

# Morphology of the Left Atrial Appendage: Introduction of a New Simplified Shape-Based Classification System

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<b>Background</b>	The left atrial appendage (LAA) is a heart structure with known prothrombogenic and pro-arrhythmic properties.
<b>Aim</b>	The aim of this study was to evaluate the specific anatomy of the LAA and to create a simple classification system based on the shape of its body.
<b>Method and Results</b>	This study investigated 200 randomly selected autopsied human hearts (25.0% females, 46.6±19.1 years old). Three (3) types of LAAs were distinguished: the cauliflower type (no bend, limited overall length, compact structure [36.5%]); the chicken wing type (substantial bend in the dominant lobe [37.5%]), and the arrowhead type (no bend, one dominant lobe of substantial length [26.0%]). Additional accessory lobes were present in 55.5% of all LAAs. Significant variations between category types were noted in LAA length (chicken wing: 35.7±9.8 mm, arrowhead: 30.8±10.1 mm, cauliflower: 22.3±9.6 mm [p<0.001]) and in the thickness of pectinate muscles located within the LAA apex (arrowhead: 1.2±0.7 mm; cauliflower: 1.1±0.6 mm; chicken wing: 0.9±0.6 mm [p<0.001]). Left atrial appendage volume and orifice size were not affected by the type of LAA shape. The age of the donor was positively correlated with LAA volume (r=0.29, p=0.005), body length (r=0.26, p=0.012), and area of the orifice (r=0.36, p<0.001). Donors with an oval LAA orifice were significantly older than those with round orifices (50.2±16.6 vs 43.7±20.4 years [p=0.014]) and had significantly heavier hearts (458.2±104.8 vs 409.6±114.1g [p=0.002]).
<b>Conclusions</b>	This study delivered a new simple classification system of the LAA based on its body shape. An increase in age and heart weight was associated with LAA enlargement and a more oval-shaped orifice. Results of current study may help to estimate the different thrombogenic properties associated with each LAA type and be an assistance during planning and performing interventions on LAA.
<b>Keywords</b>	Left atrial appendage occlusion • Stroke • Atrial fibrillation • Ablation • Left atrium • Cardiac anatomy • Thromboembolism • LAA shape

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## Introduction

The left atrial appendage (LAA) is an embryonic remnant of the primitive atrium originating from the posterolateral aspect of the left atrium. The LAA contains stretch-sensitive receptors that can influence heart rate and is an important place of natriuretic peptide secretion in response to change in atrial pressure. Moreover, the LAA acts as a reservoir during left ventricular systole, a conduit for blood transiting from the pulmonary veins to the left ventricle during early diastole, an active contractile chamber that augments left ventricular filling in late diastole, and a suction source that refills itself in early systole [1]. It also plays an important role in cardiac thrombogenesis and arrhythmogenesis [2]. Many thrombi originate in the LAA owing to its specific predisposing factors. This frequently multilobular structure has many trabeculations, a relatively small orifice, a narrow neck, and turbulent blood flow, which increase the risk for cardio-embolic events [3]. The prothrombotic properties of the LAA are exponentiated by atrial tachyarrhythmias [4]. Thrombi created within the LAA account for 91% of strokes in non-valvular atrial fibrillation and 15–38% of strokes in non-atrial fibrillation patients with a cardiomyopathy [2]. Procedures aiming for exclusion of the LAA are commonly performed; however, it has not been clearly proven by any randomised study that LAA isolation or resection is a beneficial procedure and thus should be performed based on narrow indications [5]. On the other hand, it is suggested that instead of being beneficial, LAA exclusion may be a cause of heart failure deterioration [6]. Moreover, many studies indicate that the LAA acts as an important arrhythmogenic substrate in atrial and ventricular arrhythmias [7]. It is estimated that the LAA may be the electrical trigger in as many as a third of patients developing recurrent atrial fibrillation/tachycardia after undergoing ablation procedures [8]. The role of the LAA in pathophysiological processes has led to the development of new surgical and percutaneous techniques to functionally and electrically isolate the LAA [5,8].

Owing to its clinical significance, it is imperative to understand the morphology of the LAA. Not all LAAs are made equal: there are considerable differences in its size, shape, and the types of spatial relationships it has with adjacent cardiac and extracardiac structures [9,10]. These variations have implications on the pathogenicity of the LAA, on imaging accuracy, and on the types of interventional procedures, which can be used within this anatomical region [11]. Thrombotic potential has been closely linked to the shape of the LAA body. As such, several classification systems have been put in place to categorise this structure based either on post-mortem studies [10,12] or imaging data [13–17]. The most commonly used system remains the one outlined by Wang *et al.* [17], which was designed based on computed tomography (CT) findings. However, owing to the large discrepancies in distribution types observed in both cadaveric and imaging studies and the high inter- and intra-observer variations, it has been suggested that this classification system may not be replicable and exact. This has cast

doubt on whether this classification system is capable of accurately predicting the correlation between different LAA types and their associated risks for stroke or arrhythmia [9,18–24].

The aim of this study was to investigate and document the detailed anatomy of the LAA. It also sought to devise a simple classification system of the shape of the LAA, which would allow estimation of the different thrombotic properties associated with each type. The secondary aim was to find correlations between different LAA features and anthropometric parameters.

## Material and Methods

This study was conducted at the Department of Anatomy, at the Jagiellonian University Medical College and was approved by the Bioethical Committee of the Jagiellonian University in Cracow, Poland. The study was conducted according to the principles expressed in the 1975 Declaration of Helsinki. The methods were carried out in accordance with the approved guidelines.

