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Anatomical and morphometric variation of the orifice of the left atrial appendage

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Abstract

Background. Knowledge of the anatomical variations of the shape and size of the left atrial appendage orifice, along with the relationship of its size with the number of left atrial appendage lobes, the size of its neck, the left atrioventricular orifice, the left atrioventricular fibrous ring and the distance to it, as well as with the overall dimensions of the heart is important in personalized surgical planning for the installation of occluder device and left atrial appendage clipping to prevent thromboembolic complications.
Aim. To identify anatomical variations in the shape and size of the left atrial appendage orifice and analyze the dependence of these parameters on the number of left atrial appendage lobes, cardiac dimensions, mitral orifice area and the distance from the orifice to the left atrioventricular fibrous ring.
Material and methods. We studied 37 heart specimens fixed in 10% formalin in adults who died of non-cardiac causes. Morphometry was performed by an ShTsTs-1-200 digital calliper, drawing needle calliper and 4UM goniometer. We used nonparametric analysis of variance, Spearman correlation coefficient (Rs), univariate regression analysis, cross-tabulation analysis. The results are presented as the mean and standard deviation. The significance of differences was assessed by using the Mann–Whitney U-test.
Results. The left atrial appendage was single-lobed in 16.2% of cases, two-lobed in 62.2%, and three-lobed in 18.9%. The length of the orifice was 12.7±4.03 mm, and the width was 9.5±3.62 mm. The elliptical shaped orifices were 3.1 times more common than round ones (28/37 and 9/37, p=0.0027). In 17 of 28, oval orifices were located predominantly horizontally, in nine predominantly vertical, in one case obliquely. Vertically oriented orifices were significantly longer and slightly wider compared with others. The number of the left atrial appendage lobes was not a reliable predictor for the orifice shape (p=0.055). The size of the appendage orifice, variants of its shape and the distance to the left atrioventricular opening were unrelated to each other. The length and width of the orifice were correlated with each other (Rs 0.68) and correlated with the diameters of the left atrioventricular fibrous ring size. The orifice length correlated with the length of the ventricular complex (Rs 0.47) and heart width (Rs 0.53). The orifice width correlated only with the heart width (Rs 0.4) but not with other dimensions. As the length and width of the ventricular complex increased, the orifice length increased exponentially. The distance from the left atrial appendage orifice to the left atrioventricular opening did not depend on either the orifice shape or its orientation.
Conclusion. In a normal human adult heart, the shape of the left atrial appendage orifice was oval, less often round, and the size of the orifice depends on the length and the width of the ventricles.
Keywords: human anatomy, heart, left atrium, atrial auricle, atrial appendage.

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Background

The left atrium (LA) is the least studied cardiac chamber [1]. However, a literature analysis has shown that interest in the LA anatomy has increased considerably in the last decade. In particular, the number of publications on the LA size, the anatomy of the pulmonary vein orifices, and the left cardiac auricle (LCA) has increased [2].

The LCA represents an additional cavity of the LA. In contrast to the right cardiac auricle, in most cases, the LCA has a well-defined orifice and neck, and is characterized by various forms. Although the LCA wall structure is well studied with data on its dimensions [1, 3–7], LCA orifice studies are represented by single publications [8–10]. The clinical significance of LCA orifice studies is because of its

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anatomical characteristics, and the LCA often becomes a site of thrombus generation and a source of thromboembolism of the systemic circulatory system [11].

There are few data on the quantitative ratios of the LCA orifice size with neighboring heart structures in the literature on normal anatomy. Only a few sources contain information about age-related variability of LCA parameters and correlative relationships between LCA and heart sizes [3]. Meanwhile, such data are necessary for forming a “digital platform that characterizes the normative indicators of the human body structure at various levels of its organization,” provided by the certificate of the specialty “Human Anatomy.” Morphometric studies of typical and variant anatomy of intracardiac structures will expand the understanding of the local constitution of the heart and improve the criteria for its normal structure.

