Cardiovascular Topics

Analysis of risk factors for thrombosis of the left atrium/left atrial appendage in patients with non-valvular atrial fibrillation

He Du, Ke Bi, Lisha Xu, Feng Chen, Wenfeng Xiong, Yin Wang

Abstract

Objectives: Left atrial appendage (LAA) morphology is a powerful predictor of thrombogenesis of the left atrium (LA) in patients with non-valvular atrial fibrillation (NVAF). However, it remains unknown whether LAA morphology is useful for stroke risk stratification in patients with NVAF.

Methods: A total of 555 atrial fibrillation patients were divided into thrombus and non-thrombus groups according to transoesophageal echocardiography. We analysed the correlation between LAA morphology and the CHADS 2 score. We determined the L2CHADS2 score and compared the ability to predict LA/LAA thrombosis of the CHADS 2, L2CHADS2, and CHA2DS2-VASc scores from the area under the curve (AUC).

Results: The odds ratio of non-chicken wing LAA morphology was 11.48. Non-chicken wing LAA morphology was significantly correlated with LA/LAA thrombosis. We incorporated LAA morphology into the CHADS 2 score and named it the L2CHADS2 score. The AUC of the L2CHADS2 score (0.767) in predicting LA/LAA thrombosis was significantly higher than that of the CHADS 2 (0.558) or CHA2DS2-VASc scores (0.557). The positive and negative predictive values of the L2CHADS2 score (13.1 and 98.7%) were higher than those of the CHADS 2 (8.7 and 94.2%) and CHA2DS2-VASc scores (6.9 and 6.9%).

Conclusions: Non-chicken wing LAA morphology was a powerful predictor of LA/LAA thrombosis in NVAF patients. The AUC, sensitivity and specificity of the L2CHADS2 score were higher than those of the CHADS 2 and CHA2DS2-VASc scores.

Keywords: atrial fibrillation, thrombus, stroke, left atrial appendage morphology

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Atrial fibrillation (AF) is one of the most common arrhythmias, which is an independent risk factor for stroke. It is estimated that AF incidence will double by 2035.1-3 The most valuable evaluation systems for stroke are the CHADS 2 and CHA2DS2-VASc scores, but the risk factors these scoring systems utilise are relatively limited and less than half of all known possibilities. This means that some important risk factors have not been defined, such as left atrial (LA) diameter, non-chicken wing left atrial appendages (LAA), and persistent AF.1-4

As early as 1909, Welch proposed that cardiac stroke associated with AF was mainly caused by emboli originating from a LAA thrombus.4,5 Previous research has shown that LAA morphology has a close relationship with thrombosis, with the type with obvious bending in the main lobe less likely to form thrombus. In 2010, Wang et al. first divided LAA morphology into four types, namely chicken wing, cauliflower, cactus and windsock, in order to guide LAA closure.6 Di Biase et al. then reported that these different LAA morphologies are associated with stroke or transient ischaemic attack (TIA). They also pointed out that the chicken wing LAA morphology (which has an obvious bend in the main lobe) is less likely to form thrombus compared with other LAA morphologies. These discoveries have attracted extensive attention.

In 2013, Kimura et al. found that cauliflower LAA was the main predictor of stroke/TIA in non-valvular atrial fibrillation (NVAF) patients with low CHADS2 scores, and the results of multivariable logistic regression analysis suggested that cauliflower LAA was an independent risk factor for stroke or TIA (OR: 3.4; 95% CI: 1.243–9.055; p = 0.017).1 These studies
revealed that LAA morphology has a close relationship with stroke.

The LAA is the main site for thrombosis in NVAF patients, and LAA morphology affects the incidence of stroke. In this study, we sought to determine whether LAA morphology could predict the formation of LA/LAA thrombus in patients with NVAF.

Methods

This study was a retrospective review of transoesophageal echocardiography (TEE) and electronic clinical records. The ethics committee of Changhai Hospital approved the study protocol and written informed consent was obtained from all patients before enrollment.

