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Research Article

Evaluation of Heart Diseases in Rabbits with Echocardiography Cardiac Diseases

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Abstract

The New Zealand White rabbit laboratory animal has an important place in cardiological studies as well as in many scientific studies. In this respect, echocardiographic methods are the gold standard in the diagnosis of cardiac diseases in veterinary medicine. Cardiac diseases such as congestive heart failure, congenital heart disease, cardiomyopathy, tricuspid, mitral valve disease and diastolic dysfunction are observed in rabbits. Therefore, periodic echocardiographic studies are required in healthy rabbits. All rabbits were examined by color Doppler echocardiographic method using a 5-7.5 mHz transducer. In the studies, images were obtained from the 2nd to 4th intercostal space, parasternal long axis, parasternal short axis, apical four-chamber and modified four-chamber windows using two-dimensional (2D) mode, M-mode and color Doppler echocardiography methods. In the examination, the anatomy and functions of the rabbit heart were examined one by one. When the values obtained in this study were compared with the studies conducted on cats and dogs in routine veterinary medicine, it was observed that rabbits also had cardiac problems. In addition, it was determined that the changes in right ventricular parameters were compatible with the changes in left ventricular occupancy parameters. Our aim in this study is to bring rabbits into our lives not only as laboratory animals but also as healthy pets.

Keywords: Diagnostic Techniques; Echocardiography; Heart, Rabbit

Introduction

Rabbits are a model animal used in human medicine due to their anatomical and physiological characteristics [1]. Rabbits are valuable experimental animals because they are used in human medicine and in laboratories because of their anatomical and physiological characteristics, and because we want to see animals in laboratories as models [1,2].

In recent years, he has shown intense interest in the diastolic and systolic capacity of the heart. Color Doppler echocardiography has been used to evaluate the flows in the mitral valve, tricuspid valve, aortic valve, pulmonary and left and right atria, left ventricular outflow tract, pulmonary valve, and right ventricular outflow tract, including congestive heart failure, arrhythmias, cardiomyopathies (hypertrophic cardiomyopathy, dilated cardiomyopathy), and congenital heart disease [3].

With the advent of echocardiography, M-mode and B-mode (2D) echocardiography have become frequently used, while in recent years, Pulsed Wave (PW) Doppler echocardiography has begun to be used in veterinary medicine [4]. Information about transplantation is obtained by assessing right ventricular (RV) and left ventricular

(LV) systolic and diastolic capacities. Studies using color Doppler echocardiography have primarily focused on valvular insufficiency and intracardiac shunts.

With this method, moving anatomical slices can be displayed with dimensions and velocities coded by color coverage, consistent with cardiac motion. The color Doppler method provides two-dimensional anatomical images at Doppler frequencies for all flows from all slices [4]. For example, left ventricular volume and size determinations were made in normal and hypertensive mice.

Flows, age, sex, and heart rate were assessed in the mitral valve, left atrium, tricuspid valve, right atrium, aortic valve, left ventricular outflow tract, pulmonary valve, and right ventricular outflow tract of normal and feline cats [5].

New Zealand rabbits have been used in a variety of animal experiments in cardiology. Nagueh ve ark (2000), presented echocardiographic data in 24 rabbits as a control group in their study [6,7]. In the New Zealand rabbit, Pelosi., *et al.* (2011) examined B-mode (2D) echocardiographic parameters in healthy male New Zealand White rabbits anesthetized with a xylazine-ketamine combination (Figure 1).

In recent years, cardiac examinations, like those performed on cats, have become quite accessible. Why not utilize genetic resources in rabbits, particularly the gold standard of cardiography, echocardiography? It was deemed appropriate to conduct such a study, separating rabbits with heart disease from those in good health to determine their diagnostic and treatment potential. In the diagnostic examination of the heart, electrocardiography, echocardiography, radiologic imaging and blood tests should be used after questioning the complaints and medical history spent before the examination.

