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ORIGINAL RESEARCH

Synergistic Effect of the CHA_2DS_2-VASc Score and Left Atrial Epicardial Adipose Tissue Volume on Predicting Atrial Fibrillation Recurrence After Ablation

Chuanyi Sang[1,*], Renjie Gu[1,*], Tian Xia[1,*], Yameng Shao[2], Ye Zhu[1], Fukun Chen[1], Lei Sun[1], Xiang Gu[1], Chaoqun Zhang[3]

[1]Department of Cardiology, Northern Jiangsu People's Hospital, Yangzhou, 225000, People's Republic of China; [2]Department of Cardiology, Luoyang Central Hospital Affiliated to Zhengzhou University, Luoyang, 471000, People's Republic of China; [3]Department of Cardiology, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, 221000, People's Republic of China

*These authors contributed equally to this work

Correspondence: Xiang Gu, Department of Cardiology, Northern Jiangsu People's Hospital, Yangzhou, 225000, People's Republic of China, Email xgsubeidsl@163.com; Chaoqun Zhang, Department of Cardiology, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, 221000, People's Republic of China, Email xyfyxnkdsl@163.com

Objective: The CHA_2DS_2-VASc score and left atrial epicardial adipose tissue (LA-EAT) volume have been identified as potential risk factors for atrial fibrillation (AF) recurrence after ablation. However, there is currently a lack of research specifically examining the interaction between these two AF risk factors. This study aims to evaluate the predictive potential of combining CHA_2DS_2-VASc score and LA-EAT volume in predicting recurrence in patients with AF who undergo ablation.

Methods: The study encompassed a cohort of 507 patients who underwent ablation for AF finally. Follow-up assessments were conducted 1, 3, 6, and 12 months after ablation, including clinical evaluation, a 12-lead ECG, and 24-hour Holter monitoring. Recurrence was characterized by symptomatic or asymptomatic AF episodes or atrial tachycardia lasting more than 30 seconds, as evidenced by any ECG following the 3-month BP. Patients were stratified into groups based on the defined cut-off values of CHA_2DS_2-VASc score and LA-EAT volume. Cox regression analysis was employed to estimate the risk factor of AF recurrence after ablation. The interaction between CHA_2DS_2-VASc score and LA-EAT volume was assessed using the relative excess risk due to interaction (RERI), attributable proportion (AP), and synergy index (SI).

Results: 140 patients experienced AF recurrence after ablation during the follow-up period. Multivariable Cox regression analysis demonstrated that CHA_2DS_2-VASc score and LA-EAT volume were independent risk factors for AF recurrence. Patients with higher CHA_2DS_2-VASc score and LA-EAT volume exhibited a higher risk of recurrence than those with lower score and volume. Furthermore, a significant synergistic interaction existed between CHA_2DS_2-VASc score and LA-EAT volume. The LA-EAT volume and clinical model combination improved the predictive value reclassification, and discriminant abilities improved significantly.

Conclusion: There is a significant additive interaction between CHA_2DS_2-VASc score and LA-EAT volume, with the coexistence of both factors significantly increasing the risk of AF recurrence after ablation.

Keywords: atrial fibrillation, catheter ablation, CHA_2DS_2-VASc score, left atrial epicardial adipose tissue, recurrence

Introduction

Atrial fibrillation (AF) is presently the most common persistent arrhythmia linked to adverse cardiovascular incidents, such as stroke and heart failure (HF), leading to a reduced quality of life and an increased risk of mortality for patients.[1] Pulmonary vein isolation (PVI) has emerged as the cornerstone in the clinical therapy strategy of drug-refractory AF.[2] However, AF recurrence rates are high, about 10%-30%, during the post-ablation follow-up period.[2,3] Identification of

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reliable predictors for the recurrence of AF after PVI could enhance patient selection, identify high-risk individuals for AF recurrence, and improve the success rate of the procedure.

Previous studies suggest that inflammatory and metabolic risk factors promote atrial remodeling and are directly associated with the occurrence and maintenance of AF.[4–6] The CHA_2DS_2-VASc score, including risk factors for AF, is widely used to predict ischemic strokes and vascular events in patients with AF.[7] Previous studies have demonstrated high CHA_2DS_2-VASc score associated with different left atrial (LA) substrate properties and increased risk of AF recurrence after ablation.[8,9] Left atrial epicardial adipose tissue (LA-EAT) has been confirmed to secrete proinflammatory and fibrotic factors, promoting myocardial fibrosis and associated with AF.[10–12] The CHA_2DS_2-VASc score and LA-EAT are significantly associated with the LA substrate properties of AF. They could promote each other through a complex and multifactorial inflammatory and metabolic mechanism, ultimately contributing to AF recurrence.[13,14] However, the prognostic value of CHA_2DS_2-VASc score and LA-EAT volume following AF ablation and their synergistic effect remains unclear.