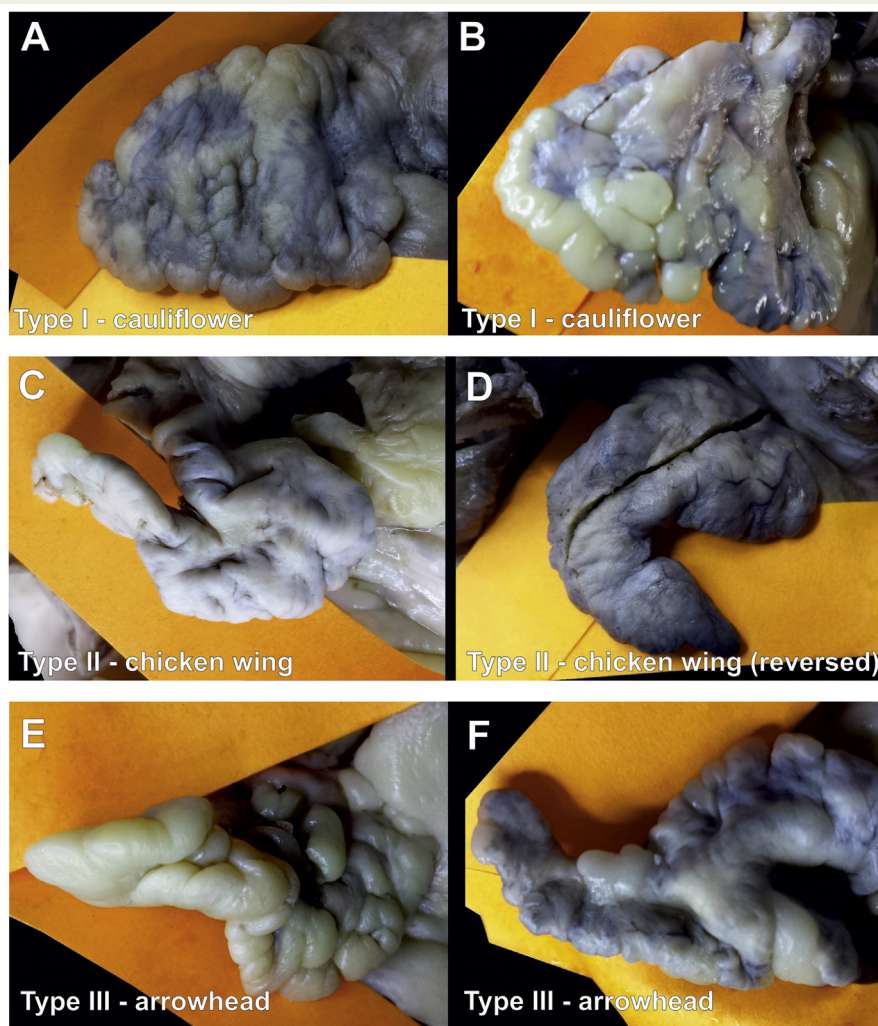
## Study Population

A total of 200 randomly selected autopsied human hearts (Caucasian) of both sexes (25.0% females) with a mean age of  $46.6 \pm 19.1$  years and an average measured body mass index (BMI) of  $26.5 \pm 4.8$  kg/m<sup>2</sup> were included and prospectively investigated. Hearts were collected during routine forensic medical autopsies performed at the Department of Forensic Medicine of the Jagiellonian University Medical College in Cracow, Poland, from December 2016 to June 2019. Hearts that had past cardiac surgery, heart grafts, previous heart trauma, evident severe macroscopic pathologies, vascular or cardiac anatomical defects, and macroscopic signs of cadaver decomposition were excluded from this study. Among the studied cases, there were no donors with either a history of persistent atrial fibrillation or a thrombus identified in the LAA during autopsy.

## Dissection and Measurements

Each heart, along with parts of its accompanying great vessels, was dissected from the chest cavity in a routine manner. All specimens were then briefly inspected, washed of excess blood, weighed, and then placed in a 10% paraformaldehyde buffered solution until the time of the next observations and measurements.

Based on its external and internal appearance, the shape of the LAA body was determined using modified classifications previously described in literature, dividing the LAA into three types (see also [Figure 1](#)): (1) Type I – the cauliflower shape. In this type, the body of the LAA is without obvious bends, it is compact with a relatively limited length, and has a variable number of lobes ([Figure 1A](#) and [B](#)). (2) Type II – the chicken wing shape. In this type, the body of the LAA has a substantial bend in the proximal or middle part of the dominant lobe (the bend is larger than 90°), and it may



**Figure 1** Photographs of cadaveric heart specimens showing different types of left atrial appendage shapes. (A, B) Cauliflower type. (C) Chicken wing type. (D) Reverse chicken wing type. (E, F) Arrowhead type.

present with secondary lobes (Figure 1C). Among chicken wing LAAs a reverse chicken wing subtype may be further distinguished (the tip of the wing is directed posteriorly and more laterally) (Figure 1D). (3) Type III – the arrowhead type. In this type, the body of the LAA is without obvious bends, it has one dominant lobe of substantial length and there are also secondary lobes extending from the base of the LAA in any direction (Figure 1E and F).

Shape assessment was performed independently by two researchers. In case of a disagreement, a third researcher was asked to also examine the specimen – all observers were then required to reach a consensus by discussing the most appropriate category in which the LAA belonged to.

Several other defining features and measurements were taken afterwards. The researchers noted the number of secondary to main lobes. The maximum length of the LAA (from base to apex) and the width of the LAA base were measured. The LAAs that were classified as having a chicken

wing shape had their length measurement divided into two parts – one measurement was taken from the base to the bend and another was taken from the bend to the apex of the appendage. The angle of the bend was also measured. Moreover, any variations in the left-sided pulmonary vein ostia and/or variations in the relative position of the LAA in relation to the pulmonary veins were noted.