We searched the TEE databases of Changhai Hospital for patients undergoing consecutive TEE imaging between 2010 and 2016 while in drug-refractory NVAF undergoing catheter ablation or cardioversion. Excluded NVAF patients were those taking warfarin with an international normalised ratio (INR) ≥ 1.5, subjects injecting low-molecular weight heparin subcutaneously, taking heparin intravenously or taking new anticoagulants, and those with chronic kidney disease, malignant tumour, connective tissue disease, valvular heart disease or hyperthyroidism. Patients were also excluded if they had rheumatic valve disease or a history of mitral valve repair or mechanical valve implantation. Finally, 555 patients were selected for analysis in this study.

All NVAF patients were divided into two groups, a thrombus and a non-thrombus group, according to TEE. The thrombus group had a thrombus or a change of ‘mud’ in the LA/LAA, and the non-thrombus group had no changes in the LA/LAA.

LA/LAA imaging was obtained using 320-channel cardiac CT angiography (Toshiba Aquilion ONE) with volume-rendering post-processing technology (using the Vitrea Enterprise Suite) to reconstruct its three-dimensional structure. The atria were imaged at optimal gain settings. Mud signals (Fig. 1A) on TEE reveal a mass structure that is relatively clear with a gelatinous appearance. Thromboembolism (Fig. 1B) is visualised through multiple angles as a discrete mass from multiple windows and the mass is independent of the endocardium and pectinate muscles. Generally TEE can identify a thrombosis larger than 2 mm. In our study we categorised mud and thrombosis images as LA/LAA thrombus-positive. Images without LA/LAA mud or thrombus were classified as negative for clots (Fig. 1C).

LAA morphology was classified on the basis of the number of bends in the lobes, the location of origin from the LA and the number of lobes. The radiologists who interpreted the CT images were blinded to the history of the patients, to minimise the risk of bias.

Chicken wing LAA consists of a main lobe and has an obvious bend in the middle or on the base of the main lobe, or the LAA main lobe has an anatomical fold towards the direction of the LAA openings. This LAA morphology usually has secondary lobes or twigs.

In the cauliflower LAA there is usually no main lobe, but there are secondary lobes of varied number among individuals and with limited length. This LAA morphology usually has a complex internal structure. Because of the large variability in morphology, the LAA ostia have less regularity and could be oval or round.

The cactus LAA morphology mainly has a dominant central lobe with secondary lobes extending in both superior and inferior directions. The windsock LAA has a long main lobe with a variety of possible morphologies related to the location and number of secondary or even tertiary lobes (Fig. 2).

eGFR (ml/min/1.73 m²) = 186.3 × [serum creatinine (mg/dl)]⁻¹⁵⁴ × age (years)⁻²⁰³ (or if female × 0.742).¹³

TEE is currently the gold standard for diagnosis of LA/LAA thrombosis. Before a LA/LAA thrombosis develops, the blood in the LA/LAA manifests two dynamic changes, ‘smoke’ and ‘mud’. During the smoke phase, spontaneous ultrasound imaging of the LA reveals dynamic swirling (or smoke-like) echo signals when imaged at optimal gain settings. Mud signals (Fig. 1A) on TEE reveal a mass structure that is relatively clear with a gelatinous appearance.

Fig. 1. Spontaneous ultrasound imaging of different changes of blood in the LA/LAA. A: with mud variation in the LAA, B: with thrombus variation in the LAA, C: without mud or thrombus variation in the LAA.
Statistical analysis

We used SPSS 17.0 software for data analysis. Continuous variables are expressed as mean (minimum and maximum) values, and if they were normally distributed with homogeneity of variance, the statistical analyses were performed using the Student’s t-test. If they were not normally distributed, the Wilcoxon rank-sum test was used. Count data are shown with ratios, and were performed with the chi-squared test. Stepwise multivariate logistic regression was used to screen for related risk factors for LA/LAA thrombosis, to devise a new scoring system denoted as the LCHADS2 score, and to calculate a receiver operating characteristic (ROC) curve. This approach was used to contrast this LCHADS2, value with that of the CHADS2, and CHADS2-VASc scores in predicting LA/LAA thrombosis through the AUC, sensitivity and specificity. A p-value < 0.05 was considered statistically significant.

