Morphological changes in the orifices of the left atrial appendage and left atrium in patients with atrial fibrillation

Xin Tian¹#, Cen Wang²#, Duo Gao¹#, Bu-Lang Gao¹, Cai-Ying Li¹

¹Department of Medical Imaging, The Second Hospital of Hebei Medical University, Shijiazhuang, China; ²Radiology Department, Beijing Nuclear Industry Hospital, Beijing, China

Contributions: (I) Conception and design: CY Li; (II) Administrative support: BL Gao; (III) Provision of study materials or patients: D Gao; (IV) Collection and assembly of data: C Wang; (V) Data analysis and interpretation: X Tian; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

#These authors contributed equally to this work.

Correspondence to: Cai-Ying Li. Department of Medical Imaging, The Second Hospital of Hebei Medical University, 215 West Heping Road, Shijiazhuang 050011, China. Email: licaiying63@163.com.

Background: As an integral part of the left atrium (LA), the left atrial appendage (LAA) plays an important role in atrial fibrillation (AF). However, the relationship between LAA remodeling and AF has not been clearly defined. This retrospective case-control study aimed to assess the morphological and functional features of the LA and the LAA in AF patients using images obtained by computed tomography angiography (CTA).

Methods: A total of 140 AF patients and 64 patients without AF or other cardiovascular diseases who underwent CTA scans between September 2016 and August 2017 were enrolled in this observational study as the experimental and the control groups, respectively. The major and minor axes, area, and perimeter of the LAA orifice, the LAA depth, and the volume of both the LAA and LA were analyzed. The data of the AF group and the control group were compared. The $t$-test was used to analyze the normally distributed data, and the Wilcoxon rank-sum test was used for abnormally distributed data. The best critical value of predictors of AF was calculated using receiver operating characteristic (ROC) curve analysis. The correlation of the LAA volume change with the major and minor axes, area, and perimeter of the LAA orifice, and the LAA depth were analyzed using the Pearson correlation coefficient.

Results: The LAA orifice's minor axis, LAA volume, and LA volume were significantly greater (P=0.004, P=0.010, and P<0.001, respectively) in patients with AF than in those without AF. The LAA volume [95% confidence interval (CI): 1.01 to 1.30; P=0.038] and LA volume (95% CI: 1.03 to 1.07; P<0.001) were significantly independent predictors of AF. An LAA volume of 8.75 mL had the highest predictive value for AF [area under the curve (AUC), 0.612], with a sensitivity of 76.6% and a specificity of 48.6%. In contrast, an LA volume of 97.15 mL had the highest predictive value for AF (AUC, 0.771), with a sensitivity of 90.6% and a specificity of 53.6%. The change of LAA volume was positively weakly correlated with the area and perimeter of the LAA orifice (r=0.1703 and r=0.1378, respectively). The LAA emptying fraction was negatively correlated with the major axis and the area of the LAA orifice. The major and minor axes, area, and perimeter of the LAA orifice, and LA volume were significantly greater in female than in male patients (P=0.003, P=0.003, P=0.001, P=0.019, and P<0.001, respectively).

Conclusions: The AF patients had a longer minor axis of the LAA orifice than that of the control group, resulting in a more circular LAA orifice. The LAA orifice area and perimeter were positively correlated with LAA volume change. The LAA orifice major and minor axes, area, and perimeter, and the LA depth of the female patients were significantly greater than those of their male counterparts in AF patients.

Keywords: Left atrial appendage (LAA); orifice; emptying function; atrial fibrillation (AF); left atrium (LA)
Introduction

Atrial fibrillation (AF) is a common tachyarrhythmia (1). The left atrial appendage (LAA) plays an important role in AF, and changes in the morphology and anatomy of the LAA have been shown to be significantly associated with the occurrence, development, and recurrence of AF (2). When the heart rhythm is normal, the LAA contraction and relaxation occur at a certain rhythm. However, AF involves irregular contraction of the left atrium (LA), and the LAA loses the normal contraction rhythm (3), resulting in a reduced contraction ability of the auricle wall and incomplete emptying of blood from the LAA. Incomplete emptying, accompanied by slow blood flow and damage to the cardiovascular endothelium, results in morphologic changes of the LAA, which are likely to cause thrombosis and severe ischemic stroke events. Although the mechanism of initiation of thrombosis is very complicated (4), the LAA morphologic change plays a crucial role in stroke (5).