Next, in order to expose the posterolateral region of the left atrium and the orifice of the LAA the anterior wall of the left atrium was dissected. The transverse diameter ( $D_1$ , parallel to the mitral valve annulus) and the antero-posterior diameter ( $D_2$ , perpendicular to the mitral valve annulus) of the LAA orifice were measured. If the difference between these two diameters was  $>3$  mm, the shape of the orifice was classified as oval, otherwise it was classified as a round. The area ( $A$ ) of the LAA orifice was calculated using the following formula:  $A = \pi \times \frac{1}{2} D_1 \times \frac{1}{2} D_2$ . The volume of the LAA was determined by filling its body with a known

volume of water. Lastly, the LAA was cut longitudinally from its base to the apex. The thickness of 10 representative pectinate muscles in both the base and apex of the LAA were measured for each appendage.

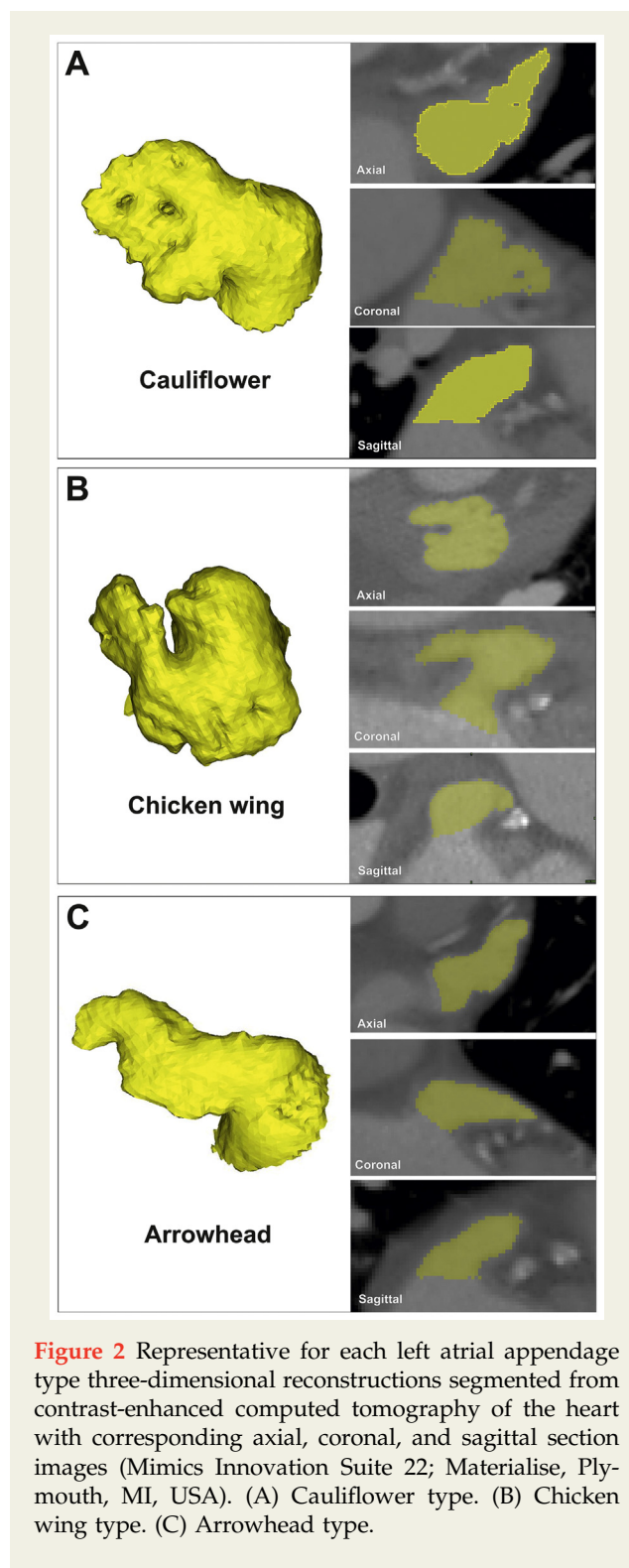
All linear measurements were conducted with a 0.03 mm precision electronic caliper (YT-7201; YATO, Wrocław, Poland). Angle measurements were taken using a 1° precision circle protractor. In order to reduce human bias, all measurements were recorded by two independent researchers. If results between the two observers varied by more than 10%, both measurements were repeated. The mean of the two new values was calculated and reported as the final length.

### Three-Dimensional Visualisations of the LAA Body

To prove the new LAA classification system in the clinical environment 50 randomly selected patients were retrospectively investigated (Caucasian, 50% females, mean age  $49.7 \pm 12.4$  years). The standard contrast-enhanced electrocardiogram-gated multi-slice CT was performed at the John Paul II Hospital in Cracow as a part of the coronary artery disease diagnostic process. The detailed cardiac CT protocol was described in a previous study [25]. The DICOM files were implemented in the three-dimensional reconstruction and visualisation software (Mimics Innovation Suite 22; Materialise, Plymouth, MI, USA). The LAA body was identified in all patients and reconstructed three dimensionally to identify its shape (Figure 2).

