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Predictive value of echocardiography combined with CT angiography for left atrial appendage thrombosis in patients with non-valvular atrial fibrillation

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Abstract. – OBJECTIVE: The aim of this study was to investigate the detection rate of left atrial appendage thrombus (LAAT) formation in non-valvular atrial fibrillation (NVAF) patients using three methods and the efficacy of combined electrocardiogram (ECG) and Computed Tomography Angiography (CTA) in the diagnosis of LAAT.

PATIENTS AND METHODS: A total of 80 NVAF patients who underwent Transesophageal echocardiography (TEE) at our hospital from August 2018 to August 2022 were included in the study. The baseline data of patients were observed, and the positive rates of LAAT formation by ECG, CTA, and TEE were compared. The efficacy of combined ECG and CTA in the diagnosis of LAAT was also evaluated.

RESULTS: Among the 80 NVAF patients, 23 were LAAT positive and 57 were LAAT negative. There were statistically significant differences between the two groups in terms of age, body mass index (BMI), N-terminal prohormone of brain natriuretic peptide NT-probNP, fibrinogen, CHA2DS2-VASC [congestive Heart Failure, Hypertension, Age (75 or older), diabetes mellitus, stroke, vascular disease, age (65-74), sex category] score, paroxysmal atrial fibrillation, renal insufficiency, D-dimer, heart failure, and serum uric acid ($p<0.05$). The positive rate of LAAT detected by ECG combined with CTA was closest to the gold standard TEE, but the difference was not statistically significant ($p>0.05$). Statistically significant differences were found between LAAT positive and negative patients in various parameters related to left atrial and left ventricular dimensions and function ($p<0.05$), while some parameters showed no significant differences ($p>0.05$).

CONCLUSIONS: ECG combined with CTA has a high diagnostic value for LAAT formation in NVAF patients, with a high degree of confidence and reduced patient intolerance. The sensitivity, accuracy, and negative predictive value of ECG combined with CTA for the diagnosis of LAAT formation in NVAF patients are high and have good predictive value.

Key Words:
Echocardiography, CT angiography, Non-valvular atrial fibrillation, Left ear thrombus, Formation, Predictive value.

Introduction

Non-valvular atrial fibrillation (NVAF) is the most common persistent arrhythmia worldwide and has become a major public health burden as the population ages[1]. The presence of atrial fibrillation is strongly associated with cardiovascular hospitalization and all-cause mortality and even counteracts the prognostic ability of cardiac calcification in patients with multiple cardiovascular risk factors[2]. Stroke is the most clinically significant complication observed in patients with NVAF[3], with a 4-5 times higher risk than in patients without[4]. Strokes can be fatal (up to 20%) or severely disabling (about 60%)[5]. The formation of LAAT is known to be a major cause of cardiogenic stroke in patients with NVAF[6].

Thrombosis occurs within the left atrial appendage (LAA), particularly in the case of LAAT in the context of NVAF, which is due to reduced contractility and blood stasis instability that has been shown[7,8] to be associated with an increased risk of thromboembolism. The prevalence of LAAT has been reported[9,10] to range from 0.6% to 27% in different populations of NVAF patients. Although Transesophageal echocardiography (TEE) is the gold standard for the diagnosis of LAAT, this invasive test limits patients with heart failure, severe arrhythmias, esophageal ulcers, or varices[11]. Electrocardiogram (ECG) is now an important tool in the diagnosis of cardiac disease

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due to its safety, simplicity, and comprehensive diagnostic information[12], but there are still strict empirical requirements and poor reproducibility[13]. Computed Tomography Angiography (CTA) has a higher resolution and has been used in the diagnosis of coronary heart disease and has gained wide acceptance[14]. This paper examines the clinical value of ECG in combination with CTA for the diagnosis of LAAT in patients with NVAF.

Patients and Methods

Study Population

Patients (n=80) with NVAF who underwent TEE at our hospital between August 2018 and August 2022 were included.

Inclusion criteria[15,16]

- patients with NVAF aged >40 years.
- patients who have completed TEE, ECG or CTA
- with adequate and complete clinical information.

Exclusion criteria[17]

- patients with valvular atrial fibrillation.
- combined acute coronary artery disease.
- acute ischemic stroke; hyperthyroidism; severe hepatic and renal dysfunction; infectious diseases.

The study was approved by the Review Committee of our Ethics Committee. All patients and their families gave informed consent.

