QL and they supervised the manuscript. HXX helped in the process of revising the article. All authors have read and agreed to the published version of the manuscript.

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Data availability

Data is provided within the supplementary information files.

Declarations

Ethics approval and consent to participate

All the procedures followed were in accordance with the ethical guidelines of the Helsinki Declaration. This retrospective study was approved by the Affiliated Hospital of Nantong University Institutional Review Board, and exception to the requirement of informed consent was approved (Affiliated Hospital of Nantong University Institutional Review Board No.2018-K020).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Ma LY, Wang ZW, Fan J, et al. Summary of the China Cardiovascular Health and Disease Report 2021 [J]. *Chin J Interventional Cardiol*. 2002;30(07):481–96.
2. Cardiac electrophysiology and Pacing Branch of Chinese Medical Association, Arrhythmia Professional Committee of Chinese Medical Doctor Association. Chinese expert consensus on the ablation of atrial fibrillation by cryoballoon catheter [J]. *Chin J Arrhythm*, 20,24(02): 96–112.
3. HINDRICKS G, POTPARA T, DAGRES N, et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-thoracic surgery (EACTS)[J]. *Eur Heart J*. 2021;42(5):373–498.
4. KRZEMINSKA J, WRONKA M, MLYNARSKA E, Arterial hypertension-oxidative stress and Inflammation[J]. *Antioxid (Basel)*, 2022,11(1).