Results

A total of 555 NVAF patients were recruited, of whom 35 were classified into the thrombus group and 520 into the non-thrombus group. Baseline demographics, clinical characteristics and LAA measurements of patients with and without LA/LAA thrombosis are shown in Table 1. There were no differences in age and gender, CHADS2, and CHADS2-VASc scores, windsock LAA morphology, prevalence of hypertension, diabetes, stroke/TIA and vascular disease, and lipoprotein(a) levels between the thrombus and non-thrombus groups. There were significant differences between the two groups in brain natriuretic peptide (BNP), D-dimer and fibrinogen levels, eGFR, outside and inside diameter of the LAA, LAA volume, LA diameter, chicken wing, cactus and cauliflower LAA morphology, history of heart failure and renal dysfunction.

Patients with cauliflower or cactus LAA morphology were more likely to have thrombosis (p < 0.001). Eighty and 28.1% of the patients with non-chicken wing LAA were distributed in the thrombus and non-thrombus groups, respectively, and the difference was statistically significant (p < 0.001).

A regression model was built by adding all the covariates listed in Table 1. The results of multivariate logistic regression analysis (Table 2) showed that D-dimer (OR: 1.74; 95% CI: 1.073–2.807; p = 0.025), BNP (OR: 3.00; 95% CI: 1.709–9.677; p = 0.002), LA diameter (OR: 4.07; 95% CI: 1.709–9.677; p = 0.002), non-persistent AF (OR: 5.14; 95% CI: 1.911–13.818; p = 0.001) and non-chicken wing LAA (OR: 11.48; 95% CI: 4.157–31.684; p = 0.000) were independent risk factors for LA/LAA thrombosis.

| Table 1. Comparison of general data and related clinical data between the thrombus and non-thrombus groups |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Characteristic | Overall | Thrombus group | Non-thrombus group | c2/t/Z | p-value |
| No of patients | 555 | 35 | 520 | | | |
| Age, years (SD) | (59.1 (19–85)) | (59.8 (34–78)) | (59.1 (19–85)) | 0.368 | 0.713 |
| < 65, n (%) | 375 (67.6) | 24 (68.6) | 351 (67.5) | 0.017 | 0.896 |
| ≥ 75, n (%) | 148 (26.7) | 9 (25.7) | 139 (26.7) | 0.017 | 0.895 |
| Male/female, n (%) | 23 (5.8) | 2 (5.7) | 21 (4.0) | 0.000 | 0.998 |
| CHADS2 score ≥ 2, n (%) | 21 (3.8) | 2 (5.7) | 19 (3.7) | 0.382 | 0.536 |
| CHADS2-VASc score ≥ 2, n (%) | 152 (27.0) | 17 (4.9) | 135 (25.8) | 0.116 | 0.25 |
| CHA2DS2-VASc score ≥ 2, n (%) | 248 (44.7) | 17 (48.6) | 231 (44.4) | 0.288 | 0.633 |
| Fibrinogen, g/l (SD) | (3.00 (0.07–6.89)) | (2.97 (0.07–6.89)) | 2.74 | 0.006 |
| D-dimer, mg/ml (SD) | (0.44 (0.07–6.89)) | (2.97 (0.07–6.89)) | 3.02 | 0.003 |
| eGFR, ml/min/1.73 m2 (SD) | (98.6 (5.125–178.125)) | (99.3 (5.125–178.125)) | 3.60 | 0.000 |
| Lipoprotein (a), mg/dl (SD) | (18.1 (1.96–81.9)) | (18.9 (1.75–75.1)) | 0.85 | 0.39 |
| BNP, pg/ml (SD) | (72.9 (4–1560)) | (235 (27–1560)) | 8.66 | 0.000 |
| LA diameter, mm (SD) | (3.11 (1.6–7.5)) | (4.19 (2.10–7.50)) | 6.09 | 0.000 |
| Outside diameter of LAA, mm (SD) | (1.67 (0.60–3.90)) | (1.88 (0.60–3.40)) | 2.08 | 0.007 |
| Inside diameter of LAA, mm (SD) | (3.14 (0.90–3.90)) | (2.99 (0.90–3.40)) | 3.02 | 0.001 |
| LAA volume, ml (SD) | (6.73 (1.00–41.00)) | (6.55 (3.00–41.00)) | 3.76 | 0.000 |
| Chicken wing LAA, n (%) | 377 (67.9) | 7 (20) | 370 (71.2) | 0.93 | 0.000 |
| Non-chicken wing LAA | | | | | |
| Windsock LAA, n (%) | 62 (11.2) | 20 (57.1) | 42 (12.9) | 44.45 | 0.000 |
| Cactus LAA, n (%) | 104 (18.7) | 3 (8.6) | 101 (19.4) | 0.20 | 0.302 |
| Cauliflower LAA, n (%) | 12 (2.2) | 4 (17.1) | 8 (1.5) | 18.312 | 0.000 |

