Relation of Left Atrial Appendage Morphology Determined by Computed Tomography to Prior Stroke or to Increased Risk of Stroke in Patients With Atrial Fibrillation

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Left atrial appendage (LAA) morphology is considered to be associated with ischemic stroke, non-Chicken Wing LAA morphology increases the risk of thromboembolic events. However, existing classification of LAA morphology remains not well quantifiable and therefore may leave room for substantial subjective interpretation. This study aimed to assess interobserver and intraobserver agreements in LAA morphology and its real value in stroke prediction. A total of 2,264 atrial fibrillation patients who underwent computed tomography to explore the LAA anatomy were enrolled. All computed tomography images were given to 3 reviewers to judge the LAA morphology independently. A consensus between all 3 reviewers was only reached in 655 cases (28.9%). In which, 86 patients had previous stroke. Poor intraobserver consistency was observed between 2 times of reading in all the 3 reviewers (Kappa = 0.368, p = 0.014; Kappa = 0.350, p = 0.014; Kappa = 0.333, p = 0.015). Multivariate analysis showed that persistent atrial fibrillation (odds ratio [OR] 1.679; 95% confidence interval [CI] 1.031 to 2.736; p = 0.037), female gender (OR 1.761; 95% CI 1.037 to 2.994; p = 0.036) and age (OR 1.029; 95% CI 1.004 to 1.056; p = 0.025) were associated with previous stroke. LAA morphology was not associated with previous stroke and non-Chicken Wing LAA morphology did not increase the risk of stroke (OR 1.392; 95% CI 0.847 to 2.288; p = 0.192). In conclusion, high interobserver and intraobserver variabilities suggested that existing classification of LAA morphology was unreliable, the interpretation of the relation between LAA morphology and stroke needs caution. **© 2019 Published by Elsevier Inc.** **(Am J Cardiol 2019;123:1283−1286)**

Atrial fibrillation (AF) is the most prevalent sustained cardiac arrhythmia seen in clinical practice and the most frequent cause of cardioembolic events. Left atrial appendage (LAA) thrombi are the main source of thromboemblus especially in nonvalvular AF. Di Biase L et al firstly categorized LAA morphology into 4 types: Cactus, Chicken Wing, Windsock, and Cauliflower in 2012. They found that patients with Chicken Wing LAA morphology had lower risk of thromboembolism after controlling for co-morbidities and CHADS2 score,[1] this conclusion has been widely cited since then.[2−6] However, existing classification of LAA morphology which remains not well quantifiable may leave room for substantial subjective interpretation. This study aimed to assess the interobserver and intraobserver variabilities in LAA morphology as well as the real world relation of LAA morphology and stroke in AF.

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Methods

We analyzed data on patients with nonvalvular AF in Fuwai hospital from April 2011 to December 2017. All patients accepted multidetector computed tomography (CT) examination to fully explore the anatomy of the LAA. Paroxysmal AF was defined as AF that terminated spontaneously or with intervention within 7 days of onset, persistent AF was defined as continuous AF sustained beyond 7 days.[7] The study was approved by the local ethical research committee.

The CT scan strategy was previously reported.[8] Electrocardiograph-gated CT was conducted using a 64-slice spiral scanner (Lightspeed Volume CT, GE Healthcare, Little Chalfont, United Kingdom) during a single breath-hold, the scanning range for early-phase scanning was from the diaphragm to the aortic arch, and late-phase scanning from aortic arch to the middle of left ventricle, mainly aimed at the LAA area. Detector collimation was 64×0.625 mm and the gantry rotation time was 350 ms. Electrocardiograph-based tube current modulation was applied to guarantee high-quality images. A bolus of contrast media (50 to 60 ml) was injected at an infusion rate of 5 ml/s followed by an injection of saline (40 ml, 5 ml/s). All patients underwent examination under a heart rate <70 beats per minute. Three-dimensional structures of the LAA and left atrium were constructed in multiple orthogonal views.

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Table 1
The computed tomography images reading results by individual panel members

	Observer 1	Observer 2	Observer 3	Agreement
Cactus	449 (19.8%)	519 (22.9%)	337 (14.9%)	103
Chicken Wing	472 (20.8%)	989 (43.7%)	341 (15.1%)	187
Windsock	553 (24.4%)	261 (11.5%)	758 (33.5%)	93
Cauliflower	799 (35.3%)	508 (22.4%)	837 (37.0%)	272
Total	2264	2264	2264	655 (28.9%)

All CT images were given to panel members including 3 observers who were asked to carefully judge the morphology independently blinded to patient history. All the 3 observers were experienced doctors in cardiology and were familiar with cardiac imaging. A second reading was repeated 3 months later on the same CT images rearranged in a random sequence for the analysis of intraobserver variability, all members were blinded to previous reading results. The same definitions were used for the assessment of agreement in the interpretation of LAA morphology.

