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ORIGINAL RESEARCH

Inflammatory Burden Index Associated with Recurrence of Atrial Fibrillation After Radiofrequency Catheter Ablation

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Background: Recurrence rates of atrial fibrillation (AF) remain high after radiofrequency catheter ablation (RFCA), and inflammation plays an important role in the process. Inflammatory burden index (IBI) as a new inflammatory marker has been found to be associated with worse prognosis in cardiovascular disease. But there are no studies on its role in predicting AF recurrence. The aim of this study was to assess the value of IBI in predicting recurrence of AF after RFCA.

Methods: This was a single-center retrospective observational study. Consecutive enrolment of PersAF who underwent first-time radiofrequency ablation between January 2021 and June 2024. Inflammatory Burden Index (IBI) was calculated as C-reactive protein (CRP) × neutrophil/lymphocyte (NLR).

Results: A total of 142 (27.2%) patients experienced recurrence after RFCA. Multivariate analysis showed that PersAF (OR = 1.599; 95% CI: 1.028 ~ 2.486, p = 0.018), CHA_2DS_2-VASc score≥2 (OR = 1.769; 95% CI: 1.142 ~ 2.741, p = 0.011), LAD (OR = 1.098; 95% CI: 1.054 ~ 1.145, p < 0.001) and IBI (OR = 1.028; 95% CI: 1.007 ~ 1.050, p = 0.009), were independent predictors of recurrence. ROC analysis shows superiority of IBI (AUC=0.695, 95% CI: 0.647 ~ 0.743, p < 0.001) over CRP and NLR in predicting AF recurrence. When IBI was integrated into the traditional model (including PersAF, LAD and CHA_2DS_2-VASc Score), the discrimination and reclassification accuracy for the recurrence were significantly improved.

Conclusion: Inflammatory load index associated with the recurrence of AF after RFCA. Integration of IBI can improve the model about the recurrence of AF after RFCA.

Keywords: atrial fibrillation, radiofrequency catheter ablation, recurrence, inflammation, inflammatory burden index

Introduction

The incidence of atrial fibrillation (AF) increases with age and has been shown to cause or aggravate heart failure, stroke, myocardial infarction and vascular dementia.[1–4] Although catheter ablation currently has a better success rate in restoring sinus rhythm, 20–30% of patients still experience recurrence after ablation.[5,6] How to identify risk factors for recurrence by non-invasive means has become an important clinical issue.

Inflammation and endothelial dysfunction are the strongest predictors of AF and actually promote the development of AF at almost all stages. Coronary artery disease is one of the strongest risk factors for AF, which is closely related to inflammation.[7–9] Previous studies have identified induction of atrial remodelling by inflammatory factors and alteration of membrane potential fluctuations as important factors in the development and maintenance of AF.[10,11] Current clinical indicators of inflammation, including high sensitivity C-reactive protein (hs-CRP), Lymphocyte, Neutrophil and ST2, have been shown to be associated with AF recurrence after Radiofrequency ablation (RFCA).[11,12] As the most widely used inflammatory factor, hs-CRP has been extensively studied and basic research has shown that it can promote the progression of AF through the complement activation pathway.[13] However, compared to the use of a single inflammatory factor, composite inflammatory markers calculated from several haematological markers, such as SII, NLR, SIRI, etc.,

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have a better clinical value in predicting recurrence.[14,15] It is now being studied extensively because it is more readily available and can provide better information about immune activity.

Inflammatory Burden Index (IBI), calculated from C-reactive protein (CRP) × neutrophil/lymphocyte (NLR), is now widely used in tumour-associated diseases as a novel indicator of inflammation.[16,17] A recent study suggests that IBI is associated with adverse cardiovascular outcomes,[18] but there are no studies on its role in predicting AF recurrence. The aim of this study was to assess the value of IBI in predicting recurrence of AF after RFCA.