Multiple imaging modalities are available to assess cardiac morphology and function (6). Echocardiography is a widely used means of non-invasively assessing cardiac anatomy (7). Transesophageal ultrasound is the “gold standard” for diagnosing thrombus in LAA (8). However, variations in the imaging plane and imaging angle implemented by different technicians affect how morphological structures are displayed. Therefore, the measurement is subjective (9). Cardiac magnetic resonance imaging (MRI) can accurately measure the volume and blood flow velocity in LAA, and the results are highly consistent with those of transesophageal ultrasound (10). Nonetheless, MRI is time-consuming and expensive. In contrast, multi-slice spiral computed tomography (CT) has the advantages of flexibility, noninvasiveness, high accuracy, and 3D imaging when obtaining the LAA and coronary artery parameters.

So far, the correlation between static geometric features and the function of the LAA is unknown. Understanding this correlation may provide basic information to investigate the mechanism of AF thrombosis. We aimed to investigate the LAA morphology, function, and their possible relationship in AF patients for clinical reference in making treatment plans. We present the following article in accordance with the STROBE reporting checklist (available at https://qims.amgroups.com/article/view/10.21037/qims-22-218/rc).

Methods

Research participants

This retrospective observational case-control study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional Ethics Committee of The Second Hospital of Hebei Medical University, and informed consent was provided by all participants. A total of 140 patients with AF were enrolled in the experiment group, while 64 participants without AF were enrolled in the control group. All participants underwent a computed tomography angiography (CTA) scan between September 2016 and August 2017. The AF group was clinically diagnosed by physical examination and electrocardiogram (ECG) and included 85 males and 55 females with an age range of 30 to 80 (mean, 58.09±10.19) years. The inclusion criteria of the AF group were patients with AF that had been confirmed clinically and diagnosed by a physical examination and ECG with 256-slice spiral CT examination, including paroxysmal and persistent AF. Episodes of AF that terminated spontaneously were classified as paroxysmal; those that were sustained beyond 7 days without spontaneous conversion to sinus rhythm were classified as persistent. The exclusion criteria were as follows: poor quality CTA images, pacemaker implantation, valvular and congenital heart disease, and previous medication for AF. The control group underwent a CTA examination for chest tightness or a routine physical examination, including 40 males and 24 females aged 24–81 (mean, 56.56±7.91) years. The exclusion criteria were as follows: poor quality CTA images, pacemaker implantation, valvular and congenital heart disease, and previous medication for AF. The control group underwent a CTA examination for chest tightness or a routine physical examination, including 40 males and 24 females aged 24–81 (mean, 56.56±7.91) years. The inclusion criteria of the control group were candidates who had a normal heart rhythm and normal blood pressure <140/90 mmHg. The exclusion criteria were poor quality CTA images, pacemaker placement or other cardiac implants, valvular and congenital heart disease, and cardiovascular diseases (Figure 1).

CT scanning technology

Patients were trained before scanning to respire properly according to guidance. Metoprolol was used to control...
the heart rate and heartbeat rhythm in patients with AF. The nonionic contrast agent iohexol (350 mgI/mL, 0.8 mL/kg) was injected venously using a double-barrel high-pressure syringe with a scan range from 0.5 cm below the tracheal bifurcation to the palpebral surface of the heart, which used the bolus tracking technique (11,12). Using the retrospective ECG gating technology, the scanning parameters were as follows: tube voltage 80–120 kV, tube current 280–350 mAs/rev, collimation 128×0.625, pitch 0.18, matrix 512×512, rotation time 330 ms, and scanning field of view (FOV) 250 mm, with adjustment of the scan voltage and current according to the patient’s body mass index (BMI) to reduce scanning dose.