Values depicted for n are mean (minimum and maximum) or percent. TIA, transient ischaemic attack; eGFR, estimated glomerular filtration rate; AF, atrial fibrillation; BNP, brain natriuretic peptide; LA, left atrium; LAA, left atrial appendage. Comparison between thrombus and non-thrombus groups.
In multivariable logistic regression analysis (Table 2), non-chicken wing LAA was found to have the highest OR, at 11.48. The CHADS2 risk score is the most popular risk stratification tool used, so we further analysed the correlation between LAA morphology and the CHADS2 score. Among the thrombus group in subjects with a CHADS2 score of zero or one point, the chicken wing LAA had the lowest prevalence. The non-chicken wing LAA was significantly more prevalent in the thrombus group compared with the chicken wing morphology (85.2 vs 14.8%). In the non-thrombus group with a CHADS2 score of two points or more, the chicken wing LAA had the highest prevalence, which was significantly more prevalent in the non-thrombus group compared with the non-chicken wing morphology (65.5 vs 34.5%). The prevalence of cauliflower LAA was highest (66.7%), followed by cactus and windsock LAA, with the chicken wing LAA the lowest (1.9%).

We hypothesised that LAA morphology might be useful for predicting LA/LAA thrombosis in NVAF patients, especially when incorporating it with the CHADS2 score. We therefore endowed the non-chicken wing LAA morphology with two points (the highest score) and derived the L2CHADS2 score based on the CHADS2 score. The L2CHADS2 score was composed of a total of six risk factors, namely, congestive heart failure, hypertension, diabetes, age ≥ 75 years, history of stroke or TIA, and chicken wing morphology (85.2 vs 14.8%). Among the thrombus group in subjects with a CHADS2 score of two points or more, the chicken wing morphology (85.2 vs 14.8%) endowed the non-chicken wing LAA morphology with two points or more.

In the non-thrombus group with a CHADS2 score of two points or more, the chicken wing LAA had the highest prevalence, which was significantly more prevalent in the non-thrombus group compared with the non-chicken wing morphology (65.5 vs 34.5%). The prevalence of cauliflower LAA was highest (66.7%), followed by cactus and windsock LAA, with the chicken wing LAA the lowest (1.9%).

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According to their CHADS2 scores, 12 (34.3%) and 15 (42.9%) subjects were classified as zero and one point, respectively, non-chicken wing LAA had a lower prevalence of subjects above two points, namely the high-risk category. It was only with the L2CHADS2 score that the percentage of subjects classified in each category increased along with the score and most of the subjects were distributed between two points or more.

