





# The Utility of Speckle Tracking Echocardiographic Parameters in Predicting Atrial Fibrillation Recurrence After Catheter Ablation in Patients with Non-Valvular Atrial Fibrillation

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**Background:** Despite the efficacy of catheter ablation (CA) as a treatment for non-valvular atrial fibrillation (NVAF), many patients still experience atrial fibrillation (AF) recurrence after CA. This study aimed to evaluate the predictive value of speckle tracking echocardiographic (STE) parameters for AF recurrence post-ablation.

**Methods:** A total of 380 NVAF patients treated with CA at the First Affiliated Hospital of Guangxi Medical University from January 2020 to March 2023 were prospectively recruited. The mean age was  $59.4 \pm 10.8$  years, and 72.1% were male, including 150 patients (39.5%) with persistent AF and 230 patients (60.5%) with paroxysmal AF. STE was used to evaluate baseline left atrial (LA) function before CA within 48h. Over a median follow-up of 9 (interquartile range, 4–17) months, AF recurrence occurred in 132 patients (34.7%).

**Results:** The recurrence group showed lower left ventricular ejection fraction, LA reservoir strain (LASr), and conduit strain (LAScd), but higher LA stiffness than non-recurrence group (all  $P < 0.05$ ). Multivariable Cox regression identified LA stiffness and LASr as independent risk factors. Time-dependent ROC analysis showed that LA stiffness (AUC 0.768, 95% CI 0.705–0.831) and LASr (AUC 0.755, 95% CI 0.691–0.820) were better at predicting 1-year AF recurrence than other risk factors. For 2-year AF recurrence post-catheter ablation, LA stiffness (AUC 0.866, 95% CI 0.804–0.928) and LASr (AUC 0.860, 95% CI 0.800–0.920) also demonstrated superior predictive performance. Kaplan-Meier curves showed a significant difference in AF recurrence rate for patients with LA stiffness  $> 0.55$  and LASr  $\leq 24.3\%$  (Log rank  $P < 0.01$ ).

**Conclusion:** Evaluation of LA function using STE assists in stratifying the risk of AF recurrence in NVAF patients and guiding follow-up management. LASr and LA stiffness are independent predictors of AF recurrence following CA in NVAF patients, and potentially outperforming other morphological parameters.

**Keywords:** non-valvular atrial fibrillation, catheter ablation, speckle tracking echocardiography, atrial fibrillation recurrence

## Introduction

Non-valvular atrial fibrillation (NVAF) is a common clinical arrhythmia, and is an independent risk factor for patient death, stroke, heart failure, and dementia. Even in patients with well-controlled anticoagulation therapy, AF can still lead to severe adverse cardiovascular events such as stroke, increased mortality, and heart failure.<sup>1</sup> Catheter ablation (CA) therapy is the preferred treatment for symptomatic NVAF patients who do not respond to medication.<sup>2</sup> The goal of CA is to block the transmission pathway of abnormal electrical signals by ablating specific areas of the heart tissue to restore normal rhythm. However, the early recurrence rate of AF after ablation can be as high as 25% to 40%, making it a major clinical challenge.<sup>3</sup> Exploring predictive factors for AF recurrence after CA is of significant importance for improving patient outcomes.

The treatment outcomes of patients with NVAF may vary significantly due to different clinical characteristics and AF phenotypes. The latest evidence indicates that left atrial (LA) remodeling is the most important factor affecting the success of ablation surgery. LA fibrosis is a key process in the enlargement of the atrium and structural remodeling, playing an important role in the pathogenesis and recurrence of AF.<sup>4</sup> Atrial fibrosis involves the accumulation of collagen between atrial muscle cells, leading to stiffening of atrial tissues and impaired function.<sup>5</sup>

LA enlargement is widely considered a sign of LA structural remodeling and has been consistently shown to be a strong predictor of AF recurrence after cardioversion or ablation.<sup>6</sup> However, AF may also lead to significant microstructural changes in the LA, impacting LA myocardial contraction and relaxation even before LA enlargement occurs. With the continuous advancements in ultrasound technology, LA strain analysis can sensitively reflect microstructural changes in the LA, outperforming traditional parameters of LA structure and function.<sup>7</sup> Speckle tracking echocardiography (STE) detecting LA strain has been proven to have greater value in predicting AF recurrence after ablation compared to structural parameters like LA diameter and volume. Assessing LA function using STE to predict AF recurrence may assist in risk stratification and clinical management of patients with NVAF.<sup>8</sup> LA stiffness is significantly correlated with LA volume index and strain function. LA stiffness can be used to evaluate fibrotic remodeling of the LA in NVAF patients.<sup>9</sup> Recent studies have indicated that LA stiffness is a key factor influencing the physiological and pathological status as well as clinical outcomes of NVAF patients. An increase in LA stiffness suggests reduced compliance of the LA, typically associated with atrial fibrosis and chamber dilation.<sup>10</sup> Atrial fibrosis leads to electrophysiological and structural remodeling, increasing the risk of AF recurrence. Evaluating LA stiffness in NVAF patients before ablation may become an important indicator for predicting AF recurrence after ablation.

The objective of this study was to utilize STE for the evaluation of LA function and to investigate the prognostic significance of LA strain parameters in predicting AF recurrence following CA in patients with NVAF.

