



Anatomical and histological structure and morphometric features of the heart of the red fox (*Vulpes vulpes*)

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The heart is the central organ of the cardiovascular system, ensuring continuous blood circulation, the delivery of oxygen and nutrients to tissues, and the removal of metabolic waste products. Despite numerous studies describing the cardiac morphology of various animal species, the morphometric and histological characteristics of the heart of the red fox (*Vulpes vulpes* Linnaeus, 1758) remain insufficiently investigated. The aim of this study was to examine the anatomical, histological, and morphometric organization of the heart of sexually mature red foxes, including the determination of its linear dimensions, organometric parameters, ventricular and atrial morphometry, and the cytometric characteristics of cardiomyocytes. The study was conducted on clinically healthy sexually mature animals ($n = 5$) using anatomical, histological, morphometric, and statistical methods. Novel data were obtained on the macromorphological, histological, and cytomorphometric organization of the red fox heart. The heart was found to be ellipsoidal in shape and to belong to the broadened-shortened type. Its height was 6.52 ± 0.19 cm, width 4.42 ± 0.02 cm, circumference 11.8 ± 0.27 cm, and cardiac development index $147 \pm 3.76\%$. The ventricles represented the most developed structural components, as confirmed by their morphometric parameters. The thickness of the left ventricular wall was significantly greater ($P \leq 0.001$), exceeding that of the right ventricle by 3.23-fold, whereas the thickness of the left atrial wall exceeded that of the right atrium by 1.40-fold. The absolute heart weight was 40.6 ± 1.96 g, corresponding to $0.46 \pm 0.015\%$ of body weight, while the net heart weight without epicardial fat was 38.2 ± 1.85 g ($0.43 \pm 0.01\%$ of body weight). The left ventricle accounted for the largest proportion of the net heart mass (52.1%), followed by the right ventricle (26.1%), whereas the atria together constituted 21.8%. The established ventricular-to-atrial mass ratios characterize the structural organization of the heart in this species. Histologically, the myocardium of both ventricles and atria consisted of cardiac striated muscle tissue formed by contractile cardiomyocytes arranged into myocardial fibers of varying thickness. These fibers were separated by layers of loose fibrous connective tissue containing blood and lymphatic vessels that provide trophic support and maintain myocardial functional activity. Cytometric analysis demonstrated that cardiomyocytes of the left ventricle were the largest. Their length was significantly greater than that of the right ventricle by 1.28-fold, while their width exceeded the corresponding value by 1.13-fold. The highest mean cardiomyocyte volume was also recorded in the left ventricular myocardium ($7602 \pm 78 \mu\text{m}^3$), compared with $4728 \pm 114 \mu\text{m}^3$ in the right ventricle and $3425\text{--}3699 \mu\text{m}^3$ in the atria. Conversely, the nuclear-to-cytoplasmic ratio was lowest in left ventricular cardiomyocytes and highest in atrial cardiomyocytes, reflecting the functional specialization of different cardiac chambers. The findings substantially expand current knowledge of the morphofunctional organization of the red fox heart and may serve as reference data for comparative anatomy, cardiac morphology, veterinary morphology, clinical diagnostics, pathological anatomy, forensic veterinary medicine, and experimental studies of the cardiovascular system.

Keywords: micromorphology; cardiovascular system; dissection; linear parameters; cytoarchitecture; cardiomyocytes.

Introduction

A fundamental aspect of organismal function is the interaction among its organs and systems (Bartsch et al., 2015; Lehnertz et al., 2020). A living organism is a complex biological system that has evolved through phylogenetic development and functions through the physiological integration of organs and tissues, forming a unified biological complex encompassing the organism and its environment (Duclos et al., 2019; Logvinenko et al., 2023). At every level of biological organization (cellular, tissue, organ, and systemic) essential physiological processes are coordinated to maintain the viability of the organism as a whole (Ayres, 2020; Wilson & Metzler-Wilson, 2024). Through their synergistic activity, organs and organ systems ensure adaptive responses to a wide range of environmental factors, including temperature, humidity, light, and other physical and chemical conditions (Buchko et al., 2019; Wishart, 2019). For example, the cardiovascular system adapts to physical exercise by regulating blood circulation and oxygen delivery to skeletal muscles (Cooper & Loxham, 2019; Eckhardt & Wu, 2021), whereas the respiratory system adjusts to fluctuations in ambient oxygen availability (Horalskyi et al., 2023).

These adaptive responses are coordinated by the nervous system, which transmits signals from the external environment to internal organs, enabling the organism to respond rapidly to environmental changes (González et al., 2023; Horalskyi et al., 2024). Thus, the organism is not a closed system but continuously interacts with its environment, thereby ensuring its survival, homeostasis, and evolutionary development (Simões-Costa et al., 2005; Buijtenendijk et al., 2020).

In response to environmental influences, the organism, as an integrated biological system, depends on the coordinated morphofunctional activity of all organs and organ systems, including the cardiovascular system, whose central organ is the heart (Kots et al., 2021; Raiola et al., 2023). The heart ensures continuous blood circulation, delivering oxygen and nutrients to tissues and organs while facilitating the removal of metabolic waste products (Zhurenko et al., 2018; Protsenko et al., 2020). Therefore, the coordinated function of the heart is essential for maintaining homeostasis and overall health, as it sustains arterial blood pressure, which is critical for adequate perfusion of all organs and tissues (Cesarovic et al., 2020; Christoffels & Jensen, 2020; Somberg et al., 2020). Equally important is the interaction of the cardiovascular system with other physiological systems,

particularly the nervous and endocrine systems, which enables the organism to adapt effectively to environmental changes, stress, and physical activity (Binu et al., 2017). Through this integrated regulation, the organism maintains homeostasis, adapts to changing environmental conditions, and preserves its functional integrity and viability (Michel, 2018).