The objective of this study was to examine the predictive significance of both the CHA_2DS_2-VASc score and LA-EAT volume in individuals who undergo AF ablation. Furthermore, we sought to investigate the potential synergistic impact resulting from the combination of the CHA_2DS_2-VASc score and LA-EAT volume.

Methods

Study Population

This study protocol was reviewed and approved by the Local Ethics Committee, the Affiliated Hospital of Xuzhou Medical University, approval number [KL223-01]. All methods were carried out by the Declaration of Helsinki.[15] Written informed consent was obtained from all patients, allowing for the retrospective utilization of their de-identified data for health-related research purposes. Patients who underwent AF catheter ablation were consecutively enrolled in the analysis at our institution between July 2019 and July 2022. Before ablation, all patients underwent routine LA computed tomography angiography (CTA) to rule out the presence of LA thrombus. Paroxysmal atrial fibrillation (PAF) and persistent atrial fibrillation (PersAF) were defined according to current guidelines.[1] Exclusion criteria: (1) previous history of catheter ablation and cardiac surgery; (2) history of rheumatic heart disease, valvular heart disease, and congenital heart disease; (3) severe hepatic and renal insufficiency, thyroid dysfunction, and malignant tumor; (4) patients with uninterpretable CT images (Figure 1). Those who did not receive regular follow-up for at least one year after the ablation procedures were excluded. Demographic characteristics, medical history, personal history, and medication usage data were obtained via the electronic medical record system. Each patient's CHA_2DS_2-VASc score was calculated following the current guidelines. All participants underwent transthoracic echocardiography, during which measurements of left ventricular ejection fraction (LVEF) and left atrial diameter (LAD) were obtained and documented.

Cardiac Computed Tomography Imaging

To acquire CT imaging data, a 128-row spiral CT system (SOMATOM Definition, SIEMENS, Germany) was utilized to perform scans on all patients. An intravenous injection protocol was employed, with iopamidol administered at a volume of 60–80 mL and an infusion rate of 5 mL/s. Following that, an additional 50 mL of saline was injected at the same flow rate. Enhanced scanning-trigger planes were initiated at the level of the ascending aorta root using contrast agent tracking technology, with a trigger threshold set at 90HU ~ 100HU. Scanning commenced after a 6-second delay, and the duration ranged from 5 to 12 seconds. The scanning spanned from 1 cm below the tracheal carina to 1.5 cm below the lower edge of the heart. The scanning parameters included a tube current of 280–350 mA and a tube voltage of 120 kV. All images were reconstructed using retrospective ECG gating, with a slice thickness of 0.5 mm and an overlapping of 0.3 mm.

EAT Volume Analysis

The detection of EAT has been previously described.[16] In brief, EAT was defined as a specific visceral fat deposit located between the myocardium and the visceral layer of the pericardium. Using the Advantage Workstation 4.6 software (GE, USA), total EAT was identified by setting the adipose tissue CT threshold value between −50 hU and −200 hU. The

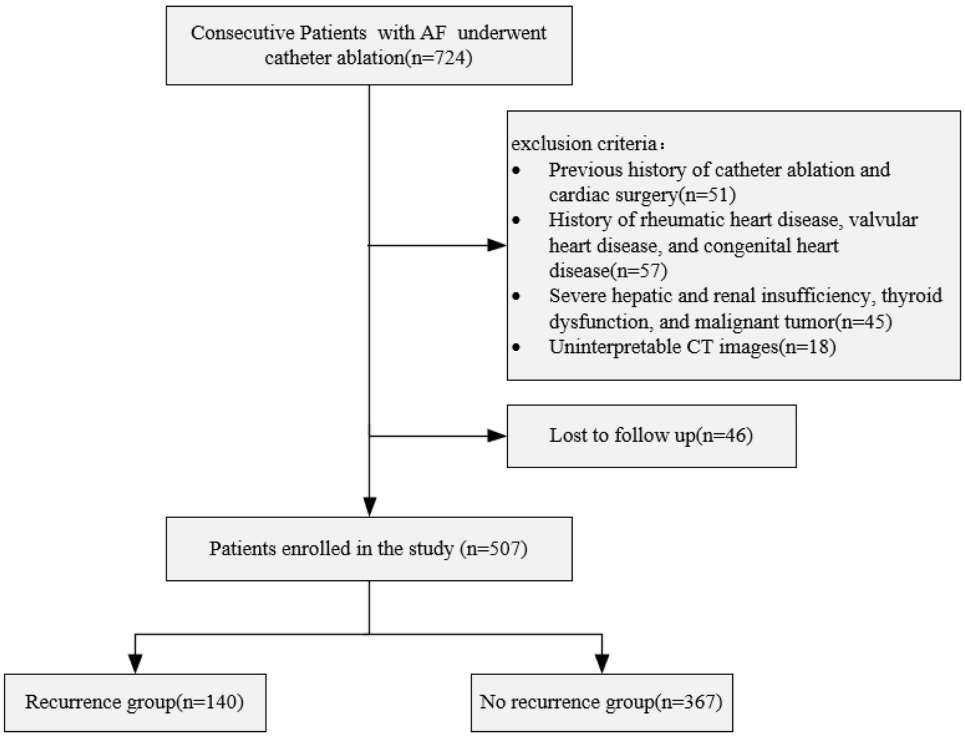

Figure 1 Study flowchart.