From the point of view of clinicians, knowledge of the shape and size variants of the LCA orifice, as well as the relationship of its size with the number of LCA lobes, its neck size, the left atrioventricular orifice, and the left annulus fibrosis (LAF) and the distance to it, as well as with the overall heart dimensions, is significant for personalization of the strategy when installing occluders and performing clipping of the auricle orifice to prevent thromboembolic complications [2, 11].

Aim

This study determines the shape options and normative (reference) values of the LCA orifice size. It analyzes the dependence of these dimensions on the number of auricle lobes, the overall heart dimensions, the left atrioventricular orifice diameters, and the distance from the auricle orifice to the LAF.

The study design was observational and non-randomized, and *the sampling method* was continuous. The study was performed at the Department of Human Anatomy of the Ural State Medical University from February to July 2021.

Materials and methods

Heart specimens (n = 37) were taken from the deceased whose bodies were not claimed for burial, so informed consent was not available. When working with sectional material, the requirements of Art. 5 of the Federal Law No. 8 “On Burial and Funeral Business” dated January 12, 1996 (as amended, in the current version) were considered.

The study protocol was approved by the local ethics committee of the Ural State Medical University (protocol No. 8 dated November 20, 2020).

Criteria for inclusion in the study:

1) Typical left-sided location of the heart;
2) Externally regular-shaped heart;
3) Concordant ratio of the cardiac chambers and cardiac vessels;
4) Heart weight 250–400 g.

Restriction criteria:

1) The age of the deceased under 18 years and over 90 years;
2) Heart disease in the structure of the pathoanatomical diagnosis as a primary, competing disease, or complication of the underlying disease;
3) Detection of macroscopic signs of complications of coronary heart disease, cardiomyopathies, diseases of the atrioventricular valves, and signs of heart surgery at the opening of the heart ventricles;
4) Damage or deformity of the LCA or its orifice, including the opening of the LCA in a case of suspected thromboembolism from cryptogenic stroke;
5) An atypical number of orifices of the pulmonary veins in the LA wall.

The specimens were washed in running water, post-mortem clots were removed, and they were fixed by immersion in 10% formalin so that the heart chambers were maximally filled with fixative.

Three overall heart dimensions were measured, the length of the ventricular complex (from the apex of the heart to the extreme right point of the aortic bulb in the coronary sulcus), the width of the heart (the largest distance between the pulmonary surfaces of the heart immediately below the coronary sulcus and parallel to it), the anteroposterior heart dimension (the largest distance between the sternocostal and diaphragmatic surfaces of the heart at the same level perpendicular to the width).

The number of auricle lobes was determined. The boundary between the lobes was considered a notch on the lower edge of the LCA, the depth at which was at least 1/3 of the auricle width at the location of the notch (Fig. 1).

If there were no notches, the auricle was considered single-lobed. Next, the posterior wall (“roof”) and partially the lower wall of the LA were cut off. The walls of the LA are named as they are oriented in a living person in an orthograde position. The LA was measured and the largest and smallest diameters of the LCA orifice (after this referred to as its length and width), the shortest distance from the LCA orifice to LAF, and the largest and smallest diameters of the left atrioventricular orifice.

If the orifice length exceeded its width by 1.25 times or more, the orifice was considered oval, and if it had a smaller ratio, it was considered round. If the long axis of the orifice was parallel to the conditional intercommissural line (largest diameter) of

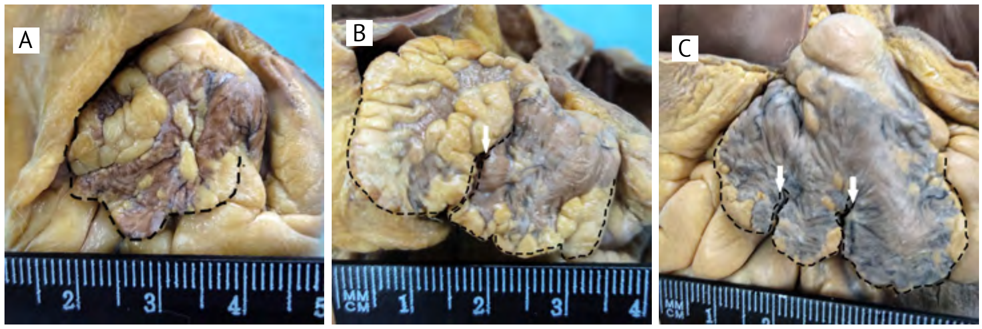

Fig. 1. Shape variants of the left cardiac auricle: A—single-lobed; B—two-lobed; C—three-lobed. Notches located on the lower edge (black dotted line) and dividing the auricle into lobes are shown by arrows.