Materıals and Methods

Ethics statement

Ankara Training and Research Hospital's local animal ethics committee approved the use of experimental animals. Written informed consent was obtained.Toplantı tarihi: 21.02.2024

- Meeting number: 2024/0080
- Study protocol number: 760

Animal selection

Twenty-five New Zealand white rabbits (with cardiac problems), 30-45 cm long, and weighing 2-3 kg, were used in the study.

Congenital and subsequent cardiac findings were evaluated during echocardiography. Rabbits with cardiac problems including systolic and diastolic dysfunction, valvular insufficiency and stenosis, congenital malformations, pericardial and pleural effusions, and increased cardiac chamber size and wall thickness were included in the study Rabbits without cardiac problems or with minimal problems should not be included. Echocardiographic measurements were taken on all rabbits using a Mindray Vetüs 5 Expert color Doppler ultrasound device with a 5-7.5 mHz transducer. Because the chest area where the transducer would be placed was severely deformed, it was shaved, and gel (Medical Mitsubishi Ultrasound Gel) was applied to this area. To prevent movement, the rabbits were placed on their left sides, with two people They hold their feet.

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Echocardiographic Techniques

Echocardiographic studies in rabbits were performed in the parasternal long-axis view, starting from the 2nd to 4th intercostal spaces, where they join the left and right sternums. The probe was maneuvered 300-900 degrees along the midline of the sternum, between the 3rd and 4th intercostal spaces, to obtain images in the parasternal short-axis view.

As with echocardiography systems, two-dimensional (2D), M-mode, and color Doppler distributions were recorded in rabbits. The left ventricular effect was captured using the Teicholz method in the parasternal long-axis view. Parasternal short-axis views included the aortic valve, mitral valve, tricuspid valve, pulmonary valve, left ventricular papillary muscle, pulmonary arteries, right ventricle, and right atriumValuable information was obtained by shifting the probe slightly below the sternum and obtaining a modified cross-sectional view, unlike the apical views. In the apical view, the transducer was placed at the apex of the heart, and echocardiographic studies were performed using images from 2, 3, 4, and 5 chamber views. Left ventricular segmental assessment was performed under the guidance of the American Society of Echocardiography, with scoring based on a 16-segment model obtained from the parasternal short-axis and apical 2, 3, and 4 chamber views. Wall motion of each segment was scored as 1 = normal, 2 = hypokinesia, 3 = akinesia, and 4 = dyskinesia. Echocardiographic evaluation was considered inadequate if more than two segments and four or more of the 16 segments within the infarct area could not be visualized.

Echocardiographic parameters

Doppler echocardiography provided insights into the diastolic filling function, including maximal premature velocity (E) detected from the mitral and tricuspid valves, maximal atrial filling velocity (A) and their ratio (E/A), acceleration time (AT), deceleration time (DT), ejection time (ET), and isovolumic relaxation time (IVRT), E velocity-time integral (EVTI), and A velocity-time integral (AVTI). In our study, left ventricular parameters, LVIDD (left ventricular end-diastolic dimension), LVIDS (left ventricular end-systolic dimension), IVDS (interventricular septum thickness), LVPWD (posterior wall thickness), LVM (left ventricular mass), EF (ejection fraction), (FS) Fraction shortening, EDV (end-diastolic volume), SV (stroke volume), AO (aortic diameter), LA (left atrium diameter), RA (right atrium), SI (Stroke index), Left ventricular mass (LVM), HR (Heart rate) values were obtained with B mode (2D) and M mode echocardiography.

Because these animals were not discriminated against by age, breed, sex, or weight, the chance of finding a suitable animal was quite high. Unexpected cardiac problems were encountered in the rabbits. Cardiac parameters were determined from the images obtained.

Results

The study employed B-mode (2-D), M-mode, and color Doppler echocardiography techniques. Echocardiography diagnostic methods and protocols used in other domestic animals (cats, dogs) and humans were used.

