วารสารสัตวแพทยศาสตร์ มข.
KKU Veterinary Journal
ISSN 0858-2297

RESEARCH ARTICLE

Understanding cardiac parameters in rabbits using chest radiography and electrocardiography

Phawida Wiphusunti[1*], Kanit Chukanhom[2], Kwankate Kanistanon[2], Sompoth Weerakhun[2]

[1]*Graduate Student, Master of Science program, Faculty of Veterinary Medicine, Khon Kaen University, Khon Kaen, Thailand*
[2]*Department of Veterinary Medicine, Faculty of Veterinary Medicine, Khon Kaen University*
[*]***Corresponding author*** *E-mail: P.wiphusunti@gmail.com*

Received 28 August 2019, **Revised** 30 July 2020 **Accepted** 3 August 2020, **Published** 20 October 2020

Abstract

Objective: To compare selected parameters of the heart, using the vertebral heart score (VHS) and electrocardiogram (ECG), between different breeds of healthy pet rabbits.

Materials and Methods: Included in the analysis were 99 healthy rabbits, with no preselection for sex, age, or weight. Rabbits were classified according to their breed: Holland lop (n=51), Thai (n=32), or Netherland dwarf (n=16). Animals underwent anesthesia for a general surgical procedure. Anesthesia was performed using intramuscular ketamine-xylazine injection. Under anesthesia, chest radiography was performed to measure the size of the heart in the ventro-dorsal and right lateral recumbent positions, using the VHS method and ECG.

Results: The heart-to-thoracic size ratio was ≤60% in both positions. In the right recumbent position, there was no difference in heart size, width, and length and overall size between breeds. There was also no difference in heart rate and the following ECG parameters between the breeds: P wave (s), P wave (mV), PR interval (s), QRS complex (s), R wave (mV), and T wave (s). However, the QT interval (s) was different between the Holland lop and Thai breeds ($P<0.05$), with the difference being in the ST segment, with an elevation of >0.05 mV in 56.6% of animals and a maximum elevation of 0.12 mV. The mean electrical axis (MEA) was between -90º and 180º in 55.6% of animals, between -30º to -90º in 7.1%, and between 90º and 180º in 37.4%.

Conclusion: There were no significant differences in heart size or heart rate among the three breeds of rabbits. ECG showed a specific difference in the QT interval. ST elevation was different than that in normal dogs and cats, but remained within the normal values for humans. The MEA was between -90º and 180º.

Keywords: Heart size, VHS, heart rate, electrocardiography, rabbit

บทความวิจัย

ค่าตัวแปรของหัวใจกระต่ายเลี้ยง ด้วยภาพถ่ายรังสีช่องอกและคลื่นไฟฟ้าหัวใจ

ภาวิดา วิภูสันติ[1*], คณิต ชูคันหอม[2], ขวัญเกศ กนิษฐานนท์[2], สมโภชน์ วีระกุล[2]

[1]นักศึกษาปริญญาโท คณะสัตวแพทยศาสตร์ มหาวิทยาลัยขอนแก่น อ.เมือง จ.ขอนแก่น 40002

[2]ภาควิชาอายุรศาสตร์ คณะสัตวแพทยศาสตร์ มหาวิทยาลัยขอนแก่น

[*]ผู้ประพันธ์บรรณกิจ อีเมล์: P.wiphusunti@gmail.com

บทคัดย่อ

วัตถุประสงค์ การศึกษาค่าตัวแปรที่สำคัญของหัวใจ ได้แก่ ขนาดหัวใจ อัตราการเต้นของหัวใจ และคุณสมบัติทางคลื่นไฟฟ้าหัวใจในกระต่ายเลี้ยงสุขภาพดี ด้วยวิธีการวัด Vertebral heart score (VHS) และ Electrocardiogram (ECG) เพื่อเปรียบความแตกต่างค่าพารามิเตอร์ในกระต่ายแต่ละสายพันธุ์