**Image post-processing technology**

A Philips i128CT EBW 4.5 workstation (Philips Healthcare, Amsterdam, Netherlands) was used to reconstruct the original images into 10 phases ranging from a 5% phase to a 95% phase, with an interval of 10%. The thickness of the reconstructed layer was 0.9 mm, and the interval was 0.45 mm. The 3D image of the LAA was obtained using the post-processing software for cardiac function. The volume of the LAA and LA was measured in each of the 10 phases. Then, the maximal volume of the LAA and LA and the minimal volume of the LAA and LA were also determined for the calculation of the emptying fraction of the LAA and LA (13).

The original images in the 75% phase of the cardiac cycle were used for multiplanar reconstruction (MPR) imaging on the Philips EBW 4.5 workstation. At the 75% phase of the cardiac cycle, the structural parameters of the LAA changed minimally (14). Then, MPR images were applied to measure the parameters of the LAA orifice at different angles. The LAA 3D images were obtained using the cardiac function processing software, and the LAA depth was measured.

**Measurement methods**

All parameters were analyzed by two experienced radiologists, who reached a consensus for each examination.

(I) **Measurement of the LAA morphology:** the LAA and LA on the cross-sectional images were identified, and a positioning line was fixed at the vertical LAA and LA junction for multiplanar reorganization. The position line was perpendicular to the LAA and LA junction, and the cross-sectional image of the LAA orifice was obtained (Figure 2A-2C). The LAA orifice’s long diameter, short diameter, area, and perimeter were measured (Figure 2D,2E). The major axis line at the orifice of the LAA was the long diameter, and the minor axis was the diameter of the midpoint through the vertical length.

(II) **LAA and LA volume:** 3D images of the LAA and
LA were obtained with cardiac function processing software. The total volume of the LAA and LA was obtained, and the LAA was cut at the LA junction to obtain a separate image of the LAA. The software automatically calculated the volume of the LAA and LA (Figure 3).

(III) LAA depth: the distance from the farthest point of the LAA tip to the central point of the LAA plane was measured on the cut LAA 3D image (Figure 3).

(IV) LAA emptying volume and LAA emptying fraction were calculated as follows:

\[
\text{LAA emptying volume} = \text{maximal LAA volume} - \text{minimal LAA volume} \tag{1}
\]

\[
\text{LA emptying volume} = \text{maximal LA volume} - \text{minimal LA volume} \tag{2}
\]

\[
\text{LAA emptying fraction} = \frac{(\text{maximal LAA volume} - \text{minimal LAA volume})}{\text{maximal LAA volume}} \times 100\% \tag{3}
\]

\[
\text{LA emptying fraction} = \frac{(\text{maximal LA volume} - \text{minimal LA volume})}{\text{maximal LA volume}} \times 100\% \tag{4}
\]
Statistical analysis

The data were analyzed using the SPSS 21.0 statistical software (IBM Corp., Armonk, NY, USA). The normality of data was tested with the Shapiro-Wilk test method, and when the P value was >0.05, the data were considered normally distributed. The data of the AF group and the control group were compared. The t-test was used to analyze the data in a normal distribution, and the Wilcoxon rank-sum test was used for the data without a normal distribution. The chi-square test was used to compare the gender ratios of the AF group. The measurement data obtained in a normal distribution were expressed as the mean ± standard deviation (SD), and the abnormally distributed measurement data were expressed as the median (interquartile range). The best critical value of predictors of AF was calculated by receiver operating characteristic (ROC) curve analysis. The correlation of the LAA volume change with the major and minor axes, area, and perimeter of the LAA orifice, and LAA depth were analyzed using the Pearson correlation coefficient. A P value <0.05 was considered statistically significant.

Results

Participants characteristics

A total of 140 patients with AF and 64 participants without AF but with a sinus rhythm were enrolled (Figure 1). Baseline characteristics are listed in Table 1. There was no significant (P>0.05) difference in age, gender, or BMI between the AF and the control groups.

Morphological and functional parameters of the LAA and LA and their correlation

Morphological and functional parameters of the LAA and LA are listed in Table 2. The LAA orifice minor axis (P=0.004), LAA volume (P=0.010), and LA volume (P<0.001) were significantly greater in patients with AF than in the controls. However, no significant difference (P>0.05) existed in the major axis, area, and perimeter of the LAA orifice and the LAA depth between the two groups. A comparison of the LA function between the AF group and control group revealed that the maximal and minimal LAA
The correlation of the LAA emptying fraction and LAA emptying volume with LA volume, LAA orifice major and minor axes, area, and perimeter were analyzed. The LAA emptying fraction was negatively correlated with the major axis and the area of the LAA orifice (Table 4). The LAA emptying volume was not significantly correlated with the above parameters (Table 5).