During evolution, the structure and function of the heart have undergone substantial modifications in response to environmental conditions, physiological demands, and the metabolic requirements of different animal species (Monahan-Earley et al., 2013). In most vertebrates, particularly mammals and birds, the heart is four-chambered, allowing complete separation of oxygenated and deoxygenated blood and thereby supporting highly efficient circulation and elevated metabolic activity (Brown et al., 2020; Somberg, 2020). In contrast, reptiles and amphibians possess a three-chambered heart, reflecting their comparatively lower oxygen demands and different circulatory requirements (Schmidt-Ukaj et al., 2022; Jensen & Christoffels, 2024). In invertebrates, such as mollusks and crustaceans, the circulatory system is considerably simpler, with the heart pumping hemolymph rather than blood (Kodirov, 2011). These structural differences represent evolutionary adaptations driven by natural selection.

The morphology of the heart in humans and mammals has been extensively investigated from developmental, age-related, species-specific, and comparative perspectives (Slaby, 2018; Araújo Júnior et al., 2021; Shah et al., 2022; Ragulya et al., 2024). Comparative studies have demonstrated that the structural organization of the heart exhibits pronounced species-specific characteristics that reflect evolutionary adaptation to diverse ecological conditions and lifestyles (Poelmann & Gittenberger-de Groot, 2019). Nevertheless, many aspects of cardiac morphology, particularly those concerning the quantitative organization of its macro-, histological, and cytological structures, remain insufficiently understood and continue to be the subject of scientific discussion (Stakhurska & Pryshliak, 2014; Anderson & Ho, 2023). Most previous investigations have focused primarily on descriptive and comparative anatomy, whereas relatively few studies have provided comprehensive quantitative histomorphometric and cytometric analyses of the myocardium and its structural components (Rowlatt, 1990; Ragulya et al., 2024). Such quantitative data are essential for the objective interpretation of normal cardiac organization and for establishing reliable reference values applicable to both fundamental and applied research. Moreover, limited attention has been devoted to the integrated morphological organization of individual cardiac structures and their functional interactions, despite their critical role in the regulation of cardiac performance and systemic circulation.

Therefore, comprehensive investigation of the anatomical, histological, and morphometric organization of the heart remains an important task in modern morphology. Such studies are essential for advancing comparative anatomy, evolutionary biology, veterinary and human medicine, fur animal science, wildlife conservation, and experimental cardiovascular research, thereby providing the scientific rationale for the present study.

Materials and methods

The study was performed on the hearts of the red fox (*Vulpes vulpes* Linnaeus, 1758), a mammalian species belonging to the order Carnivora and the family Canidae. All experimental procedures complied with the principles of Good Laboratory Practice (GLP, 1981), the General Ethical Principles for Animal Experiments approved by the First National Congress on Bioethics (Kyiv, 2001), the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986) (European Convention, 1986), the Regulations for the Use of Experimental Animals approved by Order No. 281 of the Ministry of Health of Ukraine (November 1, 2000), and the Law of Ukraine "On the Protection of Animals from Cruelty" (No. 3447-IV, February 21, 2006) (Nichiporuk et al., 2022).

Hearts were collected together with the pericardial sac from clinically healthy sexually mature red foxes ($n = 5$). After the initial weighing, the pericardium was removed and the major vessels were

trimmed. The aorta and pulmonary trunk were transected at the free margins of the semilunar valve cusps, whereas the pulmonary veins and the cranial and caudal venae cavae were cut approximately 5 mm from the base of the atria. Blood clots were carefully removed from the cardiac chambers before the hearts were weighed again to determine their net mass.

Linear morphometric measurements were obtained using a metal ruler with an accuracy of 0.1 mm. Heart length (height) was measured as the distance from the origin of the aorta to the cardiac apex. Heart width was measured between the lateral surfaces of the organ at the level of the ventricular base, whereas thickness was determined as the maximum craniocaudal dimension, usually at the same level. Heart circumference was measured around the widest part of the ventricles. Cardiac shape was assessed based on the relationship among the principal linear dimensions (height, width, and thickness), allowing classification of the heart according to its geometric configuration (e.g., round, oval, or elongated) (Horalskyi et al., 2024). These measurements enabled comparative evaluation of cardiac morphology.

Absolute heart weight was determined using a PS 6000/C/2 analytical balance (RADWAG, Poland). Relative heart weight was calculated according to the following formula: Relative heart weight (%) = (absolute heart weight / body weight) $\times$ 100.

The cardiac development index was calculated as the ratio of heart height to heart width using the following equation: Cardiac development index (%) = (heart height / heart width) $\times$ 100.

Cardiac dissection was performed according to a standardized protocol. Initially, a circumferential incision was made through the atria, followed by longitudinal incisions extending through the atrioventricular orifices into the ventricular walls. The thickness of each atrial wall was measured at standardized locations within the dorsal and caudal regions of the atrial appendages. In the right ventricle, the incision was made between the two parietal leaflets of the right atrioventricular valve. In the left ventricle, the incision extended from the anterior margin of the posterior leaflet of the left atrioventricular (mitral) valve to the cardiac apex, passing between the papillary muscles. All dissections were performed with particular care to avoid damage to adjacent cardiac structures and to ensure accurate morphometric measurements. The dimensions of the anatomical structures were measured using a digital caliper with an accuracy of 0.05 mm.

For histological examination, tissue samples were fixed in chilled 10–12% aqueous formalin for at least 24 h. Following fixation, the specimens were dehydrated, embedded in paraffin according to standard histological procedures (Horalskyi et al., 2019), and sectioned at a thickness of 10–12 μ m using an MC-2 sliding microtome.