วัสดุ อุปกรณ์ และวิธีการ ทำการตรวจเพื่อทำการคัดเลือกกระต่ายสุขภาพดี จำนวน 99 ตัว โดยไม่คำนึงถึงเพศ อายุ หรือน้ำหนัก จากนั้นแบ่งกระต่ายเป็น 3 กลุ่มคือ สายพันธุ์ฮอลแลนด์ลอป ไทย และเนเธอร์แลนด์ดวอร์ฟ จากนั้นวางยาสลบเพื่อให้อยู่ในสภาวะที่สงบ โดยฉีดไซลาซีนไฮโดรคลอไรด์ร่วมกับเคตามีนไฮโดรคลอไรด์เข้ากล้ามเนื้อ จากนั้นทำการถ่ายภาพทางรังสีช่องอกเพื่อวัดขนาดหัวใจ ในท่านอนหงายและตะแคงขวา การวัดคลื่นไฟฟ้าหัวใจ ด้วยวิธีการวัด Vertebral heart score (VHS) และ Electrocardiogram (ECG)

ผลการศึกษา ในกระต่ายสายพันธุ์ฮอลแลนด์ลอป 51 ตัว ไทย 32 ตัว และเนเธอร์แลนด์ดวอร์ฟ 16 ตัว พบว่าอัตราส่วนขนาดหัวใจต่อขนาดทรวงอก มีอัตราส่วนไม่เกินร้อยละ 60 ทั้งในภาพรังสีท่านอนตะแคงขวาและท่านอนหงาย ในท่าตะแคงขวาพบว่าขนาดหัวใจด้านกว้าง ด้านยาว และขนาดโดยรวม ไม่มีความแตกต่างกันระหว่างกลุ่ม อัตราการเต้นและคลื่นไฟฟ้าหัวใจ P wave (s), P wave (mV), PR interval (s), QRS complex (s), R wave (mV) และT wave (s) พบว่าไม่มีความแตกต่างกันระหว่างกลุ่ม แต่พบว่า QT interval (s) มีความแตกต่างในสายพันธุ์ฮอลแลนด์ลอปกับไทย ($P<0.05$) ลักษณะ ST segment ที่แตกต่างจากสัตว์ชนิดอื่นพบว่ามี ST elevation ร้อยละ 56.6 โดยค่าสูงสุดอยู่ที่ 0.12 mV ส่วน ST depression ไม่มีการพบ และ MEA ทั้งหมดอยู่ในช่วงระหว่าง -90 ถึง 180 องศา โดยร้อยละ 55.6 อยู่ในช่วงระหว่าง -30 ถึง 90 องศา ซึ่งเป็นค่าปกติเมื่อเทียบกับในมนุษย์ร้อยละ 7.1 อยู่ในช่วงระหว่าง -30 ถึง -90 องศา และร้อยละ 37.4 อยู่ในช่วงระหว่าง 90 ถึง 180 องศา ไม่มีช่วง -90 ถึง -180

สรุป ขนาดของหัวใจและอัตราการเต้นของหัวใจในกระต่ายทั้งสามสายพันธุ์ไม่มีความแตกต่างกัน คลื่นไฟฟ้าหัวใจพบว่ามีเฉพาะ QT interval (s) ที่มีความแตกต่างกัน ส่วน ST elevation ที่เกิดขึ้นมีความแตกต่างกับค่าปกติในสุนัขและแมว แต่ไม่เกินค่าปกติในมนุษย์ และ MEA อยู่ในระหว่าง -90 ถึง 180 องศา

คำสำคัญ: ขนาดหัวใจ, อัตราการเต้นของหัวใจ, คลื่นไฟฟ้าหัวใจ, กระต่าย

Introduction

Nowadays, rabbits are increasingly adopted as pets, almost as commonly as dogs and cats in several countries (Praag, 2015). With good care and appropriate knowledge provided to owners, pet rabbits have an average life expectancy of >10-12 years. In 2013, Kwancum Animal Hospital provided care to 8037 rabbits (Weerakhun, 2015). Heart disease in pet rabbits includes infectious diseases and non-infectious heart failure at the end-stage of life (Chitty, 2015). Although there is currently no clear evidence of heart disease in rabbits, it is believed that the risk of heart disease increases with age, as for other animals. Between the ages of 5 and 10 years, 10% of dogs develop an underlying heart disease (Atkins et al., 2009), with this proportion likely to increase with age. A delay in the diagnosis of heart disease can result in the death of the animal before treatment is provided.