## Methods

### Study Population

A prospective consecutive cohort study was conducted on inpatients diagnosed with NVAF who underwent AF ablation at the First Affiliated Hospital of Guangxi Medical University from January 2020 to March 2023. Inclusion criteria: (1) patients with paroxysmal or persistent AF, (2) age >18 years old. Exclusion criteria: (1) congenital heart disease, cardiomyopathy, (2) moderate to severe valvular heart disease, history of valve repair or replacement, (3) acute coronary syndrome, (4) previous history of ablation therapy. All patients in this study underwent transthoracic and transesophageal echocardiography examinations within 48 hours before CA to assess cardiac function and to rule out intracardiac thrombi. Ablation was performed using a catheter-based approach guided by the CARTO 3D mapping system. This study has been approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (Approval No: 2022-KT-077) and adhered to the Declaration of Helsinki. All patients have signed informed consent forms.

### Clinical Baseline Data and Biochemical Indicators

The general and clinical data of the patients were collected, including gender, age, height, weight, blood pressure, and medical history (such as hypertension, coronary heart disease, diabetes, hyperlipidemia, peripheral vascular disease, stroke/TIA), as well as history of anticoagulant medication use (such as antiplatelet drugs, warfarin, or new oral anticoagulants). Calculate the CHA<sub>2</sub>DS<sub>2</sub>-VASc score based on the patient's medical history (detailed calculation method same as in the first chapter). After admission, fasting venous blood was drawn and analyzed by the hospital laboratory for biochemical markers such as N-terminal pro-B-type natriuretic peptide (NT-proBNP), troponin I, serum creatinine (SCr), endogenous creatinine clearance rate (Ccr). The glomerular filtration rate (eGFR) was calculated using the CKD-EPI formula, which took into account levels of SCr, age, gender, and race.

### Routine Echocardiography

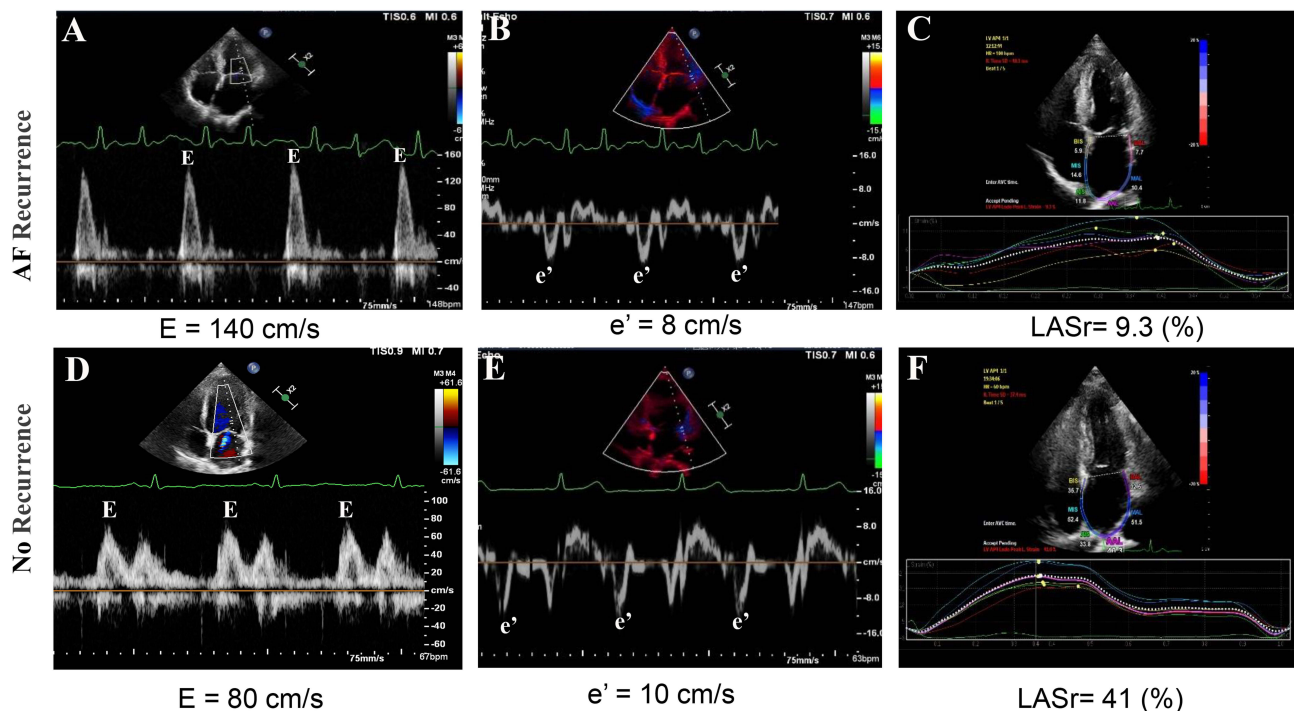
The patient was placed on the left side, a routine 6-heartbeat cycle electrocardiogram was connected for image collection and storage. All patients included in the study underwent echocardiography, and routine electrocardiogram was

connected. The PHILIP EPIQ 7C ultrasound diagnostic instrument was used for both transthoracic and transesophageal ultrasound examinations, with the S5-1 probe (frequency 1~5 MHz) and X5-1 transthoracic 3D matrix probe (frequency 1~5 MHz) used for transthoracic echocardiography examination. The X8-2t probe (frequency 2~8 MHz) was used for transesophageal echocardiography examination. Transesophageal ultrasound examination was mainly used for screening thrombi before CA therapy to exclude surgical contraindications. All echocardiographic parameters are continuously stored for 5 cardiac cycles and averaged during atrial fibrillation, and for 3 cardiac cycles during sinus rhythm.