Methods

Study Population

This is a single-centre retrospective observational clinical study. We consecutively enrolled 621 patients who underwent first-time RFCA for AF between January 2021 and June 2024. Exclusion criteria were: 1) History of rheumatic valvular disease, moderate to severe valvular stenosis or dysfunction; 2) Severe hepatic and renal insufficiency, thyroid dysfunction, respiratory disease and history of malignant tumour; 3) Previous catheter ablation for AF; 4) Hematological diseases, malignant tumors, autoimmune diseases, infections, and systemic inflammation; 5) Acute infection during or before hospitalisation. This study complies with the Declaration of Helsinki. The study protocol was reviewed and approved by the Ethics Committee of Second Affiliated Hospital of Soochow University (No. JD-LK2024034-IR01). As this was a retrospective study with no risk to patients, the requirement for written informed consent was waived. A total of 523 patients were included. (Figure 1)

According to the 2020 ESC Guidelines for the diagnosis and management of AF, PersAF was defined as AF that is continuously sustained beyond 7 days.[19]

Data Collection

Demographic information, comorbidities, admission clinical characteristics, laboratory and echocardiographic data were collected through the electronic medical record system. Venous blood was drawn within 24 hours of admission for measurement of biochemical parameters including serum total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), albumin, white blood cells (WBCs), neutrophils, and other biomarkers. Neutrophil-to-lymphocyte ratio (NLR) is calculated as neutrophil count divided by lymphocyte count. Inflammatory Burden Index (IBI) was calculated as C-reactive protein (CRP) × NLR. All patients underwent transthoracic echocardiography within 12 hours of admission to measure left ventricular ejection fraction (LVEF) and left atrial (LA) diameter.

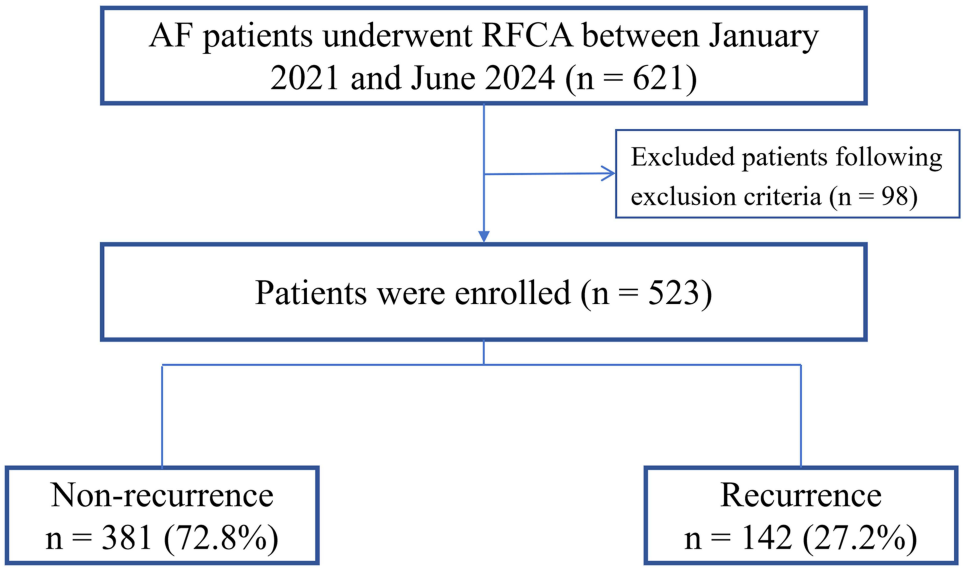

Figure 1 Patients flowchart.
Abbreviations: AF, atrial fibrillation; RFCA, radiofrequency catheter ablation.

Pulmonary Vein Isolation Procedures

All patients underwent pre-procedure transesophageal echocardiography or computed tomography to exclude left atrial thrombus. After observing the left atrial geometry, a complete electroanatomical model of the left atrium was constructed using intravenous fentanyl under conscious sedation and access to the left atrium through the interatrial septum with an ablation catheter guided by the Ensite Precision calibration system. The right and left pulmonary veins were isolated point-by-point using an TCQ or TCSE cold saline-filled ablation catheter. Radiofrequency (RF) energy was 40–45 watts (saline infusion 17–25mL/min), Lesion Size index(LSI) of 4.5–4.8 for atrial wall, roof and bottom ablation and 3.8–4.0 for posterior wall ablation, and 5–20 g was considered the optimal contact force to deliver RF energy to each site. The distance between each two ablation sites is 3–4 mm. Cardioversion for patients who do not return to sinus rhythm, after which additional ablation was performed at the discretion of the operator.