The risk factors for heart disease in rabbits have been studied for animals in crowded farming environments (Canavese et al., 2014). Marini et al. (1999) reported that combined xylazine hydrochloride and ketamine hydrochloride, used for the general anesthesia of rabbits, causes significant expansion of the heart muscle, particularly when given at a high dose. Chronic respiratory infections, caused by Pasteurella multocida, are another risk factor for heart disease in rabbits (Deeb and DiGiacomo, 2000). In humans, periodontitis, caused by Streptococcus mutans and S. sanguis, can lead to endocarditis and valvular heart disease (Shree et al., 2017; Carinci et al., 2018). This is also a possible risk factor for heart disease in rabbits as they too can develop periodontitis, generally resulting from a malocclusion that causes insufficient wearing of teeth and severe inflammation and/or infection.

Despite the acknowledgement of various possible risk factors for heart disease in rabbits, the mechanism underlying heart disease in these animals remains unclear. However, it is expected that these mechanisms would be similar to those in dogs and cats considering the similarity in the heart physiology and anatomy (Harcourt-Brown, 2002), although rabbits to have a comparatively faster heart rate (Alexander, 2005). Therefore, there is a need for physical examination strategies that are specific to rabbits to assist in the diagnosis of heart disease in these animals (Lord et al., 2010b), using radiography, electrocardiogram (ECG), and computed tomography (CT). We used chest radiography and ECG to compare features of heart anatomy and physiology between different breeds rabbits that will provide preliminary data that could be used for the diagnosis of heart disease in pet rabbits.

Materials and Methods

Ethics Statement

This study was approved by research ethics board of Khon Kaen University (Animal use license number U1-04651-2559).

Study Samples

Pet rabbits who were admitted to Kwancum Animal Hospital, Bangkok, for general treatment or a health check-up were eligible for study inclusion. Healthy rabbits who did not exhibit signs of illness, symptoms of respiratory disease, had no evidence of periodontic disease and had no history of chronic infections were included. These criteria were assessed using the standardized approach of the Health Record Model (Alice, 2015). We used a non-probability sampling strategy, with no a priori determination of sex, breed, age, and/or weight. Sampling was performed over a 12-month period. The sample size was estimated based on previous data indicating a prevalence of hidden heart disease in dogs of 10% (Atkins et al., 2009), using an infinite population proportion method (Wayne, 1995).

Anesthesia

Measurements of the heart were obtained with the animal under anesthesia. Of note, animals were being anesthetized to undergo sterilization procedure and, thus, not only for the purposes of this study. Anesthesia was administered using intramuscular injections of xylazine hydrochloride (2-3 mg/kg), followed by intramuscular injection of ketamine hydrochloride (15-20 mg/kg) after a 5 minute delay, as previously reported (James, 2013). Sedation was achieved at 15 minutes post-injection.

The Vertebral Heart Score (VHS)

A Kelex radiography system (model MD 1100) was used, with the table placed at a distance of 1.40 m from the X-ray cassette. The settings for radiography were as follows: 50-55 mA at 100 kVp, with mAs of 0.04-0.06 depending on size of the animal. Images were obtained in two positions, the ventro-dorsal (VD) and right lateral recumbent positions. On these radiographs, we evaluated the presence or absence of a large expansion of the abdo-

men over the chest. We also evaluated the size of the heart, during the inspiratory phase, in the right lateral recumbent position after infusion of a radioactive marker. The long axis of the heart was measured from the carina to the apex and the short axis at point of its widest diameter. For this measure, a line was drawn perpendicular to the long axis of the heart with a second line drawn parallel to the thoracic spine, beginning from T4 downward, equal to the length of the long and short axis of the heart. The number of thoracic spinal segments included between the two lines was counted to obtain the VHS, as previously described (Buchanan and Bucheler, 1995).

