



Echocardiographic characteristics of the morphofunctional parameters of the heart in clinically healthy rabbits

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Abstract. Rabbits are prone to developing cardiovascular system pathologies and require modern methods of diagnosis and treatment. One of the most informative and safe tools for assessing the condition of the heart is echocardiography. In this regard, the aim of the study was to determine the reference values for echocardiographic measurements in one-dimensional and two-dimensional modes in clinically healthy rabbits without the use of sedation. To diagnose the condition of the cardiovascular system in rabbits, echocardiography was used – a method that allowed for a comprehensive assessment of the morphology, size and contractile function of the heart structures using parasternal access. The study was focused on obtaining quantitative and qualitative parameters of the morphofunctional state of the main structures of the heart using echocardiography, in particular the left and right ventricles, interventricular septum, left atrium and valve apparatus. During the study, key parameters of left ventricular contractility in clinically healthy rabbits were determined. Age dynamics of the studied parameters were revealed: at 4.5 months of age, the end-diastolic size was up to 14.71 ± 1.51 mm, and the end-systolic size was up to 8.88 ± 1.64 mm. At the same time, the fractional shortening ($39 \pm 11\%$) and ejection fraction ($79 \pm 22\%$) remained relatively stable, indicating physiological adaptation of the heart to increasing body weight. In particular, a correlation was established between an increase in the total body weight of animals and an increase in the structural dimensions of the heart. Thus, it has been proven that echocardiography is a highly informative, safe and valuable tool for assessing the condition of the heart in rabbits. As a result, the scientific information presented in the article is of practical value for veterinary cardiologists and general practitioners, providing a basis for the timely diagnosis and effective treatment of heart disease in rabbits

Keywords: transthoracic echocardiography; ultrasound diagnostics; cardiology; laboratory animals; contractility indices; haemodynamics; reference values

Introduction

The development of cardiological science and clinical practice determines the need to develop and standardise the values of morphofunctional parameters of the heart for different animal species, in particular rabbits, which are widely used in experimental studies. Transthoracic echocardiography is one of the most common and accessible methods for non-invasive assessment of cardiac activity in both humans and animals. A number of researchers, including A.E.G.W. Marques *et al.* (2020), have reported that rabbits can be used as a model in cardiovascular research. The cardiac system of rabbits is similar in structure and electrophysiological characteristics to that of other mammals, making them a valuable model for studying the mechanisms of cardiac pathology and

developing new therapeutic approaches. In addition, rabbits are widely used as model subjects in scientific research and experimental work, as well as being kept as pets. This necessitates the determination of the physiological parameters of their cardiac indicators for the timely diagnosis of pathologies.

As noted by V. Jekl *et al.* (2022), echocardiography is a non-invasive method for assessing cardiovascular function, which is used in both experimental research and clinical practice. With the increase in the lifespan of rabbits kept as companion animals, the incidence of heart disease is increasing, positioning echocardiography as an important diagnostic tool alongside clinical assessment, chest X-ray and electrocardiography. According to

N. Ngosurachet *et al.* (2022), various imaging modes are used during echocardiography to analyse the morphometric parameters of the myocardium and assess the contractile function of the left ventricle. Innovative technologies, in particular two-dimensional spectral tracking (2D speckle tracking echocardiography), according to A.Y. Kabakov *et al.* (2021), open up new opportunities for detailed analysis of myocardial characteristics.

C.J. Orcutt & R.L. Malakoff (2020) found that the incidence of cardiovascular disease in rabbits usually increases with age, especially in animals older than four years, but the pathology can also occur in younger individuals. M.G. Dilek & H. Erden (2019) showed that the age and body weight of rabbits significantly affect the morphology of the heart, in particular the size of the chambers and the thickness of the myocardial walls. They also found that young rabbits may have an increased ejection fraction with a stable fractional shortening, and that the use of sedation in accordance with protocols leads to a decrease in systolic parameters compared to the active state of the animal. As noted by E.V. Praag (2015), additional factors contributing to the development of cardiovascular disease include nutritional deficiencies, excess weight, and stress factors.

According to S. Ozawa *et al.* (2021), cardiac pathologies are common in rabbits, including degenerative valve changes, cardiomyopathy, and myocarditis. The incidence of cardiovascular disease in the population is estimated at approximately 2.6% with associated symptoms (murmurs, arrhythmias, shortness of breath). Diagnosis is based on a comprehensive examination, but chest X-rays do not allow for assessment of heart function, and their interpretation is complicated by the small size of the chest. Electrocardiography allows for the determination of electrical activity but does not reflect structural characteristics. Thus, echocardiography is considered the method of choice.