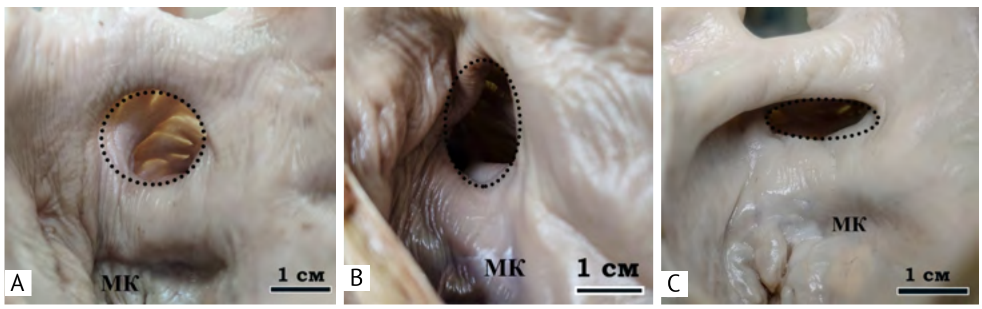

Fig. 2. Shape variants of the left auricle orifice of the heart (black dotted line): A—round; B—oval, vertical; C—oval, horizontal; MK—mitral valve.

the left atrioventricular orifice or deviated from it by no more than 20°, the orifice position was considered horizontal. If the angle between this axis and the intercommissural line varied from 70° to 110°, the orifice was considered vertical.

A 4UM goniometer (MIK PRO, vernier 10', accuracy 1°) was used. Linear quantities were measured using a spring compass, and an electronic sliding caliper ShCC-1-200 0.01 (Chelyabinsk, Chelyabinsk instrument plant; verification 2018) were used. When performing a morphometric analysis of intracardiac structures, the needles of the legs of the caliper were placed on the points of morphometry. Then, after removing the caliper from the LA, the distances between the ends of the needles were measured with a caliper (measurement error 0.03 mm according to ShCC-1-200).

The Statistica 10.0 program (StatSoft Inc, USA) was used to evaluate the distribution of values using the Shapiro–Wilk W test. For analysis of variance, the Kruskal–Wallis H test was used, and then for paired comparisons, the Mann–Whitney *U*-test was used. The results were presented as the mean value, standard deviation (M ± SD), median (Me), and extreme values. Spearman's correlation coefficient (r) was determined, and a one-way regression analysis was performed. The cross-tabulation method analyzed the significance of differences in qualitative attributes, and the significance level α was equal to 0.05.

Results

The width of the heart was 99.8 ± 10.57 mm (Me 98 mm), the anteroposterior size was 60.5 ± 10.87 mm (Me 61.2 mm), and the length of the ventricular complex was 100.1 ± 11.04 mm (Me 100.9 mm). The LCA could be single-lobed (6 of 37, 16.2%), three-lobed (7 of 37, 18.9%), but usually, it comprised two lobes (23 of 37, 62.2%; Fig. 1). In 20 of 23 cases, the two-lobed auricles were adjacent to the surface of the heart. They were located horizontally, and on only three specimens, they were oriented vertically.

Oval LCA orifices were 3.1 times more common than round orifices (28 of 37 and 9 of 37, $p = 0.0027$). In 17 of 28 cases, the oval orifices were located predominantly horizontally, predominantly vertically in 9 cases, and obliquely in one case (Fig. 2). Compared with other groups, vertically oriented orifices were significantly longer (Table 1) and somewhat wider (U = 41.0; $p = 0.059$) than horizontally oriented orifices.