For the evaluation of the cytoarchitecture and histoarchitecture of the heart, paraffin sections were deparaffinized and stained with hematoxylin (Diapath, Italy) and eosin (Leica Geosystems, Germany). In addition, Heidenhain's iron hematoxylin staining was employed to enhance visualization of the striated myocardium and to evaluate the cytological features of cardiomyocytes. The prepared histological sections were subsequently used for qualitative histological assessment and quantitative histomorphometric analysis.

Histomorphometric measurements, including cardiomyocyte length, width (diameter), and nuclear volume, were performed using light microscopy with a Micros microscope equipped with a digital imaging system (Micros, Austria) and an MBS-10 stereomicroscope (Micromed, China), following the procedures described by Horalskyi et al. (2019). Histological sections were photographed using a CAM V-200 digital camera (Inter Med, China). Anatomical and histological terminology followed the International Veterinary Anatomical and Histological Nomenclature.

Statistical analysis was performed using Statistica version 7.0 (StatSoft Inc., Tulsa, OK, USA). Quantitative data were analyzed using one-way analysis of variance (ANOVA), and differences were considered statistically significant at $P < 0.05$ after Bonferroni correction for multiple comparisons.

Results

The heart of the red fox is located within the thoracic cavity, positioned almost horizontally and asymmetrically, with a slight displace-

ment toward the left side between the lungs and cranial to the diaphragm.

The base of the heart is directed cranially and is situated approximately at the level of the third to fourth ribs, whereas the apex is directed caudally and lies at the level of the seventh to eighth ribs. The auricles are relatively poorly developed (Fig. 1). The left auricle is broad and short, whereas the right auricle is narrow and elongated.

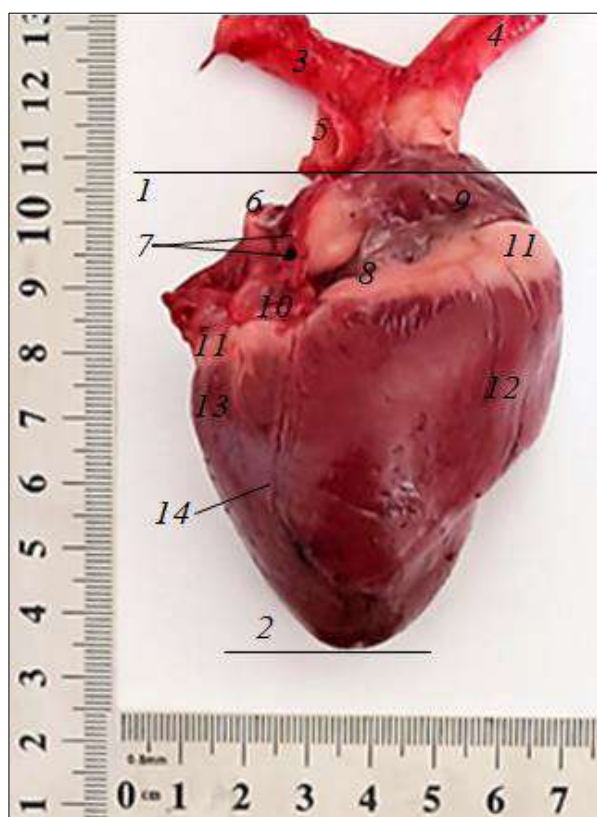


Fig. 1. Gross morphology of the heart (right lateral view) of a sexually mature red fox. 1 – base of the heart; 2 – apex of the heart; 3 – aorta; 4 – brachiocephalic trunk; 5 – pulmonary trunk; 6 – pulmonary veins; 7 – cranial and caudal venae cavae; 8 – right atrium; 9 – right auricle; 10 – pericardial attachment line; 11 – subepicardial fat; 12 – right ventricle; 13 – left ventricle; 14 – subsinuosal interventricular groove; gross specimen

According to the morphometric analysis, the heart of the red fox measured 6.52 ± 0.19 cm in height, 4.42 ± 0.02 cm in width, and 11.8 ± 0.27 cm in circumference. The cardiac development index was $147.0 \pm 3.8\%$, indicating that the heart has an ellipsoidal configuration and belongs to the broadened-shortened morphological type (Table 1). The ventricles represented the most developed anatomical components of the heart, followed by the left and right atria, which corresponded well with the thickness of their respective walls. The left ventricular wall (8.42 ± 0.17 mm) was significantly thicker ($P \leq 0.001$), exceeding the thickness of the right ventricular wall (2.60 ± 0.15 mm) by 3.23-fold. Likewise, the wall of the left atrium (3.04 ± 0.15 mm) was significantly thicker ($P \leq 0.05$) than that of the right atrium (2.18 ± 0.09 mm), with a 1.4-fold difference (Table 1). Organometric analysis demonstrated that the absolute heart weight of sexually mature red foxes was 40.6 ± 1.96 g, corresponding to $0.46 \pm 0.015\%$ of body weight. After removal of epicardial fat, the net heart weight was 38.2 ± 1.9 g, representing $0.43 \pm 0.01\%$ of body weight.

Based on the net heart weight, the absolute weight of the left atrium was 5.88 ± 0.38 g, accounting for $15.50 \pm 0.16\%$ of the total heart mass. The right atrium weighed 2.40 ± 0.18 g ($6.32 \pm 0.20\%$), which was 2.45-fold lower than the left atrium ($P < 0.01$). Together, both atria weighed 8.30 ± 0.14 g, representing $21.82 \pm 0.29\%$ of the net heart weight (Table 2).