volume of total EAT was then semi-automatically reconstructed by tracing the pericardium sac boundary from the apex of the heart to the pulmonary artery trunk in axial sections at 10 mm intervals. Subsequently, the EAT volume was subtracted from the epicardial adipose tissue in the left ventricle in front of the mitral annulus, the epicardial adipose tissue in the right atrium in front of the right superior pulmonary vein, and the epicardial adipose tissue below the plane of the coronary sinus. The remaining epicardial adipose tissue was referred to as LA-EAT (Figure 2).

Catheter Ablation Protocol

The ablation procedure has been described in detail elsewhere.[17] All antiarrhythmic drugs were discontinued for at least 5 half-lives before the procedure, except amiodarone, which was ceased 1 month before the procedure. The ablation procedure was performed under local anesthesia. We used a smart-touch catheter (35W;43°C) with a pressure monitoring function to improve ablation energy and constructed a complete left atrial electrical anatomical model under the guidance of the 3D electroanatomic mapping system (CARTO-3, Biosense Webster Inc, USA). Circumferential pulmonary vein isolation (CPVI) under ablation index (AI) guidance was performed as the initial step (contact force 5g to 30g) in all patients. If AF was still present after CPVI, sinus rhythm was restored by electrical cardioversion. After CPVI, a force-sensing ablation catheter was used to map the LA matrix by creating a detailed 3-D voltage map during sinus rhythm. All the electrograms in low-voltage zones (defined as bipolar voltage ranges of 0.1–0.4 mV) were ablated to improve the matrix.

Follow-Up Visits

Follow-up assessments were conducted 1, 3, 6, and 12 months after ablation, including clinical evaluation, a 12-lead ECG, and 24-hour Holter monitoring. During this blanking period (BP) of 3 months, recurrence was managed with antiarrhythmic drugs (AADs) and/or cardioversion if necessary. Additional ECGs and Holter recordings were obtained when patients exhibited symptoms suggestive of AF. Recurrence was characterized by symptomatic or asymptomatic AF episodes or atrial tachycardia lasting more than 30 seconds, as evidenced by any ECG following the 3-month BP.

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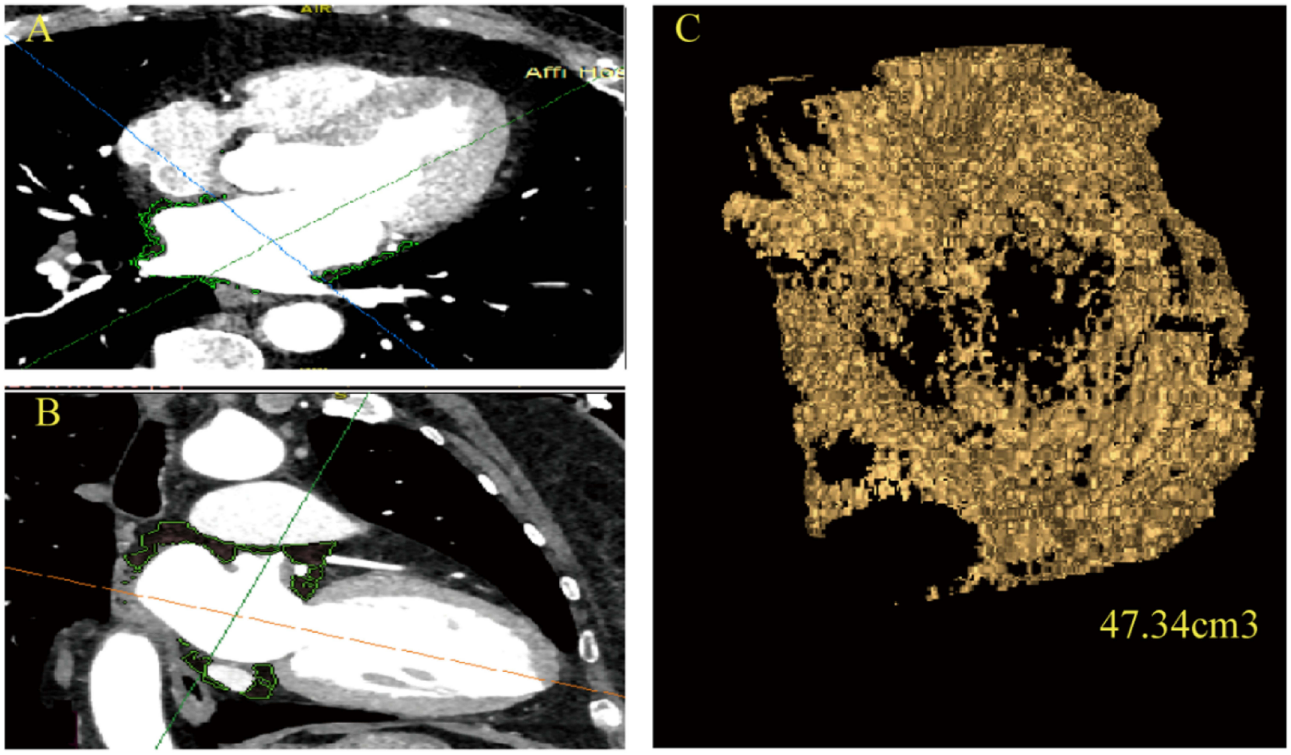