Electrocardiography

Considering the more rapid heart rate in rabbits than in other animals (dogs and cats), the speed of the paper was set at 50 mm/s and the sensitivity to 2 mm/mV, rather than the usual setting of 1 mm/mV. The ECG was recorded with the rabbit in the right lateral recumbent position on an insulated table, according to the methods of Turner et al. (2015). Alcohol gel was applied to the electrodes to increase the electrical conductivity. The front limb electrodes were placed on the skin above the elbow, with the hind limb electrodes placed along the midline between the knee and groin. The limbs were stretched out in front of the animal for the recording, with an insulated separator placed between the limbs to avoid contact. The ECG was used to record the heart rate and rhythm (normal or arrhythmia). The following lead II cardiac parameters were recorded: P wave (s), P wave (mV), PR interval (s), QRS complex (s), R wave (mV), QT interval (s), T wave (s), and the mean electrical axis (MEA). Measurements obtained were robust, based on 8-10 PQRST complex recorded at each lead. To measure the MEA and QRS, we first identified the positive or negative values calculated from R-(Q+S) from lead I and Lead aVF, and values were then recorded on the hexaxial reference system. If a negative value was identified (with the current traveling from the positive to the negative electrode), the signal was then transposed to the axis of lead I on the left (negative) side. The same transposition process was performed if a positive value was obtained at the aVF lead, with the signal shifted superiorly to the point of intersection between a line perpendicular to lead I and to lead aVF, indicating the end-point of the mean QRS vector.

Results

Of the 139 animals eligible for our study, 99 met our inclusion criteria and were included in our analysis. The sample comprised of 51 Holland lop rabbits, 32 Thai rabbits, and 16 Netherland dwarf rabbits.

Chest radiograph (VHS)

The heart-to-thoracic ratio was <60% in both VD and right lateral recumbent positions. The size of the heart measured in the right lateral recumbent position is summarized in Table 1.

Electrocardiography (ECG)

The QT interval was significantly different between the Holland lop and Thai breed, at the 95% CI ($P<0.05$), but with no difference for the Netherlands dwarf breed. There were no differences between the breeds with regard to the other measured ECG parameters ($P>0.05$). No case of sinus arrhythmia was identified in our study sample.

ST segment characteristics

With regard to the ST segment, an isoelectric segment was identified in 43.4% of animals (n=43), with an elevated ST in the other 56 animals (56.6%). Among these, ST elevation was >0.05 mV in 19 rabbits (33.9%) and ≤0.05 mV in 37 rabbits (66.1%). The highest ST elevation identified was 0.12 mV (Figure 1).

Measurement of the mean electrical axis (MEA) using the QRS complex

The distribution of the MEA across the 99 rabbits was as follows: 55.6% between -90º and 180º; 7.1% between -30º to -90º; and 37.4% between 90º and 180º. Of note, there were no cases between the range of -90º to -180º. The MEA values for rabbits compared to those of humans are shown in Table 3.

Discussion

The administration of general anesthesia, as in our study for sterilization, requires that ECG be monitored. Our findings provide a reference for determining if ECG is normal or not, which is often difficult in rabbits. This is particularly important as it is known that the administration of anesthetic agents can induce an expansion of the heart in rabbits. Anesthesia also causes an increase in heart and respiration rate. Thus, our finding also provides a reference

Table 1. Comparison of rabbit heart sizes in each breed

	Breed		
	Holland lop (n=51)	Thai (n=32)	Netherland dwarf (n=16)
Vertebral heart scale (VHS) and Right lateral recumbency			
Right lateral-Short axis (RL-SA)	3.47 ± 0.33	3.40 ± 0.26	3.45 ± 0.33
Right lateral-Long axis (RL-LA)	4.19 ± 0.38	4.21 ± 0.36	4.14 ± 0.33
Overall heart size (VHS Right)	7.67 ± 0.61	7.69 ± 0.51	7.65 ± 0.49

There was no difference among the three breeds, at the 95% confidence interval (95% CI) level, with regard to the length, width, and overall size of the heart (P> 0.05).