The incidence of thrombosis in the CHADS2 and CHA2DS2-VASC scores showed an increasing trend with the scores increasing gradually (Fig. 4). The L2CHADS2 score increased more obviously and the thrombosis incidence was obviously higher than that of the CHADS2 and CHA2DS2-VASC scores in the high-risk group.

Using a score ≥ one, one and two as cut-off points for the CHADS2, CHA2DS2-VASC and L2CHADS2 risk-stratification schemes in the thrombus group.

These results confirmed that the L2CHADS2 score was superior to the CHADS2 and CHA2DS2-VASC scores for prediction of the development of LA/LAA thrombi. The positive and negative predictive values of the L2CHADS2 score (13.1 and 98.7%) were higher than those of the CHADS2 (8.7 and 94.2%) or CHA2DS2-VASC scores (6.9 and 6.9%) (Fig. 5).

Table 2. Multivariate OR for LA/LAA thrombosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>D-dimer</td>
<td>1.735</td>
<td>1.073–2.807</td>
<td>0.025</td>
</tr>
<tr>
<td>BNP (pg/ml)</td>
<td>3.002</td>
<td>1.683–5.355</td>
<td>0.000</td>
</tr>
<tr>
<td>LA diameter</td>
<td>4.066</td>
<td>1.709–9.677</td>
<td>0.002</td>
</tr>
<tr>
<td>Non-persistent AF</td>
<td>5.139</td>
<td>1.911–13.818</td>
<td>0.001</td>
</tr>
<tr>
<td>Non-chicken wing LAA</td>
<td>11.476</td>
<td>4.157–31.684</td>
<td>0.000</td>
</tr>
<tr>
<td>BNP, brain natriuretic peptide; LA, left atrium; LAA, left atrial appendage.</td>
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</tbody>
</table>

Table 3. LAA morphology and risk of LA/LAA thrombus in the thrombus group with a CHADS2 score of zero or one point, in the non-thrombus group with a CHADS2 score of two points or more, and thrombosis ratio of chicken wing and non-chicken wing LAA morphology

<table>
<thead>
<tr>
<th>Variable</th>
<th>Chicken wing (%)</th>
<th>Windsock (%)</th>
<th>Cactus (%)</th>
<th>Cauliflower (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombus group</td>
<td>14.8</td>
<td>85.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(CHADS2 score 0 or 1 point)</td>
<td></td>
<td></td>
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<tr>
<td>Non-thrombus group</td>
<td>65.5</td>
<td>34.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(CHADS2 score 2 points or more)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombosis ratio</td>
<td>1.9</td>
<td>11.4</td>
<td>12.5</td>
<td>66.7</td>
</tr>
</tbody>
</table>

Fig. 3. Prevalence (percentage) of patients classified in each score according to the CHADS2, CHA2DS2-VASC and L2CHADS2 risk-stratification schemes in the thrombus group.

Fig. 4. Prevalence (percentage) of LA/LAA thrombosis in each score according to the CHADS2, CHA2DS2-VASC and L2CHADS2 risk-stratification schemes.
and the L2CHADS2 score was superior to the CHADS2 and CHA2DS2-VASc scores in predicting LA/LAA thrombosis.

Two score systems have been criticized.19 The CHA2DS2-VASc score is commonly used for this risk stratification with regard to the need for anticoagulant therapy.20 The CHADS2 score is commonly used for this risk stratification in patients with NVAF. The main findings were as follows: (1) LAA morphology was closely related to LA/LAA thrombus; (2) the L2CHADS2 score could reliably predict LA/LAA thrombi, and the L2CHADS2 score was superior to the CHADS2, and CHA2DS2-VASc scores in predicting LA/LAA thrombosis.