Figure 2 Green regions represent epicardial adipose tissue in the axial position (**A**) and the sagittal position (**B**). The LA-EAT volume is calculated by post-processing software(**C**).

Statistical Analysis

SPSS Statistics (IBM, SPSS, Version 16) and R statistical software (R version 4.0.5, R Foundation for Statistical Computing) were used to analyze the data statistically. Continuous variables were presented as either the mean ± standard deviation (SD) or medians with interquartile range (IQR), and their statistical comparisons were conducted using independent samples Student's *t*-test or Mann–Whitney *U*-test. Categorical variables were expressed as frequencies and percentages, and their comparisons were performed using either the chi-square test or Fisher's exact test. The receiver operating characteristic (ROC) curve analysis was conducted to determine the optimal cut-off values (CHA_2DS_2-VASc score: 2.5 points, LA-EAT volume: 26.07cm^3) for predicting AF recurrence. The total cohort was divided into two groups: the low-risk (LR) group (CHA_2DS_2-VASc score ≤2.5) and the high-risk (HR) group (CHA_2DS_2-VASc score >2.5), based on the cut-off value of CHA_2DS_2-VASc score. The baseline characteristics of the patients were described and compared based on the cut-off value of the CHA_2DS_2-VASc score and LA-EAT volume.

Kaplan–Meier analysis with Log rank test was used to calculate AF-free survival and compare the rate of AF recurrence in the respective groups defined by the cut-off value of the CHA_2DS_2-VASc score and LA-EAT volume. Variables with a significance level of $P < 0.05$ in the univariate Cox regression analysis model were included in the multivariate Cox regression analysis model. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated accordingly. To evaluate the combined predictive value of the CHA_2DS_2-VASc score and LA-EAT volume for AF recurrence, patients were divided into four groups: Group 1: LA-EAT volume≤26.07cm^3 and LR, Group 2: LA-EAT volume >26.07 cm^3 and LR, Group 3: LA-EAT volume≤26.07 cm^3 and HR, and Group 4: LA-EAT volume >26.07 cm^3 and HR. Kaplan–Meier analysis with Log rank test was employed to calculate AF-free survival in these four groups. The multivariate Cox regression analysis model further included the combined predictive value. To test the interaction between the CHA_2DS_2-VASc score and LA-EAT volume, we calculated relative excess risk due to interaction (RERI), attributable proportion (AP), and synergy index (SI).[18] The net reclassification index (NRI) and integrated discrimination index (IDI) were used to characterize accuracy improvement in predicting a binary outcome when new variables were added to regression models. $P < 0.05$ was considered to be statistically significant.

Result

Baseline Characteristics

A total of 553 patients were included in the follow-up, with 46 patients (8.3%) lost to follow-up, resulting in 507 patients for analysis. Among these the follow-up of patients with AF (mean age 60.8 ± 10.7 years; 36.1% female), 140 (27.6%) had at least one episode of AF recurrence. Based on ROC analysis and the maximum value of the Youden index, CHA_2DS_2-VASc score =2.5 and LA-EAT volume =26.07cm^3 were determined as the optimal cut-off values for predicting AF recurrence (Supplement Figure 1). The total cohort was divided into two groups based on the optimal cut-off value of CHA_2DS_2-VASc score, with 305 patients (60.2%) scoring less than or equal to 2.5, constituting the LR group and 202 patients (39.8%) scoring greater than 2.5, constituting the HR group. Table 1 displays the general characteristics of the study population stratified by the cut-off value of the CHA_2DS_2-VASc score. As expected, compared to the LR group, the HR group had older patients, a higher proportion of females, and patients with PersAF and showed higher levels of BMI, CRP, and LAD and lower levels of LVEF. The HR group also had a higher proportion of patients with comorbidities such as CAD, Stroke/TIA, HF, and diabetes, and a higher proportion of patients receiving medication treatment with I & III class AADs, Beta-Blockers, ACEI/ARB, and statins than the LR group. Additionally, the LA-EAT volume was significantly larger in the HR group compared to the LR group. Furthermore, the recurrence rate during follow-up was significantly higher in the HR group (19.7% vs 39.6%, $P< 0.001$).