M. Kaya & M.A. Cetinkaya (2025) analysed the results of a comprehensive study of 58 healthy adult New Zealand white rabbits, which aimed to determine reference intervals for radiographic cardiac indices. The authors found that vertebral heart size (VHS) measurements were 7.94 ± 0.31 vertebrae (range 7.2-8.6 vertebrae) in the right lateral projection and 8.67 ± 0.33 vertebrae (7.8-9.2 vertebrae). At the same time, the size of the left atrium and its relationship with other heart structures showed marked gender independence, which opens up opportunities for the development of universal reference values. A study by M.G. Sousa *et al.* (2020) confirmed that most echocardiographic parameters of rabbits are similar to those of other rodents, which facilitates their use as experimental models. Despite the available data, N. Ngosurachet *et al.* (2022) noted significant variability in the obtained indicators, which complicates their clinical use. At the systemic level, the British Society of Echocardiography proposed a comprehensive approach that emphasised the importance of clinical context and indexing to body size parameters (Harkness *et al.*, 2020).

An analysis of current research shows that there is a global lack of systematic and standardised reference values for morphological and functional parameters of the heart in healthy rabbits. This gap complicates the correct interpretation of results and the differentiation of physiological changes from pathological ones. Given the relevance of the topic, the aim of this study was to establish such parameters for B-mode (two-dimensional imaging of heart structures) and M-mode echocardiography (assessment of wall and valve motion over time) that can serve as a basis for improving the diagnosis, treatment, and prevention of cardiovascular pathologies.

Materials and Methods

The research was conducted in June 2025 at the Department of Veterinary Surgery named

after Academician I.O. Povazhenko of the Faculty of Veterinary Medicine of the National University of Life and Environmental Sciences of Ukraine. The object of the study was 13 clinically healthy female rabbits of the Hiplus breed from a single line. The age of the animals at the time of measurement was between 3 and 4.5 months; only non-pregnant and non-lactating individuals were selected for the group. Given the specifics of establishing reference values, this study was pilot in nature and aimed to establish indicative normative indicators that require further verification on expanded population samples. To ensure the statistical power and scientific validity of the results obtained with a given number of animals, the experiment was designed as a longitudinal study (repeated measures design). This approach involved conducting a series of sequential echocardiographic examinations of each individual, which made it possible to obtain a representative data set for analysis. Particular attention was paid to the homogeneity of the sample: the animals were identical in breed, sex, and lineage and were kept in uniform conditions. This minimised inter-individual variability caused by genetic or environmental factors and significantly increased the internal validity of the study.

All rabbits were kept at the Department of Veterinary Surgery named after Academician I.O. Povazhenko of the National University of Life and Environmental Sciences of Ukraine and were housed in individual mesh cages measuring 30x50x45 cm in a separate room with an area of 20 m². The cages were equipped with bunker feeders, a nipple watering system and plastic ramps (24x40 cm) to prevent limb injuries. The space ratio per animal, temperature and ventilation parameters of the holding room complied with the SOU 85.2-37-736:2011 (2011) standard. The experimental study was conducted in accordance with the ARRIVE (n.d.)

recommendations, Law of Ukraine No. 3447-IV (2006) and Directive 2010/63/EU (2010).

Echocardiographic examination was performed on the same individuals three times at different ages (3 months, 3.5 months and 4 months), which allowed to track the dynamics of the parameters under study. At the time of the echocardiographic examination, a veterinarian performed a clinical examination of the animals using physical examination methods, which included an assessment of the rabbits' physique, the condition of their coat and skin, and selective measurement of body temperature, pulse rate and respiratory movements. At the beginning of the study, the rabbits were weighed and transported in animal carriers to the ultrasound diagnostics room. Assistants secured the animals and shaved the fur on the chest wall (corresponding to the topographical boundaries of the heart) using an animal clipper, after which they applied ultrasound gel to improve contact with the skin.

Echocardiographic examination of rabbits was performed using a modern veterinary ultrasound scanner SIUI Apogee 2100V (China). To obtain high-quality images, a C6LN microconvex sensor with parameters R17.5, a frequency range of 4.5–7.5 MHz and a central frequency of 6 MHz was used, which allowed for a detailed assessment of cardiac structures in rabbits. During the examination, the rabbits were placed in a right lateral position, which provided the most optimal access to the chest and facilitated the high-quality acquisition of ultrasound data. The study itself was conducted in long and short right parasternal projections, which corresponded to the generally accepted standards of veterinary echocardiography for small animals. It is important to note that echocardiography in rabbits was performed without sedation, which minimised additional stress and the effect of drugs on cardiac function.