Inspection Methods

TEE was performed using a PhilipsE33 Color Doppler ultrasound machine (Kunshan He Chuang Ultrasound Instrument Co., Ltd., Kunshan, Jiangsu, China), a 2-7MHz X7-2t transesophageal ultrasound probe (Jiangsu Anmao Medical Technology Co., Ltd., Xuzhou, Jiangsu, China), and a 2-5MHz S5-1 cardiac probe (Jiangsu Anmao Medical Technology Co., Ltd., Xuzhou, Jiangsu, China). Echocardiography was performed to measure the anterior-posterior left atrial diameter, left atrial internal diameter, left atrial transverse diameter, left atrial upper and lower diameters, left ventricular end-diastolic internal diameter, and left ventricular ejection fraction levels in both groups. Long and short left auricular opening diameter, long left auricular opening diameter/short left auricular opening diameter, left auricular opening area, left auricular depth, maximum and minimum left auricular volume, and left auricular ejection fraction levels were measured or calculated in both groups using 64-layer spiral CT (Lightspeed VCT, GEMedical System: Boston, MA, United States) in combination with cardiac gated scanning. All patients were examined prior to percutaneous left ventricular occlusion and complete images were obtained with an interval of <48 hours between each examination. The criteria[18] conformed to the use of echocardiography in the diagnosis of left atrial accessory thrombus in patients with non-valvular atrial fibrillation.

The ECG is measured using CTA and TEE parameters from the records of the medical hospital system. LAAT was defined as a dense LAAT block with well-defined abnormalities seen in ≥2 slices using TEE.

Observed Indicators

Data collection

We collected baseline information of all patients, including age, gender, smoking status, BMI, paroxysmal Atrial fibrillation (AF), coronary artery disease, heart failure, hypertension, renal insufficiency, history of stroke, transient ischemic attack (TIA), diabetes, history of vascular disease, CHADS2 score ≥2, CHA2DS2-VASc score ≥2, fibrinogen, D-dimer, serum uric acid, NT-proBNP, and alcohol consumption.

The formulas used to calculate diagnostic efficacy were:

1. Diagnostic sensitivity=[TP/(TP+FN)] ×100%.
2. Diagnostic specificity=[TN/(TN+FP)] ×100%.
3. Expected value of positive results=[TP/(TP+FP)] ×100%.
4. Expected value of negative results=[TN/(TN+FN)] ×100%.
5. Accuracy=[TP+TN/(TP+FP+TN+FN)] ×100%.

In the formulas, TP is true positive, TN is true negative, FP is false positive, and FN is false negative.

Statistical Analysis

The 80 NVAF patients included in the study were divided into two groups (LAAT-positive and LAAT-negative groups). Measured variables were expressed as mean ± standard deviation (s), and a *t*-test was used with degrees of freedom for comparison between groups. Count variables were expressed as percentages, and comparisons were made using the χ^2 test. Receiver operating characteristic (ROC) curves were used for analysis and to determine appropriate cut-off points for risk factors predicting LAAT. Logistic regression analyses were performed to find independent risk factors for LAAT, and results were expressed as an odds ratio (OR) with a 95% confidence

interval (CI). All statistical analyses were performed using SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). A p-value lower than 0.05 was considered statistically significant.

Results

Age, BMI, N-terminal prohormone of brain natriuretic peptide NT-proBNP, fibrinogen, paroxysmal atrial fibrillation, renal insufficiency, D-dimer, heart failure, and serum uric acid are associated with LAAT positivity. We included 80 patients with NVAF, of whom 23 were LAAT-positive and 57 were LAAT-negative. In both groups, age, BMI, NT-proBNP, fibrinogen, paroxysmal atrial fibrillation, renal insufficiency, D-dimer, heart failure, and serum uric acid were analyzed for their association with LAAT positivity.

Statistically significant differences were observed in the CHA2DS2-VASc score for paroxysmal cases and were found in the comparison of atrial fibrillation, renal insufficiency, D-dimer, heart failure, and serum uric acid. All other data were not statistically significant when compared, $p>0.05$ (Table I).

The Positive LAAT Detection Rate for ECG Combined with CTA is Closer to the Gold Standard Detection Rate

According to the results, the positive detection rate of LAAT was 32.50% for TEE, which is the gold standard, 18.75% for ECG, 48.75% for CTA, and 31.25% for ECG combined with CTA. The positive detection rate of LAAT using ECG, CTA, and TEE was statistically significant at $p<0.05$, while the positive detection rate of ECG combined with CTA was not statistically significant at $p>0.05$ (Table II). The findings suggest that ECG combined with CTA has the closest positive detection rate to the gold standard for LAAT (Table II, Figure 1).

