Original Article

Use of left atrial automated functional myocardial imaging to identify patients with paroxysmal atrial fibrillation at high risk of stroke

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Background: Left atrial automated functional myocardial imaging (AFILA) is a new software program for analyzing the structure and function of the left atrium (LA). The present study sought to analyze the correlation between the LA function parameters as measured by AFILA echocardiography and the risk of cerebral ischemic stroke (CIS) in patients with non-valvular paroxysmal atrial fibrillation (NVPAF) to explore the diagnostic value of LA strain in patients with congestive heart failure, hypertension, age of ≥75 years (doubled), diabetes mellitus, stroke or transient ischemic attack (TIA) (doubled), age of 65–74 years, and sex category (female) (CHA2DS2-VASc) scores of <2.

Methods: A total of 205 patients with NVPAF were included in the study and divided into the no-CIS group (154 patients) and the CIS group (51 patients). The baseline clinical data for the 2 groups were analyzed, and routine echocardiography examinations were performed. AFILA was used to evaluate the LA function of all the patients.

Results: Compared to the no-CIS group, the LA emptying fraction and the LA reservoir strain were decreased, the LA contractile strain (S_CT) was increased, and the S_CT value changed from negative to positive in the CIS group, and the difference between the 2 groups were statistically significant (P<0.001). However, there were no significant differences in the volume at the onset of LA contraction, LA evacuation volume, LA minimum volume, LA maximum volume, and LA conduit strain between the 2 groups. The multifactorial regression analysis showed that age, hypertension, and the S_CT were independently associated risk factors for patients with CIS. After correcting for the clinical factors included in the CHA2DS2-VASc score, the S_CT was shown to predict to NVPAF with stroke [odds ratio (OR): 1.234, 95% confidence interval (CI): 1.101–1.383, P=0.000]. In addition, we included the CHA2DS2-VASc score (instead of age, diabetes, coronary artery disease, and hypertension) in a multiple regression analysis, and found that the S_CT was still significant (OR: 1.252, 95% CI: 1.118–1.402, P=0.000). The difference between the 2 groups in the CHA2DS2-VASc score for the S_CT was statistically significant, especially when the CHA2DS2-VASc score was <2. The S_CT equaled –4.5% was the cut-off value for the presence or absence of CIS in the NVPAF patients, with an area under the curve (AUC) of 0.866, sensitivity of 0.80, and specificity of 0.75 (P<0.0001).

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Conclusions: Comparison with LA volume parameter, measuring LA strain by AFILA provides a better index for the dynamic assessment of impaired LA function in patients with NVPAF combined with CIS, especially in those with a CHA2DS2-VASc score of <2. In addition, a LA S_CT of >–4.5% is a valuable cut-off for patients with NVPAF. The results of the current study may form the basis for a large prospective multicenter interventional study in which patients with impaired LA S_CT are randomized to receive oral anti-coagulant (OAC) therapy or no OAC therapy for the primary prevention of stroke.

Keywords: Non-valvular paroxysmal atrial fibrillation (NVPAF); cerebral ischemic stroke (CIS); left atrial automated functional myocardial imaging (AFILA); left atrial contractile strain (S_CT); CHA2DS2-VASC score

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Introduction

Non-valvular paroxysmal atrial fibrillation (NVPAF) is a common type of atrial fibrillation (AF) (1). Cerebral ischemic stroke (CIS) is the most serious complication of AF. Acute cerebral infarction with NVPAF often results in more severe brain dysfunction and has higher mortality and recurrence rates than valvular AF (2-7). Rasmussen *et al.* reported that the incidence of stroke in patients with paroxysmal atrial fibrillation (PAF) was equivalent to that in patients with persistent and permanent AF (8). However, European and American studies have found that the incidence of PAF was higher than that of persistent AF in CIS and transient ischemic attacks (TIAs) (9). Thus, PAF plays an important role in the occurrence of stroke. Research has shown that left atrium (LA) remodeling in patients with AF is closely related to CIS (10,11). Thus, the evaluation of LA function has been an important research topic in recent years.

Four-dimensional automated left atrial quantitative analysis (4D LAQ) is a new ultrasonic technology specifically used to measure LA function. It employs a semi-automatic segmentation algorithm to calculate the LA strain and 3-dimensional (3D) volume data. The software automatically obtains the LA volume and strain parameters. However, this technique requires high-quality images; the analysis results are more variable when the image quality is poor or when the LA envelope is incomplete at the time of image acquisition. Left atrial automated functional myocardial imaging (AFILA) is a new method for evaluating LA function, which is applied in 2-dimensional (2D) echocardiography with speckle tracking to measure the LA volume and overall strain. The operator can easily and quickly obtain parameters, such as LA strain, LA volume, and LA emptying fraction (LA EF). In combination with the 3 planes, it can also be used for PAF episodes and persistent AF. Compared to the 4D Auto LAQ software (GE Healthcare, Chicago, IL, USA), it is easy to operate, reproducible, and less affected by image quality.