Multivariate analysis (Table 6) showed that the LAA volume [95% confidence interval (CI): 1.01 to 1.30; \(P=0.038\)] and LA volume (95% CI: 1.03 to 1.07; \(P<0.001\)) were two significant and independent risk factors of AF. The LAA orifice minor axis was not a significant (\(P=0.597\)) risk factor for AF, with a 95% CI of 0.88 to 1.07. The covariance expansion factor of the LAA volume and LA

### Table 1 Baseline characteristics in the AF and control group

| Variables          | AF group (n=140) | Control group (n=64) | Z/t value | P value |
|--------------------|------------------|----------------------|-----------|---------|
| Male               | 85 (60.71)       | 40 (62.50)           | 0.059     | 0.877   |
| Age (years)        | 58.09±10.19      | 56.56±7.91           | -1.861*   | 0.063   |
| BMI (kg/m\(^2\))  | 26.67±4.84       | 25.58±3.85           | -1.742    | 0.082   |

Data are presented as mean ± SD or n (%). *, t value. AF, atrial fibrillation; BMI, body mass index; SD, standard deviation.

### Table 2 Comparison of morphological and functional parameters of the LAA and LA between AF and control groups

| Variables                  | AF                  | Control             | Z/t value | P value |
|----------------------------|---------------------|---------------------|-----------|---------|
| Maximal LAA volume (mL)    | 11.15 (7.98, 13.50) | 8.05 (6.70, 10.65)  | -3.152    | 0.002*  |
| Minimal LAA volume (mL)    | 4.90 (3.63, 7.00)   | 3.15 (2.10, 3.98)   | -4.515    | <0.001* |
| LAA emptying fraction      | 47.34 (34.75, 62.13)| 63.72±7.88          | -3.960    | <0.001* |
| LAA emptying volume (mL)   | 5.39±2.16           | 5.30 (4.10, 6.20)   | -0.053    | 0.958   |
| Maximal LA volume (mL)     | 117.15 (103.53, 137.65) | 90.92±17.97      | -4.609    | <0.001* |
| Minimal LA volume (mL)     | 76.10 (54.68, 110.65)| 45.06±11.30        | -5.576    | <0.001* |
| LA emptying fraction       | 27.95 (16.24, 43.12)| 52.19 (47.38, 53.68)| -5.913    | <0.001* |
| LA emptying volume (mL)    | 37.15 (19.75, 48.25)| 45.86±9.49         | -3.099    | 0.002*  |
| LAA volume (mL)            | 8.30 (6.33, 11.03)  | 7.37±2.30           | -2.576    | 0.010*  |
| LA volume (mL)             | 99.75 (80.65, 120.43)| 76.58±15.82       | -6.206    | <0.001* |
| LAA orifice major axis (mm)| 26.25±5.22          | 26.45±3.80         | -0.845    | 0.398   |
| LAA orifice minor axis (mm)| 17.8±14.65          | 16.26±2.92         | 2.896*    | 0.004*  |
| LAA orifice area (m\(^2\))| 364.43 (268.32, 486.97)| 343.47±95.31      | -1.135    | 0.256   |
| LAA orifice perimeter (mm)| 71.40±15.50         | 69.73±9.72         | -0.259    | 0.795   |
| LAA depth (mm)             | 41.09±8.25          | 42.39±6.08         | -1.264*   | 0.208   |

Data are presented as mean ± SD or median (interquartile range). *, t value; *, P<0.05. LAA, left atrial appendage; LA, left atrium; AF, atrial fibrillation; SD, standard deviation.
volume was less than 5, which indicated that the LAA volume and LA volume had no collinearity.

**Predictive value of LA and LAA volumes**

The ROC curve analysis showed that an LAA volume of 8.75 mL had the highest predictive value for AF [area under the curve (AUC), 0.612], with a sensitivity of 76.6% and a specificity of 48.6%, whereas an LA volume of 97.15 mL had the highest predictive value for AF (AUC, 0.771), with a sensitivity of 90.6% and a specificity of 53.6% (Figure 4).