Table 1

Morphometric parameters of the heart of the red fox ($x \pm SD$, $n = 5$)

Parameter	Value
Heart height, cm	6.52 ± 0.19
Heart width, cm	4.42 ± 0.02
Heart thickness, cm	3.50 ± 0.18
Heart circumference, cm	11.80 ± 0.27
Cardiac development (shape) index, %	147.0 ± 3.76
Mean ventricular wall thickness, mm	5.52 ± 0.16
Left ventricular wall thickness, mm	8.42 ± 0.17
Right ventricular wall thickness, mm	2.60 ± 0.15
Mean atrial wall thickness, mm	2.94 ± 0.25
Left atrial wall thickness, mm	3.04 ± 0.15
Right atrial wall thickness, mm	2.18 ± 0.09

Table 2

Morphometric characteristics of the heart, ventricles, and atria of the red fox ($x \pm SD$, $n = 5$)

Parameter	Absolute weight, g	Relative weight, %
Whole heart	40.60 ± 1.96	0.460 ± 0.015
Heart without epicardial fat (net heart weight)	38.20 ± 1.85	0.43 ± 0.01
Left atrium	5.88 ± 0.38	15.50 ± 0.16
Right atrium	2.40 ± 0.18	6.32 ± 0.20
Left and right atria (combined)	8.30 ± 0.14	21.82 ± 0.29
Left ventricle	19.78 ± 0.48	52.06 ± 0.59
Right ventricle	9.92 ± 0.42	26.12 ± 0.74
Left and right ventricles (combined)	29.72 ± 0.54	78.18 ± 0.87

The left ventricle constituted the largest cardiac compartment, with an absolute weight of 19.78 ± 0.48 g ($52.06 \pm 0.59\%$), whereas the right ventricle weighed 9.92 ± 0.42 g ($26.12 \pm 0.74\%$). The combined ventricular mass reached 29.72 ± 0.54 g, corresponding to $78.18 \pm 0.87\%$ of the total net heart weight. Consequently, the total ventricular mass was significantly greater than the combined atrial mass ($P < 0.001$), exceeding it by 3.6-fold.

The ratio of ventricular mass to the net heart weight was 0.78, whereas the corresponding ratio for the atria was 0.22. In addition, the atrial-to-ventricular myocardial mass ratio was 0.28, reflecting the predominance of ventricular myocardium in the structural organization of the red fox heart (Table 2).

The wall of the red fox heart consists of three layers: the outer epicardium, the middle myocardium, and the inner endocardium. The myocardium represents the principal structural and functional component of both the ventricular and atrial walls (Fig. 2a). Morphologically, the myocardium of the right and left ventricles of the red fox heart consists of two superficial layers, outer and inner, whose muscle fibers are oriented in an oblique longitudinal direction, two deeper layers, also outer and inner, and a single deepest layer.

The myocardium of the right and left atrial walls is composed of only two muscular layers: an outer layer common to both atria and a deep layer. The myocardial fibers of the outer layer are arranged transversely, extending from the right to the left auricle. In contrast, the fibers of the deep myocardial layer of both atria are oriented longitudinally. In the regions surrounding the venous orifices, the myocardial fibers form circular bundles.

This distinctive myocardial architecture, particularly the more pronounced development of the ventricular myocardium compared with that of the atria, reflects the different functional loads imposed on these cardiac chambers. Consequently, owing to the greater contractile workload of ventricular cardiomyocytes, the ventricular walls are substantially thicker than the atrial walls.

Microscopically, the myocardium of the ventricles and atria is composed of cardiac striated muscle tissue, whose principal structural elements are contractile cardiomyocytes. These cells are interconnected to form muscle fibers separated by layers of loose fibrous connective tissue containing blood and lymphatic vessels (Fig. 2b). Within the myocardium, contractile cardiomyocytes form a network of striated muscle fibers of varying thickness, classified as small, medium, and large. In histological sections stained by the Heidenhain method, these fibers exhibit differences in staining intensity (Fig. 2c).