The congestive heart failure, hypertension, age of ≥75 years (doubled), diabetes mellitus, stroke or TIA (doubled), age of 65–74 years, and sex category (female) (CHA2DS2-VASc) score is the most widely used clinical method for stratifying thromboembolism risk in patients with AF. It is also used to guide clinical anti-coagulation therapy. This score is not suitable for all patients with AF. Indeed, a number of NVPAF patients have CHA2DS2-VASc scores of <2, which does not reach the threshold for clinical anti-coagulation treatment, however, such patients also have a risk of stroke (12). The present study was the first to explore the relationship between the LA function parameters measured by AFILA and the risk of ischemic stroke in patients with NVPAF and to define the cut-off value for the CHA2DS2-VASc score as <2. Our findings provide an ultrasonic reference standard for the clinical anti-coagulation treatment of this group of patients.

Methods

Study population

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Board of The Second Affiliated Hospital of Nanchang University, and the requirement of individual consent for this retrospective analysis was waived. The investigators were blinded to the clinical outcomes of the patients. A total of 205 patients with NVPAF treated

at the Department of Cardiology between August 2019 and August 2022 were included in the study. Among them, 51 patients with ischemic stroke served as the case group (CIS group), and 154 patients with NVPAF without stroke served as the control group (no-CIS group). To be eligible for inclusion in this study, the patients had to meet the following inclusion criteria: (I) have PAF confirmed by an electrocardiogram (ECG); (II) have been diagnosed with non-valvular AF using echocardiography; and (III) if the patient had experienced CIS, they have been diagnosed with AF-related stroke by a neurologist [the clinical judgment criteria were based on magnetic resonance imaging (MRI), brain infarct morphology and the score for the targeting of AF (13), the LA diameter, age, a diagnosis of stroke or TIA, the smoking scoring system (14), and a history of AF]. Patients were excluded from the study if they met any of the following exclusion criteria: (I) had persistent and permanent AF; (II) also had rheumatic mitral stenosis, and had undergone mitral valvuloplasty and repair, and prosthetic valve replacement; (III) had primary myocardial and pericardial disease; (IV) had congenital heart disease; and/or (V) had incomplete medical records. All the participants were scored according to the CHA2DS2-VASc criteria for thromboembolism risk. The patients were divided into the subgroups based on whether they had a CHA2DS2-VASC of <2 (i.e., a score of 0 or 1) or ≥2. All the patients were examined by routine echocardiography and evaluated by an AFILA analysis.

Image acquisition

The GE vivid E95 ultrasonic diagnostic instrument (GE Vingmed Ultrasound, Horten, Norway) with a M5S probe (frequency: 1.5–4.6 MHz), equipped with EchoPAC 204 software (GE Healthcare), was used for imaging. First, the ECG leads were connected, and the probe was placed at the apex. After verifying that the 2D-section standard was stable, the apical 4- and 2-chamber views with >5 cardiac cycles were acquired with an image frame rate of >40 frames per second (fps). Clear dynamic images were saved for the software analysis.

AFILA analysis

The images were imported into the EchoPAC 204 software. After clicking "measure" and selecting AFILA to enter the measurement mode, the apical 4-chamber view was chosen to ensure that the sampling point was placed in the septal base, lateral wall base, and LA apex as shown in the upper right corner. The LA volume and strain parameters of the 4-chamber view were then obtained after a waiting period of a few seconds. After clicking "Approve and Select Next", the apical 2-chamber view images were activated. The tracing line was modified as necessary and the LA volume and strain results of the 2-chamber view were obtained. The LA parameter average of the biplane was also recorded.

The following volume parameters were measured: volume at onset of LA contraction (LA VpreA); left atrial minimum volume (LA Vmin); left atrial maximum volume (LA Vmax); left atrial evacuation volume (LA EV); and left atrial emptying fraction (LA EF). The following LA strain parameters were measured: left atrial reservoir strain (S_R), which occurs when the left ventricular end-systolic mitral valve opens first and the LA receives blood flow from the pulmonary veins, and reflects the storage function of the LA and the maximum strain value at that time; left atrial conduit strain (S_CD), which occurs when the mitral valve opens and the LA blood empties rapidly until the LA pressure equals the left ventricular pressure and the strain decreases, and is the conduit stage of the LA; left atrial contractile strain (S_CT), which occurs in the late stage of ventricular diastole, when the LA contraction further drains blood into the left ventricle, and the strain parameter decreases further, equal to the difference between the absolute value of S_R and S_CD (this stage reflects the LA systolic function). During the reservoir phase, the LA wall is lengthened, and thus the S_R parameter is expressed as a positive value in this phase. In the other 2 phases, the LA wall is shortened, and thus the S_CD and S_CT parameters in these phases are expressed as negative values (*Figures 1*,*2*).