In two-dimensional echocardiography, the diameter of the left atrium (LA) and aorta (Ao) was measured at the level of the aorta and aortic valves in the right parasternal short-axis view. The ratio of the left atrium diameter to the aortic diameter (LA/Ao) was automatically calculated by the ultrasound system. M-mode echocardiography was performed to measure the size of the chamber and the thickness of its wall in the right parasternal four-chamber projection along the short axis. The thickness of the interventricular septum at end-diastole (IVSd) and end-systole (IVSs) was measured, the internal diameter of the left ventricle at the end of diastole (LVIDd) and systole (LVIDs), (LVIDs)), as well as the thickness of the posterior wall of the left ventricle at the end of diastole (LVPWd) and systole (LVPWs). Fractional shortening (FS) and ejection fraction (EF) were determined and calculated using ultrasound system software according to the Teichholz method.

Statistical data processing was performed using descriptive statistics to determine the mean values and standard deviation ($M \pm SD$) in different age groups. Additionally, Pearson's correlation analysis was performed to assess the relationship between echocardiographic parameters and rabbit body weight. This analysis was aimed at identifying the relationship

between the structural and functional parameters of the heart (measured in B and M modes) and the individual body weight of each animal within one age point (i.e., separately for 3 months, 3.5 months, and 4.5 months). No comparison of correlation relationships between different age groups was performed, nor was it the purpose of this study. The analysis allowed to assess the strength of the linear relationship between the parameters and body weight at a specific moment of ontogenesis. The significance of the correlation coefficient was assessed using the t-test with $df = n - 2$. A two-tailed level of statistical significance was accepted at $P < 0.05$. To compare parameters between age points, Student's paired t-test was used.

Results and Discussion

In order to assess the age-related dynamics of the morphofunctional parameters of the heart in clinically healthy rabbits, an analysis of echocardiographic parameters was performed in three consecutive age periods. Given the longitudinal nature of the study design (repeated measures design), this allowed to track individual and group variability in cardiac structures as the animals grew. Descriptive statistical characteristics of the studied parameters ($M \pm SD$) are presented in Table 1.

Table 1. Echocardiographic parameters in rabbits of different ages, $n = 13$, $M \pm SD$

Parameter	Age of animals		
	3 months	3.5 months	4.5 months
Body weight (BW), g	3,400.00 \pm 1,366.35	4,295.38 \pm 422.02	4,438.46 \pm 529.93
Heart rate (HR), bpm	254.38 \pm 29.26	229.85 \pm 27.09	248.77 \pm 49.46
B-mode			
Aortic diameter (Ao), mm	8.12 \pm 0.75	8.24 \pm 0.53	8.57 \pm 0.96
Left atrium (LA), mm	9.85 \pm 0.73	10.15 \pm 0.88	11.02 \pm 1.27
Left atrium to aorta ratio (LA/Ao)	1.22 \pm 0.12	1.24 \pm 0.14	1.27 \pm 0.24
Pulmonary artery (PA), mm	7.38 \pm 0.62	7.45 \pm 0.43	7.62 \pm 0.92
Pulmonary vein (PV), mm	2.45 \pm 0.50	2.80 \pm 0.56	2.69 \pm 0.72
Right pulmonary artery (RPA), mm	2.88 \pm 0.58	3.12 \pm 0.67	3.19 \pm 0.89
Pulmonary vein to right pulmonary artery ratio (PV/RPA)	0.86 \pm 0.10	0.91 \pm 0.11	0.86 \pm 0.12

Table 1. Continued

Parameter	Age of animals		
	3 months	3.5 months	4.5 months
Mitral valve E-point to septal separation (EPSS), mm	2.48 ± 0.52	2.75 ± 0.79	3.24 ± 1.66
M-mode			
Left ventricular posterior wall thickness at end-diastole (LVPWd), mm	4.10 ± 0.64	4.13 ± 0.71	4.25 ± 0.99
Interventricular septum at end-diastole (IVSd), mm	3.86 ± 0.62	3.92 ± 0.29	4.05 ± 0.66
Left ventricular internal diameter at end-diastole (LVIDd), mm	14.14 ± 1.31	14.21 ± 1.46	14.71 ± 1.51
Left ventricular posterior wall thickness at end-systole (LVPWs), mm	5.73 ± 0.94	5.42 ± 0.95	5.85 ± 1.63
Interventricular septum at end-systole (IVSs), mm	5.15 ± 0.73	5.65 ± 0.61	6.14 ± 1.52
Left ventricular internal diameter at end-systole (LVIDs), mm	9.06 ± 0.54	8.97 ± 1.47	8.88 ± 1.64
Fractional shortening (FS), %	35.0 ± 8.0	37.0 ± 7.0	39.0 ± 11.0
Ejection fraction (EF), %	71.0 ± 16.0	74.0 ± 14.0	79.0 ± 22.0