Table 2. Comparison of the electrocardiogram of rabbits in each breed

	Breed		
	Holland lop (n=51)	Thai (n=32)	Netherland dwarf (n=16)
Heart Rate (bpm)	179.23 ± 33.07	176.93 ± 43.86	202.18 ± 38.18
P-wave duration (s)	0.021 ± 0.008	0.022 ± 0.011	0.018 ± 0.008
P-wave amplitude (mV)	0.040 ± 0.020	0.043 ± 0.029	0.038 ± 0.020
PR interval (s)	0.062 ± 0.008	0.063 ± 0.012	0.057 ± 0.007
QRS duration (s)	0.036 ± 0.008	0.039 ± 0.009	0.037 ± 0.005
R-wave amplitude (mV)	0.174 ± 0.126	0.224 ± 0.133	0.178 ± 0.104
QT interval (s)	0.157 ± 0.021a	0.169 ± 0.023b	0.154 ± 0.019ab
T-wave amplitude (mV)	0.080 ± 0.059	0.090 ± 0.068	0.048 ± 0.037

[a]P-value < 0.05 vs a, [b]P-value < 0.05 vs b., [ab]P-value > 0.05 vs a,b.

Table 3. Comparison of MEA values in rabbits with normal degrees in humans

Degree	Rabbit (percent)	Human
-30 to 90	55.6	normal zone
-30 to -90	7.1	left axis deviation or pathological left axis
90 to 180	37.4	right axis deviation or pathological right axis
-90 to -180	0	gray zone or indeterminate axis

Adapted from Anthony Dupre, Sarah Vincent, and Paul A Iaizzo (2005).