ECG Combined with CTA is of Greater Diagnostic Value for LAAT

The study found statistically significant differences between LAAT-positive and negative patients in terms of several ECG and TEE parameters. Anteroposterior left atrial diameter, transverse left atrial diameter, inferior and superior left atrial diameter, and left ventricular ejection fraction, all showed significant differences between the two groups ($p<0.05$). However, there were

Table I. Baseline information.

Index	NVAF patients (n=80 cases)	LAAT positive group (n=23 cases)	LAAT negative group (n=57 cases)	t/χ^2	p
Sex (Cases)					
male	42 (52.5)	13 (56.52)	29 (50.88)	0.009	0.925
female	40 (50)	12 (52.17)	28 (49.12)		
Age (Cases)					
<65 years old	31 (38.75)	5 (21.74)	26 (45.61)	3.936	0.047
≥65 years old	49 (61.25)	18 (78.26)	31 (54.39)		
BMI (kg/m^2)	25.11±3.34	23.15±3.28	25.86±3.41	3.252	0.002
NT-proBNP (pg/mL)	1,082.34±92.84	1,285.41±97.84	1,066.79±91.77	9.463	0.000
Fibrinogen (g/L)	3.79±1.51	3.56±1.49	4.37±1.64	2.051	0.044
Coronary heart disease (cases)	20 (25.00)	6 (26.09)	14 (24.56)	0.020	0.887
Paroxysmal atrial fibrillation (cases)	20 (25.00)	12 (52.17)	8 (14.04)	12.713	0.000
Stroke/TIA (cases)	6 (7.50)	2 (8.70)	4 (7.02)	0.045	0.833
Renal insufficiency (cases)	5 (6.25)	4 (17.39)	1 (1.75)	4.430	0.035
CHA2DS2-VASc score≥2points (cases)	14 (17.50)	4 (17.39)	10 (17.54)	0.095	0.757
CHADS2score≥2points (cases)	28 (35.00)	7 (30.43)	21 (36.84)	0.296	0.587
History of vascular disease (cases)	16 (20.00)	6 (26.09)	10 (17.54)	0.309	0.578
Diabetes (cases)	16 (20.00)	6 (26.09)	10 (17.54)	0.309	0.578
D-dimer (μg/mL)	3.67±0.73	4.18±0.76	3.37±0.72	4.483	0.000
Heart failure (cases)	8 (10.00)	6 (26.09)	2 (3.51)	6.943	0.008
Serum uric acid (μmol/L)	382.67±28.46	401.87±29.87	370.11±28.26	4.476	0.000
Smoke (cases)	44 (55.00)	14 (60.87)	30 (52.63)	0.449	0.503
Hypertension (cases)	16 (20.00)	6 (26.09)	10 (17.54)	0.309	0.578
Drink (cases)	45 (56.25)	15 (65.22)	30 (52.63)	1.055	0.304

Table II. Left atrial appendage thrombus (LAAT) detection rates of different examination methods.

	TEE					
	LAAT positive	LAAT negative	Total	Positive rate (%)	χ^2	*p*
ECG (n=80)						
Positive	14	1	15 (48.75)	18.75	3.968	0.046
Negative	12	53	65 (81.25)			
Total	26	54	80			
CTA (n=80)						
Positive	25	14	39 (48.75)	48.75	4.379	0.036
Negative	1	40	41 (51.25)			
Total	26	54	80			
ECG combination CTA (n=80)						
Positive	23	2	25 (31.25)	31.25	0.029	0.865
Negative	3	52	55 (68.75)			
Total	26	54	80			

no statistically significant differences in left atrial internal diameter or left ventricular end-diastolic internal diameter between LAAT-positive and negative patients ($p>0.05$) (Table III).

A comparison between the gold standard TEE and CTA parameters showed statistically significant differences between LAAT-positive and negative patients in various measures, including left atrial opening length, left atrial opening short diameter, left atrial opening area, maximum left atrial volume, minimum left atrial volume, and left atrial ejection fraction ($p<0.05$). However, there were no statistically significant differences in left atrial opening length/left atrial opening short diameter and left atrial depth between LAAT-positive and negative patients ($p>0.05$). Additionally, no statistically significant differences were found in terms of left ventricular opening length/ventricular opening short diameter and left ventricular depth between LAAT-positive and negative patients ($p>0.05$), as shown in Table IV.