Cross-tabulation showed that oval orifices were more typical of two-lobed auricles than single- or three-lobe ones ($p = 0.055$). When analyzing the dimensions of the auricle orifice, the width of the orifice of the three-lobed auricles was 1.8 times larger than the same parameter of the single-lobed auricles (H = 6.82, $p = 0.033$; U = 5.0, $p = 0.027$). No statistically significant differences were found between the lengths of the auricle orifices with different numbers of lobes (Table 2).

Table 1. Dimensions of the left cardiac auricle orifice with different shapes of the orifice and different orientations of its long axis.

Orifice size, mm; statistic parameter		Oval horizontal orifice	Oval vertical orifice	Round orifice	H; *p*
Width	M (SD)	9.25 (4.05)	10.9 (3.83)	9.0 (2.56)	2.89; 0.24
	Me	7.65	10.0	8.45	
Length	M (SD)	12.7 (4.08)	15.3* (4.08)	10.1* (2.46)	9.65; 0.008
	Me	11.2	14.3	9.8	

Note: *differences were significant at a Mann–Whitney *U*-test value of 10.0; $p = 0.005$; M (SD)—mean value and its standard deviation; Me—median; H—Kruskal–Wallis test; *p*—the level of significance.

Table 2. Dimensions of the left auricle orifice in hearts with different numbers of auricle lobes.

Orifice size, mm; statistical parameter		Number of auricle lobes			Combined sample value
		one	two	three	
Width	M (SD)	7.3 (1.49)	9.1 (2.91)	12.9 (5.13)	9.5 (3.62)
	Me	6.77*	8.0	12.0*	8.0
Length	M (SD)	10.3 (3.03)	12.4 (3.36)	15.7 (5.63)	12.7 (4.03)
	Me	8.94	11.5	14.6	11.8

Note: *differences were significant at a Mann–Whitney *U*-test value of 5.0; $p = 0.027$; M (SD)—mean value and its standard deviation; Me—median.

The values of the length and width of the LCA orifice formed a correlation pair with each other (Rs = 0.68). In addition, the length of the LCA orifice correlated with the length of the ventricular complex (Rs = 0.47) and the width of the heart (Rs = 0.53), and the values of the orifice width from three overall heart dimensions formed a correlation pair only with the width of the heart (Rs = 0.4). As the length and width of the ventricular complex increased, the length of the LCA orifice increased exponentially (Fig. 3). The dependence of the length of the LCA orifice on the size of the heart can be described by the following equations.

$$(1)\ L = 3.1525 \times e\ (0.0134X_1),$$
$$(2)\ L = 2.4634 \times e\ (0.016X_2),$$

where L is the length of the orifice of the auricle; X_1 is the length of the ventricular complex; X_2 is the width of the heart.

The distance from the LCA orifice to the LAF ranged from 4.33 to 20 mm (11.7 ± 3.02 mm). Oval and round orifices were at the same distance from the LAF ($U = 110$, $p = 0.49$), while the position of the orifice (horizontal or vertical) did not matter ($H = 0.49$; $p = 0.77$). Small and large diameters of LAF were 19.9 ± 4.45 mm (Me 18.9 mm) and 29.8 ± 5.54 mm (Me 29 mm), respectively. Between both LAF diameters and both LCA orifice sizes, a direct average correlation was revealed (Rs = 0.36–0.53).