The modified Simpson's method was employed to calculate left ventricular volumes and ejection fraction (EF) from the apical two-chamber and four-chamber views. Left ventricular mass was determined using the validated Devereux formula, where various measurements are taken into account. LA volume was measured using the biplane Simpson's method by capturing data from both the apical two-chamber and four-chamber views. Left ventricular mass and LA volume was adjusted for body surface area to calculate left ventricular mass index (LVMI) and LA volume index (LAVI). The peak velocity of early diastolic trans mitral Doppler flow (E) was measured in the apical four-chamber view. Tissue Doppler imaging was used to measure the septal and lateral  $e'$  velocities at the mitral annulus and then averaged to obtain the  $e'$  value. The  $E/e'$  ratio was determined by dividing the E velocity by the average  $e'$  value.

## Speckle Tracking Echocardiography

According to the guidelines, using the starting point of the QRS wave group as the zero-reference point (R-R gating), two-dimensional speckle tracking technique was used to measure LA strain. Utilizing the apical four-chamber view, tracing starts from the endocardial border of the mitral valve annulus and extends along the endocardial border of the left atrium, excluding the pulmonary veins and LA appendage, up to the other side of the mitral valve annulus. The ROI width was set at 3 mm, adjusting the size and shape of the ROI to include the thickness of the LA wall while excluding the pericardium. The LA strain curve was obtained through STE to measure the LA reservoir strain (LASr) and LA conduit strain (LAScd). LA stiffness (LA stiffness) was defined as the ratio between  $E/e'$  and LA reservoir strain, LA stiffness = (Mean  $E/e'$ ) / LASr, as shown in Figure 1.



**Figure 1** The measurements of left atrial stiffness using Transthoracic echocardiography (A–C) The measurements of left atrial stiffness ( $(E/e') / \text{LASr} = 1.88$ ) in NVAF patients with atrial fibrillation recurrent after catheter ablation, (D–F) The measurements of left atrial stiffness ( $(E/e') / \text{LASr} = 0.20$ ) in NVAF patients without recurrence after catheter ablation).

# Follow-Up and Detection of Outcomes

After CA, patients were routinely followed up in the outpatient clinic at 1 month, 3 months, 6 months, 1 year, and longer. Follow-up examinations include routine surface electrocardiography or 24-hour dynamic electrocardiography to assess the recurrence of AF. Recurrence of AF was defined as the occurrence of any symptomatic or asymptomatic atrial tachyarrhythmia (such as AF, atrial tachycardia, or atrial flutter) lasting  $\geq 30$  s after 3 months post CA (with the first 3 months being a blanking period).

# Statistical Analysis

Statistical analyses were performed using SPSS 25.0. The Shapiro–Wilk test was used to test for normal distribution of continuous variables. For data that followed a normal distribution, continuous variables were expressed as mean  $\pm$  SD, and independent sample *t*-tests were conducted for analysis. For variables that did not follow a normal distribution, median and interquartile range were used, and comparisons were done using the Mann–Whitney test. Categorical variables were represented as rates and percentages, and statistical analysis was conducted using Pearson’s chi-square test or Fisher’s exact test. Single-factor Cox regression analysis was performed on all variables to determine important factors associated with the recurrence of AF. Clinical and echocardiographic-related variables with  $P < 0.05$  in the single-factor Cox analysis were further analyzed using multiple-factor Cox regression analysis to identify independent risk factors for AF recurrence after CA in patients with NVAf. Time-dependent ROC curves were plotted using R language (4.2.1) to find the optimal cutoff value, and Kaplan–Meier survival curves were drawn based on the best cutoff value. A significance level of  $P < 0.05$  was considered statistically significant for differences.

# Results

This study prospectively included 380 patients, with an average age of  $59.4 \pm 10.8$  years, and a male proportion of 72.1%. Among them, 150 patients (39.5%) had persistent AF and 230 patients (60.5%) had paroxysmal AF. After CA, routine outpatient follow-up was conducted with a median follow-up time of 9 (interquartile range, 4–17) months. During the follow-up period, 132 cases (34.7%) experienced AF recurrence.