### Statistical Analysis

The data from this study are presented as mean values with corresponding standard deviations or determined percentages. Shapiro–Wilk tests were used to determine if the quantitative data were normally distributed. Levene’s test was performed to verify a relative homogeneity of variance. Student’s *t*-tests and the Mann–Whitney *U*-tests were used for statistical comparisons. The analysis of variance or non-parametric Kruskal–Wallis tests were used to compare values between different groups. Detailed comparisons were performed using Tukey’s post-hoc analyses. Qualitative variables were compared using chi square tests of proportions with Bonferroni corrections to account for the multiple comparisons. Correlation coefficients were calculated to assess whether there was a statistical dependence between the measured parameters. In particular, the correlations between the LAA features, anthropometric parameters of the donors, and heart parameters were investigated. To detect a simple correlation ( $r=0.25$ ) with 80% power and a 5% significance level (two-tailed;  $\alpha=0.05$ ;  $\beta=0.2$ ), the required minimal sample size was set at approximately 123 cases. A *p*-value  $<0.05$  was considered to be statistically significant. Statistical analyses were performed using StatSoft STATISTICA 13.1 software for Windows (StatSoft, Tulsa, OK, USA).



**Figure 2** Representative for each left atrial appendage type three-dimensional reconstructions segmented from contrast-enhanced computed tomography of the heart with corresponding axial, coronal, and sagittal section images (Mimics Innovation Suite 22; Materialise, Plymouth, MI, USA). (A) Cauliflower type. (B) Chicken wing type. (C) Arrowhead type.

## Results

Three (3) different LAA body types were distinguished: type I (cauliflower [36.5%; Figure 1A and B]); type II (chicken wing [37.5%; reverse chicken wing in 2.5%] [Figure 1C]); and type

**Table 1** Prevalence and basic characteristic of the left atrial appendage (LAA) according to its shape.

Parameter	LAA Shape		
	Cauliflower (%)	Chicken Wing (%)	Arrowhead (%)
n (%)	73 (36.5)	75 (37.5), including reverse chicken wing: 5 (2.5%)	52 (26.0) according to previous classification: cactus: 31 (15.5) and windsock: 21 (10.5)
No additional lobes (% of cases)	23.3	46.7	71.1
One additional lobe (% of cases)	46.6	49.3	13.5
Two or more additional lobes (% of cases)	30.1	4.0	15.4

III (arrowhead [26.0%; Figure 1E and F]). Interobserver agreement for the assessment of the three different LAA types was excellent: 95.9% for the cauliflower, 96.0% for the chicken wing, and 92.3% for the arrowhead type. The sex and age of donors did not affect the LAA type. Using the original LAA classification by Wang et al. [17] the prevalence of the cactus and the windsock LAA types (that are now combined into arrowhead type) would be 15.5% and 10.5%, respectively. In the set of analysed cardiac computed tomography (CT) data the LAA body types were identified as follows: cauliflower in 38.0% (Supplementary Figure 1), chicken wing in 40.0% (Supplementary Figure 2), and arrowhead in 22.0% (Supplementary Figure 3), which proves clinical reliable of the proposed new classification system.

At least one or more additional accessory lobes were present in 55.5% of all examined specimens. The number of secondary lobes varied based on the type of LAA body shape ( $p < 0.001$ ; Table 1).

Table 2 shows the measured parameters divided by LAA type. The total length of the body of the LAA was longest in the chicken wing type ( $35.7 \pm 9.8$  mm) and shortest in the cauliflower type ( $22.3 \pm 9.6$  mm;  $p < 0.001$ ). In 27.0% of all cases the length of the LAA was less than twice the LAA orifice diameter. The thickness of the pectinate muscles at the LAA apex was significantly thinner in the chicken wing type than in the cauliflower and arrowhead types ( $0.9 \pm 0.6$  vs  $1.1 \pm 0.6$  vs  $1.2 \pm 0.7$  mm, respectively [ $p < 0.001$ ]). Also, irrespective of body type, pectinate muscles located within the LAA base were significantly thicker than those located within the LAA apex ( $p < 0.001$ ; Table 2). Interestingly, LAA volume and orifice size did not vary with the type of LAA shape. Moreover, the shape of the orifice of the LAA was not influenced by the LAA body type. The orifice was oval in 50.7% of cauliflower types, in 40.0% of chicken wing types, and in 44.2% of arrowhead types – the remainder of specimens had round orifices ( $p = 0.422$ ). Also, appendages with numerous lobes did not differ in their volume capacity ( $p > 0.05$ ).

Owing to its unique architecture, the chicken wing type had additional morphometric parameters assessed. Therefore, the angle of the bend of the main lobe ( $134.5 \pm 21.0^\circ$ ), the length of the LAA body from the base to the bend ( $20.0 \pm 6.2$

mm), and the length from the bend to the apex ( $16.5 \pm 7.4$  mm) are included in Table 2.

Other trends and correlations were noticed, which were independent of the LAA body type. The LAA volume correlated with BMI ( $r = 0.27$ ,  $p = 0.02$ ), body weight ( $r = 0.29$ ,  $p = 0.004$ ), body height ( $r = 0.20$ ,  $p = 0.04$ ), age ( $r = 0.29$ ,  $p = 0.005$ , growth rate: 0.02 mL/year), and heart weight ( $r = 0.32$ ,  $p < 0.001$ ). Moreover, the total length of the LAA increased with age ( $r = 0.26$ ,  $p = 0.012$ , growth rate: 0.12 mm/year) and cardiac weight ( $r = 0.28$ ,  $p = 0.003$ ). The area of the orifice of the LAA was also positively correlated with age ( $r = 0.36$ ,  $p < 0.001$ , growth rate: 0.02 cm<sup>2</sup>/year) and heart weight ( $r = 0.26$ ,  $p < 0.001$ ). Donors with an oval LAA orifice (45.0%) were significantly older than those with a round (55.0%) orifice ( $50.2 \pm 16.6$  vs  $43.7 \pm 20.4$  years,  $p = 0.014$ ) and they had significantly heavier hearts ( $458.2 \pm 104.8$  vs  $409.6 \pm 114.1$  g;  $p = 0.002$ ). No other statistically significant correlations were observed. The sex of the donor did not affect any LAA dimensions.