Data Analysis

Numerical variables are expressed as mean ± standard deviation. Normal distribution of numerical data was tested using the Kolmogorov–Smirnov test. For normally distributed data, two-group comparisons were made using the Student's *t*-test; for non-parametric distributions, the Mann-Whitney *U*-test was used. Categorical variables were expressed as percentages and compared using the chi-squared test or Fisher's exact test. Univariate logistic regression analysis was used to compare risk factors between patients with and without recurrence. Forward stepwise multivariate logistic regression analyses were used to detect any independent significant predictors (expressed as odds ratio [OR] and 95% confidence interval). Variables that were statistically significant ($p < 0.05$) or near significant ($p < 0.1$) in univariate analyses were included in the multivariate logistic regression risk model. Restricted cubic splines (RCS) were used to explore the dose-response relationship between IBI and recurrence of AF. The area under the curve (AUC) was determined using receiver operating characteristic (ROC) curve analysis and calculated for optimal sensitivity and specificity. All statistical analyses were performed using SPSS version 23.0 (IBM, Armonk, NY, USA). p values < 0.05 were considered statistically significant. A power analysis was conducted to confirm the adequacy of the sample size for detecting meaningful differences. All statistical analyses were performed with SPSS version 23.0 (IBM, Armonk, NY, USA).

Results

Baseline Characteristics of the Study Population

From 523 patients who underwent RF ablation, 142 (27.2%) patients experienced recurrence AF. Compared with the non-recurrent group, the recurrent group was on average older, had a larger left atrial diameter (LAD) and more people with persistent AF. In addition, The proportion of patients with CHA_2DS_2-VASc score≥2 was higher in the recurrence group. In inflammatory factors, CRP, Neutrophil, Lymphocyte, IBI, NLR were different in both groups ($p<0.05$) (Table 1).

Logistic Regression Analysis for Recurrence of AF

Univariate analysis showed that Age, PersAF, LAD, IBI and CHA_2DS_2-VASc score≥2 associated with recurrence ($p<0.05$). Multivariate regression analysis was then performed on all indicators with p-value < 0.05. Multivariate analysis showed that PersAF (OR = 1.599; 95% CI: 1.028 ~ 2.486, p = 0.018), CHA_2DS_2-VASc score≥2 (OR = 1.769; 95% CI: 1.142 ~ 2.741, p = 0.011), LAD (OR = 1.098; 95% CI: 1.054 ~ 1.145, p < 0.001) and IBI (OR = 1.028; 95% CI: 1.007 ~ 1.050, p = 0.009), were independent predictors of termination (Table 2). RCS results indicated a non-linear dose-response relationship between IBI and recurrence of AF, both before and after adjustment, suggesting that higher IBI may increase the risk of recurrence of AF (Figure 2).

Value of IBI in Predicting Recurrence of AF

The ROC was used to analyze the variables as the critical value for predicting the AF recurrence after RFCA. The cut-off value of IBI was, the sensitivity was 82.4%, and the specificity was 50.7% (AUC=0.695, 95% CI: 0.647 ~ 0.743, p < 0.001). Based on the results of the multivariate regression analysis, a traditional model including PersAF, LAD and CHA_2DS_2-VASc score was developed. ROC analysis of the traditional model showed the sensitivity was 65.5%, and the specificity was 65.4% (AUC=0.708, 95% CI: 0.660 ~ 0.756, p<0.001). Then, a new model was developed after integrating IBI, ROC analysis