The baseline demographic characteristics, clinical features, biochemical indicators, and anticoagulant use of the two groups of patients were showed in Table 1. In the baseline data, included NVAf patients had some underlying diseases, with 50% having hypertension, 14.2% having diabetes, 30.7% having hyperlipidemia, 17.1% with a history of stroke or TIA, and 19.2% having coronary heart disease. However, there were no statistically significant differences in comparison between the

**Table 1** Comparison of Baseline Clinical Characteristics and Biochemical Parameters of 380 Patients with NVAf Who Experienced Atrial Fibrillation Recurrence After Catheter Ablation

Variable	Cohort			P value
	Overall (n=380)	No Recurrence (n=248)	Recurrence (n=132)	
<b>Demographics</b>				
Age, years	59.43 ± 10.8	57.81 ± 11.04	62.47 ± 9.65	< 0.001
Female sex, n (%)	106 (27.9)	76 (30.6)	30 (22.7)	0.129
Body surface area, m²	1.75 ± 0.23	1.76 ± 0.24	1.73 ± 0.2	0.258
SBP, mmHg	127.97 ± 18.09	126.86 ± 17.6	130.04 ± 18.88	0.111
DBP, mmHg	79.93 ± 12.09	78.77 ± 11.66	82.12 ± 12.62	0.012
<b>Medical history</b>				
Hypertension, n (%)	190 (50.0)	119 (47.9)	71 (53.8)	0.332
Diabetes, n (%)	54 (14.2)	31 (12.5)	23 (17.4)	0.248
Dyslipidemia, n (%)	117 (30.7)	82 (33.1)	35 (26.5)	0.230
Previous stroke/TIA, n (%)	65 (17.1)	43 (17.3)	22 (16.7)	0.982
Vascular disease, n (%)	152 (40.0)	90 (36.2)	62 (47.0)	0.056
CAD, n (%)	73 (19.2)	42 (16.9)	31 (23.5)	0.160

(Continued)

**Table 1** (Continued).

Variable	Cohort			P value
	Overall (n=380)	No Recurrence (n=248)	Recurrence (n=132)	
HF, n (%)	25 (6.6)	10 (4.0)	15 (11.4)	0.011
Persistent AF, n (%)	174 (45.8)	88 (35.5)	86 (65.2)	< 0.001
CHA <sub>2</sub> DS <sub>2</sub> -VASc score	2 (1, 3.25)	2 (1, 3)	2 (1, 4)	0.050
<b>Laboratory data</b>				
Scr, $\mu\text{mol/L}$	85.6 $\pm$ 35.94	81.08 $\pm$ 18.72	94.1 $\pm$ 54.44	0.009
Ccr, mL/min	77.66 $\pm$ 18.41	79.99 $\pm$ 17.42	73.29 $\pm$ 19.48	0.001
eGFR, mL/min per 1.73 m <sup>2</sup>	82.93 $\pm$ 19.4	85.46 $\pm$ 17.87	78.17 $\pm$ 21.26	< 0.001
NT-proBNP, pg/mL	559 (119, 1095)	337 (91, 1008)	1095 (491, 1970)	< 0.001
Troponin I, ng/L	0 (0, 0.01)	0 (0, 0.01)	0.01 (0, 0.01)	0.829
<b>Medication</b>				
Antiplatelet, n (%)	44 (11.6)	27 (10.9)	17 (12.9)	0.682
Warfarin, n (%)	20 (5.2)	8 (3.2)	12 (9.1)	0.028
NOAC, n (%)	250 (65.8)	161 (64.9)	89 (67.4)	0.707

**Abbreviations:** DBP, diastolic blood pressure; HF: heart failure; LAVI, left atrial volume index; LV, left ventricle; LVEDV, left ventricular end diastolic volume; LVESV, left ventricular end systolic volume, SBP: systolic blood pressure.

AF recurrence group and the non-recurrence group ( $P > 0.05$ ). Furthermore, there were differences in AF phenotype comparison between the two groups, with a higher proportion of persistent AF in the recurrence group ( $P < 0.01$ ). There was no statistically significant difference in CHA<sub>2</sub>DS<sub>2</sub>-VASc scores between the two groups ( $P > 0.05$ ), and in terms of anticoagulant drug use, there was no statistically significant difference in the comparison of novel oral anticoagulants between the AF recurrence group and the non-recurrence group ( $P > 0.05$ ). In the comparison of baseline data of NVAf patients, there were significant differences in echocardiographic parameters between the two groups (Table 2). LVEDV, LVESV, LVMI, LAD, and LAVI were all higher in the AF recurrence group compared to the non-recurrence group (all  $P < 0.01$ ). Compared to the non-recurrence group, NVAf patients in the AF recurrence group had lower LVEF, LASr, and LAScd, and higher LA stiffness index, with statistically significant differences (all  $P < 0.05$ ). Furthermore, in the comparison of hemodynamic parameters, the recurrence group had higher E peak velocity and greater E/e' ratio (both  $P < 0.05$ ).

**Table 2** Comparison of Baseline Echocardiographic Characteristics of 380 Patients with NVAf Who Experienced Atrial Fibrillation Recurrence After Catheter Ablation