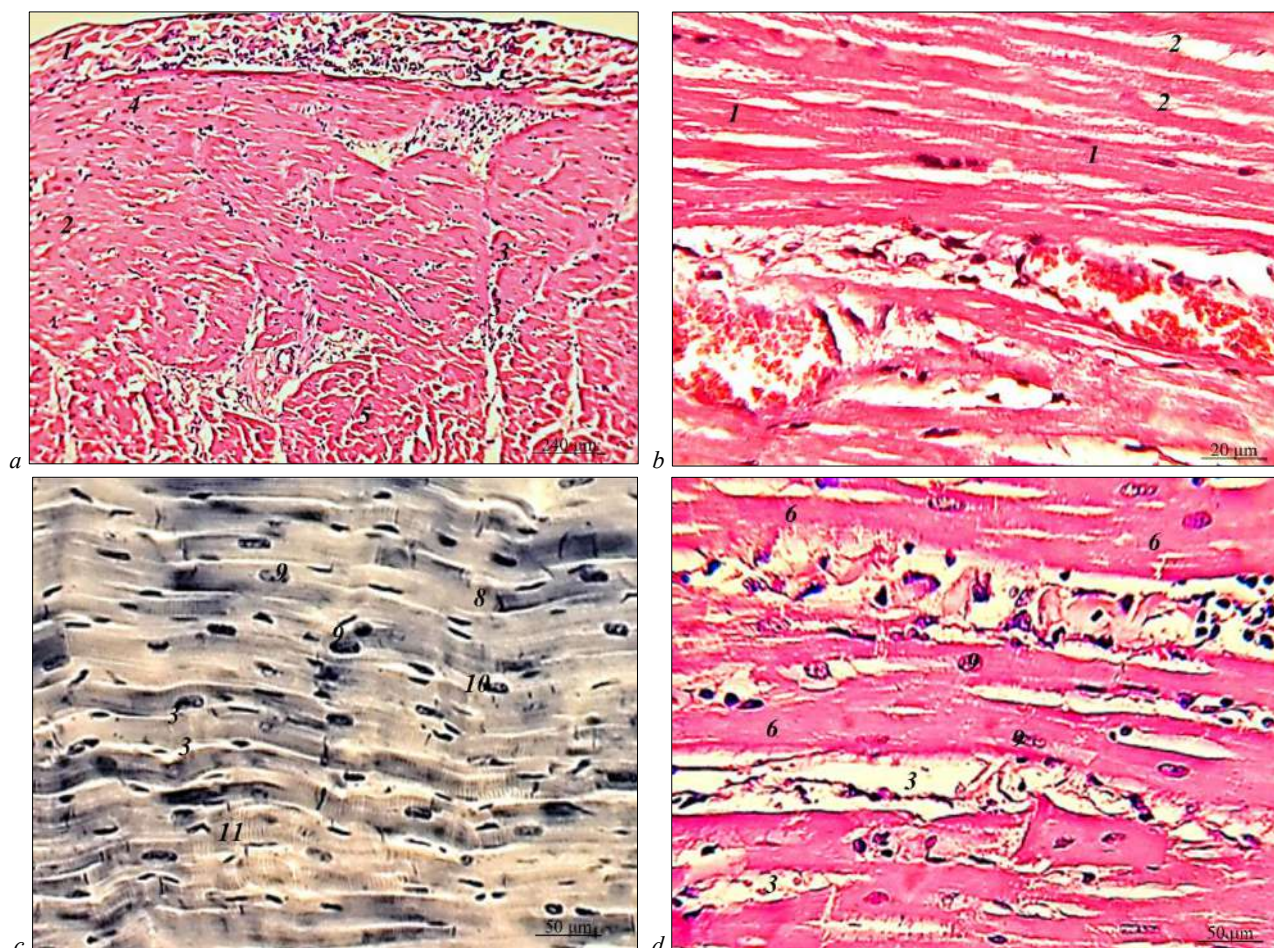


Fig. 2. Microscopic structure of the red fox heart: *a* – left ventricular wall; *b*, *c*, *d* – myocardium of the left ventricle; 1 – outer layer (epicardium); 2 – middle layer (myocardium); 3 – intermuscular connective tissue; 4 – outer superficial myocardial layer; 5 – inner superficial myocardial layer; 6 – muscle fibers; 7 – blood vessels; 8 – cardiomyocytes; 9 – cardiomyocyte nuclei; 10 – intercalated discs; 11 – cross-striations; hematoxylin and eosin staining (*a*, *b*, *d*); Heidenhain staining (*c*)

The longitudinally oriented myocardial fibers are interconnected by numerous anastomoses, forming a complex network that constitutes a continuous contractile system of the heart (Fig. 3b). In longitudinal sections, cardiomyocytes exhibit a rectangular appearance (Fig. 2c), whereas in cross-sections they appear circular (Fig. 3c), reflecting their characteristic cylindrical shape.

Microscopically, each cardiomyocyte, the principal contractile cell of the myocardium, consists of a well-defined sarcolemma, sarcoplasm, myofibrils, and one or more nuclei. The sarcoplasm exhibits distinct cross-striations produced by the orderly arrangement of myofibrils, as well as longitudinal striations resulting from the parallel organization of actin and myosin filaments (Fig. 3c).

In longitudinal sections of the myocardium, the myofibrils appear as fine parallel filaments extending along the long axis of the cardiomyocyte. In transverse sections, they are observed as numerous small dots distributed throughout the sarcoplasm. Sites where myofibrils pass through anastomotic connections from one muscle fiber to another are frequently observed, providing structural continuity and facilitating synchronized contraction of the myocardium.

In regions where the density of myofibrils is relatively low, the longitudinal striations of the muscle fibers are more distinct, whereas the cross-striations are less prominent. Conversely, thicker muscle fibers generally exhibit weaker staining characteristics, resulting in less distinct cross-striations and a more delicate appearance of the myofibrils. In thinner muscle fibers, the myofibrils are more densely packed.

The sarcoplasm of cardiomyocytes usually contains one, and occasionally two, centrally located nuclei of oval or elongated shape. In cross-sections, the nuclei occupy a central position within the cell. The nucleoplasm contains chromatin in the form of fine or coarse granules distributed throughout the nucleus (Fig. 2d).

Cardiomyocytes are interconnected by intercalated discs, which are particularly evident in sections stained by the Heidenhain method. These specialized junctional complexes mechanically and electrically couple adjacent cardiomyocytes into continuous muscle fibers, providing structural support for the contractile myofilaments and ensuring coordinated propagation of excitation and synchronous contraction of the myocardium. Consequently, the cardiac muscle functions as a functional syncytium.

According to the cytometric analysis, cardiomyocytes of the left ventricular myocardium were significantly larger than those of the right ventricle. The mean length of left ventricular cardiomyocytes ($89.94 \pm 1.04 \mu\text{m}$) was significantly greater ($P \leq 0.05$), exceeding that of the right ventricle ($70.23 \pm 1.19 \mu\text{m}$) by 1.28-fold. Likewise, the mean width of left ventricular cardiomyocytes ($12.77 \pm 0.36 \mu\text{m}$) was significantly greater ($P \leq 0.05$) than that of the right ventricle ($11.23 \pm 0.42 \mu\text{m}$), with a 1.13-fold difference. The smallest cardiomyocytes were observed in the atrial myocardium, where the mean cell length and width measured $66.30 \pm 0.99 \mu\text{m}$ and $9.98 \pm 0.31 \mu\text{m}$, respectively (Table 3). Calculated cardiomyocyte volumes also differed among the cardiac chambers. The largest mean cell volume was recorded in the left ventricle ($7602.32 \pm 78.38 \mu\text{m}^3$). In the right ventricle, the corresponding value was significantly lower ($P \leq 0.05$), measuring $4728 \pm 114 \mu\text{m}^3$, which was 1.6-fold smaller than that of the left ventricle. The smallest cardiomyocyte volume was observed in the atrial myocardium ($3425 \pm 70 \mu\text{m}^3$, Table 3).