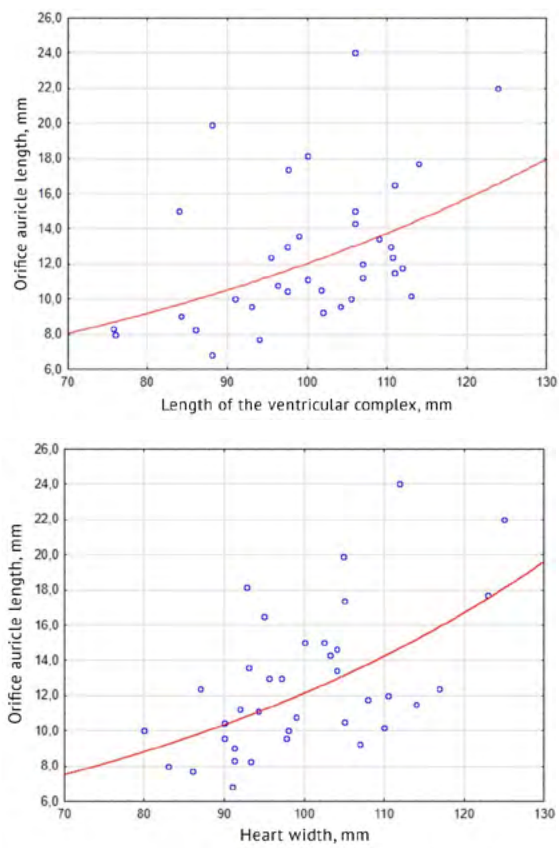

Fig. 3. Dependence of the orifice length of the left cardiac auricle on the length of the ventricular complex and the width of the heart.

Discussion

During the study, we answered questions about the range of variability in the auricle orifice size and whether any shape and position variants of this orifice could be determined based on objective morphometric parameters. The data obtained confirmed the existence of such variants.

The degree of variability of the length and width of the auricle orifice is specified. It was established that the orifice length exceeded its width by 1.3–1.5 times. According to the literature, the length and width of oval orifices were 14.23 ± 4.2 and 11.66 ± 3.5 mm, respectively, and the diameter of round orifices was 14.56 ± 2.6 mm [7]. According to other data, the LCA orifice diameter averaged 13.3 ± 0.2 mm and varied from 9 to 10 to 15–18 mm [9, 12].

Piątek–Koziej et al. (2020) measured the LCA orifice diameter in only one direction (parallel to the LAF) on 200 anatomical specimens and also studied the anatomy of the LA wall section between the LCA orifice and the left inferior pulmonary vein orifice and established that the LCA orifice diameter depended on the relief of this isthmus. In the group of hearts with the left lateral ridge in this isthmus, the diameter of the LCA orifice was 12.9 ± 4.6 mm and was larger than that in the group of hearts without a ridge (11.6 ± 4.4 mm, $p = 0.032$). The LCA orifice length values obtained in the present study are consistent with the data of these works [9, 10, 12].

According to our data, the narrowest orifice had a width of 5.6 mm. Values close to this are given by Piątek-Koziej et al. (2020) (4.5 and 4.7 mm), Whiteman et al. (2019) (5.0 mm), and Panyawongkhanti et al. (2020) (6.7 mm) [2, 7, 10].

According to Mikhailov (1987), the LCA orifice with a maximum diameter of less than 10 mm occurred in 4% of cases [5]. The length of the largest orifice, according to our findings, was 24 mm. This almost coincided with the maximum value of the LCA orifice diameter, which Panyawongkhanti et al. (2020) obtained in the study of sectional material (23.9 mm), and Su et al. (2008) determined when measuring casts of the LA (24.1 mm) [7, 8]. However, these data were inferior to the values obtained in the works of Cabrera et al. (2008) and Nucifora et al. (2011) [13, 14].

In a transesophageal examination of the LA, the length of the LCA orifice was 22.3 ± 4.5 mm, and the width was 16.5 ± 4.3 mm [14]. In the study of conditionally normal sectional specimens, the length of the longitudinal axis of the LCA orifice was 24.5 ± 3.5 mm (extreme values 18.3–28.5 mm), and the length of the transverse axis was 19.4 ± 2.5 mm (12.5–23.2 mm) [13]. The maximum diameter of the LCA orifice could reach 31.7 mm [7] and even 40 mm [2]. The orifice diameter ranged from 21 to 30 mm in 30% of cases, and in 2% of specimens, it was within 30 to 40 mm [5]. Such apparent differences could be because these studies were performed on heterogeneous samples that included drugs with and without heart pathology.

The monograph by Borodina et al. (2012) reports correlative relationships between the heart size and its auricles, and these relationships are the strongest during the first two periods of adulthood [3]. The present study clarified that the dependence of the length of the LCA orifice on the main overall heart dimensions is best described by an exponential function. This means that even a slight increase in the length and width of the ventricular complex will be accompanied by a significant increase in the LCA orifice.