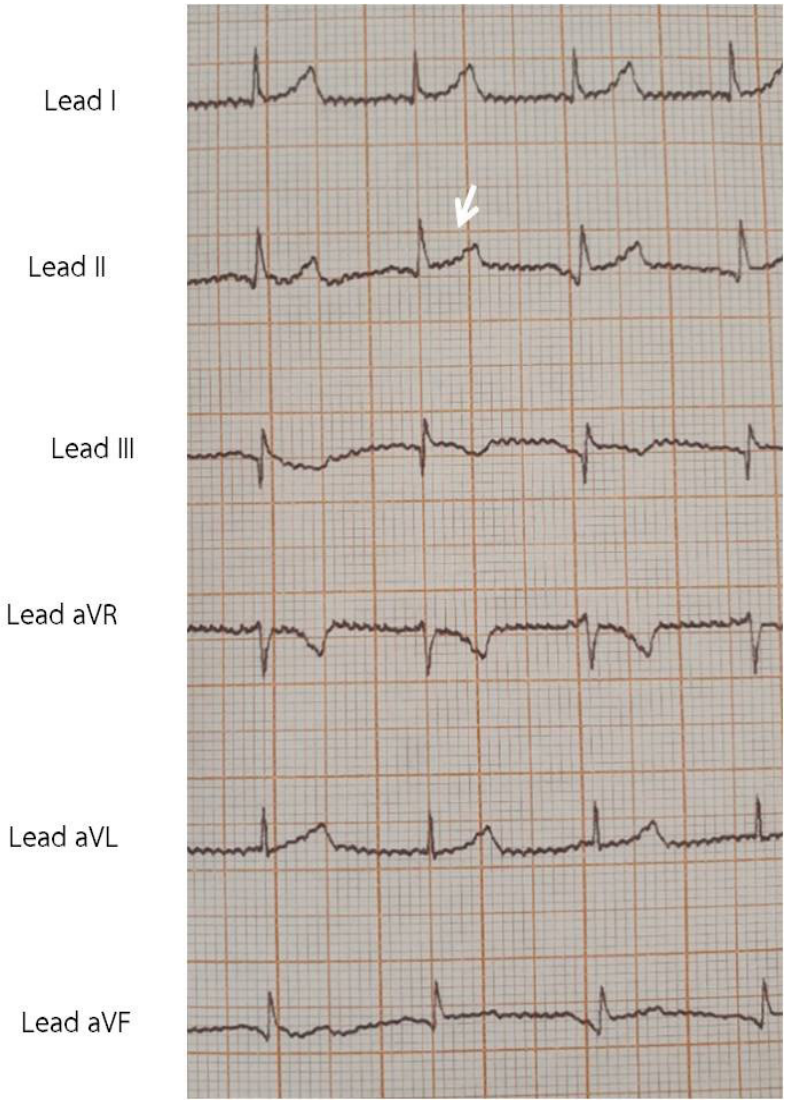

Figure 1. The electrocardiogram of rabbits with ST elevation during ST segment (arrow).

to determine if the anesthesia dose is within safe limits. This is important as high doses of anesthetic agents can adversely affect the heart muscle (Chari et al., 2001; Ruben et al., 2011).

To the authors' knowledge, this is the first study in Thailand investigating more than three different breeds. In the present study, no difference in the heart size of three breeds of rabbits in terms of the heart width, length, and overall size, which has also been reportedly found in dog breeds. Onuma et al. (2010) and Turner et al. (2015) studied the heart size of rabbits and found no difference between male and female rabbits, but left lateral was found to be significantly larger than the right lateral in both studies. In this study, only the ventro-dorsal and right lateral were measured and attempts were made to exclude fat opacity from cardiac measurements during original scoring, although some pericardial fat was included in the measurements. Nabi et al. (2014) found that the average heart size of Labrador and German Shepherd breeds was significantly larger than Indian, Split, Pug, and Native breeds ($P < 0.05$). In both studies mentioned above, the average heart size was larger than was found by Buchanan and Bucheler (1995), which is the average for common dogs. Meanwhile, Jepsen-Grant et al. (2013) found that the VHS mean in Pug, Pomeranian, Bulldog, and Boston terrier breeds were significantly greater than the published VHS references. Total body mass score does not affect VHS except for the Lhasa apso breed. Bulldog and Boston terrier breeds have higher average than other breeds. VHS is more valuable in dogs with abnormal vertebrates compared to normal dogs (Jepsen-Grant et al., 2013). However, no clear conclusion can be made for rabbits since there are few comparative studies.

Table 4. Electrocardiography of the normal rabbit

Parameter	Rabbit (New Zealand White) 100 cases*	Rabbit (Many breeds) 46 cases**
Heart rate	242	262
P wave	0.03 sec, 0.05 mV	0.03 sec, 0.08 mV
PR interval	0.05 sec	0.06 sec
QRS complex	0.05 sec	0.04 sec
R amplitude	0.18 mV	0.21 mV
T wave amplitude	0.16 mV	0.11 mV
QT interval	0.14 sec	0.12 sec

*Turner et al. (2015) and **Lord et al. (2010b).

The heart rate in all breeds wasn't different. The QT interval of Holland Lop and Thai breeds were different, but there was no difference with the Netherland Dwarf breed. The narrowest QT interval after the QT interval is the combined time interval repolarization and depolarization (Wanwarang et al., 2014). The QT interval is typically less than half of the RR interval in the same cardiac cycle (Plonsey, 1982). The QT interval will be shorter when the heart rate is faster (Loscalzo, 2013; Wanwarang et al., 2014). In a study with humans, a long QT interval may be caused by heredity, ischemic heart disease, and heart failure (Loscalzo, 2013). However, when compared to other studies, the QT interval is still considered normal (Turner et al., 2015). Another electrocardiogram study found no significant difference between groups at a 95 percent confidence level (P> 0.05). In accordance with Lord et al. (2010b), samples were divided into four groups of various breeds. No difference was discovered in the electrical wave value.