Statistical analysis

The software SPSS 23.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analyses. The categorical data are expressed as frequencies and percentages and were compared using the χ^2 test or the Kruskal-Wallis test. The continuous variables were presented as means ± standard deviations or medians with 25–75% interquartile ranges according to whether or not they were normally distributed. The independent-sample *t*-test or Mann-Whitney U test was used to compare the means or medians between the 2 groups. Logistic regression analysis was used to determine the predictors of stroke risk in patients with NVPAF. The receiver operating characteristic (ROC) curve revealed the cut-off value, which was the parameter value

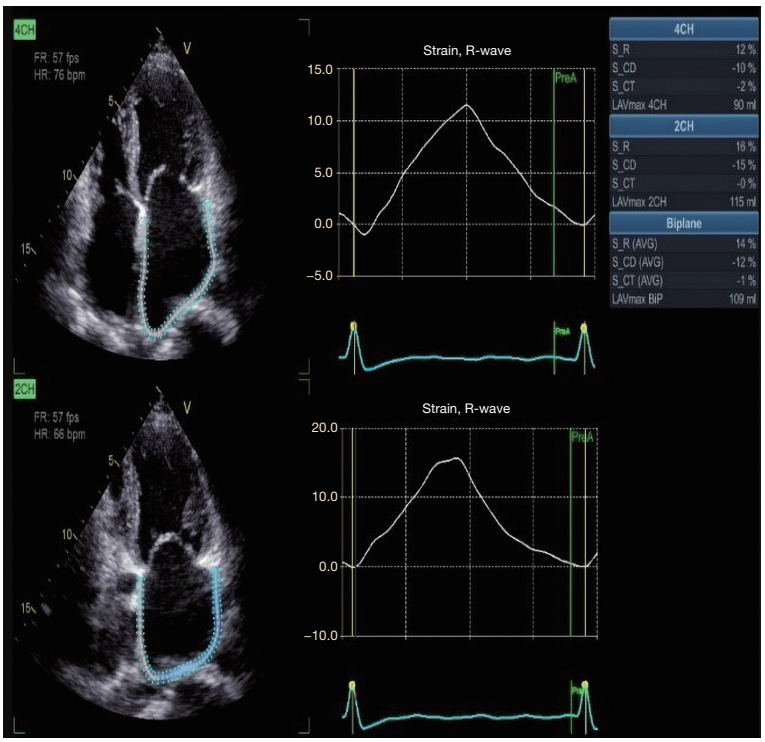

Figure 1 The strain curves. 4CH, 4-chamber; 2CH, 2-chamber; S_R, LA reservoir strain; S_CD, LA conduit strain; S_CT, LA contractile strain; LA Vmax, left atrial maximum volume.

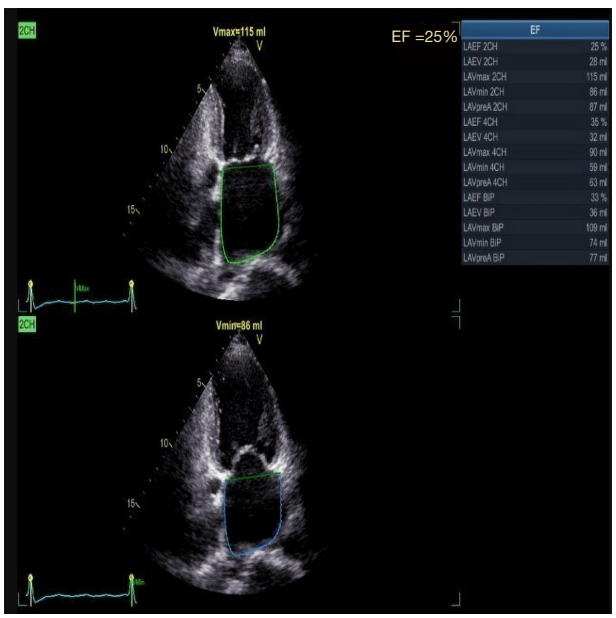

Figure 2 The volume curve. 2CH, 2-chamber; LA Vmin, left atrial minimum volume; LA Vmax, left atrial maximum volume; LA VpreA, volume at onset of left atrial contraction; LA EV, left atrial evacuation volume; LA EF, left atrial emptying fraction.