Note: there were no statistically significant results for the studied parameters compared to their values in 3-month-old rabbits

Source: authors' own work

The results show that there was only a tendency for the body weight of rabbits to increase with age. Thus, the body weight of 3.5-month-old rabbits differed by 26.33% ($P < 0.05$) compared to 3-month-old rabbits. The observed tendency towards an increase in body weight in rabbits from 3 to 4.5 months of age indicated a regular gain in body mass during growth. Age-related changes in cardiac dimensions in rabbits are consistent with the findings of M.G. Dilek & H. Erden (2019) who reported a gradual increase in cardiac chamber dimensions during rabbit growth. The results confirm that the most intensive growth of the studied parameters was observed during puberty, which correlated with an overall increase in the body weight of the animals. In addition, the thickening of the left ventricular myocardium indicates the adaptation of the cardiovascular system to the growing haemodynamic needs of the body.

The diameter of the aorta tended to increase with the age of the rabbits, reflecting natural morphological changes in cardiovascular structures during postnatal development. From 3 to 4.5 months of age, the size of the left atrium increased by 11.88% ($P < 0.01$), which may indicate adaptive changes in atrial volume to ensure cardiac output. The ratio of the left atrium to the aorta remained relatively stable, indicating that the proportions between the atrium and the aorta were maintained as the rabbits grew. The results obtained are consistent with similar studies by M.G. Dilek & H. Erden (2019) on New Zealand white rabbits, where the authors observed an increase in the systolic and diastolic diameters of the left ventricle, as well as the size of the aortic root, which correlated with an increase in body weight.

The diameter of the pulmonary artery tended to increase over the entire period, while

the sizes of the PV and RPA increased unevenly, reflecting individual growth rates and adaptive changes in the heart muscle. The PV/RPA ratio remained stable (0.86-0.91), indicating that optimal heart chamber proportions were maintained. The EPSS distance with the age of rabbits showed a tendency to increase by 30.65% compared to that in 3-month-old animals, which may indicate an adaptive change in left ventricular systolic function.

LVPWd and IVSd values tended to increase, reflecting morphological maturation of the heart muscle. The left ventricular diameter in diastole gradually increased throughout the study period, while the left ventricular diameter in systole remained relatively stable, indicating preserved normal contractility. The thickness of LVPWs and IVSs increased moderately without reaching statistical significance, reflecting

the adaptation of the heart muscle to increased load against the background of a tendency to change body weight. The tendency to increase these parameters may reflect the optimisation of the pumping efficiency of the heart, which is important for differentiating physiological growth from pathological hypertrophy.

To assess the effect of body weight on cardiovascular parameters in 3-month-old rabbits, a Pearson correlation analysis was performed. The correlation coefficient (*r*) between the animal's body weight and the main echocardiographic parameters in B- and M-modes was determined. The use of this statistical approach made it possible to establish the degree of dependence between the overall somatic growth of the organism and the proportional increase in the linear dimensions of the chambers and the thickness of the heart walls (Table 2).

Table 2. Correlation analysis between body weight and echocardiographic parameters in 3-month-old rabbits, n = 13

Parameter	M ± SD	r
Body weight, g	3,400.00 ± 1,366.35	
B-mode		
Aortic diameter (Ao), mm	8.12 ± 0.75	0.50***
Left atrium (LA), mm	9.85 ± 0.73	0.21*
Left atrium to aorta ratio (LA/Ao)	1.22 ± 0.12	-0.30**
Pulmonary vein (PV), mm	7.38 ± 0.62	0.17
Pulmonary vein (PV), mm	2.45 ± 0.50	0.27
Right pulmonary artery (RPA), mm	2.88 ± 0.58	0.33**
Pulmonary vein to right pulmonary artery ratio (PV/RPA)	0.86 ± 0.10	-0.10
Mitral valve E-point to septal separation (EPSS), mm	2.48 ± 0.52	0.02
M-mode		
Left ventricular posterior wall thickness at end-diastole (LVPWd), mm	4.10 ± 0.64	-0.31**
Interventricular septum at end-diastole (IVSd), mm	3.86 ± 0.62	-0.45***
Left ventricular internal diameter at end-diastole (LVIDd), mm	14.14 ± 1.31	0.14
Left ventricular posterior wall thickness at end-systole (LVPWs), mm	5.73 ± 0.94	-0.20*
Interventricular septum at end-systole (IVSs), mm	5.15 ± 0.73	0.02
Left ventricular internal diameter at end-systole (LVIDs), mm	9.06 ± 0.54	-0.13
Fractional shortening (FS), %	35 ± 8	0.15
Ejection fraction (EF), %	71 ± 16	0.15