Left ventricular filling parameters measured with pulsed Doppler using a modified four-chamber (rarely apical four-chamber) view, with a sample volume placed over the mitral valve, are presented (Table 1). Peak E and A flow velocities, E/A ratio, deceleration time, acceleration time, isovolumic relaxation time, and isovolumic contraction time were recorded using pulsed-wave Doppler, with a sample volume placed over the mitral and tricuspid valves, and transmitral and tricuspid flows (Figure 2).

Left ventricular filling parameters measured with pulsed Doppler using a modified four-chamber (rarely apical four-chamber) view with a sample volume placed over the mitral valve are presented (Table 1). Peak E and A flow velocities, E/A ratio, deceleration time, acceleration time, isovolumic relaxation time, and isovolumic contraction time were recorded using pulsed wave Doppler using a sample volume placed over the mitral and tricuspid valves, and transmitral and tricuspid flows were recorded using pulsed wave Doppler (Figure 2). VTIE – VTIA values, the area covered by the E and A waves, were evaluated as physiological factors affecting diastolic filling. In diastolic dysfunction, left ventricular compliance decreases, and left ventricular pressure and left atrial pressure increase, leading to left atrial dilatation. In our studies, left ventricular parameters (LVIDD) left ventricular end-diastolic dimension, (LVIDS) left ventricular end-systolic dimension, (IVDS) interventricular septum thickness, (LVPWD) posterior wall thickness, (LVM) left ventricular mass, (EF %) ejection fraction, (FS %) Fraction shortening, (EDV) end-diastolic volume, (SV) stroke volume, (Ao) aortic diameter, (LAD) left atrium diameter, (RA) right atrium, (SI), Stroke index, (LVM) left ventricular mass, (HR) Heart rate values were measured using B and M mode echocardiography (Table 2). Left ventricular parameter values obtained using B- and M-mode echocardiography in rabbits guided us toward determining whether they were cardiacly healthy or not. The B-mode technique was used to visually assess both regional and global LV systolic function. The M-mode technique measured left ventricular cavity dimensions, wall motion, and thickness. If the parameters were within the upper limit, we investigated the cause of the elevated values and sought to identify cardiac problems.

Left ventricular systolic function was assessed by measuring posterior wall and septal thickness. Wall thickness increased in systole and decreased in diastole. Scar tissue development due to dilated cardiomyopathy or previous myocardial infarction was observed. EF% and FS% were calculated using the Teicholz method from the parasternal long-axis view on B-mode and M-mode echocardiography. Left ventricular parameters were obtained in rabbits using the Teicholz method and manual B- and M-mode echocardiography.

In 8 (eight) rabbits, the diagnosis of left congestive heart failure was supported by mitral valve regurgitant flow and dilatation of the left heart chambers on B-mode echocardiography. Prolapse, thickening and degeneration of the mitral valve causing regurgitant flow were observed in 4 (four) rabbits. In apical 4-chamber and parasternal short-axis views, thinning of the interatrial septum and aneurysmal appearance were observed in 4 (four) rabbits. Suspicious ventricular septal defect was observed in one rabbit on parasternal long-axis and apical 5-chamber views. Dilated cardiomyopathy was observed in two rabbits on B-mode and M-mode echocardiographic images from parasternal long-short and apical sections. Pericardial fluid and pleural fluid images were obtained on B-mode and subcostal views in four rabbits. Pulsed Doppler echocardiography diagnosed diastolic dysfunction in four rabbits.

The parameters routinely examined in echocardiographic studies in rabbits are the same as those in studies conducted in other animal groups and humans.

In the guidelines of the American Society of Echocardiography, parameter measurements examined with two-dimensional (B mode), M mode and color Doppler echocardiography are the same all over the world.

	Average	Min-Max
Maximal early velocity E (m/s)	52.70	25-72
Maximal atrial filling flow velocity A (m/s)	37.75	20-53
E/A	1.340	1.2-1.4
Deceleration time DT (m/s)	44.70	32-64
Acceleration time AT (m/s)	50.90	40-70
Ejection time ET (m/s)	96.30	98-144
Isovolemic relaxation time IVRT (m/s)	69.30	64-115
E velocity-time integral, EVTI (m/s)	0.080	0.05-0.18
A velocity-time integral, AVTI (m/s)	0.040	0.02-0.08

Table 1: Left ventricular filling parameters in rabbits using color Doppler method.