corresponding to the Youden index with maximum points (Youden index = sensitivity + specificity −1). Statistical significance was considered when $P<0.05$. The intra-group correlation coefficient (ICC) was used to evaluate the consistency of the AFILA parameters. The ICC values ranged from 0 to 1. An ICC value of <0.5 indicated poor consistency, an ICC value of 0.5–0.75 indicated medium consistency, an ICC value of 0.75–0.9 indicated good consistency, and an ICC value of >0.9 indicated excellent consistency.

Results

Clinical characteristics

The patients in the CIS group were older, had higher CHA2DS2-VASc scores, were more likely to have hypertension, diabetes, coronary artery disease, and use anti-coagulants than those in the no-CIS group ($P<0.05$). Left ventricular ejection fraction, body mass index, sex, the number of heart failures, a previous history of cerebral infarction, a course of AF, carotid plaque, and deep vein

Table 1 Baseline characteristics of the study subjects

Clinical characteristic	No-CIS (n=154)	CIS (n=51)	P value
Male gender, n (%)	104 (67.5)	30 (58.8)	0.257
Age (years), median [IQR]	60 [53–65.25]	68 [64–78]	<0.001
LVEF (%), mean ± SD	59.27±8.88	59.06±8.23	0.879
BMI (kg/m^2), mean ± SD	22.81±2.86	23.07±2.48	0.549
Antiplatelet and anti-coagulant, n (%)	29 (18.8)	18 (35.3)	0.015
Comorbid conditions, n (%)			
History of heart failure	15 (9.7)	7 (13.7)	0.425
Hypertension	51 (33.1)	37 (72.5)	<0.001
Diabetes	11 (7.1)	13 (25.5)	<0.001
Coronary artery disease	14 (9.1)	13 (25.5)	0.003
Previous TIA or stroke	14 (9.1)	9 (17.6)	0.093
Carotid plaque	49 (31.8)	22 (43.1)	0.141
Deep vein thrombosis	2 (1.3)	3 (5.9)	0.100
Course of NVPAF (years), n (%)			0.117
<3	91 (59.1)	33 (64.7)	
3–5	21 (13.6)	11 (21.6)	
>5	42 (27.3)	7 (13.7)	
CHA2DS2-VASc score, n (%)			<0.001
<2	112 (72.7)	15 (29.4)	
≥2	42 (27.3)	36 (70.6)	

CIS, cerebral ischemic stroke; IQR, interquartile range; LVEF, left ventricular ejection fraction; SD, standard deviation; BMI, body mass index; TIA, transient ischemic attack; NVPAF, non-valvular paroxysmal atrial fibrillation; CHA2DS2-VASc, congestive heart failure, hypertension, age of ≥75 years (doubled), diabetes mellitus, stroke or TIA (doubled), age of 65–74 years, and sex category (female).

thrombosis did not differ significantly between the 2 groups (*Table 1*).

Univariate analysis of AFILA

The LA EF (26.78±9.67 *vs.* 33.45±14.31, P<0.001) and S_R {6 [2–10] *vs.* 9.5 [6–17], P<0.001} were lower in the CIS group than the no-CIS group. However, the S_CT [0 (–2 to 3) *vs.* –6 (–9 to –2), P<0.001] values were greater in the CIS group than the no-CIS group. The LA Vmin, LA Vmax, LA VpreA, LA EV, and S_CD did not differ significantly between the 2 groups (*Table 2*).

Logistic regression analysis

The multivariate regression analysis examined the factors that were found to be statistically significant in the single-factor analysis. Given the multicollinearity, the CHA2DS2-VASc score was not included in the analysis, and age, hypertension, and the S_CT were independent risk factors of CIS. The risk of CIS in patients with hypertension was 2.772 times that of those without hypertension, and the risk of CIS increased 1.068 times with each additional year of age. After correcting for the clinical factors included in the CHA2DS2-VASC score, the S_CT was shown to predict to NVPAF with stroke [odds ratio (OR): 1.234, 95% confidence interval (CI): 1.101–1.383, P=0.000] (*Table 3* and *Figure 3)*. In addition, we used the CHA2DS2-VASc score instead of age, diabetes, coronary artery disease, and hypertension to perform the multiple regression analysis, and found that the S_CT was still significant (OR: 1.252, 95% CI: 1.118–1.402, P=0.000).