AF is an independent risk factor for thromboembolic stroke and peripheral emboli. One of the key steps in preventing stroke associated with AF is effective risk stratification to guide decision making with regard to the need for anticoagulant therapy.20 The CHADS2 score is commonly used for this risk stratification in patients with AF. The CHA2DS2-VASc score was recommended by the European Society of Cardiology and the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines in 2012 and 2014, respectively, for stroke risk stratification in NVAF patients.21,22 However, these two score systems have been criticized.19

Yarmohammadi et al.24 reported in a substudy of the ACUTE trial that the CHADS2 score could not reliably predict embolic risk in patients with NVAF because 10% of the patients ranked with zero points had LA thrombi. Fruhauf et al.25 also reported a case involving a NVAF patient who had CHADS2, and CHA2DS2-VASc scores of zero points; this patient then developed recurrent LA thrombi after radiofrequency catheter ablation. Therefore, although the current stroke risk-stratification schemes appear to be practical, they still have some defects and limitations.

We found that patients with non-chicken wing LAA morphology had a significantly higher risk of LA/LAA thrombosis compared with chicken wing morphology. The chicken wing morphology was the most common LAA form (67.9%) in our population and the least associated with a history of LA thrombosis, which was in accordance with the Di Biase et al. studies.7 To date, there have been no data incorporating LAA morphology into stroke risk stratification.

Our data indicated that LAA morphology remained the most powerful independent predictor of LA/LAA thrombosis with multivariable regression analysis (OR: 11.48; 95% CI: 4.157–31.684; p = 0.000). According to Clark et al., the CHADS2 risk score was the most commonly used scoring system for the evaluation of stroke risk.20 We found that there were 27 subjects (77.1%) with a CHADS2 score of zero or one in the thrombus group but they all developed a LA/LAA thrombus. Of these 27 individuals, 23 (85.2%) had non-chicken wing LAA and only four (14.8%) had chicken wing LAA. Moreover, there were 84 subjects (16.2%) with a CHADS2 score of two or more in the non-thrombus group. In these 84 cases, 55 (65.5%) had chicken wing LAA and 29 (34.5%) had non-chicken wing LAA. This suggested that LAA morphology might be useful for predicting the risk of thromboembolism in NVAF patients with low and high CHADS2, scores (Tables 1, 3). We therefore incorporated LAA morphology (L with highest points of two) into the CHADS2 score, leading to the L2CHADS2 risk score.

The utility of the L2CHADS2 score for predicting risk of systemic emboli, as indicated by the results of the AUC calculation, was higher than that of either the CHADS2 or CHA2DS2-VASc scores. These results indicated that the L2CHADS2 score was superior to either the CHADS2, or the CHA2DS2-VASc scores for predicting LA thrombus formation. The CHADS2 score had high specificity but poor sensitivity (Fig. 5). This led to missed opportunities for anticoagulant therapy for a majority of patients with a high risk of stroke. The CHA2DS2-VASc score increased the sensitivity at the cost of reducing specificity to 0.225. This observation was in agreement with the USA and Portuguese TEE and European clinical outcomes studies.11,13–20 On the other hand, compared to the CHADS2 score, the L2CHADS2 score had higher sensitivity and specificity (0.427 and 0.606, respectively). These observations suggested that the L2CHADS2 score could identify ‘truly low-risk’ patients without sacrificing overall predictive ability. Therefore the findings were consistent in showing the advantage of the L2CHADS2 risk score.

The risk for stroke may be balanced by the risk of bleeding, which can be a deadly complication in patients with NVAF who are treated with anticoagulants.26 The 2016 AHA/ACC guidelines pointed out that patients with NVAF and a CHA2DS2-VASc score of one point, taking aspirin or anticoagulant drugs or not taking any medications (Class IIb, C), had similar outcomes. That is to say, the clinical decision making is still controversial in patients with intermediate risk.31 The CHADS2 score has been criticised for categorising a great number of patients with NVAF as intermediate risk.32 Compared with the CHADS2 score, the CHA2DS2-VASc and L2CHADS2 scores placed a smaller percentage of patients in the intermediate-risk group; there was a reduction to 43 (18.8%) and 73 (31.9%) patients, respectively. Because the L2CHADS2 score reduced these percentages to a greater extent, utilising it may reduce uncertainties about the benefits of anticoagulant therapy in patients with intermediate risk.