Note: * – $P < 0.05$; ** – $P < 0.01$; *** – $P < 0.001$, statistically significant indicators, correlated with body weight in 3-month-old rabbits

Source: authors' own work

In B-mode, there was a moderate positive correlation between rabbit body weight and aortic diameter ($P < 0.001$), indicating an increase in Ao in rabbits with greater body weight. A weak positive correlation was found between the left atrial index and the body weight of rabbits ($P < 0.05$), while the LA/Ao ratio was moderately negatively correlated ($P < 0.01$), which may reflect proportional changes in the structure of the atrium relative to the aorta. A weak positive correlation was found between the diameter of the PA and PV indices of rabbits and body weight, which was not statistically significant. The right pulmonary artery index in rabbits had a weak but significant positive correlation ($P < 0.01$), indicating an increase in this parameter in rabbits with higher body weight. The PV/RPA and EPSS ratios did not show a significant relationship with the body weight of rabbits. In M-mode, a moderate negative correlation with body weight ($P < 0.01$) was determined for IVSd and LVPWd thickness, indicating adaptive morphological changes in

the heart in rabbits of different weights. Weak or insignificant correlations were observed for other M-mode parameters.

Correlation analysis of rabbit body weight with echocardiographic parameters at 3.5 months of age is presented in Table 3. Thus, in rabbits aged 3.5 months, during echocardiographic examination in B-mode, a moderate positive correlation was observed between body weight and aortic diameter ($P < 0.001$), indicating an increase in Ao in rabbits with greater body weight. A positive correlation was found between left atrial indices and body weight in rabbits ($P < 0.05$). No significant relationship was found between LA/Ao indices and pulmonary artery diameter and body weight in rabbits. A weak positive correlation was found between the pulmonary vein index and the body weight of rabbits ($P < 0.05$), while the RPA and EPSS indices did not show a statistically significant dependence. A moderate positive correlation was found between the PV/RPA ratio and the body weight of rabbits ($P < 0.01$).

Table 3. Correlation analysis between body weight and echocardiographic parameters in 3.5-month-old rabbits, n = 13

Parameter	Mean ± SD	r
Body weight, g	4,295.38 ± 422.02	
B-mode		
Aortic diameter (Ao), mm	8.24 ± 0.53	0.42***
Left atrium (LA), mm	10.15 ± 0.88	0.23*
Left atrium to aorta ratio (LA/Ao)	1.24 ± 0.14	-0.08
Pulmonary vein (PV), mm	7.45 ± 0.43	0.01
Pulmonary vein (PV), mm	2.80 ± 0.56	0.19*
Right pulmonary artery (RPA), mm	3.12 ± 0.67	0.05
Pulmonary vein to right pulmonary artery ratio (PV/RPA)	0.91 ± 0.11	0.25**
Mitral valve E-point to septal separation (EPSS), mm	2.75 ± 0.79	0.05
M-mode		
Left ventricular posterior wall thickness at end-diastole (LVPWd), mm	4.13 ± 0.71	0.05
Interventricular septum at end-diastole (IVSd), mm	3.92 ± 0.29	0.11
Left ventricular internal diameter at end-diastole (LVIDd), mm	14.21 ± 1.46	0.02
Left ventricular posterior wall thickness at end-systole (LVPWs), mm	5.42 ± 0.95	-0.02
Interventricular septum at end-systole (IVSs), mm	5.65 ± 0.61	-0.27**

Table 3. Continued

Parameter	Mean ± SD	r
<i>M-mode</i>		
Left ventricular internal diameter at end-systole (LVIDs), mm	8.97 ± 1.47	0.08
Fractional shortening (FS), %	37 ± 7	-0.10
Ejection fraction (EF), %	74 ± 14	-0.10

Note: * – $P < 0.05$; ** – $P < 0.01$; *** – $P < 0.001$, statistically significant indicators, correlated with body weight in rabbits at 3.5 months of age

Source: authors' own work

In M-mode, the most pronounced negative correlation was between the left ventricular interventricular septal thickness in systole and the body weight of rabbits ($P < 0.01$). No statistically significant correlations were found for other M-mode parameters, such as LVPWd, IVSd, LVIDd, LVPWs, and LVIDs. The shortening and ejection fractions remained independent of the body weight of rabbits. The results obtained are consistent with the data of studies by M.S. Young *et al.* (1990) and M. Kaya & M.A. Cektinkaya (2025), who noted the stability of functional parameters in healthy rabbits, which, as a rule, did not depend on body weight.