LAA morphology was characterized as Cactus, Chicken Wing, Windsock, or Cauliflower.[1] Before the study was performed, all observers read the CT images of another 100 patients together and discussed the classification of LAA morphology in order to obtain a maximum of objectiveness.

All patients underwent transthoracic echocardiogram examination and were screened for the previous history of stroke which was confirmed by imageological diagnosis carefully. The parameters of the 4 cardiac chambers were abstracted. Other information including demographic data and co-morbidities were abstracted.

Statistical analyses were performed using SPSS 19.0 software (SPSS Inc, Chicago, Illinois). Comparisons of continuous variables between groups were performed with the Student's *t* Test or Wilcoxon test. Chi-square analysis was used to compare the categorical variables between groups. For the multivariate logistic regression analysis, the continuous variables were appropriately transformed where required to render them normally distributed. The consistency detection between the 2 times of readings was analyzed using the Kappa statistics. All tests were 2-tailed and a statistical significance was established at a $p < 0.05$.

Table 2
Comparison of clinical characteristics in patients with and without prior stroke who reached in consensus

	With prior stroke (n = 86)	Without prior stroke (n = 569)	p Value
Age, (years)	58.8 ± 9.1	56.6 ± 9.9	0.043
Male	63 (73.3%)	365 (64.1%)	0.098
Persistent AF	48 (55.8%)	268 (47.1%)	0.132
Median AF history, (months)	36 (1−360)	36 (1−480)	0.957
Echocardiography parameters			
LAD, (mm)	40.3 ± 6.3	39.5 ± 5.7	0.214
LVEDD, (mm)	48.4 ± 3.3	47.9 ± 4.8	0.342
LVEF, (%)	61.1 ± 6.8	62.5 ± 6.7	0.081
Co-morbidities			
Hypertension	48 (55.8%)	287 (50.4%)	0.353
Diabetes mellitus	10 (11.6%)	68 (12.0%)	0.820
Vascular disease	14 (16.3%)	71 (12.5%)	0.395
CHA_2DS_2-VASc score	1 (0−7)	1 (0−6)	0.547
Chicken Wing LAA	29 (33.7%)	158 (27.8%)	0.255
Non-Chicken Wing LAA	57 (66.3%)	411 (72.2%)	0.255

AF = atrial fibrillation; LAD = left atrial diameter; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; LAA = left atrial appendage.

Results

A total of 2,357 consecutive AF patients who underwent CT scan of LAA were enrolled. In which, 93 patients were excluded from the study because of poor CT quality or LAA agenesis. Therefore, there were 2,264 patients enrolled. The mean age at inclusion was 54.1 ± 15.2 years, and 1,502 (66.3%) patients were male.

Of the 2,264 CT images, a consensus between all 3 reviewers was reached in only 655 (28.9%) cases (Table 1). A consensus between 2 reviewers was reached in 998 cases (44.1%), including 200 cases of Cactus morphology, 179 cases of Chicken wing, 315 cases of Windsock, and 304 cases of Cauliflower. In the remaining 611 (27.0%) patients, no agreement could be reached. The differentiation between Cauliflower, Chicken wing, and Cactus morphology were often puzzled (Figure 1). Poor intraobserver consistencies were observed between the 2 times of reading in all the 3 reviewers, respectively (Kappa = 0.368, p = 0.014; Kappa = 0.350, p = 0.014; Kappa = 0.333, p = 0.015).

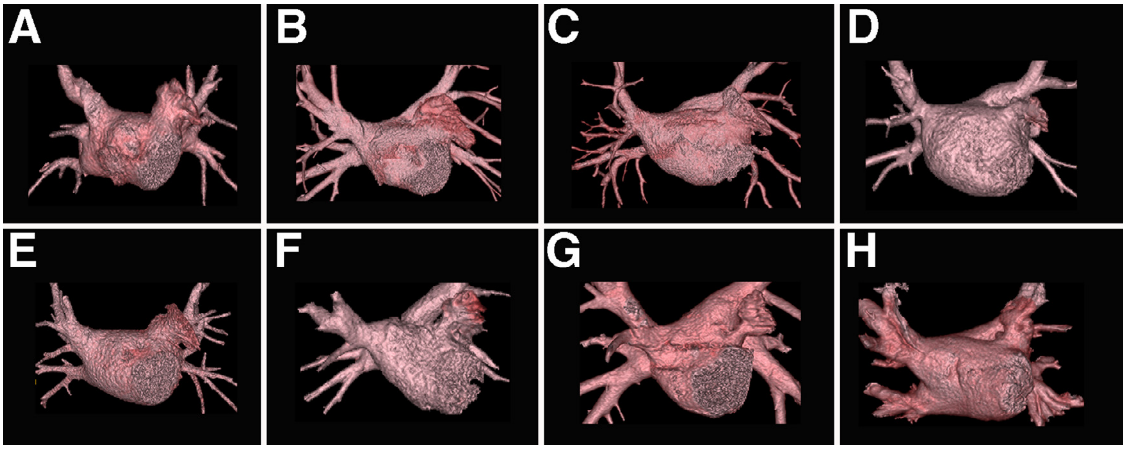

Figure 1. Examples of left atrial appendage morphology difficult to differentiation. (***A*** to ***D***) The observer 2 classified as Chicken Wing while the other two observers classified as Cauliflower; (***E* and *F***) Disagreement existed between Cauliflower and Cactus; ***G* and *H***) No agreement could be reached.