**LAA axis and volumes comparison between genders**

The LAA axis and volumes of the males and females in the AF group were compared after standardization based on their body surface area. The major and minor axes, area, and perimeter of the LAA orifice and LAA depth in female patients were significantly greater (P<0.05) than those in male patients (Table 7).

**Volume-time curves of LA and LAA**

The volume-time curves of LA and LAA were presented. Compared with non-AF patients, the LAA volume in patients with AF had a greater amplitude of increase even though the volume-time curves remained the same, whereas the LA volume in patients with AF had a smaller amplitude of increase over time (Table 8; Figure 5).

**Discussion**

Our study demonstrated that AF patients tended to have a...
more circular LAA orifice, which was positively correlated with LAA volume change. Also, the LAA orifice major axis and area were negatively correlated with the LAA emptying function. In addition, LAA anatomic parameters varied between males and females. As 3D cardiac CT is a vital tool to effectively evaluate the LAA size, these parameters may be potentially useful in guiding clinicians to choose devices properly (15).

The LAA plays an important role in AF (16). However, the relationship between LAA remodeling and AF has not

| Variables                      | Males           | Females         | Z value | P value |
|--------------------------------|-----------------|-----------------|---------|---------|
| LAA orifice major axis (mm)    | 12.98±2.79      | 14.39±3.05      | −2.955  | 0.003*  |
| LAA orifice minor axis (mm)    | 8.71±2.55       | 9.95±2.53       | −2.989  | 0.003*  |
| LAA orifice area (mm²)         | 188.22±88.39    | 220.24±88.80    | −3.287  | 0.001*  |
| LAA orifice perimeter (mm)     | 34.83±8.42      | 39.98±8.61      | −2.340  | 0.019*  |
| LAA depth (mm)                 | 20.31±5.01      | 22.61±6.50      | −3.484  | 0.000*  |
| LAA volume (mL)                | 4.63±2.27       | 4.71±2.23       | −0.143  | 0.886   |
| LA volume (mL)                 | 99.50 (82.30, 114.95) | 59.18±27.24     | −1.623  | 0.104   |

Data are presented as mean ± SD or median (interquartile range). *, P<0.05. LAA, left atrial appendage; LA, left atrium; AF, atrial fibrillation; SD, standard deviation.

Figure 4 ROC curve analysis was performed for the volume of the LAA and LA. Correlation analysis was conducted between the LAA volume change with the area (P=0.043) and perimeter (P=0.04) of the LAA orifice. ROC, receiver operating characteristic; LA, left atrium; LAA, left atrial appendage.
been defined clearly. It is believed that LAA morphology relates to the burden of silent cerebral ischemia in AF patients as a potential risk marker (17). Thus, the major axis, minor axis, and perimeter of the LAA orifice, as well as the depth and volume of the LAA, were measured in all AF patients and controls. The LAA orifice minor axis and LAA volume were significantly greater in AF patients than in control participants, but the LAA depth and the LAA orifice major axis, area, and perimeter were not. The minor axis of the LAA orifice in the AF group was longer than that of the control group, but the major axis of the two groups was similar. As a result, the shape of the LAA orifice changed from oval to circular in AF patients, which might affect the hemodynamics and accelerate thrombus formation of the LAA (18,19), even though it was not an independent risk factor of AF as compared with LAA volume and LA volume.

Besides the shape of the LAA orifice, the morphology of the LAA is another important indicator of embolic stroke.

Table 8 Changes in LA and LAA volumes over time in the phase of the cardiac cycle

| Variables | Phase of cardiac cycle |
|-----------|------------------------|
|           | 5% | 15% | 25% | 35% | 45% | 55% | 65% | 75% | 85% | 95% |
| N-LA (mL) | 45.76 | 54.47 | 70.19 | 84.68 | 90.78 | 81.71 | 68.40 | 68.37 | 65.83 | 48.27 |
| AF-LA (mL) | 95.09 | 103.87 | 113.74 | 119.22 | 124.85 | 120.42 | 116.22 | 111.06 | 108.79 | 98.31 |
| N-LAA (mL) | 3.33 | 5.00 | 6.42 | 7.91 | 8.51 | 6.94 | 6.29 | 6.42 | 6.07 | 3.52 |
| AF-LAA (mL) | 7.01 | 8.58 | 9.74 | 10.39 | 11.03 | 9.91 | 9.52 | 8.78 | 8.96 | 7.20 |

LA, left atrium; LAA, left atrial appendage; N-LA, LA volume in patients without AF; AF, atrial fibrillation; AF-LA, LA volume in patients with AF; N-LAA, LAA volume in patients without AF; AF-LAA, LAA volume in patients with AF.