The correlation analysis of rabbit body weight with echocardiographic parameters at

4.5 months of age is presented in Table 4. As a result of assessing the effect of body weight on the cardiovascular parameters of rabbits and body weight in B-mode, it was found that the LA/Ao ratio was moderately negatively correlated with the body weight of rabbits ($P < 0.001$). The results obtained indicate a change in the proportions of the atrium relative to the aorta in rabbits with a higher body weight. A weak negative correlation was found between PV parameters and the PV/RPA ratio with the body weight of rabbits ($P < 0.01$), while no statistically significant relationship was found for Ao, LA, PA and RPA indicators. EPSS tended to have a negative relationship, but did not reach the level of significance.

Table 4. Correlation analysis between body weight and echocardiographic parameters in 4.5-month-old rabbits, $n = 13$

Parameter	Mean ± SD	r
Body weight, g	4,438.46 ± 529.93	
<i>B-mode</i>		
Aortic diameter (Ao), mm	8.57 ± 0.96	-0.08
Left atrium (LA), mm	11.02 ± 1.27	-0.11
Left atrium to aorta ratio (LA/Ao)	1.27 ± 0.24	-0.51***
Pulmonary vein (PV), mm	7.62 ± 0.92	-0.18
Pulmonary vein (PV), mm	2.69 ± 0.72	-0.27**
Right pulmonary artery (RPA), mm	3.19 ± 0.89	-0.11
Pulmonary vein to right pulmonary artery ratio (PV/RPA)	0.86 ± 0.12	-0.27**
Mitral valve E-point to septal separation (EPSS), mm	3.24 ± 1.66	-0.29
<i>M-mode</i>		
Left ventricular posterior wall thickness at end-diastole (LVPWd), mm	4.25 ± 0.99	0.02
Interventricular septum at end-diastole (IVSd), mm	4.05 ± 0.66	-0.18
Left ventricular internal diameter at end-diastole (LVIDd), mm	14.71 ± 1.51	-0.45***
Left ventricular posterior wall thickness at end-systole (LVPWs), mm	5.85 ± 1.63	-0.48***
Interventricular septum at end-systole (IVSs), mm	6.14 ± 1.52	-0.36***

Table 4. Continued

Parameter	Mean ± SD	r
<i>M-mode</i>		
Left ventricular internal diameter at end-systole (LVIDs), mm	8.88 ± 1.64	0.14
Fractional shortening (FS), %	39 ± 11	-0.42***
Ejection fraction (EF), %	79 ± 22	-0.42***

Note: * – $P < 0.05$; ** – $P < 0.01$; *** – $P < 0.001$, statistically significant indicators, correlated with body weight in rabbits at 4.5 months of age

Source: authors' own work

In M-mode, moderate and pronounced negative correlations were observed for most structural and functional parameters: LVIDd ($P < 0.001$), LVPWs ($P < 0.001$), IVSs ($P < 0.001$), FS ($P < 0.001$) and EF ($P < 0.001$). No statistically significant correlations with rabbit body weight were found for other M-mode parameters, such as LVPWd, IVSd and LVPWs. The data obtained may indicate that myocardial wall thickness in diastole and end-systolic ventricular diameter are more stable parameters that are less dependent on body weight fluctuations during this age period compared to active contractility indicators. To assess the effect of body weight on cardiovascular parameters in 4.5-month-old rabbits in B-mode, it was found that the LA/Ao ratio was moderately negatively correlated with body weight ($P < 0.001$), indicating a change in the proportions of the atrium relative to the aorta in rabbits with greater body weight. A weak negative correlation was found between pulmonary vein indices and the PV/RPA ratio with the body weight of rabbits ($P < 0.01$), while no statistically significant relationship was found for Ao, LA, PA, and RPA. The EPSS indicator showed a tendency towards a negative correlation with the body weight of rabbits.