Parameters	Average	Min-Max
Left ventricular end-diastolic diameter (LVIDD, mm)	12.12	9.9-14.2
Left ventricular end-systolic diameter (LVIDS, mm)	7.93	5.8-10.1
Interventricular septum diastolic thickness (IVSd, mm)	2.65	2-3.3
Interventricular septum systolic thickness (IVSs, mm)	2.73	1.6-3.4
Left ventricular posterior wall diastolic thickness (LVPWDd, mm)	3.0	2.2-4.0
Left ventricular posterior wall systolic thickness (LVPWDs, mm)	3.21	2.1-5.3
Left atrium size (LA, mm)	7.85	6.5-8.9
Aortic diameter (AC, mm)	6.60	6.4-8.4
Right atrium (RA, mm)	5.95	3.6-7.3
Right ventricle (RV, mm)	6.32	5.5-8
Pulmonary artery diameter (PAC, mm)	4.61	3.4-6.2
Right ventricular posterior wall thickness (RVPWD, mm)	2.4	1.4-3.2
Left ventricular end-diastolic volume (EDV, ml)	3.49	2.0-5.2
Left ventricular end-systolic volume (ESV, ml)	1.17	0.5-1.8
Left Ventricular stroke volume (SV, ml)	2.35	1.3-3.4
Ejection fraction (EF, %)	67.15	60-80
Fraction shortening (FS, %)	33.45	28-43
Stroke index (SI, ml)	33.45	4.3-25.4
Left ventricular mass (g)	4.62	3.0-9.0
Heart rate (min)	125	120-250

Table 2: Left ventricular parameters in B-mode and M-mode echocardiography using the Teicholz method in rabbits.

Figure 1: Parasternal short-axis view in B-mode echocardiography, LA (left atrium), RA (right atrium), PA (pulmonary artery), RVOT (right ventricular outflow tract), AoV (aortic valve).

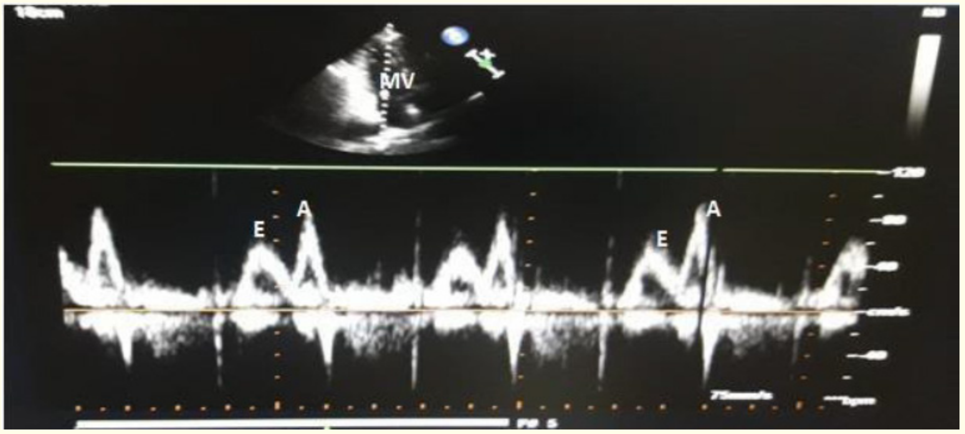

Figure 2: E/A ratios (Left ventricular diastolic dysfunction-LVDD) with PW Doppler over the mitral valve from the apical 4-chamber view.

Discussion

The rabbit is the most preferred animal model for scientific studies in human and veterinary medicine due to its anatomical and physiological characteristics. Echocardiographic parameter measurements are important for the diagnosis and treatment of heart diseases [8-10].