A similar pattern was observed for cardiomyocyte nuclear volume. The largest nuclei were found in the left ventricle ($203.5 \pm 7.1 \mu\text{m}^3$), followed by the right ventricle ($187.9 \pm 6.1 \mu\text{m}^3$), whereas the smallest nuclear volume was recorded in the atria ($160.2 \pm 3.9 \mu\text{m}^3$, Table 3).

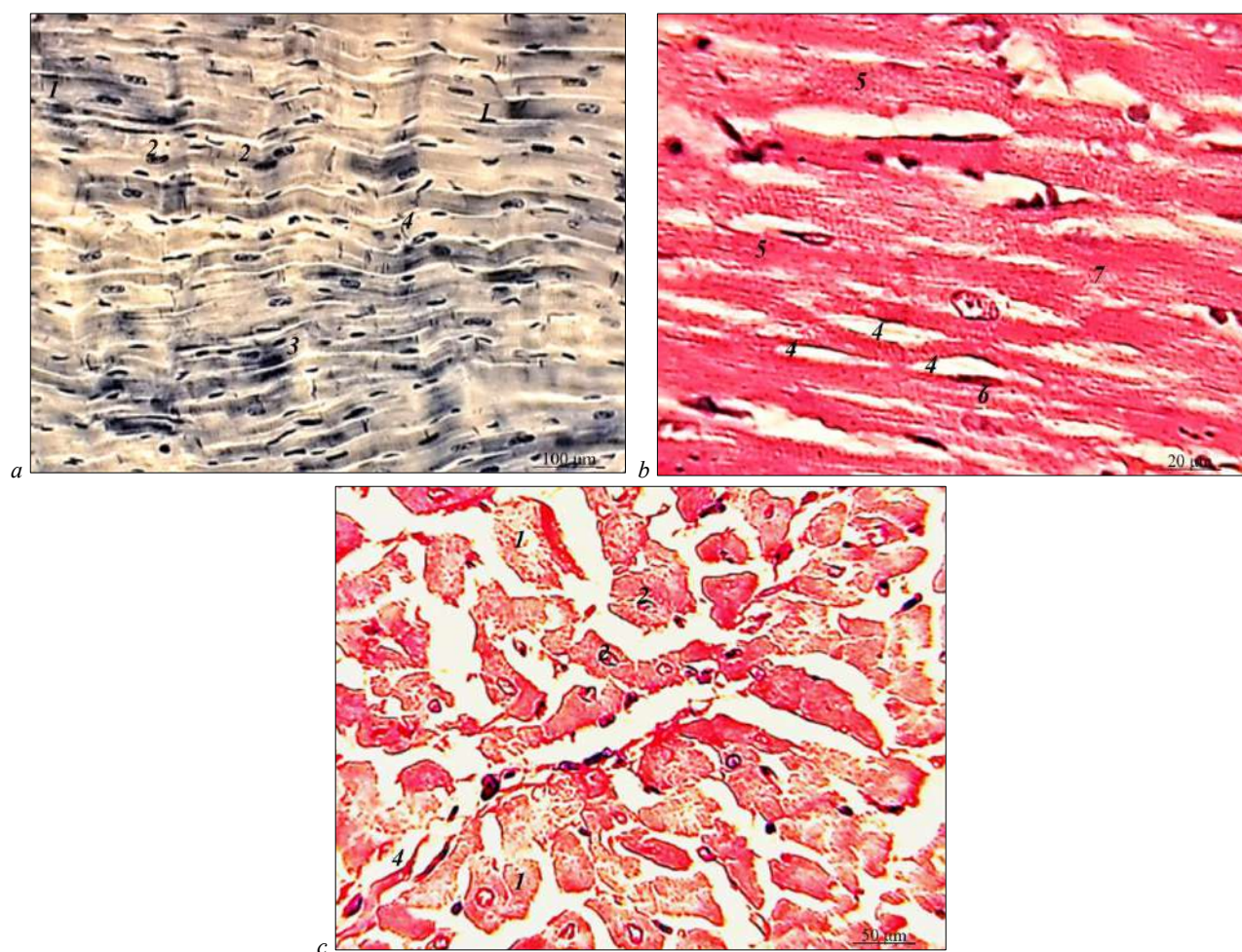


Fig. 3. Microscopic structure of the myocardium: *a, b* – right ventricle of the red fox; *c* – right atrium of the red fox heart (cross-section); 1 – cardiomyocytes; 2 – cardiomyocyte nuclei; 3 – intercalated discs; 4 – intermuscular connective tissue; 5 – muscle fibers; 6 – nuclei of muscle fibers; 7 – anastomoses; Heidenhain staining (*a*); hematoxylin and eosin staining (*b, c*)

The nuclear-to-cytoplasmic ratio also differed among the cardiac chambers. The lowest value was observed in left ventricular cardiomyocytes (0.0277 ± 0.0163), whereas the corresponding ratio in right ventricular cardiomyocytes (0.0419 ± 0.0231) was significantly higher ($P \leq 0.05$), exceeding that of the left ventricle by 1.51-fold. The highest nuclear-to-cytoplasmic ratio was recorded in atrial cardiomyocytes (0.0498 ± 0.0344), reflecting chamber-specific differences in cardiomyocyte structural organization and functional specialization (Table 3).