Comparing the results obtained at different ages of rabbits, it can be noted that in the early stage of the postnatal period of ontogenesis, an increase in the body weight of rabbits was associated with a proportional increase in Ao, which corresponded to the normal development of the cardiovascular system. By 4.5 months of age,

the proportional relationship weakened, probably due to individual growth rates or adaptive changes in cardiac output. Based on the LA to Ao ratio, a change in the proportions of the atrium relative to the aorta can be observed. At the beginning of the study, the growth of the atrium in rabbits was proportional to the aorta. However, by 4.5 months of age, rabbits with a higher body weight had a relatively lower intensity of growth of LA parameters compared to Ao, which explains the strong negative correlation. This may be an adaptive mechanism to maintain optimal cardiac output. In 3-month-old rabbits, changes in body weight stimulated the growth of the heart ventricles. However, in older animals, there was a regulatory decrease in the thickness and volume of the heart chambers in relative proportions, possibly due to the adaptation of the heart to physiological load. The adaptive thickening of the interventricular septum of the heart, which stabilised over time, reflected the physiological maturation of the heart.

The publication by A.P. Fontes-Sousa *et al.* (2006) describes M-modal and Doppler reference values for healthy male New Zealand white rabbits. In this study, the average heart rate during echocardiography was 155.0 ± 29 beats per minute. At the same time, the authors also studied morphometric indicators: the thickness of the interventricular septum, which was 2.03 ± 0.37 mm in diastole and 3.05 ± 0.45 mm in systole; the internal dimension of the left ventricle – 14.37 ± 1.49 mm in diastole and

10.25 ± 1.22 mm in systole, and the thickness of the free wall – 2.16 ± 0.25 mm in diastole and 3.48 ± 0.55 mm in systole. The results of the functional parameters studied showed a fractional shortening of 30.13 ± 2.98% and an ejection fraction of 61.29 ± 4.66%, indicating good systolic heart function in these animals. Changes in functional parameters (FS, EF) indicate adaptive regulation of systolic function as a result of an increase in the body weight of rabbits and a decrease in the correlation between heart function and body weight in the early stages of development of these animals. The results obtained coincide with the results of studies conducted by Z. Popovi *et al.* (2005), D. Casamian-Sorrosal *et al.* (2014b) and N. Ngosurachet *et al.* (2022), who proved that functional parameters are scaled allometrically according to the size of the heart ventricles and the duration of their filling, which leads to their relative stability during the growth and development of the organism. As noted by M.G. Dilek & H. Erden (2019), establishing reference values for echocardiographic parameters for healthy rabbits, taking into account their age and body weight, is extremely important for the correct interpretation of data. The results obtained in the current study can serve as a basis for comparing similar parameters in experimental models of certain pathological conditions. For example, understanding the physiological development of the heart in rabbits is the basis for studying various pathologies, since rabbits are used to model conditions that lead to cardiac remodelling, such as hypertrophy. In particular, in rabbits with obesity and hypertension, echocardiography was used to diagnose the development of concentric and eccentric hypertrophy, as well as diastolic filling disorders, which, according to S. Minegishi *et al.* (2011), must be differentiated from physiological growth.

The shortening fraction and ejection fraction are key indicators for assessing left

ventricular systolic function. FS is a one-dimensional parameter, while EF is a volumetric parameter (Levy & Deutschman, 2004). The sensitivity of FS to symmetrical LV contraction makes EF a more accurate parameter in cases of asymmetrical remodelling, but both indicators correlate closely in animals with normal LV geometry (Szmitko *et al.*, 2003). Since the present study demonstrated preservation of normal geometry and contractility of the left ventricle (LVIDs remained stable), both FS and EF are informative. As reported by X. Chen *et al.* (2022), echocardiographic measurements in rabbits also demonstrated high reproducibility, making them a reliable tool for longitudinal studies. Understanding the development of the cardiovascular system in the postnatal period of ontogenesis is critical for assessing normal heart morphology and function, as well as for establishing baseline indicators during experimental studies. Rabbits are an important model for cardiovascular research because they are relatively accessible, yet, as noted by D. Casamian-Sorrosal *et al.* (2014a) and M.G. Dilek & H. Erden (2019), large enough to perform detailed anatomical and physiological experiments. Echocardiography allows for non-invasive assessment of the structural and functional parameters of the heart, and their correlation with body weight, according to T. Hornyik *et al.* (2021), can serve as a marker of physiological growth and adaptation of the cardiovascular system.

The data obtained in the current study emphasised the importance of understanding the dynamics of changes in cardiac structures in response to the growth and development of the organism under controlled conditions. The study revealed regular age-related changes in the structure and function of the heart in rabbits, which closely correlated with body weight gain. The structural parameters of the heart predominantly correlated positively

with body weight in the early postnatal period of ontogenesis, while functional indicators (shortening and ejection fractions) remained stable or changed less significantly, indicating physiological maturation of the heart and its adaptation to increased load during the period of active growth of the animal.