Figure 5 The volume-time curves of the LA and LAA volume over time in the cardiac cycle phase. The LAA volume in patients with AF had a greater amplitude of increase even though the volume-time curves remained the same, whereas the LA volume in patients with AF had a smaller amplitude of increase over time. LAA, left atrial appendage; N-LAA, LAA in patients without AF; AF, atrial fibrillation; AF-LAA, LAA in patients with AF; LA, left atrium; N-LA, LA in patients without AF; AF-LA, LA in patients with AF.
The LAA morphology has 4 shapes, with the chicken wing shape considered to present a low risk of stroke, while others (windsock, cactus, and cauliflower) have a high risk of stroke (20,21). However, this study does not contribute to the analysis of the LAA morphology in association with stroke.

A widely used method to obtain the LAA volume is 3D imaging software, but the approaches to measuring the LAA orifice maximal and minimal diameters vary. For example, Boucebci et al. (22) measured the maximal and minimal diameters of the orifice on a 3D volume-rendering view. In contrast, we used axial images to locate the junction between the LA and LAA before reconstructing the coronal images to obtain the orifice image when measuring the major and minor axis, area, and perimeter. Theoretically, both these approaches were considered adequate to measure orifice parameters accurately.

The correlation in the LAA function with the axes, area, and perimeter of the LAA orifice and LAA depth has not been previously reported. Some researchers analyzed LAA morphologic types and functions (23,24). In our study, we found that the LAA emptying fraction was negatively correlated with the major axis and area of the LAA orifice but was not significantly correlated with LAA depth. Therefore, the assessment of the relationship between LAA function and LAA orifice morphology parameters may be more significant than the relationship between LAA function and LAA geometric features. Compared with the LAA emptying volume, the LAA emptying fraction was a crucial function parameter to present the emptying ability because the LAA emptying volume was not significantly correlated with any of the LAA parameters.

After being standardized based on the body surface area, the major and minor axes, area, and perimeter of the LAA orifice, LAA depth, and LA volume of the female patients were significantly greater than those of the male patients, but no statistical difference existed in the LAA volume between male and female patients. These results indicated that the LAA might have similar volumes between females and males even though its shape is different in AF patients. This may be related to the fact that the LAA is like a mountain with multiple peaks, and its volume cannot be simply calculated as its depth multiplied by the orifice area. Korhonen et al. (25) found that the area and depth of the LAA were related to the body surface area of the participant, with a greater depth of the LAA in females than in males, which was consistent with our study.

The closure device shape should be considered for different genders. However, Roh et al. (26) reported that gender differences only became evident in non-paroxysmal AF patients under 55 years old. However, the effect of age on the orifice shape in different genders was not analyzed because of insufficient data, which was limited by the number of patients. In the future, more investigation should be performed on this aspect.

In our study, the morphologic change of the LAA orifice in AF patients was more circular than that of the control participants, and the LAA parameters varied between genders, which might be vital for clinicians to choose a proper LAA closure device based on our outcomes because CT measurement is reliable on cardiac imaging (25,27). To avoid the influence of structural heart diseases, we excluded those patients with valvular and congenital heart disease and cardiovascular diseases.

Some limitations existed in this study; it had a retrospective design, only a small cohort of patients were enrolled, only Chinese patients were enrolled, and it was a single-center study. Future studies are needed to resolve these issues for better outcomes.

**Conclusions**

In the study, AF patients had a longer minor axis of the LAA orifice than that of the controls, which made the LAA orifice more circular. The LAA orifice area and perimeter positively correlated with LAA volume change. The major and minor axis, area, and perimeter of the LAA orifice and LAA depth of the females were significantly greater than those of their male counterparts in AF patients.