Based on the optimal cut-off value determined by LA-EAT volume, the patients were categorized into two groups: LA-EAT volume≤ 26.07 cm^3 and LA-EAT volume >26.07 cm^3. Supplement Table 1 displays the general characteristics of the study population, categorized based on the cut-off value of LA-EAT volume. Compared to the LA-EAT volume≤26.07 cm^3 group, patients in the LA-EAT volume >26.07 cm^3 group were older and had higher proportions of PersAF, Stroke/TIA, and HR. Additionally, LA-EAT volume >26.07 cm^3 exhibited higher levels of serum uric acid and LAD than the LA-EAT volume≤26.07 cm^3 group. Furthermore, the LA-EAT volume >26.07 cm^3 group had a higher recurrence rate during the follow-up period than the LA-EAT≤26.07 cm^3 group (16.4% vs 36.5%, $P< 0.001$).

Table 1 Baseline Characteristics Between the LR Group and HR Group

	LR Group (n=305)	HR Group (n=202)	*P*
Age (years)	58.83±9.84	63.79±11.16	<0.001
Gender (female)	74(24.3%)	109(54.0%)	<0.001
BMI (kg/m^2)	25.69±3.31	26.44±3.65	0.017
PersAF (n, %)	104(34.1%)	91(45.0%)	0.013
CAD (n, %)	36(11.8%)	78(38.6%)	<0.001
Stroke/TIA (n, %)	7(2.3%)	104(51.5%)	<0.001
HF (n, %)	30(9.8%)	45(22.3%)	<0.001
Hypertension (n, %)	88(28.9%)	147(72.8%)	<0.001
Diabetes (n, %)	22(7.2%)	71(35.1%)	<0.001
CRP (mg/L)	0.80(0.50,2.35)	1.40(0.50,3.33)	0.003
SUA (μmol/L)	311.00(266.50,360.50)	309.00(255.00,372.50)	0.664
LVEF (%)	58.70±7.01	57.10±7.62	0.016
LAD (mm)	40.07±5.89	41.57±5.77	0.005
I & III class AAD (n, %)	160(52.5%)	125(61.9%)	0.036
Beta-Blockers (n, %)	164(53.8%)	129(63.9%)	0.024
ACEI/ARB (n, %)	72(23.6%)	97(48.0%)	<0.001
Statins (n, %)	168(55.1%)	139(68.8%)	0.002
LA-EAT volume(cm^3)	27.83±11.16	31.04±12.33	0.003
Recurrence (n, %)	60(19.7%)	80(39.6%)	<0.001

Abbreviations: LR low risk; HR high risk; BMI body mass index; CAD coronary artery disease; PersAF persistent atrial fibrillation; TIA transient ischemic attack; HF heart failure; CRP C-reactive protein; SUA serum uric acid; LVEF left ventricle ejection fraction; LAD left atrial diameter; AAD antiarrhythmic drugs; ACE-I indicates angiotensin-converting enzyme inhibitor; ARB angiotensin receptor blocker; LA-EAT left atrial epicardial adipose tissue.

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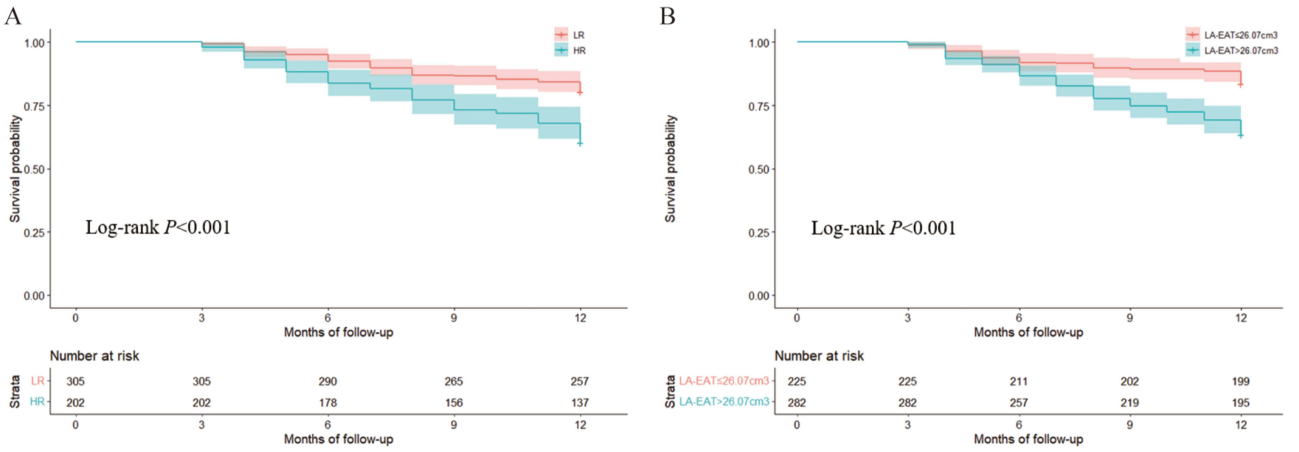

Figure 3 Kaplan–Meier survival curves according to the CHA_2DS_2-VASc score(**A**) and LA-EAT volume(**B**).