Most of the examined hearts (91.5%) had a classical pattern of left-sided pulmonary venous drainage (i.e., with one inferior and one superior pulmonary vein ostium), while the remaining 8.5% had a single common left pulmonary vein ostium. No differences in LAA dimensions were observed between these two groups ( $p > 0.05$ ). The orifice of the LAA was located at the level of left inferior pulmonary vein in 48.5% of hearts and at the level of the left superior pulmonary vein in 51.5% of hearts.

## Discussion

Currently, the most frequently used classification system is the one developed by Wang et al. [17], which distinguishes between four types of LAA body shape: chicken wing, cauliflower, cactus, and windsock [26]. Some shapes are less pathogenetic than others. For instance, patients with a chicken wing LAA morphology are significantly less likely to suffer from thrombo-embolic events than patients with other LAA shapes [18,26]. Meanwhile, cauliflower LAA body types are an independent predictor for stroke, even in patients with a low CHADS<sub>2</sub> score [16]. Nevertheless, studies

**Table 2** The morphometric characteristics of the left atrial appendage (LAA).

Parameter	All, n=200 (100%)	LAA Shape			P-value ANOVA*	Pairwise Comparisons		
		Cauliflower, n=73 (36.5%)	Chicken Wing, n=75 (37.5%)	Arrowhead, n=52 (26.0%)		P-value Cauliflower vs Chicken Wing	P-value Cauliflower vs Arrowhead	P-value Chicken Wing vs Arrowhead
LAA length (mm)	32.1±10.2	22.3±9.6	Total: 35.7±9.8 Base to bend: 20.0±6.2 Bend to apex: 16.5±7.4	30.8±10.1	<0.001	<0.001	<0.001	0.006
Width of LAA base (mm)	19.0±6.5	19.2±7.1	19.5±6.9	18.1±5.0	0.689	NS	NS	NS
Anteroposterior LAA ostium diameter (mm)	12.1±4.6 (range, 3.4–29.1)	12.5±4.6 (range, 5.5–29.1)	11.3±4.0 (range, 3.9–20.83)	12.6±5.2 (range, 3.4–26.5)	0.349	NS	NS	NS
Transverse LAA ostium diameter (mm)	13.0±4.7 (range, 2.6–31.3)	13.6±4.7 (range, 4.2–31.3)	12.4±4.4 (range, 2.6–21.5)	12.9±4.8 (range, 3.1–26.1)	0.396	NS	NS	NS
LAA orifice area (cm <sup>2</sup> )	1.3±0.9	1.4±1.1	1.2±0.7	1.4±0.9	0.379	NS	NS	NS
LAA volume (mL)	3.1±2.0	3.2±2.0	3.0±2.0	3.2±2.0	0.801	NS	NS	NS
Pectinate muscles thickness at the LAA base (mm)	1.7±0.8	1.8±0.8	1.6±0.7	1.8±0.9	0.257	NS	NS	NS
Pectinate muscles thickness at the LAA apex (mm)	1.2±0.6	1.1±0.6	0.9±0.6	1.2±0.7	<0.001	0.011	1.000	0.012

Data are mean±standard deviation unless otherwise stated.

Abbreviations: ANOVA, analysis of variance; NS, not significant.

by Wu et al. [24] and Khurram et al. [19] have raised concerns about the unreliability of the classification model, and about the limitations pertaining to the interpretation of the relationship between the morphology of the LAA and its associated stroke potential. One of the main problems concerns the very broad ranges that cover the prevalence of each LAA type. For instance, it was reported that the chicken wing type had an incidence of between 13% and 52%, the cauliflower type occurred in between 3% and 40% hearts, the cactus type occurred in 5–38% of hearts, and the windsock prevailed in 10–37% of hearts [26]. Such wide spectrums were also reported in an analysis of comparable study groups. Furthermore, huge inconsistencies were also present when comparing the distribution of LAA types in cadaveric studies versus imaging studies. In a study of autopsied hearts, the distribution of LAA types was as follows: chicken wings represented 12% of all specimens; cauliflowers represented 26%; cactuses represented 24%; and windsocks represented 38% [9].

Several factors are responsible for the major discrepancies in prevalence distribution. Firstly, the LAA body has a complex, three-dimensional structure that is often assessed in a two-dimensional plane. Stöllberger et al. [27] showed that the

imaging plane influenced the appearance of the overall shape and it could also affect the number of lobes detected. Secondly, Wang et al. [17] did not use quantitative morphometric data to qualify each subtype: they provided subjective descriptions of each category type, which could lead to confusion about certain specimens. Thirdly, the shape of the LAA can be viewed using two different techniques. Its form can be determined by examining the LAA wall (this technique is known as the myocardial model) or by exploring its cavity (this technique is referred to as the blood pool model). As the cauliflower and arrowhead types are also difficult to distinguish with the two-dimensional visualisation techniques, three-dimensional imaging should always be the preferred approach for adequate LAA visualisation in order to minimise any confusion (Figure 2, Supplementary Figures 1–3).