Table III. Comparison of efficacy of combined electrocardiogram (ECG) parameters in patients with positive and negative left atrial appendage thrombus (LAAT) detected by the gold standard.

Parameters	LAAT positive group (n=23 cases)	LAAT negative group (n=57 cases)	*t*	*p*
Anterior-posterior left atrial diameter (mm)	45.68±3.52	40.11±4.37	5.436	0.000
Left atrial internal diameter (mm)	42.86±5.64	40.95±5.47	1.401	0.165
Left atrial transverse diameter (mm)	45.31±4.96	42.11±4.92	2.627	0.010
Upper and lower left atrial diameter (mm)	60.14±4.92	54.26±4.95	4.817	0.000
Left ventricular end-diastolic internal diameter (mm)	47.06±5.34	46.12±5.30	0.716	0.476
Left ventricular ejection fraction (%)	61.02±8.65	66.26±8.71	2.426	0.018

Table IV. Comparison of Computed Tomography Angiography (CTA) parameters for left atrial appendage thrombus (LAAT) positive and negative patients detected by the gold standard.

Parameters	LAAT positive group (n=23 cases)	LAAT negative group (n=57 cases)	*t*	*p*
Long diameter of left auricular opening (cm)	3.19±0.28	2.91±0.27	4.154	0.000
Short diameter of left ventricular opening (cm)	2.09±0.29	1.90±0.25	2.937	0.004
Left auricular opening length/left auricular opening	1.53±0.21	1.57±0.20	0.798	0.427
Left auricular opening area (cm^2)	5.61±0.73	4.92±0.71	3.902	0.000
Depth of left heart ear (cm)	4.56±0.35	4.39±0.30	1.601	0.114
Maximum left ventricular volume (mL)	13.86±2.89	11.62±2.86	3.161	0.002
Minimum left heart ear volume (mL)	8.74±1.75	6.34±1.66	5.763	0.000
Ejection fraction of the left heart ear (%)	37.64±6.34	44.28±6.29	4.212	0.000