Table 1 Baseline Characteristic

	Total (n = 523)	Non-Recurrence (n = 381)	Recurrence (n = 142)	P
Age, years	61.28 ± 10.73	60.46 ± 10.94	63.49 ± 9.84	0.004
BMI, kg/m^2	25.48 ± 3.11	25.39 ± 3.07	25.73 ± 3.20	0.265
Female, n (%)	193 (36.90)	146 (38.32)	47 (33.10)	0.271
PersAF, n(%)	218 (41.68)	135 (35.43)	83 (58.45)	<0.001
WBC, 10^9/L	5.96 ± 1.46	5.93 ± 1.49	6.02 ± 1.39	0.559
Neutrophil, 10^9/L	3.77 ± 1.25	3.67 ± 1.23	4.02 ± 1.28	0.004
Lymphocyte, 10^9/L	1.75 ± 0.55	1.79 ± 0.56	1.62 ± 0.52	<0.001
HGB, g/L	140.25 ± 14.37	140.46 ± 14.64	139.69 ± 13.64	0.584
Plt,10^9/L	205.71 ± 73.36	203.16 ± 54.16	212.54 ± 109.35	0.194
ALB, g/L	43.41 ± 3.98	43.40 ± 4.19	43.42 ± 3.39	0.962
Uric Acid, μmol/L	214.29 ± 142.37	207.22 ± 144.50	233.24 ± 135.15	0.063
FBG, mmol/L	5.63 ± 1.50	5.59 ± 1.32	5.73 ± 1.91	0.356
Total cholesterol, mmol/L	4.05 ± 0.99	4.03 ± 0.96	4.10 ± 1.05	0.466
Triglycerides, mmol/L	1.58 ± 0.93	1.60 ± 0.87	1.54 ± 1.08	0.510
HDL-C, mmol/L	1.26 ± 4.33	1.32 ± 5.08	1.09 ± 0.31	0.589
LDL-C, mmol/L	2.40 ± 0.83	2.40 ± 0.81	2.40 ± 0.87	0.994
eGFR, mL/min/1.73 m^2	101.44 ± 17.61	101.66 ± 17.82	100.87 ± 17.09	0.648
LAD, mm	39.90 ± 5.59	38.95 ± 5.47	42.46 ± 5.10	<0.001
LVEF, %	58.49 ± 7.08	58.52 ± 7.05	58.42 ± 7.19	0.889
CRP, mg/L	2.34 (0.80, 3.30)	1.90 (0.60, 3.10)	2.67 (1.90, 3.89)	<0.001
IBI	4.24 (1.62, 7.82)	3.12 (1.33, 7.00)	6.48 (3.83, 10.19)	<0.001
NLR	2.10 (1.64, 2.80)	2.02 (1.56, 2.59)	2.46 (1.80, 3.27)	<0.001
HF, n(%)	70 (13.38)	47 (12.34)	23 (16.20)	0.249
Hypertension, n (%)	244 (46.65)	170 (44.62)	74 (52.11)	0.127
Diabetes mellitus, n (%)	92 (17.59)	65 (17.06)	27 (19.01)	0.602
Stroke, n (%)	90 (17.21)	60 (15.75)	30 (21.13)	0.147
CAD, n(%)	113 (21.61)	77 (20.21)	36 (25.35)	0.204
CHA_2DS_2-VASc score≥2, n(%)	309 (59.08)	208 (54.59)	101 (71.13)	<0.001

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; HDL-C, high-density leptin cholesterol; LDL-C, low-density leptin cholesterol; CRP, C-reactive protein; FBG, fasting blood glucose; CAD, coronary artery disease; NLR, neutrophil/lymphocyte; IBI, inflammatory burden index; LAD, left atrial diameter; PersAF, persistent atrial fibrillation.

Table 2 Association of Patient Characteristics with Recurrence: Univariate and Multivariate Regression Analysis

	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Age, years	1.028 (1.009 ~ 1.048)	0.004		
BMI, kg/m^2	1.036 (0.974 ~ 1.102)	0.265		
Female, n (%)	0.796 (0.531 ~ 1.195)	0.272		
PersAF, n (%)	2.563 (1.728 ~ 3.802)	<0.001	1.599 (1.028 ~ 2.486)	0.037
WBC, 10^9/L	1.040 (0.913 ~ 1.184)	0.558		
Neutrophil, 10^9/L	1.239 (1.067 ~ 1.440)	0.005		
Lymphocyte, 10^9/L	0.528 (0.360 ~ 0.777)	0.001		
CRP, mg/L	1.177 (1.079 ~ 1.283)	<0.001		
IBI	1.037 (1.014 ~ 1.059)	0.001	1.028 (1.007 ~ 1.050)	0.009
NLR	1.365 (1.163 ~ 1.602)	<0.001		
HGB, g/L	0.996 (0.983 ~ 1.010)	0.584		

(*Continued*)

Table 2 (Continued).