Parameters	Cohort			P value
	Overall (n=380)	No Recurrence (n=248)	Recurrence (n=132)	
LVEDV, mL	125.55 $\pm$ 35.79	121.04 $\pm$ 30.97	134.02 $\pm$ 42.26	0.002
LVESV, mL	49.07 $\pm$ 29.69	44.42 $\pm$ 23.95	57.83 $\pm$ 36.75	< 0.001
LVMI, g/m <sup>2</sup>	118.52 $\pm$ 32.6	113.93 $\pm$ 31.33	127.15 $\pm$ 33.29	< 0.001
LV ejection fraction, %	63.14 $\pm$ 10.91	65.03 $\pm$ 9.47	59.58 $\pm$ 12.46	< 0.001
LAD, mm	39.75 $\pm$ 6.92	38.31 $\pm$ 6.78	42.46 $\pm$ 6.37	< 0.001
LAVI, mL/m <sup>2</sup>	39.53 $\pm$ 15.42	35.51 $\pm$ 14.12	47.09 $\pm$ 14.95	< 0.001
E, cm/s	90.17 $\pm$ 22.74	86.01 $\pm$ 22.08	97.98 $\pm$ 21.96	< 0.001
Mean E/e' ratio	10.63 $\pm$ 4.02	9.92 $\pm$ 3.65	11.97 $\pm$ 4.36	< 0.001
LASr, %	21.99 $\pm$ 7.72	24.63 $\pm$ 7.28	17.02 $\pm$ 5.89	< 0.001
LAScd, %	11.09 $\pm$ 6.9	13.29 $\pm$ 6.97	6.96 $\pm$ 4.41	< 0.001
LA stiffness	0.53 $\pm$ 0.27	0.41 $\pm$ 0.19	0.78 $\pm$ 0.24	< 0.001

**Notes:** Values are mean  $\pm$  SD, n (percentage), or median (25th, 75th percentile).

**Abbreviations:** LAScd, left atrial conduit strain; LASr, left atrial reservoir strain; LAVI, left atrial volume index; LV, left ventricle; LVEDV, left ventricular end diastolic volume; LVESV, left ventricular end systolic volume; LVMI, left ventricular mass index.

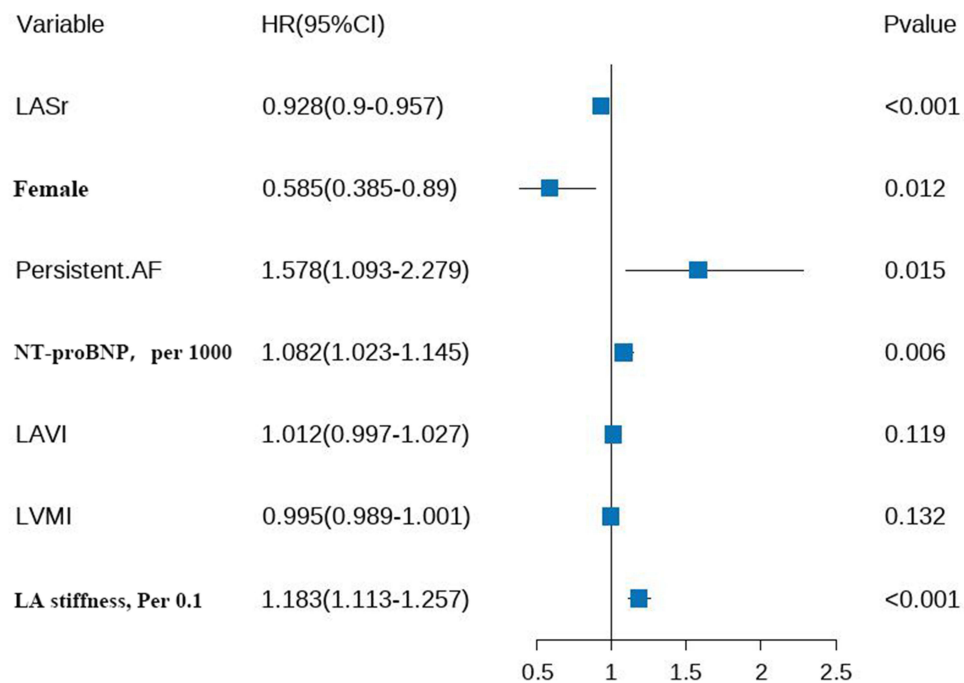


Based on single-factor and multiple-factor Cox regression analyses of baseline clinical data and echocardiographic data, used to predict AF recurrence during follow-up after CA, the results showed that baseline levels of LA stiffness, LASr, persistent AF, female, and NT-proBNP were independent risk factors for predicting AF recurrence in NVAf patients after CA. The results were shown in Table 3 and Figure 2. Subsequently, the comparison of various parameters in predicting the value of CA for non-valvular atrial fibrillation patients was conducted (Figure 3). The results showed that LA stiffness (AUC 0.768, 95% CI 0.705–0.831) and LASr (AUC 0.755, 95% CI 0.691–0.820) had better predictive performance in 1-Year AF recurrence than other independent risk factors. The stiffness (AUC 0.866, 95% CI 0.804–0.928) and LASr (AUC 0.860, 95% CI 0.800–0.920) also superior in predicting 2-Year AF recurrence after CA.