Table 2 Univariate analysis of the AFILA-related parameters between the 2 groups

Variable	No-CIS (n=154)	CIS (n=51)	Z/t	P value
LA Vmin, median [IQR]	50 [25–66]	49 [33–54]	–0.860	0.390
LA Vmax, median [IQR]	67 [48–87]	66 [52–74]	–0.708	0.479
LA VpreA, median [IQR]	59 [39–81]	56 [37–63.50]	–1.618	0.106
LA EV, median [IQR]	21 [14–26]	19 [15.5–23]	–0.774	0.439
LA EF, mean ± SD	33.45±14.31	26.78±9.67	–3.749	<0.001
S_R, median [IQR]	9.5 [6–17]	6 [2–10]	–4.271	<0.001
S_CD, median [IQR]	–6 [–10 to –1]	–7 [–11 to –1]	–0.716	0.474
S_CT, median [IQR]	–6 [–9 to –2]	0 [–2 to 3]	–6.945	<0.001

AFILA, left atrial automated functional myocardial imaging; CIS, cerebral ischemic stroke; LA Vmin, left atrial minimum volume; IQR, interquartile range; LA Vmax, left atrial maximum volume; LA VpreA, volume at onset of left atrial contraction; LA EV, left atrial evacuation volume; LA EF, left atrial emptying fraction; S_R, left atrial reservoir strain; S_CD, left atrial conduit strain; S_CT, left atrial contractile strain.

Table 3 Multivariate logistic regression analysis of variables for the prediction cerebral ischemic stroke

Variable	Coefficient	SE	OR	95% CI	P value
Age	0.066	0.020	1.068	1.027–1.111	0.001
Diabetes	0.270	0.604	1.310	0.401–4.281	0.655
Coronary artery disease	0.856	0.544	2.353	0.811–6.828	0.116
Hypertension	1.020	0.443	2.772	1.163–6.607	0.021
Antiplatelet and anti-coagulant	–0.684	0.465	0.504	0.203–1.255	0.141
S_CT	0.210	0.058	1.234	1.101–1.383	0.000
S_R	0.046	0.054	1.047	0.942–1.163	0.398
LA EF	–0.012	0.027	0.988	0.937–1.042	0.659

SE, standard error; OR, odds ratio; CI, confidence interval; S_CT, left atrial contractile strain; S_R, left atrial reservoir strain; LA EF, left atrial emptying fraction.

Correlation between the S_ CT and CHA2DS2-VASc score

The no-CIS and CIS patients were divided into 2 subgroups based on whether the patients' CHA2DS2-VASc scores were ≥2 or <2. The S_CT differed significantly between the 2 groups (P<0.0001 and P=0.0357, respectively). Further, the S_CT was more significant in CIS patients with scores of <2 than in groups with scores of ≥2 (P=0.009) *(Figure 4)*. The diagnostic value of the S_CT1 for a CHA2DS2-VASc score of <2 was better than that for a score ≥2 [S_CT1 area under the curve (AUC): 0.866, P<0.0001 *vs.* S_CT2 AUC: 0.639, P=0.0357]. In the CHA2DS2-VASc score of <2 group, there were 127 patients with CHA2DS2-VASc score of <2, 15 of which had stroke. Further, the maximum Youden index was 0.55 with a corresponding S_CT value of –4.5. The cut-off value for the NVPAF patients with CIS was a S_CT of –4.5, which had a sensitivity of 0.80, a specificity of 0.75, and an AUC of 0.866 (P<0.0001) *(Figure 5)*.

Consistency test on ultrasonic AFILA measurement parameters

The LA strain and volume parameters of AFILA were measured and analyzed by the same operator over different periods using the same method in 20 randomly selected cases to examine inter-observer variability. In addition, another operator with the same qualifications used the