	Univariate		Multivariate	
	OR (95% CI)	**P**	**OR (95% CI)**	**P**
Plt,10^9/L	1.002 (0.999 ~ 1.004)	0.226		
ALB, g/L	1.001 (0.954 ~ 1.051)	0.962		
Uric Acid, μmol/L	1.001 (1.000 ~ 1.003)	0.064		
FBG, mmol/L	1.059 (0.937 ~ 1.198)	0.358		
Total cholesterol, mmol/L	1.075 (0.885 ~ 1.306)	0.466		
Triglycerides, mmol/L	0.930 (0.749 ~ 1.154)	0.51		
HDL-C, mmol/L	0.976 (0.874 ~ 1.090)	0.665		
LDL-C, mmol/L	1.001 (0.793 ~ 1.263)	0.994		
eGFR, mL/min/1.73 m^2	0.997 (0.987 ~ 1.008)	0.647		
LAD, mm	1.128 (1.085 ~ 1.172)	<0.001	1.098 (1.054 ~ 1.145)	<0.001
LVEF, %	0.998 (0.971 ~ 1.026)	0.889		
HF, n (%)	1.374 (0.800 ~ 2.359)	0.25		
Hypertension, n (%)	1.351 (0.918 ~ 1.988)	0.127		
Diabetes mellitus, n (%)	1.141 (0.694 ~ 1.876)	0.602		
Stroke, n (%)	1.433 (0.879 ~ 2.335)	0.149		
CAD, n (%)	1.341 (0.852 ~ 2.110)	0.205		
CHA_2DS_2-VASc score≥2, n(%)	2.049 (1.353 ~ 3.103)	<0.001	1.769 (1.142 ~ 2.741)	0.011

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; HDL-C, high-density leptin cholesterol; LDL-C, low-density leptin cholesterol; CRP, C-reactive protein; FBG, fasting blood glucose; CAD, coronary artery disease; NLR, neutrophil/lymphocyte; IBI, inflammatory burden index; LAD, left atrial diameter; PersAF, persistent atrial fibrillation.

showed the the sensitivity was 76.1%, and the specificity was 60.9% (AUC=0.730, 95% CI:0.684–0.777, p<0.001) (Figures 3,4 and Supplementary Table 1).

Comparison Between Different Models

The results of the DeLong test showed that the AUC of IBI for AF recurrence was significantly higher than that of NLR (Z = 2.733, p=0.006) and CRP (Z = 3.612, p<0.001). After integrating IBI, the AUC of the new model for AF recurrence was significantly higher than that of the traditional model (Z = 3.050, p = 0.002) (Supplementary Table 2). Next, NRI and IDI were calculated and compared between the traditional and new models. The NRI was 0.276 (95% CI: 0.092 ~ 0.461),

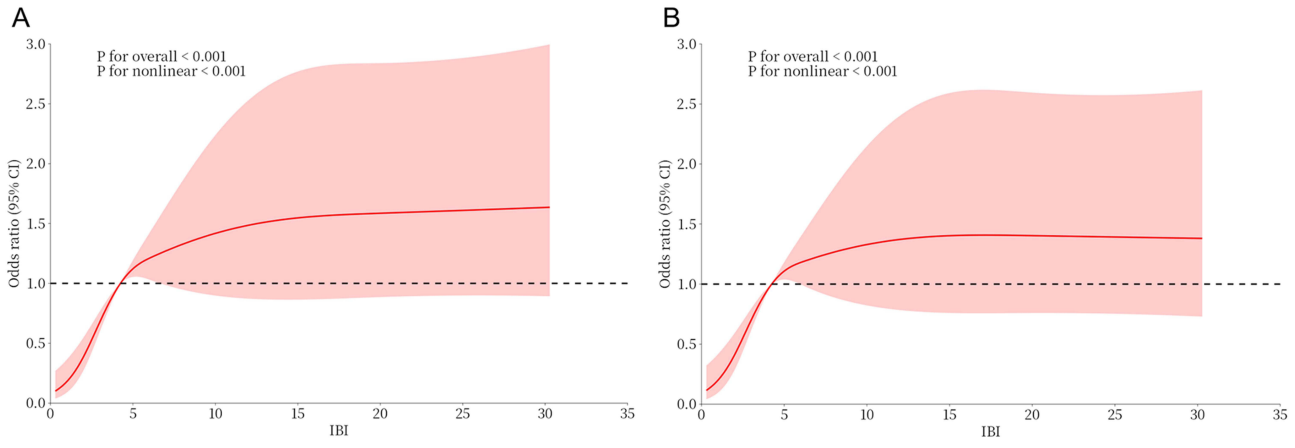

Figure 2 Dose-response relationship between IBI and the recurrence of AF. (**A**) a unadjusted dose-response relationship between IBI and the recurrence of AF; (**B**) an adjusted dose-response relationship between IBI and the recurrence of AF.
Abbreviations: IBI, inflammatory burden index; AF, atrial fibrillation.