5. Romiti GF, Corica B, Mei DA et al. Impact of chronic obstructive pulmonary disease in patients with atrial fibrillation: an analysis from the GLORIA-AF registry. *EUROPACE*. 2023; 26 (1).
6. Chan YH, Ramji DP. Key roles of inflammation in atherosclerosis: mediators involved in orchestrating the inflammatory response and its resolution in the Disease along with therapeutic avenues targeting Inflammation[J]. *Methods Mol Biol*. 2022;2419:21–37.
7. Zhu X, Cheang I, Xu F, et al. Long-term prognostic value of inflammatory biomarkers for patients with acute heart failure: construction of an inflammatory prognostic scoring system[J]. *Front Immunol*. 2022;13:1005697.
8. Pauklin P, Zilmer M, Eha J et al. Markers of inflammation, oxidative stress, and fibrosis in patients with Atrial Fibrillation[J]. *Oxid Med Cell Longev*. 2022;2022: 4556671.
9. Sohns C, Marrouche NF. Atrial fibrillation and cardiac fibrosis. *EUR HEART J*. 2020;41(10):1123–31.
10. Ding B, Liu P, Zhang F, et al. Predicting values of neutrophil-to-lymphocyte ratio (NLR), high-sensitivity C-Reactive protein (hs-CRP), and left atrial diameter (LAD) in patients with Nonvalvular Atrial Fibrillation Recurrence after Radiofrequency Ablation[J]. *Med Sci Monit*. 2022;28:e934569.
11. Kuş G, Çağirci G, Bayar N, et al. Usefulness of the systemic immune-inflammation index in predicting atrial fibrillation recurrence after direct current cardioversion[J]. *Biomark Med*. 2022;16(11):847–55.
12. Kasikara C, Davra V, Calianese D, et al. Pan-TAM tyrosine kinase inhibitor BMS-777607 enhances Anti-PD-1 mAb efficacy in a murine model of Triple-negative breast Cancer[J]. *Cancer Res*. 2019;79(10):2669–83.
13. Zhang F, Li L, Wu X, et al. Pan-immune-inflammation value is associated with poor prognosis in patients undergoing peritoneal dialysis[J]. *Ren Fail*. 2023;45(1):2158103.
14. Lin F, Zhang LP, Xie SY, et al. Pan-immune-inflammation Value: a New Prognostic Index in operative breast Cancer[J]. *Front Oncol*. 2022;12:830138.
15. Lee LE, Ahn SS, Pyo JY, et al. Pan-immune-inflammation value at diagnosis independently predicts all-cause mortality in patients with antineutrophil cytoplasmic antibody-associated vasculitis[J]. *Clin Exp Rheumatol*. 2021;39(Suppl 129):88–93.
16. Scott LJ, Li N, Dobrev D. Role of inflammatory signaling in atrial fibrillation[J]. *Int J Cardiol*. 2019;287:195–200.
17. Zhou X, Dudley SC. Evidence for inflammation as a driver of Atrial Fibrillation[J]. *Front Cardiovasc Med*. 2020;7.
18. Bi X, Zhang S, Jiang H et al. Mechanistic insights into inflammation-Induced arrhythmias: a Simulation Study[J]. *Front Physiol*. 2022;13.
19. Hu YF, Chen YJ, Lin YJ, et al. Inflammation and the pathogenesis of atrial fibrillation[J]. *Nat Rev Cardiol*. 2015;12(4):230–43.
20. Liu Y, Lv H, Tan R, et al. Platelets promote Ang II (angiotensin II)-Induced Atrial Fibrillation by releasing TGF-beta1 (transforming growth Factor-beta1) and interacting with Fibroblasts[J]. *Hypertension*. 2020;76(6):1856–67.
21. Pauklin P, Zilmer M, Eha J, et al. Markers of inflammation, oxidative stress, and fibrosis in patients with Atrial Fibrillation[J]. Volume 2022. *Oxidative Medicine and Cellular Longevity*; 2022. pp. 1–9.
22. Mei DA, Imberti JF, Bonini N et al. Performance of HAS-BLED and DOAC scores to predict major bleeding events in atrial fibrillation patients treated with direct oral anticoagulants: a report from a prospective European observational registry. *Eur J Intern Med*. 2024.
23. Hamanaka Y, Sotomi Y, Hirata A, et al. Persistent systemic inflammation is Associated with bleeding risk in Atrial Fibrillation patients. *CIRC J*. 2020;84(3):411–8.
24. Boyalla V, Harling L, Snell A, et al. Biomarkers as predictors of recurrence of atrial fibrillation post ablation: an updated and expanded systematic review and meta-analysis[J]. *Clin Res Cardiol*. 2022;111(6):680–91.
25. Meyre PB, Sticherling C, Spies F et al. C-reactive protein for prediction of atrial fibrillation recurrence after catheter ablation[J]. *BMC Cardiovasc Disord*. 2020;20(1).
26. Zhou X, Dudley SJ. Evidence for inflammation as a driver of Atrial Fibrillation[J]. *Front Cardiovasc Med*. 2020;7:62.
27. Dereli S, Bayramoğlu A, Yontar OC. Usefulness of platelet to lymphocyte ratio for predicting recurrence of atrial fibrillation after direct current cardioversion[J]. *Ann Noninvasive Electrocardiol*. 2019;24(2):e12616.
28. Luo Y, Zhang J, Liu T et al. The systemic-immune-inflammation index predicts the recurrence of atrial fibrillation after cryomaze concomitant with mitral valve surgery[J]. *BMC Cardiovasc Disord*. 2022;22(1).
29. Yano M, Egami Y, Ukita K, et al. Atrial fibrillation type modulates the clinical predictive value of neutrophil-to-lymphocyte ratio for atrial fibrillation recurrence after catheter ablation[J]. Volume 31. *IJC Heart & Vasculture*; 2020. p. 100664.
30. Weymann A, Ali-Hasan-Al-Saegh S, Sabashnikov A, et al. Prediction of New-Onset and Recurrent Atrial Fibrillation by Complete Blood Count tests: a comprehensive systematic review with meta-analysis[J]. *Med Sci Monit Basic Res*. 2017;23:179–222.
31. Kim YR, Nam GB, Han S, et al. Effect of short-term steroid therapy on early recurrence during the blanking period after catheter ablation of Atrial Fibrillation[J]. *Circ Arrhythm Electrophysiol*. 2015;8(6):1366–72.
32. Charitakis E, Tsartsalis D, Korela D et al. Risk and protective factors for atrial fibrillation after cardiac surgery and valvular interventions: an umbrella review of meta-analyses[J]. *Open Heart*. 2022;9(2).
33. Paolisso P, Bergamaschi L, Santulli G, Gallinoro E, Cesaro A, Gragnano F, et al. Infarct size, inflammatory burden, and admission hyperglycemia in diabetic patients with acute myocardial infarction treated with SGLT2-inhibitors: a multicenter international registry. *Cardiovasc Diabetol*. 2022;21(1):77.
34. Cesaro A, Gragnano F, Paolisso P, Bergamaschi L, Gallinoro E, Sardù C, et al. In-hospital arrhythmic burden reduction in diabetic patients with acute myocardial infarction treated with SGLT2-inhibitors: insights from the SGLT2-AMI PROTECT study. *Front Cardiovasc Med*. 2022;9:1012220.
35. Fuca G, Guarini V, Antoniotti C, et al. The Pan-immune-inflammation Value is a new prognostic biomarker in metastatic colorectal cancer: results from a pooled-analysis of the Valentino and TRIBE first-line trials[J]. *Br J Cancer*. 2020;123(3):403–9.
36. Murat B, Murat S, Ozgeyik M, et al. Comparison of pan-immune-inflammation value with other inflammation markers of long-term survival after ST-segment elevation myocardial infarction[J]. *European Journal of Clinical Investigation*; 2022.
37. De Giorgi U, Procopio G, Giannarelli D, et al. Association of systemic inflammation index and body Mass Index with Survival in patients with renal cell Cancer treated with Nivolumab[J]. *Clin Cancer Res*. 2019;25(13):3839–46.
38. Guven DC, Sahin TK, Erul E et al. The Association between the Pan-immune-inflammation Value and Cancer Prognosis: a systematic review and meta-analysis[J]. *Cancers (Basel)*. 2022;14(11).

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