Conclusions

As a result of the conducted study, reference morphofunctional cardiac parameters of clinically healthy rabbits were established and systematised across three consecutive age periods using B-mode and M-mode echocardiography. Age-related changes in the structure and function of the rabbit heart were identified, which correlated with the increase in body weight. In particular, the growth dynamics of the animals were accompanied by a regular increase in Left ventricular internal diameter at end-diastole (LVIDd), mm and Left ventricular internal diameter at end-systole (LVIDs), mm, as well as the thickness of the ventricular walls (Interventricular septum (IVS) and Left ventricular posterior wall (LVPW)) during different phases of the cardiac cycle. Structural cardiac parameters increased proportionally with the growth of the animals, whereas functional cardiac indices indicated maintenance or improvement of contractile efficiency. These results provide a basis for further comparison of normal and pathological cardiac morphology during the postnatal period of rabbit ontogenesis.

Analysis of the obtained results demonstrated that in 3-month-old rabbits the most pronounced changes in the heart depending on body weight dynamics were observed for Aortic diameter, Pulmonary vein, Interventricular septum at end-diastole and Left ventricular posterior wall thickness at end-diastole, which emphasised the influence of body weight on structural cardiac parameters, whereas functional

parameters (Fractional shortening, ejection fraction and mitral valve E-point to septal separation) remained practically unchanged. In rabbits aged 3.5 months the most significant dependence of cardiac parameters on body weight was observed for aortic diameter, left atrium, pulmonary vein, pulmonary vein to right pulmonary artery ratio and interventricular septum at end-systole, whereas most other structural and functional cardiac parameters remained practically independent of body weight. This indicates that structural cardiac parameters continued to correlate with body weight, while functional cardiac indices remained stable and were not influenced by minor changes in body weight at this age period. In rabbits aged 4.5 months a clear tendency towards negative correlation between body weight and structural as well as functional cardiac parameters was observed, particularly with regard to ventricular wall thickness, ventricular dimensions and fractional shortening and ejection fraction. This indicates that during this age period body weight became an important factor influencing both cardiac morphology and cardiac function in rabbits. Changes in correlation parameters with age may be explained by physiological maturation of the heart, body growth of rabbits and adaptation of the myocardium to increasing load, which is typical for growth and development during the postnatal period of ontogenesis. Prospects for further research include the study of echocardiographic parameters in rabbits and comparative analysis of reference values in other breeds and age groups. This will provide a basis for the development of unified cardiological standards necessary for timely diagnosis and monitoring of treatment effectiveness of cardiovascular diseases in veterinary practice.

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Conflict of Interest

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Ехокардіографічна характеристика морфофункціональних параметрів серця у клінічно здорових кролів

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Анотація. Кролі схильні до розвитку патологій серцево-судинної системи та потребують сучасних методів діагностики й лікування. Одним із найбільш інформативних і водночас безпечних інструментів оцінки стану серця є ехокардіографія. У зв'язку з цим, мета дослідження полягала у визначенні референтних значень для ехокардіографічних вимірювань в одномірному та двомірному режимах у клінічно здорових кролів без застосування седатії. Для діагностування стану серцево-судинної системи кролів використали ехокардіографію – метод, який дозволив комплексно оцінити морфологію, розміри та скорочувальну функціональність структур серця, використовуючи парастернальний доступ. Дослідження було спрямоване на отримання кількісних та якісних показників морфофункціонального стану основних структур серця за допомогою ехокардіографії, зокрема лівого і правого шлуночків, міжшлуночкової перегородки, лівого передсердя та клапанного апарату. У ході дослідження визначено ключові параметри скоротливості лівого шлуночка у клінічно здорових кролів. Виявлено вікову динаміку досліджуваних показників: у 4,5-місячному віці кінцево-діастолічного розміру до $14,71 \pm 1,51$ мм, а кінцево-систолічного розміру до $8,88 \pm 1,64$ мм. При цьому фракція укорочення

(39 ± 11 %) та фракція викиду (79 ± 22 %) залишалися відносно стабільними, що свідчить про фізіологічну адаптацію серця до зростаючої маси тіла. Зокрема, встановлено кореляційний зв'язок між збільшенням загальної маси тіла тварин та зростанням структурних розмірів серця. Таким чином, доведено, що ехокардіографія є високоінформативним, безпечним та цінним інструментом для оцінки стану серця у кролів. В результаті, наукова інформація, представлена у статті, має практичну цінність для ветеринарних кардіологів та лікарів загальної практики, забезпечуючи основу для своєчасної діагностики та ефективного лікування серцевих захворювань у кролів

Ключові слова: трансторакальна ехокардіографія; ультразвукова діагностика; кардіологія; лабораторні тварини; показники скоротливості; гемодинаміка; референтні значення