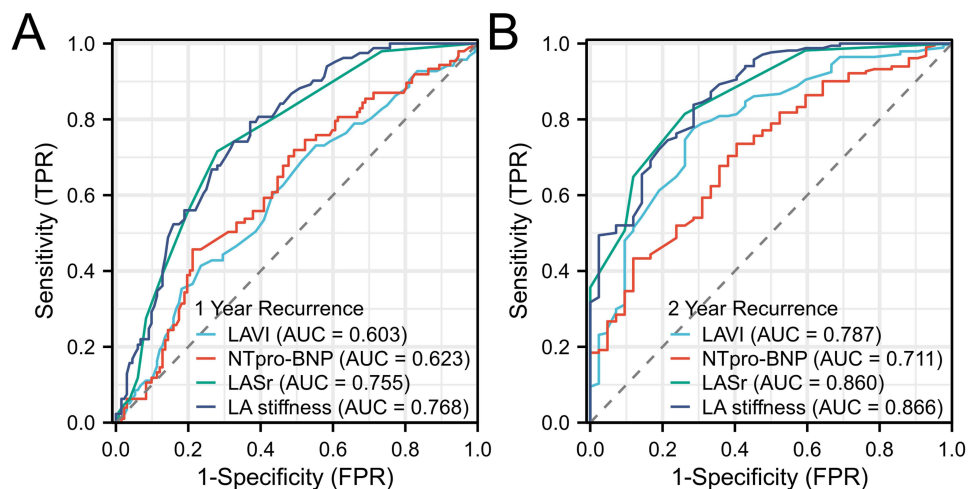
**Table 3** Univariate and Multivariate Cox Regression Analysis of Atrial Fibrillation Recurrence After Catheter Ablation Based on Baseline Data

Variable	Univariate Analysis		Multivariate Analysis			
	HR (95% CI)	P-value	HR (95% CI)	P-value		
Age, years	1.025 (1.008–1.043)	0.003	0.585 (0.385–0.890)	0.012		
Female sex, n (%)	0.624 (0.415–0.938)	0.023				
Body surface area, m <sup>2</sup>	0.782 (0.367–1.668)	0.525				
SBP, mmHg	1.005 (0.995–1.014)	0.329				
DBP, mmHg	1.012 (0.999–1.026)	0.078				
<b>Medical history</b>						
Hypertension, n (%)	1.029 (0.730–1.449)	0.872	1.578 (1.093–2.279)	0.015		
Diabetes, n (%)	1.176 (0.749–1.845)	0.481				
Dyslipidemia, n (%)	0.950 (0.645–1.400)	0.795				
Vascular disease, n (%)	1.146 (0.812–1.617)	0.439				
CAD, n (%)	1.350 (0.902–2.020)	0.145				
HF, n (%)	2.067 (1.203–3.511)	0.009				
Persistent AF, n (%)	2.534 (1.770–3.629)	< 0.001				
CHA <sub>2</sub> DS <sub>2</sub> -VAsC scores	1.041 (0.942–1.150)	0.432				
<b>Laboratory data</b>						
Scr, μmol/L	1.004 (1.001–1.007)	0.009	1.082 (1.023–1.145)	0.006		
Ccr, mL/min	0.987 (0.977–0.996)	0.006				
eGFR, mL/min per 1.73 m <sup>2</sup>	0.990 (0.982–0.999)	0.024				
NT-proBNP, ng/mL	1.071 (1.034–1.111)	< 0.001				
Troponin I, ng/L	1.742 (0.099–30.811)	0.705				
<b>Medication</b>						
Antiplatelet, n (%)	1.057 (0.635–1.762)	0.831	0.928 (0.900–0.957)	<0.001		
Warfarin, n (%)	1.570 (0.867–2.845)	0.137				
NOAC, n (%)	1.005 (0.696–1.452)	0.978				
<b>Echocardiographic parameters</b>						
LVEDV, mL	1.005 (1.001–1.009)	0.006				
LVESV, mL	1.006 (1.002–1.010)	0.001				
LVMI, g/m <sup>2</sup>	1.006 (1.001–1.010)	0.012				
LV ejection fraction, %	0.974 (0.962–0.986)	< 0.001				
LAVI, mL/m <sup>2</sup>	1.031 (1.021–1.042)	< 0.001				
E, cm/s	1.013 (1.006–1.02)	< 0.001				
Mean E/e'	1.076 (1.037–1.117)	< 0.001				
LASr, %	0.891 (0.867–0.915)	< 0.001				
LAScd, %	0.869 (0.835–0.905)	< 0.001				
LA stiffness, Per increased 0.1	1.291 (1.231–1.354)	< 0.001				

**Abbreviations:** AF, Atrial fibrillation; DBP, diastolic blood pressure; HF, heart failure; LAScd, left atrial conduit strain; LASr, left atrial reservoir strain; LAVI, left atrial volume index; LV, left ventricle; LVEDV, left ventricular end diastolic volume; LVESV, left ventricular end systolic volume; LVMI, left ventricular mass index; SBP, systolic blood pressure.



**Figure 2** The forest plot showed the results of Cox regression analysis for the recurrence of atrial fibrillation after catheter ablation.