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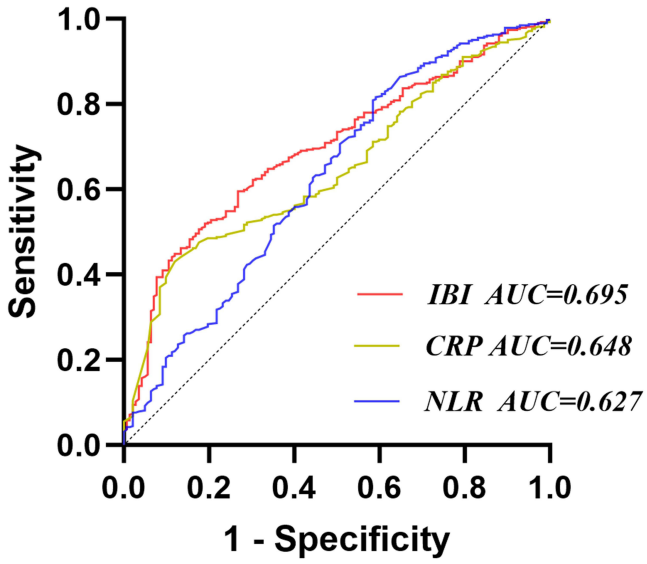

Figure 3 Receiver operating characteristic analysis (ROC) of IBI for identifying the recurrence of AF.
Abbreviations: AF, atrial fibrillation; IBI, inflammatory burden index; CRP, C-reactive protein; NLR, neutrophil/lymphocyte.

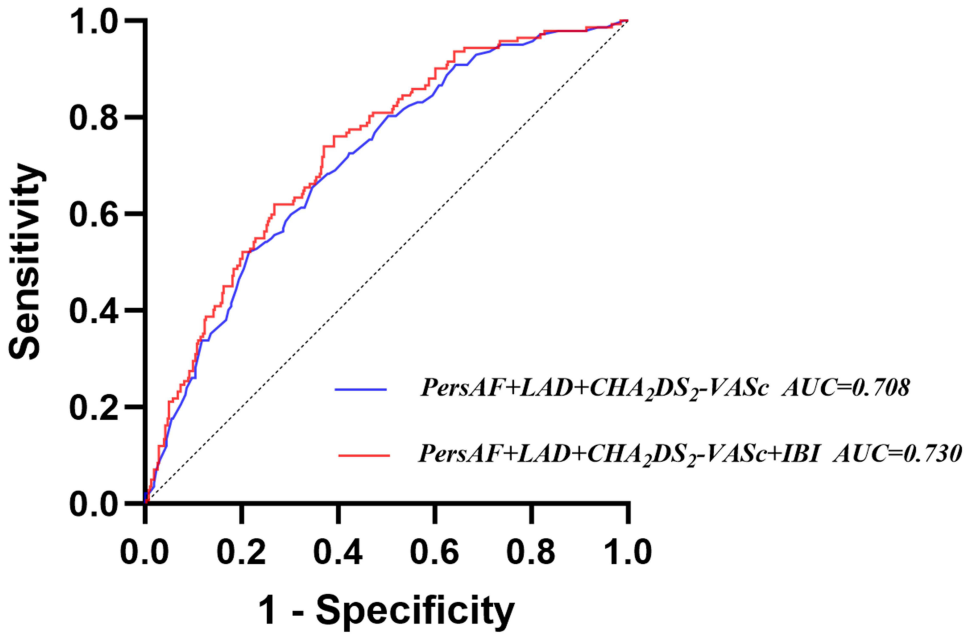

Figure 4 Receiver operating characteristic analysis (ROC) of combined parameters for identifying the recurrence of AF.
Abbreviations: AF, atrial fibrillation; IBI, inflammatory burden index; PersAF, persistent atrial fibrillation; LAD, left atrial diameter.

p=0.003, and the IDI was 0.018 (95% CI: 0.005 ~ 0.031), p=0.008. These results indicate that integration of IBI could significantly improve the ability to predict the recurrence of AF after RFCA (Table 3).

Discussion

To our knowledge, this is the first study to investigate IBI association with AF recurrence after RFCA. The main findings of this study were: 1) IBI is an independent factor for AF recurrence after RFCA and has better predictive value than CRP and NLR; 2) Integration of IBI with PersAF, LAD and CHA_2DS_2-VASc score significantly improves the models about the AF recurrence after RFCA.