An increase in the weight and overall dimensions of the heart above conventionally normal is a manifestation of many pathological processes. As noted by Mikhailov (1987), “in persons with heart disease, the LCA orifice is somewhat larger” [5, p. 69]. Several works have demonstrated the influence of cardiac pathology, primarily atrial fibrillation, heart defects, hypertrophy, and dilatation of the left ventricle on the size of the LA and LCA [12–15].

Cabrera et al. (2008) compared larger and smaller LCA orifice diameters in patients with ($n = 7$) and without structural heart disease ($n = 33$). They revealed that both diameters increased with pathology compared with controls ($p < 0.001$). A few cases in the groups and a heterogeneous nosological structure of pathology reduced the value of these results [13].

Du et al. (2020) analyzed LA dimensions in 108 patients who underwent radiofrequency catheter ablation for atrial fibrillation. Arrhythmia recurrence was noted in 24 patients 12 months after the intervention. Examination of patients by computed tomography and ultrasound showed that in the case of atrial fibrillation recurrence, the orifice area and short axis of the LCA orifice were substantially larger than in patients without recurrence [15]. Among patients with atrial fibrillation, compared with those who did not have this pathology, the LCA orifices were larger and more often had a round shape [14].

The present study revealed that the LCA orifices in a conditionally normal heart were characterized by an oval rather than a round shape. Stepanchuk et al. (2018) [9] came to the same conclusion. An exceptionally oval shape of the orifice was revealed in the study of both wet and corrosive specimens [8, 12]. According to other sources, “the shape of the LCA orifice is often slit-like or oval with a large vertical diameter” [5, p. 68]. We did not reveal any LCA orifices with a shape that could be called slit-like.

On the sectional material of the hearts of people aged 30–107 years ($n = 65$), round orifices were found in 44.6% of cases, and oval ones were noted in 55.4% [7]. Round orifices, and oval orifices, horizontal and vertical, were at the same distance from the LAF. According to Dudkiewicz et al. (2021), the distance from the LCA orifice to the LAF was 14.2 ± 4.8 mm [16], which is approximately 1.2 times higher than the same parameter value obtained in the present study. Our data on the average value and range of variation of the distance from the LCA orifice to the LAF were close to the results given in the monograph by Mikhailov (1987). According to this author, the said distance was 10–20 mm in 82.4% of cases and depended on the length of the heart [5].

The LCA orifice is often oval, but the shape of most occluders is rounded. For the personalized selection of occluders and the development and installation of sandwich-type occluders, it is essential to know how the anatomical characteristics of the orifice correlate with the neck size and the LCA lobe number [11]. According to the data obtained, oval orifices were more characteristic of the two-lobed LCA. However, the level of significance ($p = 0.055$) does not permit stating that the number of auricle lobes is a reliable predictor for determining the shape of its orifice.

Słodowska et al. (2021) compared three LCA shape variants, which differed in the number and relative position of the lobes. They revealed differences between the external LCA dimensions belonging to different variants. At the same time, neither the shape nor the LCA orifice dimensions were associated with any LCA shape variant [17], which is consistent with our results.

Kamiński et al. (2015) studied 100 LCA specimens of people aged 18–77 years and identified four auricle variants that differed in the number of lobes and their direction. The parameter that these researchers determined in the LCA orifice was its largest diameter. In most cases, this diameter varied from 12 to 16 mm [6], which was slightly larger than the results obtained by us (Table 2). We tend to believe that the main reason for these differences is the difference in the weight of the specimens studied. In [6], the weight of the heart could reach 490 g, which indicated a cardiac pathology with a high degree of probability.

Mean LCA orifice diameters ranged from 14 ± 1.3 mm in two-lobed auricles with the distal lobe oriented upwards (type 3) to 19.4 ± 4.2 mm in two-lobed auricles with the distal lobe oriented downwards (type 1). The average values of the auricle orifices diameter consisting of three lobes (types 2 and 4) were within this interval [6]. The absence in the work of Kamiński et al. (2015) the design description and the procedure for statistical processing of the data obtained significantly reduces their accuracy. In particular, it does not enable determining the relationship between the LCA shape and its orifice size.