Considering all the above issues around proper LAA categorisation, we found it necessary to design a simpler classification system. One of the main issues in the old classification system was differentiating between the cactus and the windsock LAA types. Both types were similar to each other – each type had one dominant lobe of sufficient length without any visible bends [17]. They differed in their number and location of secondary lobes. According to the

original LAA classification by Wang et al. [17] the prevalence of the cactus and the windsock LAA types in our study population would be 15.5% and 10.5%, respectively. However, as those small features were very hard to detect in both cadaveric and imaging studies, we opted to merge these two types into one category – the arrowhead type. This reasoning was further justified by previous clinical studies that did not report any significant clinical differences between these two types of LAA shape [28].

The chicken wing and the cauliflower LAA types have many clinical associations, so it is important to be able to distinguish between these types. Fortunately, this is quite easy owing to two distinguishing characteristics: the presence of a bend and the distribution of trabeculations within the LAA body. The cauliflower LAA type is characterised by extensive thick trabeculations (a potential cause of stasis and thrombus generation), especially when compared to the chicken wing type [19,29]. A study by Khurram et al. [19] revealed that small LAA orifices and extensive trabeculations were independent risk factors for thrombo-embolic events in patients with atrial fibrillation. There were other, less noteworthy differences between the two LAA body shapes. The length of the LAA was highest in the chicken wing type and the thickness of the pectinate muscles at the LAA apex was thinner in the chicken wing type (Table 2). No other significant morphometric differences were noted.

The haemodynamic properties of different LAA shapes may play a crucial role in thrombogenicity. Flow velocity within the LAA has been shown to be highest in patients with a chicken wing LAA type as opposed to non-chicken-wing morphology, which could explain the lower occurrence of ischaemic stroke within this LAA morphology [22]. However, a recent experimental computational fluid dynamics study demonstrated that besides the overall shape of the LAA, other geometric characteristics (e.g., length, tortuosity, position, and orientation) also have an impact on the haemodynamic pattern within the LAA [30]. Lastly, the number of accessory lobes, which can range from none to five, may also play a significant role in the pathogenicity of the LAA [10,31]. This would imply that the cauliflower type (which possesses several accessory lobes) would be associated with a higher thrombogenic potential.

Our study indicates that LAA volume and its orifice size do not differ between LAA type, which indicates the uniformity of the LAA orifice and overall size regardless of its shape. Furthermore, this study investigated the impact of age on the geometry of the LAA. Older donors had larger LAA volumes (0.02 mL/year increase was noted), larger total LAA lengths (0.12 mm/year increase was noted), and larger orifice areas (0.02 cm<sup>2</sup>/year increase was noted). An increase in LAA size with age may be an additional argument against LAA occlusion by devices, as the LAA orifice might increase over time, thus favouring the development of late leaks after initially successful LAA occlusion. Additionally, age affected the geometric shape of the orifice – older patients had more oval-shaped openings. Veinot et al. [10] also concluded that age played a role in LAA length, width, and orifice size, and

that these differences were most evident during the first two decades of life [10]. Age-related changes have several implications for different cardiac pathologies. Increased occurrence of atrial fibrillation has been linked to older age and left atrial remodelling [32]. Changes in LAA structure could be a contributing factor – they could potentially increase the amount of electrical activity and trigger atrial tachycardias [7,33]. In addition, the transformation in the shape of the LAA orifice from a round to a more irregular opening could have implications for interventions. For instance, irregular orifices may complicate transcatheter LAA closure procedures, as there may be a device mismatch and peridevice residual leaks even where the device was appropriately oversized [34]. There is the possibility that the more oval shape of the LAA orifice in the elderly may be linked to higher laxity of ageing heart tissue. We also proved that BMI and heart weight (which translates into the size of the heart cavities) positively correlate with the LAA size. This will possibly have two implications: it may allow for easier manipulation of the sheath and device in the left atrium and lower the risk of injury to the atrium and perforation of the LAA, and may force the implantation of larger and non-standard devices and therefore lead to peridevice residual leaks [35].

This study also explored the relationships between the LAA and the left-sided pulmonary veins. These associations are becoming increasingly more important owing to the growing number of linear ablations and electrical isolations involving the LAA [7]. Knowing the exact location of the LAA within the left atrial wall could significantly improve outcomes in electrophysiological procedures. The study by Yorgun et al. [36] found that when compared to traditional cryoballoon pulmonary vein isolation, additional LAA isolation improved 1-year outcomes in patients with persistent atrial fibrillation [36]. Moreover, Heeger et al. [37] demonstrated that LAA electric isolation in addition to pulmonary vein isolation improves clinical success of patients with atrial fibrillation not responding to pulmonary vein isolation; however, a high incidence of thrombo-embolic events and LAA thrombus was observed despite sufficient oral anticoagulation. Lastly, it is important to remember that despite the proximity between the LAA and the left-sided pulmonary veins, 59.5% of examined hearts are separated by a prominent fold of tissue (the left atrial ridge), which can be a significant obstacle in ablation procedures [25].

The current study had several limitations. Firstly, all measurements were taken from formaldehyde-preserved autopsied heart specimens, which could have minimally affected the size and shape of the tissue. However, a previous study has shown that the use of 10% paraformaldehyde in cardiac tissue preservation did not cause significant changes in atrial tissue shape and dimensions [38]. Secondly, as this study was performed post-mortem, it may not entirely represent the morphological properties of the tissues in vivo and it cannot infer much about the natural behaviour or the dimensional changes within the cardiac cycle. Moreover, no donors with atrial fibrillation were studied. Furthermore,

patients with atrial fibrillation are typically elderly patients, while the mean age of our population was  $46.6 \pm 19.1$  years. At the same time, this limitation reminds us that we cannot forget about younger patients with LAA in daily clinical practice and the possible complications resulting from this structure in those cases. Additionally, only structurally unchanged hearts were investigated, but it may be possible that cardiac diseases such as heart failure, coronary artery disease, or long-standing arterial hypertension may affect the morphology of the LAA. No correlation was obtained between autopsy findings and imaging studies of the LAA. Lastly, only Caucasian subjects were studied and therefore no inter-racial differences were studied. Despite these limitations, it is believed that they do not interfere with our morphometrical analysis of the LAA nor with the findings about the relationships between individual heart structures and their relative dimensions. This newly created LAA classification system should be further tested and validated on imaging studies, including echocardiography, computed tomography (CT), and cardiac magnetic resonance imaging. Our simplified shape-based classification system will have to prove its relevance in future studies investigating the stroke risk of these now defined three LAA types.