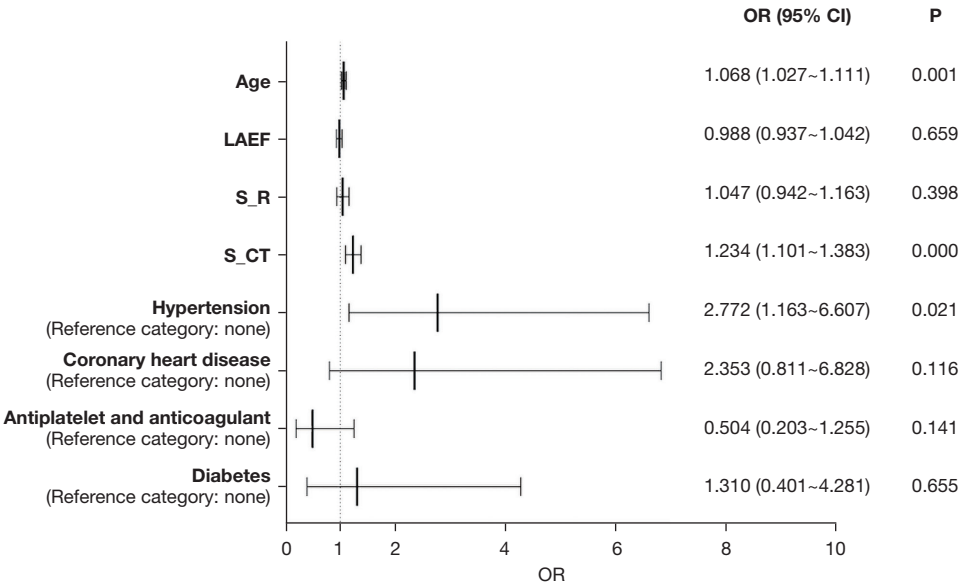

Figure 3 Logistic regression forest map of the combined risk of stroke in patients with non-valvular paroxysmal atrial fibrillation. OR, odds ratio; CI, confidence interval; LAEF, left atrial emptying fraction; S_R, left atrial reservoir strain; S_CT, left atrial contractile strain.

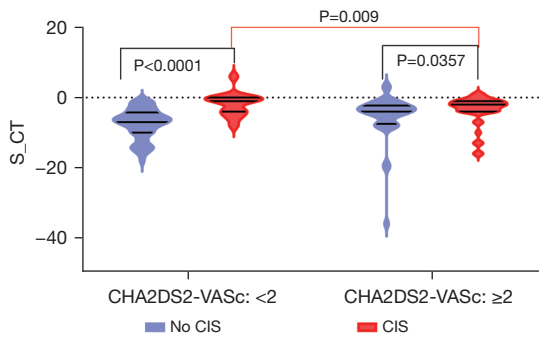

Figure 4 The S_CT in CIS and non-CIS patients. Compared to the patients without CIS, the S_CT was significantly higher in patients with CIS, irrespective of their CHA2DS2-VASc scores, and was especially high in patients with a CHA2DS2-VASc score <2. S_CT, left atrial contractile strain; CIS, cerebral ischemic stroke; CHA2DS2-VASc, congestive heart failure, hypertension, age of ≥75 years (doubled), diabetes mellitus, stroke or TIA (transient ischemic attack; doubled), age of 65–74 years, and sex category (female).

same method for the measurement and analysis. The data between the different operators were compared to determine intra-observer variability. The ICC values were all >0.9, which indicated excellent consistency *(Table 4)*.

Discussion

The present study found that compared to the no-CIS group, patients in the CIS group were older, had higher CHA2DS2-VASc scores, a history of diabetes, hypertension, and coronary heart disease, and used more anti-coagulants or platelet drugs. Of the NVPAF patients, 71% in the CIS group and 27% in the no-CIS group had CHAD2DS2-VASc scores of at least 2 points. However, only 35% in the CIS and 19% in the no-CIS group were anti-coagulants. In this study, the use of anti-coagulants referred to whether a patient had taken anti-coagulants before the diagnosis of CIS, and not to whether a patient took anti-coagulants after the diagnosis of CIS. A variety of factors, including admission to hospital, venous thrombosis of the lower limbs, previous stroke, and medication compliance, affect patients' previous anti-coagulation treatments, which might be one explanation for the high stroke rate.

LA strain is a useful indicator for the dynamic evaluation of LA function in patients with NVPAF, and is more sensitive than LA volume. Our results showed that the damage to the LAEF, S_CT, and S_R was more significant in the CIS group than the NVPAF group, whereas the damage to the LA Vmin, LA Vmax, LA VpreA, LA EV, and S_CD did not differ significantly between the 2 groups.

Age, sex, a history of hypertension, and the S_CT were shown to be independent risk factors for stroke. After adjusting for the clinical confounding factors, we found that S_CT damage was significantly correlated with stroke.