The observed cytometric and karyometric differences between ventricular and atrial cardiomyocytes are closely associated with the functional specialization of the cardiac chambers during the cardiac cycle. The atria receive venous blood returning to the heart, whereas the ventricles generate the force required to propel blood into the pulmonary and systemic circulations. Consequently, ventricular cardiomyocytes are subjected to substantially greater mechanical workload than atrial cardiomyocytes, which is reflected in their larger dimensions, greater cell and nuclear volumes, and lower nuclear-to-cytoplasmic ratio.

Table 3
Histomorphometric characteristics of cardiomyocytes in the red fox ($\bar{x} \pm SD$, $n = 30$)

Cardiac region	Cardiomyocyte length, μm	Cardiomyocyte width, μm	Cardiomyocyte volume, μm^3	Cardiomyocyte nuclear volume, μm^3	Nuclear-to-cytoplasmic ratio
Left ventricle	89.94 ± 1.04	12.77 ± 0.36	7602 ± 78	203.5 ± 7.1	0.0277 ± 0.0163
Right ventricle	70.23 ± 1.19	11.23 ± 0.42	4728 ± 114	187.9 ± 6.1	0.0419 ± 0.0231
Atria	66.30 ± 0.99	9.98 ± 0.31	3425 ± 70	160.2 ± 3.9	0.0498 ± 0.0344

Discussion

The heart of domestic mammals is a hollow, four-chambered muscular organ that maintains blood circulation throughout the vascular system. Its shape varies from conical to oval depending on the morphoarchitecture of the thoracic cavity, which largely determines the spatial configuration of the organ. In species with a relatively compact thorax, the heart typically exhibits a more rounded or oval shape, facilitating its accommodation within the limited thoracic space. Conversely, animals with a broader thoracic cavity generally possess a more elongated or conical heart (Rowlatt, 1990). Such interspecies variation in cardiac morphology reflects functional adaptation

and is important for understanding the relationship between cardiac structure and physiological performance (Meijler & Meijler, 2011; Horrell et al., 2022).

The heart is situated within the mediastinum of the thoracic cavity and is generally displaced slightly to the left. Although its overall morphoarchitecture and topographic anatomy are similar among mammalian species, species-specific anatomical differences have been described (Stephenson et al., 2017).

In the red fox, the heart is positioned almost horizontally and asymmetrically between the lungs, cranial to the diaphragm, with a slight displacement toward the left side of the thoracic cavity. The broad cardiac base lies approximately at the level of the third to

fourth ribs, whereas the apex extends to the level of the seventh to eighth ribs.

Several cardiac morphological types have been described in domestic mammals according to species, breed, and age. Cattle typically possess an elongated and narrow heart; rabbits have a shortened, narrow heart; horses exhibit a broadened and shortened heart; and dogs generally have a round-to-oval heart. In dogs, four principal cardiac shapes have been reported: ellipsoidal (43%), conical-ellipsoidal (24%), ellipsoidal-spherical (26%), and spherical (7%). In cattle, the heart may be elongated and narrow, conical, or broadened and shortened. Three major cardiac types have been described in pigs: elongated-narrow, conical, shortened-relatively narrow, and broadened-shortened triangular forms (Rudyk, 2004).

Based on the cardiac development index and gross morphological characteristics, the hearts of domestic mammals have been classified into three morphological types: broadened-shortened (cardiac development index 140–150%), broadened-elongated (151–160%), and elongated-narrow (161–170%) (Horalskyi et al., 2022). According to this classification, the hearts of rabbits, dogs, sheep, and horses belong to the broadened-shortened type, those of pigs to the broadened-elongated type, and those of cattle to the elongated-narrow type. In the present study, the red fox heart exhibited a cardiac development index of $147.0 \pm 3.8\%$, corresponding to the broadened-shortened morphological type.

According to the morphometric analysis performed in the present study, the heart of the red fox is ellipsoidal in shape and belongs to the broadened-shortened morphological type, as indicated by a cardiac development index of $147.0 \pm 3.8\%$.

The absolute and relative weights of organs are widely recognized as important indicators of their morphofunctional status and developmental maturity (Mits et al., 2016). These morphometric parameters not only characterize organ growth and functional development but also provide a basis for comparative anatomical classification and evaluation of structural organization (Linask, 2003; Belimenko et al., 2021).

In the red fox, the absolute heart weight was 40.6 ± 1.96 g, corresponding to $0.460 \pm 0.015\%$ of body weight. After removal of epicardial fat, the net heart weight was 38.2 ± 1.9 g, representing $0.43 \pm 0.01\%$ of body weight. Among the cardiac chambers, the left ventricle exhibited the greatest absolute weight (19.78 ± 0.48 g), whereas the right atrium was the lightest (2.40 ± 0.18 g). The combined absolute weight of both atria was 8.30 ± 0.14 g, while the total ventricular mass reached 29.72 ± 0.54 g.

These morphometric data demonstrate the predominance of ventricular myocardium within the overall cardiac mass. The ventricular mass represented 78% of the net heart weight, whereas the atria accounted for approximately 22%. Furthermore, the atrial-to-ventricular myocardial mass ratio was 0.28, emphasizing the structural predominance of the ventricles, which reflects their substantially greater mechanical workload during the cardiac cycle.

Quantitative cytometric analysis has become an indispensable tool in modern histomorphology because it enables objective assessment of tissue organization and facilitates the evaluation of structural relationships among cells and tissues under physiological and pathological conditions (Bodnar & Trach Rosolovska, 2011). Such analyses provide valuable information regarding quantitative cellular characteristics throughout ontogenetic and phylogenetic development and reveal adaptive structural changes associated with functional demands and species-specific characteristics (Hryhorieva & Cherniavskyi, 2018a; Hryhorieva & Cherniavskyi, 2018b).

The present findings, together with previously published studies (Mazo et al., 2017; Slaby, 2017), indicate that although the general cytoarchitecture of atrial and ventricular cardiomyocytes is similar, their quantitative cytometric characteristics differ substantially. These differences enable the detection of even subtle structural variations at the tissue and cellular levels and reflect the distinct functional loads imposed on the individual cardiac chambers (Sikora & Yarmolenko, 2013).