**Acknowledgments**

**Funding:** None.

**Footnote**

**Reporting Checklist:** The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-22-218/rc

**Conflicts of Interest:** All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-218/coif). The authors have no conflicts of interest to declare.

**Ethical Statement:** The authors are accountable for all
aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are 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 institutional ethics committee of The Second Hospital of Hebei Medical University, and informed consent was provided by all the patients.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

References

1. Massaro AR, Lip GYH. Stroke Prevention in Atrial Fibrillation: Focus on Latin America. Arq Bras Cardiol 2016;107:576-89.
2. Tsa0 HM, Hu WC, Tsai PH, Lee CL, Wang HH, Chang SL, Chao TF, Chen SA. Functional Remodeling of Both Atria is Associated with Occurrence of Stroke in Patients with Paroxysmal and Persistent Atrial Fibrillation. Acta Cardiol Sin 2017;33:50-7.
3. Ho SY, McCarthy KP, Faletra FF. Anatomy of the left atrium for interventional echocardiography. Eur J Echocardiogr 2011;12:i11-5.
4. Cabrera JA, Saremi F, Sánchez-Quintana D. Left atrial appendage: anatomy and imaging landmarks pertinent to percutaneous transcatheter occlusion. Heart 2014;100:1636-50.
5. Zhang LT, Gay M. Characterizing left atrial appendage functions in sinus rhythm and atrial fibrillation using computational models. J Biomech 2008;41:2515-23.
6. Bernard A, Comby PO, Lemogne B, Haïoun K, Ricolfi F, Chevallier O, Loffroy R. Deep learning reconstruction versus iterative reconstruction for cardiac CT angiography in a stroke imaging protocol: reduced radiation dose and improved image quality. Quant Imaging Med Surg 2021;11:392-401.
7. Herberg U, Smit F, Winkler C, Dalla-Pozza R, Breuer J, Laser KT. Real-time 3D-echocardiography of the right ventricle-paediatric reference values for right ventricular volumes using knowledge-based reconstruction: a multicentre study. Quant Imaging Med Surg 2021;11:2905-17.
8. Vira T, Pechlivanoglou P, Connelly K, Wijeysundera HC, Roifman I. Cardiac computed tomography and magnetic resonance imaging vs. transoesophageal echocardiography for diagnosing left atrial appendage thrombi. Europace 2019;21:e1-10.
9. Ernst G, Stöllberger C, Abzieher F, Veit-Dierscherl W, Bonner E, Bibus B, Schneider B, Slany J. Morphology of the left atrial appendage. Anat Rec 1995;242:553-61.
10. Hwang SH, Oh YW, Kim MN, Park SM, Shim WJ, Shim J, Choi JI, Kim YH. Relationship between left atrial appendage emptying and left atrial function using cardiac magnetic resonance in patients with atrial fibrillation: comparison with transoesophageal echocardiography. Int J Cardiovasc Imaging 2016;32 Suppl 1:163-71.
11. Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. Radiology 2010;256:32-61.
12. Yin WH, Yu YT, Zhang Y, An YQ, Hou ZH, Gao Y, Wang HP, Lu B, De Santis D, Rollins JD, Schoepf UJ. Contrast medium injection protocols for coronary CT angiography: should contrast medium volumes be tailored to body weight or body surface area? Clin Radiol 2020;75:395.e17-24.
13. Kanagala P, Arnold JR, Cheng ASH, Singh A, Khan JN, Gulsin GS, Yang J, Zhao L, Gupta P, Squire IB, Ng LL, McCann GP. Left atrial ejection fraction and outcomes in heart failure with preserved ejection fraction. Int J Cardiovasc Imaging 2020;36:101-10.
14. McGann C, Akoum N, Patel A, Kholmovski E, Revelo P, Damal K, Wilson B, Cates J, Harrison A, Ranjan R, Burgon NS, Greene T, Kim D, Dibella EV, Parker D, Macleod RS, Marrouche NF. Atrial fibrillation ablation outcome is predicted by left atrial remodeling on MRI. Circ Arrhythm Electrophysiol 2014;7:23-30.
15. Cho I, Kim WD, Lee OH, Cha MJ, Seo J, Shim CY, Pak HN, Joung B, Hong GR, Gransar H, Shin SY, Kim JS. Pre-procedural determination of device size in left atrial appendage occlusion using three-dimensional cardiac computed tomography. Sci Rep 2021;11:24107.
16. Nielsen-Kudsk JE, Korsholm K, Damgaard D, Valentin JB, Diener HC, Camm AJ, Johnsen SP. Clinical Outcomes Associated With Left Atrial Appendage Occlusion Versus Direct Oral Anticoagulation in Atrial Fibrillation. JACC Cardiovasc Interv 2021;14:69-78.
17. Yamamoto M, Seo Y, Kawamatsu N, Sato K, Sugano A, Machino-Ohtsuka T, Kawamura R, Nakajima H, Igarashi
M, Sekiguchi Y, Ishizu T, Aonuma K. Complex left atrial appendage morphology and left atrial appendage thrombus formation in patients with atrial fibrillation. Circ Cardiovasc Imaging 2014;7:337-43.