## Conclusion

The LAA comes in many shapes and sizes, and classifying its morphology based on imaging data may pose several challenges in obtaining an accurate appraisal. The present study designed a new simple classification system based on the type of LAA body shape. Three easily distinguished types of LAA were observed: the cauliflower type (36.5%), the chicken wing type (37.5%), and the arrowhead type (26.0%). These categories did not differ in their total LAA volume and orifice sizes. Additionally, LAA accessory lobes were present in 55.5% of LAAs. Age significantly affected the size of the LAA, causing LAA enlargement and a progressive transformation of the LAA orifice geometry into a more oval-shaped opening. Variations in left-sided pulmonary venous drainage had no influence on LAA morphometric features.

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## Conflicts of Interest

There are no conflicts of interest to disclose.

## Appendices. Supplementary Data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.hlc.2020.12.006>.

## References

- [1] Barbier P, Solomon SB, Schiller NB, Glantz SA. Left atrial relaxation and left ventricular systolic function determine left atrial reservoir function. *Circulation*. 1999;100:427–36.
- [2] Naksuk N, Padmanabhan D, Yogeswaran V, Asirvatham SJ. Left atrial appendage: embryology, anatomy, physiology, arrhythmia and therapeutic intervention. *JACC Clin Electrophysiol*. 2016;2:403–12.
- [3] Patti G, Pengo V, Marcucci R, Cirillo P, Renda G, Santilli F, et al. The left atrial appendage: from embryology to prevention of thromboembolism. *Eur Heart J*. 2017;38:877–87.
- [4] Watson T, Shantsila E, Lip GY. Mechanisms of thrombogenesis in atrial fibrillation: Virchow's triad revisited. *Lancet*. 2009;373:155–66.
- [5] Piccini JP, Sievert H, Patel MR. Left atrial appendage occlusion: rationale, evidence, devices, and patient selection. *Eur Heart J*. 2017;38:869–76.
- [6] Schneider B, Nazareus D, Stöllberger C. A 79-year-old woman with atrial fibrillation and new onset of heart failure. *ESC Heart Fail*. 2019;6:570–4.
- [7] Karim N, Ho SY, Nicol E, Li W, Zemrak F, Markides V, et al. The left atrial appendage in humans: structure, physiology, and pathogenesis. *EP Europace*. 2020;22:5–18.
- [8] Di Biase L, Burkhardt JD, Mohanty P, Sanchez J, Mohanty S, Horton R, et al. Left atrial appendage: an underrecognized trigger site of atrial fibrillation. *Circulation*. 2010;122:109–18.
- [9] Ucerler H, İkiz ZAA, Özgür T. Human left atrial appendage anatomy and overview of its clinical significance. *Anadolu Kardiyol Derg*. 2013;13:566–72.
- [10] Veinot JP, Harrity PJ, Gentile F, Khandheria BK, Bailey KR, Eickholt JT, et al. Anatomy of the normal left atrial appendage: a quantitative study of age-related changes in 500 autopsy hearts: implications for echocardiographic examination. *Circulation*. 1997;96:3112–5.
- [11] Beigel R, Wunderlich NC, Ho SY, Arsanjani R, Siegel RJ. The left atrial appendage: anatomy, function, and noninvasive evaluation. *JACC Cardiovasc Imaging*. 2014;7:1251–65.
- [12] Kaminski R, Kosinski A, Brala M, Piwko G, Lewicka E, Dabrowska-Kugacka A, et al. Variability of the left atrial appendage in human hearts. *PLoS One*. 2015;10:e0141901.
- [13] Li CY, Gao BL, Liu XW, Fan QY, Zhang XJ, Liu GC, et al. Quantitative evaluation of the substantially variable morphology and function of the left atrial appendage and its relation with adjacent structures. *PLoS One*. 2015;10:e0126818.
- [14] Beutler DS, Gerkin RD, Loli AI. The morphology of left atrial appendage lobes: a novel characteristic naming scheme derived through three-dimensional cardiac computed tomography. *World J Cardiovasc Surg*. 2014;4:17–24.
- [15] Cates J, Biegling E, Morris A, Gardner G, Akoum N, Kholmovski E, et al. Computational shape models characterize shape change of the left atrium in atrial fibrillation. *Clin Med Insights Cardiol*. 2015;8:99–109.
- [16] Kimura T, Takatsuki S, Inagawa K, Katsumata Y, Nishiyama T, Nishiyama N, et al. Anatomical characteristics of the left atrial appendage in cardiogenic stroke with low CHADS2 scores. *Heart Rhythm*. 2013;10:921–5.
- [17] Wang Y, Di Biase L, Horton RP, Nguyen T, Morhanty P, Natale A. Left atrial appendage studied by computed tomography to help planning for appendage closure device placement. *J Cardiovasc Electrophysiol*. 2010;21:973–82.
- [18] Di Biase L, Santangeli P, Anselmino M, Mohanty P, Salvetti I, Gili S, et al. Does the left atrial appendage morphology correlate with the risk of stroke in patients with atrial fibrillation? Results from a multicenter study. *J Am Coll Cardiol*. 2012;60:531–8.
- [19] Khurram IM, Dewire J, Mager M, Maqbool F, Zimmerman SL, Zipunnikov V, et al. Relationship between left atrial appendage morphology and stroke in patients with atrial fibrillation. *Heart Rhythm*. 2013;10:1843–9.
- [20] Kong B, Liu Y, Hu H, Wang L, Fan Y, Mei Y, et al. Left atrial appendage morphology with atrial fibrillation in China: implications for stroke risk assessment from a single center study. *Chin Med J (Engl)*. 2014;127:4210–4.
- [21] Lee JM, Seo J, Uhm JS, Kim YJ, Lee HJ, Kim JY, et al. Why is left atrial appendage morphology related to strokes? an analysis of the flow velocity and orifice size of the left atrial appendage. *J Cardiovasc Electrophysiol*. 2015;26:922–7.
- [22] Fukushima K, Fukushima N, Kato K, Ejima K, Sato H, Fukushima K, et al. Correlation between left atrial appendage morphology and flow velocity in patients with paroxysmal atrial fibrillation. *Eur Heart J Cardiovasc Imaging*. 2016;17:59–66.