Our data revealed that for NVAF subjects who had LA thrombus on TEE, more than two-thirds developed these clots despite having a low CHADS2 score of zero or one point. This suggested that a high proportion of patients with high risk of...
stroke would not receive anticoagulant therapy. This number was surprisingly high and raised questions about the use of the CHADS2 score as an independent risk-stratification tool. However, with the development of the L2CHADS2 scale, only four subjects (11.4%) with a zero or one point score developed a LA/LAA thrombus. There were 231 (44.4%) subjects with a CHADS2-VASC score of two points or more, but these patients did not have a LA/LAA thrombus. This means that almost half of these patients would have unnecessarily been exposed to oral anticoagulation. In contrast, use of the L2CHADS2 score would have minimised this number and reduced the risks of haemorrhage from unnecessary anticoagulant therapy.

Compared to the CHADS2, and CHA2DS2-VASC score, the thrombosis incidence in the low- and intermediate-risk subjects, retrospectively identified by the L2CHADS2 score, was significantly lower, and in the high-risk group it was significantly higher. This was in accord with the expectations of a thromboembolic risk-stratification system, with higher scores predicting higher incidence of LA/LAA thrombosis. Risk scores based on the CHADS2, and CHA2DS2-VASC scales had obvious limitations in our study. It therefore supported the use of modified risk scores and the need for further prospective studies on risk stratification in patients with NVAF.

The R2CHADS2 score posits that renal dysfunction is an important predictor of stroke and peripheral embolism in NVAF patients with intermediate and high stroke risk, and is based on the ROCKET-AF and ATRIA stroke risk studies proposed in 2013.13,14 But in our study, a significant independent effect of renal dysfunction on LA/LAA thrombus was not documented, and so the relationship between them was not explored further. The results of the present study indicated that we could improve the accuracy of LA/LAA thrombus prediction if we simultaneously considered LAA morphology. In addition, renal dysfunction, a significant risk factor for bleeding, was added to the R2CHADS2 scoring scheme that is intended to estimate the risk of thromboembolic events and guide antithrombotic therapy, which may not be appropriate.

The causes and mechanisms of atrial thrombi are not completely equivalent for every patient with NVAF, so the benefits of anticoagulant therapy may depend on the potential stroke risks themselves, and therefore the risk/favour ratio of different people may need comprehensive assessment to make optimal decisions regarding anticoagulant therapy. This is one reason why it can be relatively difficult to make decisions about the use of anticoagulation in patients with NVAF. Therefore, if we could develop objective criteria to assess the risk of stroke in NVAF patients and guide the use of anticoagulants in this population, it would be a good step forward.

Study limitations
This was a single-centre retrospective study of a limited number of NVAF patients, with only 35 having LA/LAA thrombus. In addition, the patients with NVAF in the study were refractory to pharmacotherapy. Their general physical condition was relatively good and they could tolerate radiofrequency ablation or cardioversion. Even in those with a history of stroke, the symptoms were mild and prognoses good, so the present results cannot be extrapolated to the overall patient population with NVAF. Because this was a retrospective study, it may have been affected by recall bias and it was difficult to select reasonable controls. Therefore, larger prospective studies would be needed to verify the conclusions. Finally, although TEE has high sensitivity and is the gold-standard test for LA/LAA clots, it cannot discern thrombi less than 2 mm and therefore may produce false negative findings.

Conclusions
This study suggests that LA/LAA morphology is a powerful predictor of thrombus formation and possible subsequent arterial embolic events in patients with NVAF. Compared with the CHADS2 and CHA2DS2-VASC schemes, the L2CHADS2 score developed here has the advantage of identifying ‘truly low-risk’ patients without sacrificing overall predictive ability. It can provide insights into the value of the L2CHADS2 score for the management of patients with NVAF, which are novel and could prove to be clinically very relevant. Of course, further prospective clinical studies on the relationship of the L2CHADS2 score to outcomes in larger populations of NVAF patients will be needed before its widespread adoption in the world.

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References