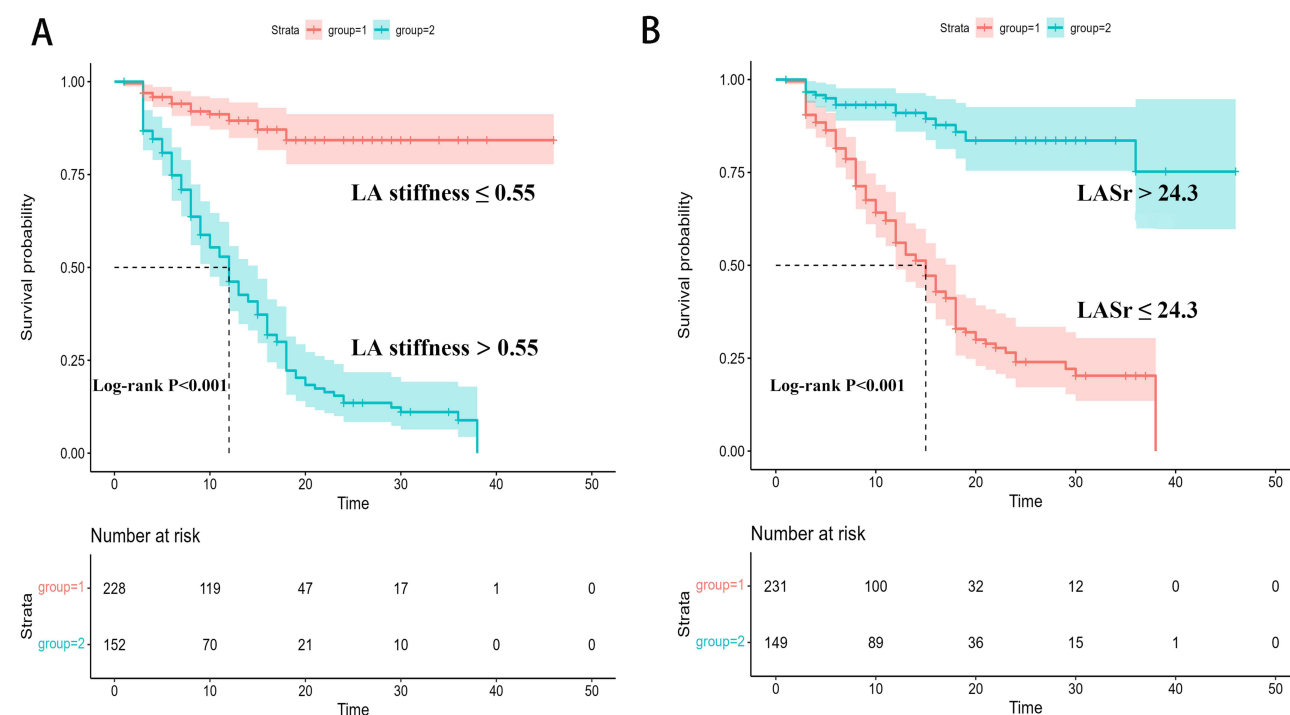


**Figure 3** ROC curve analyses were performed to compare the predictive value of various parameters for atrial fibrillation recurrence at 1 year (**A**) and 2 years (**B**) after catheter ablation.

Kaplan-Meier curves showed a significant difference in AF recurrence probability of patients with LA stiffness > 0.55 and LASr ≤ 24.3% (Log rank  $p < 0.001$ ). The results were shown in Figure 4.

## Discussion

This study demonstrates that LA strain assessed by STE can predict AF recurrence after CA. Baseline LA stiffness, LASr, persistent AF, sex, and NT-proBNP are independent risk factors for predicting AF recurrence after CA in patients with NVAf, with LA stiffness and LASr having higher diagnostic efficiency for predicting AF recurrence. Changes in LA function assessed by STE aid in stratifying the risk of AF recurrence in NVAf patients.



**Figure 4** Kaplan-Meier survival curve analyses for atrial fibrillation recurrence after catheter ablation (A) Left atrial stiffness > 0.55 indicated higher risk of atrial fibrillation recurrence; (B) Left atrial reservoir strain (LASr) ≤ 24.3% suggested higher risk of recurrence of atrial fibrillation).

Similar to the Frank-Starling mechanism in the left ventricular myocardium, the LA myocardium also exhibits similar physiological responses. When AF occurs, the LA size increases, and its blood storage and pumping function both improve to maintain appropriate blood output. However, when the atrium excessively expands beyond the ideal pressure-volume relationship, its reservoir and contraction functions may both decrease.<sup>11</sup> It is well known that the longer the duration of AF, the more severe the pathological physiological changes related to LA enlargement and dysfunction become.

Despite the effective restoration of sinus rhythm and improvement of AF symptoms with CA, there is still a possibility of recurrence in clinical practice. Evaluation of LA structure through different imaging modalities has confirmed that larger LA volume is a strong predictor of AF recurrence after CA in paroxysmal AF patients.<sup>12</sup> In this study, 34.7% of NVAf patients experienced AF recurrence, consistent with previous research findings showing similar recurrence rates post successful CA. The potential mechanisms of recurrence may include progression of atrial fibrosis in AF patients, restoration of electrical connections to isolated pulmonary veins following previous CA, and the ablation technique itself. Previous study suggested that AF recurrence after CA may be associated with age, CHA<sub>2</sub>DS<sub>2</sub>-VASc score, AF phenotype, LA size, and LA strain. LA remodeling and atrial fibrosis due to AF are important factors influencing AF recurrence. Impaired atrial reserve function in AF patients may have significant value in predicting AF recurrence.<sup>13</sup> LGE-MRI is commonly used to quantitatively evaluate the degree of atrial fibrosis, which is prevalent in AF patients and has been shown in long-term follow-ups to be an independent risk factor for recurrence after CA.<sup>14</sup>

LA strain measured by STE is considered an alternative indicator of atrial fibrosis and remodeling and may be used in risk stratification of AF patients. Studies have explored the relationship between 2D speckle tracking echocardiography (2D-STE) and LA remodeling in AF patients with high-density voltage mapping. Results showed a negative correlation between low-voltage areas in the left atrium of AF patients and LASr.<sup>15</sup> Therefore, measuring LASr by simple 2D-STE could serve as a non-invasive method to evaluate significant LA remodeling and fibrosis in AF patients. Decreased LA strain is often proportional to the degree of LA fibrosis and the risk of AF recurrence.