Prediction of AF Recurrence After Ablation Between CHA_2DS_2-VASc Score and LA-EAT Volume

According to the critical values of the CHA_2DS_2-VASc score and LA-EAT volume, a Kaplan-Meier survival curve was plotted (Figure 3). Patients in the HR group had a higher post-ablation recurrence rate than those in the LR group (Log rank test, $P<0.001$). Additionally, patients in the high LA-EAT group exhibited a higher risk of recurrence than those in the low LA-EAT group (Log rank test, $P<0.001$).

In the univariate Cox regression analysis, PersAF, LAD, HR, and LA-EAT volume were significantly associated with post-ablation recurrence during patient follow-up ($P<0.05$ for all). These variables were included in the multivariate Cox regression analysis using a stepwise forward method to eliminate confounding factors. The results showed that PersAF, HR, and LA-EAT volume remained significantly associated with recurrence during patient follow-up (Table 2). Based on the multivariate Cox regression analysis, a predictive model included PersAF and CHA_2DS_2-VASc score variables. Adding LA-EAT volume to the model resulted in a moderate yet significant enhancement in outcome prediction, as demonstrated by the reclassification and discriminant abilities (NRI 0.250, $P=0.011$; IDI 0.020, $P=0.002$) (Supplement Table 2). Multivariate Cox regression analysis

Table 2 Cox Survival Analysis of the Recurrence in Patients with AF After Ablation

	Univariate analysis		Multivariate Analysis	
	HR (95% CI)	***P***	**HR (95% CI)**	***P***
BMI	1.01 (0.97–1.06)	0.623		
PersAF	1.93(1.38–2.69)	<0.001	1.58 (1.13–2.23)	0.008
CRP	1.01 (0.98–1.05)	0.379		
SUA	1.00 (1.00–1.00)	0.741		
LVEF	1.00 (0.98–1.03)	0.846		
LAD	1.04 (1.01–1.07)	0.004		
I & III class AADs	1.24(0.88–1.73)	0.222		
Beta-Blockers	0.99(0.71–1.38)	0.942		
ACEI/ARB	1.24 (0.88–1.75)	0.217		
Statins	0.85(0.61–1.19)	0.335		
HR	2.24 (1.60–3.13)	<0.001	2.01(1.43–2.82)	<0.001
LA-EAT volume	1.03 (1.02–1.05)	<0.001	1.02 (1.01–1.04)	0.002

Abbreviations: HR high risk; BMI body mass index; PersAF persistent atrial fibrillation; CRP C-reactive protein; SUA serum uric acid; LVEF left ventricle ejection fraction; LA left atrial diameter; AAD antiarrhythmic drugs; ACE-I indicates angiotensin-converting enzyme inhibitor; ARB angiotensin receptor blocker; LA-EAT left atrial epicardial adipose tissue.

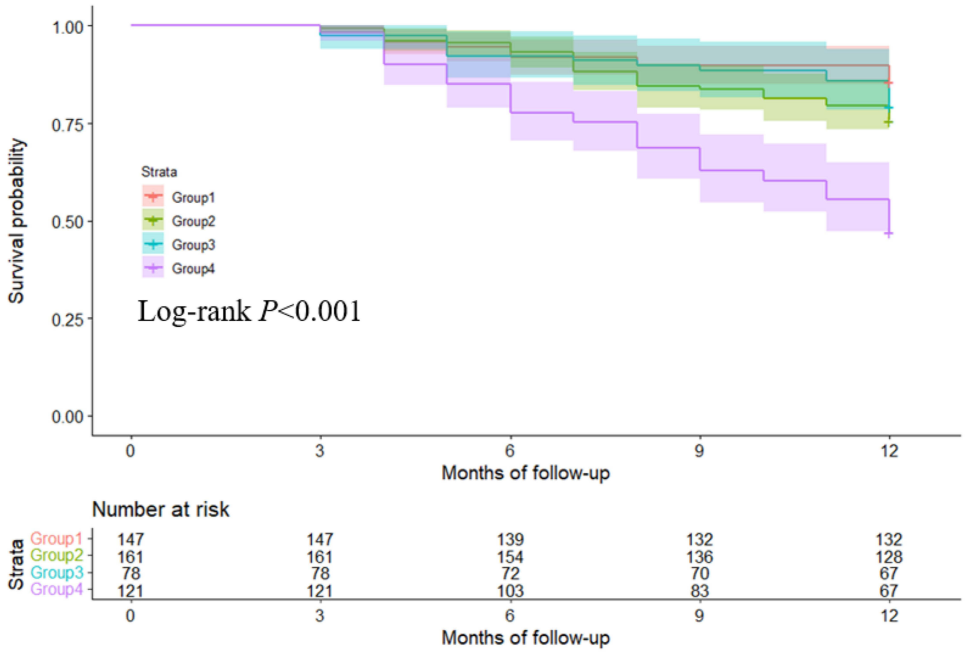

Figure 4 Kaplan–Meier survival curves across the CHA_2DS_2-VASc score and LA-EAT volume. Group 1: LA-EAT volume≤26.07cm^{3}and LR; Group 2: LA-EAT volume >26.07cm^{3}and LR; Group 3: LA-EAT volume≤26.07cm^3 and HR; Group 4: LA-EAT volume >26.07cm^{3}and HR.