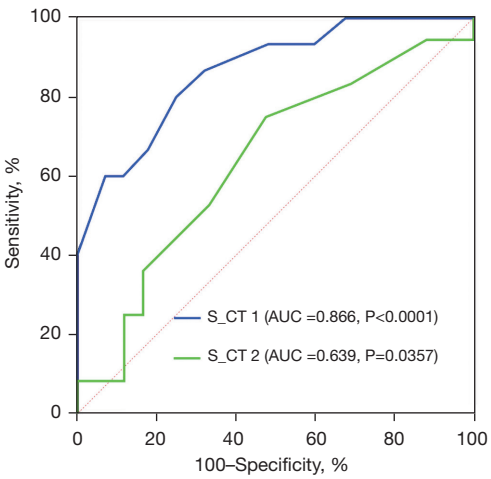

Figure 5 The S_CT ROC curve for predicting the risk of stroke in patients with a CHA2DS2-VASc score <2 and a CHA2DS2-VASc score ≥2 in non-valvular paroxysmal atrial fibrillation patients. S_CT, left atrial contractile strain; ROC, receiver operating characteristic; AUC, area under the curve; CHA2DS2-VASc, congestive heart failure, hypertension, age of ≥75 years (doubled), diabetes mellitus, stroke or TIA (transient ischemic attack; doubled), age of 65–74 years, and sex category (female); S_CT 1, S_CT in patients with a CHA2DS2-VASc score <2; S_CT 2, S_CT in patients with a CHA2DS2-VASc score ≥2.

Further, Compared to CHA2DS2-VASc score ≥2, the S_CT impairment was more obvious in the stroke group with a CHA2DS2-VASc score <2, and the diagnostic value was greater. The ROC curve showed that a S_CT equal to –4.5% was the CIS cut-off value for NVPAF patients, and had a sensitivity of 80%, a specificity of 75%, and an AUC of 0.866 (P<0.0001). All the analyses were performed in sinus rhythm, and the LA strain values of the patients with AF recorded in this study were significantly lower than those reported in previous studies. There are a number of possible reasons for the inconsistencies between these results; for example, inconsistent software and instruments were used, different cases were studied, the cut-off value in this study was for patients with AF at risk of stroke, whereas previous studies mostly examined the range of LA strain in healthy control participants, and the left ventricular strain used in previous analyses of LA strain was measured by a new ultrasonic technique that had certain errors. Today, emerging ultrasound technologies, such as 4D Auto, LAQ, and AFILA, use specialized software to study the LA, and are more accurate in theory.

It is estimated that PAF causes up to one-third of CIS cases (9). The CHA2DS2-VASc score reflects the risk factors for clinical complications. This score is composed of C (congestive heart failure), H (hypertension), A (age ≥75 years), D (diabetes), and S (previous stroke or TIA), and is the most widely used scoring system in clinical practice and is recommended by the 2014 AHA/ACC/HRS guidelines (15). Recent studies have found that in addition to clinical complications, the risk of stroke in patients

Table 4 Inter-observer and intra-observer variability

Parameter	Inter-observer variability			Intra-observer variability		
	ICC	95% CI	P value	ICC	95% CI	P value
LA Vmin	0.995	0.988–0.998	<0.001	0.990	0.976–0.996	<0.001
LA Vmax	0.999	0.996–0.999	<0.001	0.997	0.993–0.999	<0.001
LA VpreA	0.999	0.997–0.999	<0.001	0.997	0.994–0.999	<0.001
LA EV	0.993	0.983–0.997	<0.001	0.987	0.967–0.995	<0.001
LA EF	0.990	0.975–0.996	<0.001	0.976	0.940–0.990	<0.001
S_R	0.993	0.982–0.997	<0.001	0.986	0.965–0.994	<0.001
S_CD	0.990	0.974–0.996	<0.001	0.979	0.949–0.992	<0.001
S_CT	0.994	0.986–0.998	<0.001	0.989	0.972–0.995	<0.001

ICC, intra-group correlation coefficient; CI, confidence interval; LA Vmin, left atrial minimum volume; LA Vmax, left atrial maximum volume; LA VpreA, volume at onset of left atrial contraction; LA EV, left atrial evacuation volume; LA EF, left atrial emptying fraction; S_R, left atrial reservoir strain; S_CD, left atrial conduit strain; S_CT, left atrial contractile strain.

with AF is also related to cardiac function, renal function, inflammation, coagulation biomarkers, LA mechanical function impairment, and other factors (16). However, clinical complications are used as risk factors for the CHA2DS2-VASc, and the assessment is not comprehensive enough to be applicable to all patients with AF. Some PAF patients with fewer clinically relevant factors have a CHA2DS2-VASc score of 0 or 1, which indicates a low risk of cerebral thromboembolism. At present, no conventional anti-thrombotic therapy is recommended for such patients, but these patients still have a certain level of CIS risk. If the score is used to determine the risk of thrombosis in clinical practice, there will be a risk of missed diagnosis of stroke in this cohort. Thus, there is a need to improve risk stratification beyond clinical variables.