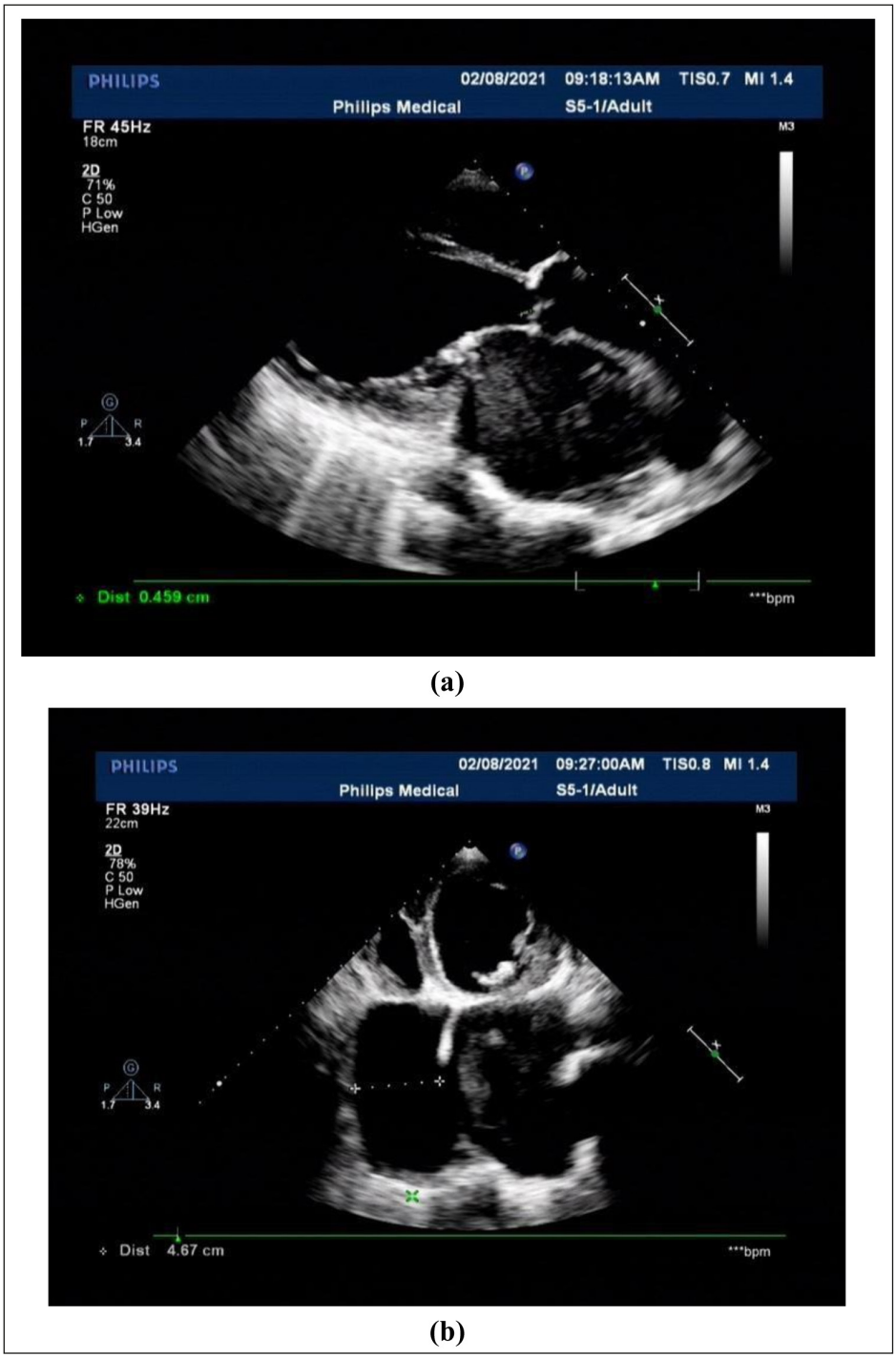

Figure 1. Echocardiogram of a patient with positive LAAT (**a**) with vertical measurement (**b**) with both vertical and horizontal measurement.

Based on the results presented in Table V and Figure 2, CTA had the highest sensitivity and negative predictive value but the lowest specificity, accuracy, and positive predictive value. On the other hand, ECG had the highest specificity and positive predictive value but the lowest sensitivity and negative predictive value. Combining ECG with CTA resulted in a greater AUC than either single test alone. Specifically, ECG had the highest sensitivity, accuracy, and negative predictive value, while ECG combined with CTA had the best diagnostic efficacy.

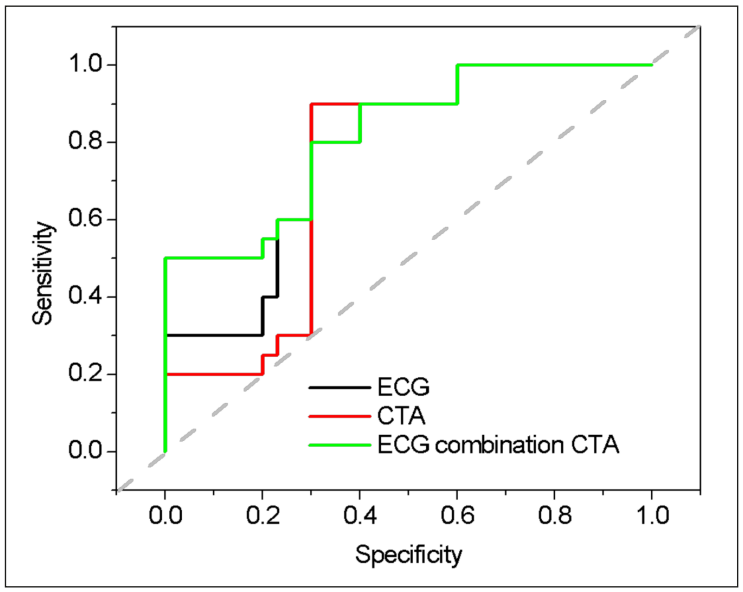

Figure 2. ROC curve.

Table V. Predictive value of the 3 screening instruments.