is performed without CHA_2DS_2-VASc score, the results showed that Gender, PersAF, Stroke/TIA, and LA-EAT volume remained significantly associated with recurrence during patient follow-up (Supplement Table 3).

Combined Predictive Value of the CHA_2DS_2-VASc Score and LA-EAT Volume for AF Recurrence

According to the critical values of the CHA_2DS_2-VASc score and LA-EAT, patients were divided into four groups. Kaplan-Meier analysis was used to compare the risk of post-ablation recurrence among the four groups. The results demonstrated that patients in the HR group and those with LA-EAT volume > 26.07 cm^3 had the highest risk of recurrence, while the LR group and those with LA-EAT volume ≤ 26.07 cm³ exhibited significantly lower recurrence rates (Log rank test, $P < 0.001$) (Figure 4). To assess the combined impact of CHA_2DS_2-VASc score and LA-EAT on post-ablation recurrence in AF, a multivariate Cox regression analysis was conducted, revealing that patients in the HR group with LA-EAT volume > 26.07 cm³ had a 4.10 times higher risk of post-ablation recurrence than those in the LR group with LA-EAT volume ≤ 26.07 cm³ (Table 3).

Interaction Between the CHA_2DS_2-VASc Score and LA-EAT Volume

Calculate the RERI, AP, and SI as measures of additive interaction, as shown in Table 4. There is a significant positive additive interaction between the CHA_2DS_2-VASc score and LA-EAT volume, where the combined effect of both factors

Table 3 Joint Association of the CHA_2DS_2-VASc Score and LA-EAT Volume with AF Recurrence

	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	***P***	**HR (95% CI)**	***P***
LA-EAT volume≤26.07cm^3 and LR	1(Reference)		1(Reference)	
LA-EAT volume >26.07cm^3 and LR	1.77 (1.04–3.01)	0.035	1.67(0.98–2.84)	0.060
LA-EAT volume≤26.07cm^3 and HR	1.46 (0.76–2.80)	0.254	1.44 (0.75–2.76)	0.270
LA-EAT volume >26.07cm^3 and HR	4.62(2.82–7.57)	<0.001	4.10(2.47–6.78)	<0.001

Abbreviations: LR low risk; HR high risk; LA-EAT left atrial epicardial adipose tissue; AF atrial fibrillation.

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Table 4 Additive Interaction of the CHA_2DS_2-VASc Score and LA-EAT Volume Concentrations Concerning AF Recurrence

	OR (95% CI)	*P*
RERI	3.89 (1.04–6.73)	0.004
AP	0.61(0.37–0.84)	<0.001
SI	3.56 (1.32–9.62)	<0.001

Abbreviation: RERI relative excess risk due to interaction; AP attributable proportion; SI synergy index.

is significantly greater than the sum of their individual effects. According to the two measures of additive interaction, the relative excess risk of AF recurrence is 3.89 due to the additive interaction, and an AP of 0.61 means that 61% of AF recurrence in individuals with both risk factors can be attributed to the additive interaction.

Discussion

The main findings of this study are as follows. 1) CHA_2DS_2-VASc score and LA-EAT volume are independent risk factors for AF recurrence after ablation. 2) Patients with higher levels of both CHA_2DS_2-VASc score and LA-EAT volume have a higher AF recurrence rate after ablation. 3) CHA_2DS_2-VASc score and LA-EAT volume have a positive additive interaction; the coexistence of both factors significantly increases the risk of AF recurrence.

The CHA_2DS_2-VASc score is widely used clinically to assess the risk of thromboembolic events and guide anticoagulation therapy in AF patients.[7] Letsas et al[9] and Jacobs et al[19] confirm that the CHA_2DS_2-VASc score is an independent predictor for predicting AF recurrence after ablation. Our study results are consistent with these findings and confirm a significantly higher recurrence rate in the HR group compared to the LR group during a one-year follow-up. Previous study has shown a correlation between the CHA_2DS_2-VASc score and the activation level of inflammation, suggesting that inflammation may act as an additional middle step between the CHA_2DS_2-VASc score and AF recurrence.[20–22] Although the predictive value of the CHA_2DS_2-VASc score for AF recurrence after ablation is relatively low (AUC 0.635), it is more easily obtainable compared to hematological markers. Therefore, it should be considered in the clinical management process after ablation.