Obokata *et al.* found that LA strain provides incremental diagnostic information that exceeds that obtained by the CHA2DS2-VASc score (17). LA strain analysis improves the current risk stratification of embolism in patients with AF, and LA strain is also predictive of the mortality risk after stroke (18). Leong *et al.* (19) and Sanchis *et al.* (20) found that strain was significantly impaired in the CIS of patients with PAF and that it was a better predictor than clinical risk factors alone. The above studies showed that LA function, especially myocardial strain, is a potential sensitive indicator of an increased risk of stroke or TIA, can be used in addition to the CHA2DS2-VASc score (21).

The systolic function of LA in patients with AF is seriously reduced, leading to atrial myocardial fibrosis and LA remodeling. LA remodeling includes the structural, functional, and electrophysiological remodeling of the LA, whereby the LA is enlarged and the atrial muscle fiber is destroyed, in patients with AF. Atrial stretching leads to cell hypertrophy and apoptosis, which promotes the abovementioned structural and electrophysiological changes. The functions of the LA include storage, conduit, and contraction. LA remodeling leads to LA strain and strain rate impairment, and LA function decline also leads to LA remodeling. Abnormal LA function is closely related to the occurrence and progression of AF and is known as LA cardiomyopathy (22,23). The evaluation of LA strain can serve as a substitute for the evaluation of LA fibrosis (24). AFILA is a new ultrasonic technology for the assessment of LA function. Its operation is extremely simple; ECG is used to obtain dynamic images of the apical 4- and 2-chamber views during a 2D echocardiography examination. The method can then be used to immediately and automatically analyze the LA volume and strain parameters. The measurement accuracy and repeatability of this technique are high. Further, it is relatively independent of the image quality compared to 4D Auto LAQ.

LA strain includes the S_R, S_CD, and S_CT. The S_R is determined by the stiffness and compliance of the atria and affects the storage function of the LA. The S_CD occurs in the early stage of ventricular diastole and is related to the early filling of the left ventricle, and its value indirectly reflects the diastolic function of the left ventricle. The S_CT occurs in the late ventricular diastole stage, and a LA contraction acts as a booster pump to further increase the left ventricular filling pressure. This function is affected by the LA preload, afterload, and the reserve capacity of the left ventricle at the end of systole. In a study of non-valvular AF, Leung *et al.* found that the LA strain of stroke patients with AF was more severely impaired than patients with AF without stroke (25). The present study also confirmed this relationship. In addition, the S_CT of the LA strain parameter was more obviously damaged in the CIS group with CHA2DS2-VASc scores of 0 or 1 than in those with scores ≥2. The diagnostic value of the S_CT was better in groups with CHA2DS2-VASc scores of <2 than in those with scores ≥2. This may be because PAF patients have fewer comorbid clinical factors, whereas patients with long-term persistent AF are more prone to heart failure and have more clinical comorbidities than PAF patients. Compared to patients with persistent AF, the CHA2DS2-VASc score of PAF patients was lower, and the LA strain parameters and clinical factors for the CHA2DS2-VASc score, such as hypertension and diabetes, had a synergistic effect (26). If these confounding factors had been excluded, the results of the present study in assessing the effect of LA strain parameters on stroke would have been more accurate.

Study limitations

The present study had a number of limitations. First, the sample size of the stroke patients with a CHA2DS2-VASc score of <2 in the no-CIS group was not large and there was no validation cohort. Thus, large-scale, multicenter prospective studies need to be conducted in the future to verify these results. Second, only the clinical and ultrasonic factors for PAF patients were included in the present analysis, and the laboratory indicators were excluded. Third, the final outcome of NVPAF was not applicable to all patients with AF. The accuracy and repeatability of the AFILA measurement depend on high-quality images, and there is a great difference in the

analysis results when the image quality is poor or the left atrial wrapping is not complete during image acquisition. Finally, different instruments, software packages, different suppliers, and different ECG gating can affect the results of analyses.

Conclusions

The S_CT of LA strain measured using AFILA was shown to have a high diagnostic efficacy in patients with NVPAF, whereas age, hypertension, and S_CT were factors independently associated with the risk of stroke. CHA2DS2-VASc scores of 0 or 1 and a S_CT of >–4.5% in NVPAF patients may be valuable in guiding clinical anticoagulation treatments in patients with NVPAF.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-1142/coif). All authors report that the study received support from the Science and Technology Research Project of Jiangxi Provincial Department of Education (No. GJJ190002) and the Research Topic of the Teaching Reform Research Subject of Jiangxi Province (No. JXJG-19-1-40). SL is an employee of the GE company. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work, including ensuring that any questions related to the accuracy or integrity of any part of the work have been appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Board of The Second Affiliated Hospital of Nanchang University, and the requirement of individual consent for this retrospective analysis was waived.

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