Review mode	AUC	Sensitivity (%)	Specificity (%)	Accuracy (%)	Positive predictive value (%)	Negative predictive value (%)	p	The 95% confidence interval falls within the rate	
								Upper limit	Lower limit
ECG	0.948	53.85	98.15	83.75	93.33	81.54	0.000	0.901	0.996
CTA	0.996	96.15	74.07	81.25	64.10	97.56	0.000	0.988	1.000
ECG combination CTA	1.000	88.46	96.30	93.75	92.00	94.55	0.000	1.000	1.000

Discussion

Predicting LAAT Formation Plays an Important Role in the Treatment of NVAF

The presence of non-valvular atrial fibrillation (NVAF) poses a significant threat to cardiovascular health[18], with a high risk of left atrial appendage thrombus (LAAT) formation. The left atrial appendage has a long and tubular structure, highly variable in shape, predominantly bilobed with many comb-like muscles and a rough surface[19]. Due to its specific and complex structure, LAAT is easily generated in NVAF[20], and in severe cases, thrombus dislodgement can lead to obstruction of vascular circulation and ischemic stroke[21]. Therefore, predicting LAAT plays a crucial role in the treatment of NVAF.

ECG Combined with CTA has a Higher Detection Rate of Positive LAAT in Patients with NVAF Compared to a Single Test

TEE is the gold standard for the detection of LAAT formation in NVAF patients and the biggest advantage is that the images are very clear and facilitate the accuracy of the diagnosis of the disease by avoiding external interference and interference from other tissues[22]. However, it can cause a certain amount of discomfort and complications. ECG is widely used in the diagnosis of heart-related diseases but requires a high level of experience.

This study included 80 NVAF patients with 23 LAAT positive and 57 LAAT negative by TEE[23].In addition, a comparison of baseline data between LAAT positive and negative patients revealed that age, BMI, NT-proBNP, fibrinogen, CHA2DS2-VASc score, paroxysmal atrial fibrillation, renal insufficiency, D-dimer, heart failure, and serum uric acid may be associated with LAAT formation in NVAF patients. In the study by Cai et al[24], it was also shown that CHA2DS2-VASc score and NT-proBNP were additional predictors of LAAT formation in patients with NVAF. In addition, it was also shown that LAAT formation in NVAF patients was associated with renal insufficiency, D-dimer, and serum NT-proBNP levels[25].

LAAT formation was detected in 80 patients by ECG, CTA and ECG combined with CTA. The

results showed that the positive LAAT detection rate was 32.50% for the gold standard for TEE, 18.75% for ECG, 48.75% for CTA and 31.25% for ECG combined with CTA. The difference between the positive LAAT detection rate of ECG combined with CTA and the gold standard is not significant, which also indicates that the detection rate of LAAT formation by ECG combined with CTA is more consistent with the gold standard results and better diagnostic.

ECG Combined with CTA Has Good Predictive Value for LAAT Formation in NVAF Patients

The comparison of ECG parameters and CTA parameters between LAAT-positive and negative patients by the gold standard showed that there were statistically significant differences between LAAT-positive and negative patients in the anteroposterior left atrial diameter, transverse left atrial diameter, upper and lower left atrial diameter, left ventricular ejection fraction, long left atrial appendage opening diameter, short left atrial appendage opening diameter, left atrial appendage area, maximum left atrial appendage volume, minimum left atrial appendage volume and left atrial appendage ejection fraction. The differences were statistically significant. In addition, CTA had better sensitivity and negative predictive value but poorer specificity, accuracy, and positive predictive value, while ECG had higher specificity and positive predictive value but poorer sensitivity and negative predictive value. The AUC of ECG combined with CTA was greater than the other two single tests, and ECG combined with CTA had the best diagnostic efficacy with better sensitivity, accuracy, and negative predictive value.

Limitations

The limitations of this study are the small sample size and the single-center retrospective nature of the study. A small amount of bias in the detection of LAAT formation by ECG combined with CTA may have an impact on its results, and therefore, a multi-center, large sample and more comprehensive study is needed.

Conclusions

In summary, ECG combined with CTA has a high diagnostic value for LAAT formation in patients with NVAF, with a high degree of confidence, and reduces intolerance in patients.

The sensitivity, accuracy and negative predictive value of ECG combined with CTA for the diagnosis of LAAT formation in patients with NVAF are high and have good predictive value.

Ethics Approval

This study was approved by the Ethics Committee of Xiangyang No. 1 Peoples Hospital (Approval number: XYRH20180722). This study was conducted in conformity with the Declaration of Helsinki.

Informed Consent

Informed consent was obtained from all participants in this study.

Authors' Contributions

Conceptualization, J.Zh., and L.X.; methodology, J.Zh. Software, L.X. Validation, J.Zh formal analysis, L.X. Writing original draft preparation, J.Zh Writing review and editing L.X, All authors have read and agreed to the published version of the manuscript.

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Data Availability

The experimental data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declared that they have no conflicts of interest to declare.

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