Obesity is a significant risk factor for the occurrence and recurrence of AF.[23] EAT was defined as a specific visceral fat deposit located between the myocardium and the visceral layer of the pericardium, which can have a paracrine effect on the myocardium and cardiac vessels by secreting several proinflammatory adipokines (such as interleukin-1β and tumor necrosis factor-α).[11,24,25] The relationship between EAT and the recurrence in patients with AF remains unclear. Maeda et al,[26] involving 218 Asian patients, confirmed that EAT was independently associated with the recurrence of AF after ablation; our study is consistent with it. However, Cruz et al,[27] involving 350 European patients, found that EAT is not an independent risk factor for AF recurrence when clinical risk factors for AF are considered. We consider that the different conclusions may be related to racial differences. EI Khoudary et al[28] and Adams et al[29] including multiple racial backgrounds, have concluded that EAT is significantly higher in the Asian population compared to White individuals. However, the mechanism of the cardiac metabolic effect of EAT across various racial populations remains unclear. Furthermore, when LA-EAT volume was added to the model (CHA_2DS_2-VASc score and PersAF), reclassification and discriminant abilities showed a moderate yet significant enhancement in outcome prediction.

We quantified the additive interaction between the CHA_2DS_2-VASc score and LA-EAT volume to reflect the biological plausibility of the interaction. The results showed that the interaction between a high CHA_2DS_2-VASc score and a high LA-EAT volume is greater than the sum of their individual effects. Specifically, 61% of AF recurrence in individuals with both risk factors can be attributed to the additive interaction. Therefore, it would be advantageous to consider these two factors together in predicting and managing the risk of AF recurrence. Although the exact mechanisms of this synergistic effect are not yet precise, previous studies have provided valuable mechanistic insights.

Components included in the CHA_2DS_2-VASc score, such as hypertension,[20] diabetes,[21] and heart failure,[30] are associated with activated inflammatory states. It is worth noting that some components of the CHA_2DS_2-VASc score are also present in metabolic syndrome and are associated with increased LA-EAT volume.[4,13,14,31] Meanwhile, several studies have shown that LA-EAT can promote the progression of components in the CHA_2DS_2-VASc score (such as vascular disease, heart failure, and stroke), leading to a high CHA_2DS_2-VASc score status.[32,33] Therefore, the synergistic additive interaction between LA-EAT volume and CHA_2DS_2-VASc score is significantly associated with atrial remodeling through inflammation, fibrosis, endothelial dysfunction, and oxidative stress mechanisms. The CHA_2DS_2-VASc score and LA-EAT volume, as risk factors for AF recurrence after ablation, combined can help better identify individuals susceptible to persistent and recurrent AF, allowing for timely interventions to improve patients' quality of life.

Additionally, atrial enlargement is commonly considered to be closely related to atrial structural remodeling.[34] However, our study found that LAD was associated with AF recurrence in univariate analysis but was not an independent risk factor in multivariate analysis. We consider this may be due to the anatomical asymmetrical shape of the LA posteriorly in the heart and the non-uniform enlargement of the LA due to physiological constraints of the chest. The LAD obtained from transthoracic echocardiography may not reflect LA enlargement accurately. Abecasis et al[35] found that assessing LA volume using multi-layer computed tomography to detect endocardial boundaries better reflects actual LA enlargement and has a higher clinical predictive value for AF recurrence after ablation.

There were several limitations in this study. 1) This study was a single-center retrospective study, and in the future, it is necessary to expand the sample size and conduct a multicenter study to validate and confirm these findings. 2) Within our research scope, the incidence of AF recurrence may be potentially underestimated when assessments are primarily based on clinical symptoms and short-duration dynamic monitoring. Consequently, future research endeavors should consider continuous cardiac rhythm monitoring systems, such as 7-day ambulatory devices or implantable cardiac monitors, to accurately assess AF recurrence.3) In a few cases, the thinness of the selected patients' pericardial CT images may have resulted in potential inaccuracies in the semi-automatic delineation of the epicardial border, leading to deviations in LA-EAT volume measurements.

Conclusion

The study confirmed that CHA_2DS_2-VASc score and LA-EAT volume are independent risk factors for AF recurrence after ablation, and we also discovered a significant positive synergistic interaction with each other, which can collectively increase the risk of recurrence following AF ablation. Multivariate Cox regression analysis is performed without CHA_2DS_2-VASc score, the results showed that Gender, PersAF, Stroke/TIA, and LA-EAT volume remained significantly associated with recurrence during patient follow-up.

Ethics Approval and Informed Consent

All methods were carried out by the Declaration of Helsinki. This study involves human participants and was approved by the Ethics Committee of the Affiliated Hospital of Xuzhou Medical University (Ethics Committee Approval: KL223-01). Written consent was obtained from each patient.

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.

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Disclosure

The authors report no conflicts of interest in this work.

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