Attention should be paid to the constancy of the ratios between the LCA orifice sizes and both LAF diameters revealed. We have been unable to find any publications containing information on size comparisons of these structures. During reconstructive surgeries on the mitral valve, it is advisable to focus on these ratios as a morphometric criterion for the harmony of the structure, and therefore, an anatomical prerequisite for the optimal functioning of the organ. From the standpoint of fundamental science, the relationship between the LCA orifice sizes and the LAF diameters, as well as the correlations between the LCA dimensions, adjacent morphometric parameters, and the size of the heart as a whole, can probably be considered a manifestation of the general biological principle of coordinated growth and development of anatomical formations that are structurally and topographically subordinate and characterized by unity of origin and, therefore, can be considered as objective criteria for the normal structure of the heart.

Study limitations

At all stages of the work, we tried to ensure the maximum compliance of the study with modern principles of evidence-based morphology. Nevertheless, we must note several aspects that may affect interpreting the results.

Specimens, fixed in 10% formalin aqueous solution, were studied. Fixation is inevitably manifested by tissue shrinkage. We do not consider this limitation significant since it has been proven that reducing the size of the macroanatomical heart structures due to fixation is within the statistical error [18].

The number of cases in the work is small, and this requires using non-parametric criteria for data analysis with a power less than that of parametric ones. It cannot be ruled out that with an increase in the number of cases, other results will be obtained both due to a decrease in the dispersion of values relative to the mean and existing differences that might not have been identified. We believe that the results obtained should be regarded as preliminary. The conclusions drawn are substantiated, but they do not have the nature of regularities so far.

We considered the LCA orifice round or oval based on its length and width ratio. We chose the value of this ratio (1.25) arbitrarily. The criteria (angular values) were also arbitrarily chosen, and according to them, we considered the orifice of an oval shape to be oriented horizontally or vertically. Changing the criteria would entail changing the results. However, in all works we know, these parameters were determined subjectively. The present study was the first to determine these parameters using objective morphometric criteria.

The patients whose drugs were included in the study were treated and died in city general hospitals. Regarding condition severity, these patients most likely differed from those discharged due to recovery, deterioration, transfer to a higher level medical institution, and recovered at home with the same pathology. The conclusions obtained in this work relate only to a specific group of patients.

The cause of death in 51.4% of cases was coronavirus infection 2019 (COVID-19). Heart lesions are recorded in 19% of patients hospitalized with COVID-19 [19]. There are limited data in the literature on COVID-19-associated myocarditis and right ventricular remodeling [19]. We included drugs in the sample only in cases when, according to the results of the examination performed in the standard volume, such lesions were ruled out. However, specific pathological changes could be unnoticed. An expanded scope of clinical, paraclinical, and pathomorphological studies would possibly reveal the actual myocardial damage. We do not consider the restriction associated with the potential influence of COVID-19 on the anatomical parameters of the LCA to be significant, as the known COVID-19-associated heart lesions do not have a direct pathogenetic relationship with a change in the auricle orifice size. Nevertheless, the study of the impact of COVID-19 on the structural organization of LA at all levels, from molecular to organ, seems promising.

Conclusion

The LCA may consist of one or more lobes, and the auricle orifice shape may be round or oval. Two-lobed LCAs are more common than single- and three-lobed LCAs, and oval orifices are 3.1 times more common than round ones. The orifice of the three-lobed auricle is 1.8 times wider than the orifice of the single-lobed auricle. The number of auricle lobes is not a reliable predictor of the auricle orifice shape. The relationship between the auricle orifice size, shape options, and the distance from the orifice to the left atrioventricular orifice was not revealed.

Correlation and regression relationships between the auricle orifice size, the left atrioventricular orifice, the length and width of the ventricular complex of the heart were revealed. These relationships can be considered a manifestation of the general biological law of coordinated growth and harmonious structure of the organ and intraorgan structures.

The quantitative values of the LCA orifice size obtained can be used as reference parameters for the normal structure of the heart.

Author contributions. A.A.Ya. was the work supervisor, developed the concept and design of the study, performed information retrieval, data analysis, and wrote the text of the article; A.A.G. performed information retrieval, prepared the specimens and made photographs, performed measurements, and data analysis.

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Conflict of interest. The authors declare no conflict of interest.

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