Table 3
Univariate and multivariate analysis for the presence of prior stroke

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Age	1.026 (1.001−1.051)	0.044	1.029 (1.004−1.056)	0.025
Female gender	1.531 (0.922−2.545)	0.100	1.761 (1.037−2.994)	0.036
Persistent AF	1.419 (0.899−2.239)	0.133	1.679 (1.031−2.736)	0.037
AF history	1.000 (0.997−1.003)	0.957	1.000 (0.977−1.003)	0.896
LAD	1.025 (0.986−1.065)	0.214	1.023 (0.977−1.071)	0.325
LVEDD	1.023 (0.976−1.073)	0.342	1.021 (0.970−1.075)	0.419
LVEF	0.973 (0.943−1.004)	0.082	0.981 (0.948−1.015)	0.273
Hypertension	1.241 (0.787−1.957)	0.353	1.171 (0.724−1.894)	0.520
Diabetes mellitus	1.032 (0.509−2.090)	0.931	1.094 (0.524−2.283)	0.811
Vascular disease	1.364 (1.054−2.545)	0.330	1.227 (0.642−2.392)	0.547
Chicken Wing LAA	1.466 (0.991−2.364)	0.116	1.392 (0.847−2.288)	0.192

The abbreviations are the same as in Table 2.

The 655 patients who reached in consensus of LAA morphology were enrolled for further analysis. In which, 86 patients had previous stroke. The characteristics in patients with and without previous stroke were shown in Table 2. Significant statistical difference was only found in age. Multivariate analysis showed that persistent AF (odd ratios [OR] 1.679; 95% confidence interval [CI] 1.031 to 2.736; p = 0.037), female gender (OR 1.761; 95% CI 1.037 to 2.994; p = 0.036) and age (OR 1.029; 95% CI 1.004 to 1.056; p = 0.025) were associated with previous stroke Table 3. LAA morphology was not associated with previous stroke, and non-Chicken Wing LAA morphology did not increased the risk of stroke (p = 0.192).

Discussion

In this study, we firstly revealed a high interobserver and intraobserver variabilities in LAA morphology assessment by CT from a large series of AF patients, and found the relation of LAA morphology to previous stroke was negligibly low.

Di Biase L et al. firstly categorized LAA morphology into 4 types and declared that patients with Chicken Wing LAA morphology had lower risk of stroke in 2012. Since then, the relation between LAA morphology and stroke has become an issue of great interest. Although most studies came to similar conclusions,[2−6] there were still a few studies expressed their various opinions. Kosiuk J et al found that LAA Chicken Wing morphology is associated with higher periprocedural thromboembolic risk in patients who underwent AF ablation.[9] Khurram IM et al reported that LAA morphology was not associated with stroke.[10] The contradictory results were confusing. One possible explanation is that the high observer variabilities in the assessment of LAA morphology led to this inconsistency.

Actually, the morphology and anatomy of the LAA is more complex, bizarre, and variable than previously thought. Many factors can affect LAA morphology, and this should be considered when reading and interpreting images of the LAA especially in patients with LAA thrombosis. Ernst G et al reported that LAA is greatly varying in volume (770 to 19,270 mm^3) and shape in 220 cases by postmortem examination.[11] The volume and shape of LAA was also impacted by many variations including age, gender, and AF classification, etc.[11−15] Although malignant LAA morphology related to embolization risk has been reported in anecdotal cases,[16] these extreme cases may not represent the majority of patients.

Current morphologic classification schemes based on stroke epidemiology showed high interobserver and intraobserver variabilities in LAA morphology assessment, it seems impractical and too complicated to do so predictably and infallibly. A deeper understanding of the effect of LAA anatomy on blood flow and thrombus formation may provide a more reliable risk estimation scheme. A few studies already showed LAA morphology is a determinant of LAA flow velocity.[3−5] Lee JM et al found that patients with a smaller LAA orifice area and higher LAA velocity had a decreased stroke risk. However, more studies are needed to confirm these conclusions.[6]

Our study has several limitations. First, we were unable to retrieve the anticoagulation status at the time of stroke. However, it is well known that the proportion of Chinese AF patients accepted long-term anticoagulant therapy is very low. Second, we did not assess more dimensions such as volume, velocity, and orifice diameter of LAA. The limitations must be taken into consideration when interpreting our results.

Disclosures

The authors have not conflict of interests to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.01.024.

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