Table 3 Incremental Value of IBI for AF Recurrence After RFCA

	NRI		IDI	
	Estimate (95% CI)	**P**	**Estimate (95% CI)**	**P**
PersAF+LAD+CHA_2DS_2-VASc	Reference	–	Reference	–
PersAF+LAD+CHA_2DS_2-VASc+IBI	0.276 (0.092 ~ 0.461)	0.003	0.018 (0.005 ~ 0.031)	0.008

Abbreviations: NLR, neutrophil/lymphocyte; CRP, C-reactive protein; IBI, inflammatory burden index; LAD, left atrial diameter; PersAF, persistent atrial fibrillation.

The incidence of AF, one of the most common clinical arrhythmias, has increased in recent years.[6] Excessively fast and disturbed heart rate can induce and promote the development of heart failure, stroke, vascular dementia and other diseases.[4,20,21] RFCA has become the first-line clinical treatment because it can effectively restore and maintain sinus rhythm.[19] However, some patients still experience recurrence after ablation.[5] Risk factors for AF recurrence include atrial enlargement, obesity, smoking and Obstructive sleep apnea hypopnea syndrome (OSAHS).[22–24] Identifying and controlling risk factors plays an important role in the postoperative management of patients with AF.

In recent years, more and more studies have demonstrated the importance of inflammation in cardiovascular diseases.[14,25,26] IBI, a novel inflammation indicator, is calculated from CRP/NLR. Recent studies have shown that IBI has a good value in predicting the prognosis of tumour-related diseases and is also important in predicting the prognosis of cardiovascular diseases.[14,17,18] In this study, IBI was found to be more effective in predicting the recurrence of atrial fibrillation than CRP and NLR. This suggests that IBI is a better indicator of the inflammatory burden in AF patients. Previous studies have indicated that CRP is independently associated with worse clinical outcomes largely attributable to the excess inflammation.[27–29] Current basic research suggests that the release of inflammatory factors and oxidative stress, leading to atrial fibrosis and ion channel alterations, promotes atrial remodelling leading to the development and maintenance of AF.[30]

Excessive accumulation of adipocytes, especially epicardial fat, leads to a chronic low-grade systemic inflammatory state, which is important for the recurrence of AF.[31,32] Existing studies have shown that the main immune cells infiltrating the atrial myocardium in patients with AF are lymphomonocytes.[33] Lymphocytes secrete inflammatory mediators such as IL-6, transforming growth factor (TGF)-βand tumour necrosis factor (TNF)-α, which contribute to atrial remodelling and are involved in the development and maintenance of AF.[33,34] Complex inflammatory factors obtained from a simple complete blood count have been shown to be more predictive of AF recurrence than single inflammatory factors.[25] Gibson et al demonstrated that elevated NLR, both pre- and post-operatively, is associated with the development of post-operative AF.[35] In addition, a number of chronic inflammatory diseases, such as inflammatory bowel disease, autoimmune diseases and chronic obstructive pulmonary disease, have been shown to increase the risk of AF.[36–38] Therefore, IBI, as a non-invasive assessment tool that can reflect the systemic inflammatory burden, is important in the postoperative management of patients with AF.

Consistent with previous studies, we also found that persistent AF, enlarged atria and higher CHA_2DS_2-VASc score were also independent risk factors for recurrence of AF. The integration of IBI significantly improved the model of AF recurrence after RFCA. Therefore, our study provides important information for AF recurrence risk stratification. Our results suggest that IBI may be another valid reference for these patients. Patients with a high IBI may benefit from receiving enhanced follow-up or anti-inflammatory intervention measures.

Limitation

This study has several limitations that need to be highlighted. First, this is a single-centre, retrospective study and the sample size is small. There may be some potential confounding factors in this study, such as medication use, lifestyle factors, or genetic predispositions. A multicenter and a prospective study design would be needed to strengthen generalizability and reduce potential biases. Secondly, loss to follow-up and exclusion of asymptomatic recurrences due to the lack of continuous rhythm monitoring again comes as a limitation. Perhaps an implantable loop recorders or extended Holter monitoring would have allowed to capture all recurrences.

Conclusion

Inflammatory load index associated with the recurrence of AF after RFCA. Integration of IBI can improve the model about the recurrence of AF after RFCA.

Data Sharing Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the correspondence upon reasonable request.

Statement of Ethics

This study complies with the Declaration of Helsinki. The study protocol was reviewed and approved by the Ethics Committee of Second Affiliated Hospital of Soochow University (No. JD-LK2024034-IR01). As this was a retrospective study with no risk to patients, the requirement for written informed consent was waived.

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Disclosure

The authors declare no conflicts of interest in this work.

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