Previous studies have indicated that LA volume and LASr are alternative indicators of LA structural remodeling and fibrosis.<sup>16,17</sup> While in our study, an increased LAVI in the recurrence group showed statistical differences compared to the non-recurrence group and demonstrated a certain predictive trend, LAVI was not an independent predictor in the



multivariable Cox regression analysis, possibly due to the characteristics of the study population and the relatively short follow-up period. Increased LA pressure promotes the occurrence and maintenance of AF, and elevated LA pressure is also associated with AF recurrence after CA. However, non-invasive evaluation of elevated LA pressure in AF patients remains challenging in clinical practice. Preoperative assessment of LA stiffness by echocardiography may have important clinical implications for predicting increased LA pressure after CA, as high LA pressure may result from increased LA stiffness.<sup>18</sup> Previous studies have shown that LA stiffness is the best predictor of elevated LA pressure among echocardiographic parameters determined by ROC curve analysis.<sup>10</sup> Decreased LA reserve function and increased LA pressure and stiffness are typical features in AF patients whose structural remodeling can lead to LA fibrosis, a possible pathological mechanism for increased LA stiffness causing elevated LA pressure and promoting AF recurrence.

Although several studies have used STE to evaluate LA function for predicting AF recurrence after CA, there are differences in the choice of time points for echocardiographic assessment and parameters used. Khan et al primarily focused on the improvement of post-ablation atrial function in maintaining sinus rhythm.<sup>19</sup> While Li et al suggested that LA strain during atrial contraction (LASct) before CA was independently predictive of AF recurrence.<sup>20</sup> Our study also indicated that LA function assessed by STE may contribute to the risk stratification of AF patients. Additionally, our study introduced a new echocardiographic parameter - LA stiffness, which was found to have slightly higher predictive value compared to LASr and LASct. This study suggests that exploring LA stiffness derived from LASr and E/e' in predicting AF recurrence is valuable, with LA stiffness being an independent predictor of AF recurrence post CA in NVAF. STE provides valuable information on LA stiffness for selecting optimal candidates for CA and perioperative management.

Certain baseline serum biomarkers may be associated with the risk of AF recurrence. A previous meta-analysis aimed to identify serum biomarkers associated with arrhythmia recurrence before ablation to screen suitable candidates for CA and reduce the risk of AF recurrence. Results showed that of 22 biomarkers, 9 were associated with AF recurrence after CA, with elevated levels of NT-proBNP, BNP, hsCRP, and IL-6 closely related to AF recurrence. This study also indicates that NT-proBNP is an independent risk factor for AF recurrence post CA. Inflammation is one of the causes of atrial myopathy, and atrial myopathy has recently been defined as structural and/or electrophysiological changes in the atria contributing to the development and maintenance of AF. Therefore, the increased levels of B-type natriuretic peptide specific to AF may be caused by inflammation and increase the likelihood of AF recurrence after ablation. Our study had suggested that LA stiffness and LASr were probably superior to NT-proBNP in predicting AF recurrence after CA.

In our study, we utilize STE to assess LA function, significantly refining the risk stratification of AF recurrence in patients with NVAF and subsequently guiding their follow-up management. Our findings highlight that LASr and the LA stiffness index, as measured by this method, serve as independent predictors of AF recurrence post-CA. These indicators indicate the potential for increased predictive power compared to traditional echocardiographic parameters, which could lead to more accurate risk assessments and more effective, personalized interventions. This highlights the promise of STE in enhancing outcomes for NVAF patients undergoing CA. A large-scale multicenter study is required to confirm this finding.

## Limitation

This study was a single-center, small sample cohort study, with a limited number of cases included, requiring validation through prospective large multicenter studies. During follow-up, asymptomatic AF episodes not captured on routine electrocardiograms may underestimate the recurrence rate. Additionally, the method of CA may influence AF recurrence, but detailed discussion on ablation technique was not conducted in this cohort as the majority underwent radiofrequency ablation, with only a minority undergoing cryoablation. The clinical follow-up period of this study was relatively short, and most follow-up was conducted within 1 year, extending follow-up time could lead to the occurrence of adverse events. Lastly, due to the thinness of the LA wall, precise speckle tracking is not easy to perform, and future studies will utilize new specialized LA speckle tracking software for analysis to reduce inter-observer and intra-observer variability.

## Conclusion

LASr and LA stiffness are independent predictors of AF recurrence in NVAF patients after CA. LA stiffness and LASr may be highly effective for predicting AF recurrence compared to other morphological parameters. Evaluation of LA function using STE assists in stratifying the risk of AF recurrence in NVAF patients and guiding follow-up management.

## Data Sharing Statement

The corresponding author will share the data underlying this article upon reasonable request.

## Ethics Approval and Informed Consent

This study has been approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (Approval No: 2022-KT-077) and adhered to the Declaration of Helsinki. All participants have signed the informed consent form.

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## Disclosure

The authors report no conflicts of interest in this work.

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