Our findings demonstrate that cardiomyocytes are structurally adapted to the functional demands imposed on the different cardiac

chambers during the cardiac cycle. During systole, cardiomyocytes generate the force required to propel blood through the circulatory system, thereby ensuring tissue perfusion and oxygen delivery. Consequently, cardiomyocytes located in the left ventricle, right ventricle, and atria exhibit distinct cytometric characteristics that reflect their chamber-specific functional roles. The largest mean cardiomyocyte volume was observed in the left ventricle ($7602 \pm 78 \mu\text{m}^3$), followed by the right ventricle ($4728 \pm 114 \mu\text{m}^3$), whereas the smallest volume was recorded in the atria ($3425 \pm 70 \mu\text{m}^3$).

A similar trend was observed for cardiomyocyte nuclear volume. The largest nuclei were found in the left ventricle ($203.5 \pm 7.1 \mu\text{m}^3$), followed by the right ventricle ($187.9 \pm 6.1 \mu\text{m}^3$), whereas the smallest nuclear volume was measured in the atria ($160.2 \pm 3.9 \mu\text{m}^3$).

These findings reflect the distinct morphofunctional characteristics of the ventricular myocardium rather than random variation. The left ventricle functions as the principal pressure-generating chamber, whereas the right ventricle primarily serves as a volume pump within the pulmonary circulation (Haligür & Dursun, 2009). Consequently, the greater length, width, cell volume, and nuclear volume, together with the lower nuclear-to-cytoplasmic ratio observed in left ventricular cardiomyocytes, are consistent with their greater mechanical workload. Left ventricular cardiomyocytes generate the force required to propel blood through the systemic circulation, whereas right ventricular cardiomyocytes pump blood through the pulmonary circulation under substantially lower pressure.

The nuclear-to-cytoplasmic ratio of atrial cardiomyocytes (0.0498 ± 0.0344) was significantly higher than that of both the right and left ventricular cardiomyocytes, exceeding the corresponding values by 1.2-fold ($P \leq 0.05$) and 1.8-fold ($P \leq 0.01$), respectively. This finding indicates the comparatively lower morphofunctional load of atrial cardiomyocytes. It is generally accepted that highly differentiated and functionally active somatic cells are characterized by a relatively low nuclear-to-cytoplasmic ratio, whereas cells with higher nuclear-to-cytoplasmic ratios are considered less functionally specialized (Anderson & Ho, 2003; Gnatjuk et al., 2010).

Conclusion

The absolute heart weight of the red fox was 40.6 ± 1.9 g, corresponding to a relative heart weight of $0.460 \pm 0.015\%$ of body weight. The net heart weight (excluding epicardial fat) was 38.20 ± 1.85 g ($0.43 \pm 0.01\%$ of body weight). Morphometric analysis demonstrated that the heart measured 6.52 ± 0.19 cm in height, 4.42 ± 0.02 cm in width, and 11.80 ± 0.27 cm in circumference. The cardiac development index was $147.0 \pm 3.8\%$, indicating that the red fox heart is ellipsoidal and belongs to the broadened-shortened morphological type.

Based on linear dimensions and chamber weights, the most highly developed anatomical components of the heart were the left ventricle, followed by the right ventricle, left atrium, and right atrium. The left ventricular wall (8.42 ± 0.17 mm) was significantly thicker than the right ventricular wall (2.60 ± 0.15 mm) by 3.24-fold ($P \leq 0.001$). Similarly, the left atrial wall (3.04 ± 0.15 mm) was significantly thicker than the right atrial wall (2.18 ± 0.09 mm) by 1.39-fold ($P \leq 0.05$). The absolute weight of the left ventricle was 19.78 ± 0.48 g ($52.06 \pm 0.59\%$), whereas the right ventricle weighed 9.92 ± 0.42 g ($26.12 \pm 0.74\%$). The combined ventricular mass reached 29.72 ± 0.54 g ($78.18 \pm 0.87\%$). The left and right atria weighed 5.88 ± 0.38 g ($15.50 \pm 0.16\%$) and 2.40 ± 0.18 g ($6.32 \pm 0.20\%$), respectively, with a combined atrial mass of 8.30 ± 0.13 g ($21.82 \pm 0.29\%$). The ventricular mass represented 78% of the net heart weight, whereas the atria accounted for 22%. The atrial-to-ventricular myocardial mass ratio was 0.28.

Left ventricular cardiomyocytes exhibited the largest mean cell volume ($7602 \pm 78 \mu\text{m}^3$), followed by those of the right ventricle ($4728 \pm 114 \mu\text{m}^3$), whereas the smallest cardiomyocytes were observed in the atria ($3425 \pm 70 \mu\text{m}^3$). Cardiomyocyte nuclear volume followed the same pattern, measuring $203.5 \pm 7.1 \mu\text{m}^3$ in the left ventricle, $187.9 \pm 6.1 \mu\text{m}^3$ in the right ventricle, and $160.2 \pm 3.9 \mu\text{m}^3$ in the atria. The nuclear-to-cytoplasmic ratio was lowest in left ven-

tricular cardiomyocytes (0.0277 ± 0.0163), significantly higher in right ventricular cardiomyocytes (0.0419 ± 0.0231 , $P \leq 0.01$), and highest in atrial cardiomyocytes (0.0498 ± 0.0344 , $P \leq 0.001$). These chamber-specific cytometric characteristics reflect the differing functional demands placed on the myocardium and its adaptation to spontaneous rhythmic contraction and blood propulsion through the systemic and pulmonary circulations.

The authors declare that they have no conflicts of interest.

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