18. Chen L, Xu C, Chen W, Zhang C. Left atrial appendage orifice area and morphology is closely associated with flow velocity in patients with nonvalvular atrial fibrillation. BMC Cardiovasc Disord 2021;21:442.

19. Khurram IM, Dewire J, Mager M, Maqbool F, Zimmerman SL, Zipunnikov V, Beinart R, Marine JE, Spragg DD, Berger RD, Ashikaga H, Nazarian S, Calkins H. Relationship between left atrial appendage morphology and stroke in patients with atrial fibrillation. Heart Rhythm 2013;10:1843-9.

20. Agmon IN, Barnea R, Shafir G, Auriel E, Peretz S, Kornowski R, Hamdan A. Left appendage morphology as risk factors for cardio-embolism in patients with stroke of undetermined source. Eur Heart J 2021;42:172.

21. Yaghi S, Chang AD, Akiki R, Collins S, Novack T, Hemendinger M, Schomer A, Grory BM, Cutting S, Burton T, Song C, Poppas A, McTaggart R, Jayaraman M, Merkler A, Kamel H, Elkind MSV, Furie K, Atalay MK. The left atrial appendage morphology is associated with embolic stroke subtypes using a simple classification system: A proof of concept study. J Cardiovasc Comput Tomogr 2020;14:27-33.

22. Boucebci S, Pambrun T, Velasco S, Duboe PO, Ingrand P, Tsu JP. Assessment of normal left atrial appendage anatomy and function over gender and ages by dynamic cardiac CT. Eur Radiol 2016;26:1512-20.

23. Kishima H, Mine T, Takahashi S, Ashida K, Ishihara M, Masuyama T. Morphologic remodeling of left atrial appendage in patients with atrial fibrillation. Heart Rhythm 2016;13:1823-8.

24. Shimada M, Akaishi M, Kobayashi T. Left atrial appendage morphology and cardiac function in patients with sinus rhythm. J Echocardiogr 2020;18:117-24.

25. Korhonen M, Parkkonen J, Hedman M, Muuronen A, Onatsu J, Mustonen P, Vanninen R, Taina M. Morphological features of the left atrial appendage in consecutive coronary computed tomography angiography patients with and without atrial fibrillation. PLoS One 2017;12:e0173703.

26. Roh SY, Shim J, Lee KN, Ahn J, Kim DH, Lee DI, Choi JI, Kim YH. Gender-related Difference in Clinical Outcome of the Patient with Atrial Fibrillation after Radiofrequency Catheter Ablation. Korean Circ J 2018;48:605-18.

27. Rajwani A, Nelson AJ, Shirazi MG, Disney PJS, Teo KSL, Wong DTL, Young GD, Worthley SG. CT sizing for left atrial appendage closure is associated with favourable outcomes for procedural safety. Eur Heart J Cardiovasc Imaging 2017;18:1361-8.

Cite this article as: Tian X, Wang C, Gao D, Gao BL, Li CY. Morphological changes in the orifices of the left atrial appendage and left atrium in patients with atrial fibrillation. Quant Imaging Med Surg 2022;12(12):5371-5382. doi: 10.21037/qims-22-218