In humans, an ST elevation greater than 0.05 mV is a disorder. Elevation of the ST segment greater than 0.15 mV or depression of the ST segment greater than 0.2 mV in leads II, III, or aVF is abnormal in the dog. ST segment elevation or depression in the cat is abnormal (Larry et al., 2008). If altered in the same way in rabbits, it can be assumed that the occurrence of ST-elevation is likely an abnormal condition, but a definitive answer has not been found. Turner et al. (2015) performed echocardiograms with rabbits, and found that rabbits with an ST elevation have a condition, but no abnormalities were found in the heart, including after undertaking an autopsy. This experiment used doping xylazine and ketamine together as a pre-anesthetic before using inhalation anesthetics. Alpha2-agonists have the potential to cause cardiovascular side effects, including bradycardia and decreasing cardiac output by up to 50 percent. Alpha2-agonists also affect ECG changes, resulting in arrhythmia or even a slower heart rate which results in QT prolongation (Ali et al., 2009; Cassu et al., 2014; Naglaa et al., 2015).

For QRS Axis (MEA), the value was found to be close to a previous study. In a sample of 100 New Zealand White rabbits, the MEA value was found to be in the range of -60 to 180 degrees, in the range of -30 to 90 degrees to 85 percent. The normal MEA range in humans is between -30 to 90 degrees, while values between 90 and 180 degrees imply right axis deviation and an electrical shape of the heart rather than vertically. MEA values between -30 and -90 degrees mean left axis deviation or an electrical shape of the heart rather than horizontally. Meanwhile, MEA values between -90 and -180 degrees are in an unclear zone and cannot be identified as left or right axis deviation (Anthony, D. and Sarah, V., 2005; Wanwarang et al., 2014). Among dogs and cats, MEA ranges from 40 to 100 degrees and 0 to 130 degrees, respectively (Wendy, 2007). Rabbits may have different electrocardiogram characteristics from humans and the other species mentioned above, while MEA has more degrees.

References

Wanwarang Wongcharoen, Arinthaya Phonminthikun, Narawutt Prasertwitthayakit, Rangsarit Kanchanawanit , Apichat Sukhonsan. 2014. Electrocardiography for medical student. 8th edition. Thailand, Chaingmai: Trick Thimk, 11-41.

Alexander JH. 2005. Comparative cardiac anatomy. In Paul AI (Ed.). Handbook of cardiac anatomy, physiology and devices. New Jersey: American International Standard institute, 81-91

Ali AS, Nasser V, Nikahval B, Alireza K. 2009. Comparison of the Effects of different doses of acepromazine-xylazine on the electrocardiogram in dogs. Iran J Vet Res 33(3), 208-215.

Anthony D, Sarah V. 2005. Basic ECG theory, recordings and interpretation. In Paul AI (Ed.). Handbook of cardiac anatomy, physiology and devices. New Jersey: American international standard institute, 191-201.

Atkins C, Bonagura J, Ettinger S, Fox P, Gordon S, Haggstrom J, Hamlin R, Keene B, Luis-Fuentes V, Stepien R. 2009. Guidelines for the diagnosis and treatment of canine chronic valvular heart disease. J Vet Intern Med 23(6), 1142–1150.

Buchanan JW, Bucheler J. 1995. Vertebral scale system to measure canine heart size in radiographs. J Am Vet Med Assoc 206(2), 194-199.

Canavese F, Dimeglio A, Barbetta D. 2014. Effect of thoracic arthrodesis in prepubertal New Zealand White rabbits on cardio-pulmonary function. Indian J Orthop 48(2), 184–192.

Cassu RN, Melchert A, Canoa JT, Martins PD. 2014. Sedative and clinical effects of the pharmacopuncture with xylazine in dogs. Acta Cir Bras 29(1), 47-52.