Since congestive heart failure, arrhythmias, cardiomyopathy, tricuspid and mitral valve diseases are frequently observed in rabbits, B-mode (2D) and M-mode techniques are used in the diagnosis of many congenital disorders such as aortic valve disorders, insufficiency, prolapse and stenosis of mitral and tricuspid valves, endocarditis, aortic aneurysms, increased pericardial effusion, hypertrophic cardiomyopathy and vitacordis [2,4].

Rabbits should be used frequently because they offer lower maintenance costs compared to other large animal models, easier echocardiographic examinations, and more detailed information. The echocardiographic imaging used in rabbits is similar to the imaging modalities routinely used in humans and animals [11].

Important findings are obtained regarding the evaluation of cardiac functions in large animal models (Horse, Cow, Mare, etc.) and the determination of the effects of treatment methods to be applied in ischemic and non-ischemic cardiomyopathiesIn our PW and CW Doppler echocardiography studies in rabbits, systolic segmental wall motion abnormalities and diastolic dysfunctions were not observed [5,12,13]. Interventricular septal defects have been diagnosed in rabbits by echocardiography [11,14]. Ventricular septal defects, patent ductus arteriosus, pulmonary hypertension, and valvular cysts have been detected at necropsy in New Zealand White rabbits [15]. In 1999, we began our first studies in rabbits, conducted under the guidance of cardiovascular surgeon Dr. Ertan Yücel, to evaluate echocardiographic findings. Measurements were made of rabbit heart diameters (ventricles, atria, and wall thickness) using surgical instruments, and these measurements were matched with anatomical structure and clinical information.

In rabbits, widening of the interventricular septum and the posterior wall (posterior wall, free wall) space was considered to be concentric left ventricular hypertrophy. The wall enlargements were considered congenitalIt has been reported that the LA (left atrium) value is increased in rabbits diagnosed with congestive heart failure [3]. In rabbits with increased LA values, signs of insufficiency due to mitral valve degeneration were observed. Because the left atrium-to-aorta ratio (LA:Ao ratio) was >1.2, the left atrium was enlarged. In studies conducted on rabbits, it was observed that there was no statistical difference depending on body weight, age and gender, and this was consistent with the findings reported for rabbits by Casamian-Sorrosal., *et al*. (2014).

Diastolic dysfunction and systolic function were investigated in rabbits with varying left ventricular ejection fraction (EF%). A decrease in EF was observed in rabbits with dilated cardiomyopathy, particularly in association with mitral valve insufficiency [1,16]. Patients with decreased EF (%) also exhibited decreased global systolic function.

Tissue Doppler imaging (TDI) is valuable for recording myocardial motion and assessing global systolic and diastolic function in patients with diastolic dysfunction [16,17]. While ultrasound devices with standard radiological color Doppler were used in veterinary medicine in the early 2000s, the TDI technique has begun to be added to veterinary echocardiography devices in recent years.

We believe that diastolic dysfunction will contribute to this in the coming years.

Congenital disease is not as common in rabbits as in cats and other animals. Although the interatrial septum is more commonly thinned and mobile, no atrial septal defect (ASD) or patent foramen ovale (PFO) was observed. Mitral valve degenerations, left atrium and left ventricular dilatation, mitral valve prolapse, and increased left ventricular and interventricular septum thickness were found to be suspicious for mitral valve disease in echocardiography [18,19].

Pericardial and pleural effusions are very common in all animal groups and in humans, but they have also been encountered in rabbits. Echocardiography provides valuable information about heart diseases in rabbits, contributing to their diagnosis and treatment.

Conclusion

Echocardiography was intended to be the most commonly used cardiac imaging technique in rabbits due to its advantages such as portability and non-invasiveness in preclinical studies. Given the frequent occurrence of congenital and acquired cardiac diseases in rabbits, it was emphasized that routine cardiac imaging should be performed to ensure that rabbits benefit from gold-standard technology like echocardiography for a better quality of life.

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