- [23] Nedios S, Kornej J, Koutalas E, Bertagnolli L, Kosiuk J, Rolf S, et al. Left atrial appendage morphology and thromboembolic risk after catheter ablation for atrial fibrillation. *Heart Rhythm*. 2014;11:2239–46.
- [24] Wu L, Liang E, Fan S, Zheng L, Du Z, Liu S, et al. Relation of left atrial appendage morphology determined by computed tomography to prior stroke or to increased risk of stroke in patients with atrial fibrillation. *Am J Cardiol*. 2019;123:1283–6.
- [25] Piątek-Koziej K, Holda J, Tyrak K, Bolechała F, Strona M, Koziej M, et al. Anatomy of the left atrial ridge (coumadin ridge) and possible clinical implications for cardiovascular imaging and invasive procedures. *J Cardiovasc Electrophysiol*. 2020;31:220–6.
- [26] Lupercio F, Carlos Ruiz J, Briceno DF, Romero J, Villablanca PA, Berardi C, et al. Left atrial appendage morphology assessment for risk stratification of embolic stroke in patients with atrial fibrillation: a meta-analysis. *Heart Rhythm*. 2016;13:1402–9.
- [27] Stöllberger C, Ernst G, Bonner E, Finsterer J, Slany J. Left atrial appendage morphology: comparison of transesophageal images and postmortem casts. *Z Kardiol*. 2003;92:303–8.
- [28] Yaghi S, Song C, Gray WA, Furie KL, Elkind MSV, Kamel H. Left atrial appendage function and stroke risk. *Stroke*. 2015;46:3554–9.
- [29] Patel A, Au E, Donegan K, Kim RJ, Lin FY, Stein KM, et al. Multidetector row computed tomography for identification of left atrial appendage filling defects in patients undergoing pulmonary vein isolation for treatment of atrial fibrillation: comparison with transesophageal echocardiography. *Heart Rhythm*. 2008;5:253–60.
- [30] Masci A, Barone L, Dedè L, Fedele M, Tomasi C, Quarteroni A, et al. The impact of left atrium appendage morphology on stroke risk assessment in atrial fibrillation: a computational fluid dynamics study. *Front Physiol*. 2019;9:1938.
- [31] Yamamoto M, Seo Y, Kawamatsu N, Sato K, Sugano A, Machino-Ohtsuka T, et al. Complex left atrial appendage morphology and left atrial appendage thrombus formation in patients with atrial fibrillation. *Circ Cardiovasc Imaging*. 2014;7:337–43.
- [32] Zulkifly H, Lip GYH, Lane DA. Epidemiology of atrial fibrillation. *Int J Clin Pract*. 2018;72:e13070.
- [33] Shirani J, Alaeddini J. Structural remodeling of the left atrial appendage in patients with chronic non-valvular atrial fibrillation: implications for thrombus formation, systemic embolism, and assessment by transesophageal echocardiography. *Cardiovasc Pathol*. 2000;9:95–101.
- [34] Rajwani A, Shirazi MG, Disney PJS, Wong DTL, Teo KSL, Delacroix S, et al. Left atrial appendage eccentricity and irregularity are associated with residual leaks after percutaneous closure. *JACC Clin Electrophysiol*. 2015;1:478–85.
- [35] Mahabadi AA, Lehmann N, Sonneck NC, Kälsch H, Bauer M, Kara K, et al. Left atrial size quantification using non-contrast-enhanced cardiac computed tomography – Association with cardiovascular risk factors and gender-specific distribution in the general population: the Heinz Nixdorf Recall study. *Acta Radiol*. 2013;55:917–25.
- [36] Yorgun H, Canpolat U, Kocyigit D, Çötelci C, Evranos B, Aytemir K. Left atrial appendage isolation in addition to pulmonary vein isolation in persistent atrial fibrillation: one-year clinical outcome after cryoballoon-based ablation. *Europace*. 2017;19:758–68.
- [37] Heeger CH, Rillig A, Geisler D, Wohlmuth P, Fink T, Mathew S, et al. Left atrial appendage isolation in patients not responding to pulmonary vein isolation: Benefit and risks. *Circulation*. 2019;139:712–5.
- [38] Holda MK, Klimek-Piotrowska W, Koziej M, Piątek K, Holda J. Influence of different fixation protocols on the preservation and dimensions of cardiac tissue. *J Anat*. 2016;229:334–40.