Chari YTH, John CBJr, Margaret MR. 2001. Effects of avertin versus xylazine-ketamine anesthesia on cardiac function in normal mice. Am J Physiol 281(5), 1938-1945.

Chitty J. 2015. Cardiovascular disease in rabbits. Companion Anim J 20(2), 74-78.

Carinci F, Martinelli M, Contaldo M, Santoro R, Pezzetti F, Lauritano D, Candotto V, Mucchi D, Palmieri A, Tagliabue A, Tettamanti 7. 2018. Focus on periodontal disease and development of endocarditis. J Biol Reg Homeos Ag 32(2), 143-147.

Deeb BJ, DiGiacomo RF. 2000. Respiratory diseases of rabbits. Vet Clin North Anim Exotic Anim Pract 3(2), 465-480.

Harcourt-Brown F. 2002. Textbook of Rabbit Medicine. 2nd edition. Burlington: Butterworth-Heinemann.

Jepsen GK, Pollard RE, Johnson LR. 2013. Vertebral heart scores in eight dog breeds. Vet Radiol Ultrasound 54(1), 3-8.

Larry T, Francis S, Mark O, Meg S. 2008. Electrocardiography. manual of canine and feline cardiology (4th Edition). Philadelphia: Saunders Elsevier. 464.

Lord B, Devine C, Smith S. 2010a. Congestive heart failure in two pet rabbits. Jo Small Anim Pract 52(1), 46-50.

Lord B, Boswood A, Petrie A. 2010b. Electrocardiography of the normal domestic pet rabbit. Vet Rec 167(25), 961-965.

Loscalzo J (Ed.). 2013. Harrison's Cardiovascular Medicine. 2nd edition. United States: McGraw-Hill Education.

Marini RP, Li X, Harpster NK. 1999. Cardiovascular pathology possibly associated with ketamine/xylazine anaesthesia in Dutch belted rabbits. Lab Anim Sci 49(2), 153–160.

Nabi SU, Wani AR, Dey S. 2014. Radiographic measurements (vertebral heart scale) of popular breeds of dogs in India. Appl Biol Res 16 (2), 242-246.

Naglaa AG, Alaa G, Ayman A. 2015. Effect of repeated intravenous administration of xylazine on sedation, analgesia and ECG parameters in donkeys *(Equus Asinus)*. Assiut Vet Med J 61(147), 130-136.

Pariaut R. 2009. Cardiovascular physiology and diseases of the rabbit. Vet Clin North Ame Exotic Anim Pract 12(1), 135-144.

Plonsey R. 1982. Electrocardiographic lead theory and lead systems. In Plonsey R, Liebman J, Gillette PC. (Eds.). Pediatric electrocardiography. Baltimore: Lippincott Williams & Wilkins. 26-39.

Praag EV. 2015. Congestive heart failure in rabbits. Retrieved January 19, 2019, from https://www.researchgate.net/publication/272151346_Congestive_heart_failure_in_rabbits.

Ruben CS, Matthew R, Dorcas O, Karen O, Chad RF, Corinne AW, Amanda GA, David AB. 2011. High doses of ketamine–xylazine anesthesia reduce cardiac ischemia–reperfusion injury in guinea pigs. J Am Assoc Lab Anim Sci 50(3), 349–354.

Shree VD, Milind SD, Basavraj SN. 2017. Periodontitis, bacteremia and infective endocarditis: a review study. Pediatr Infect Dis 5(3): e41067.

Turner GA, Ayres DA, Lima L. 2015. Determination of normal echocardiographic, electrocardiographic, and radiographic cardiac parameters in the conscious New Zealand White rabbit. J Exotic Pet Med 24(2), 223-234.

Weerakhun S. 2015. Rabbit Gastrointestinal Syndrome. Processing of the 16th KhonKaen university veterinary international annual conference, KhonKaen University, KhonKaen, Thailand.

Wendy AW. 2011. Cardiovascular disease in small animal medicine. 3rd ed. London: Manson Publishing Ltd.