

Comparison of Systolic Blood Pressure between Normal and Asymptomatic Degenerative Mitral Valve Diseased in Small Breed Dogs

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Abstract

Degenerative mitral valve disease (DMVD) is the major cause of mitral valve regurgitation and heart failure in dogs. The regurgitation of mitral valve may affect blood pressure without clinical presentation. The aims of this study were to compare the systolic blood pressure between normal dogs and dogs affected with asymptomatic DMVD (class B ACVIM classification) and to determine the relationship between echocardiographic values and blood pressure levels. The systolic blood pressure of small breed dogs, weighing less than 10 kilogram, that were normal (n=22) and newly diagnosed with DMVD (n=21) was measured. The average of systolic blood pressure determined by Doppler ultrasonic device and Oscillometer of dogs in the DMVD group was higher than that of the normal group. Three DMVD dogs had systolic blood pressure higher than 160 mmHg. The echocardiographic values did not correlate with blood pressure. In conclusion, blood pressure of asymptomatic DMVD dogs is maintained. Some diseased dogs may have systolic blood pressure higher than normal limit.

Keywords: blood pressure, degenerative mitral valve disease, dogs

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Introduction

Degenerative mitral valve disease (DMVD) or chronic valvular endocardiosis is the most common cardiac disease in dogs. It accounts for 75% of cardiovascular diseases in dogs (Häggsström et al., 2009). It is the common cause of mitral valve regurgitation and left sided congestive heart failure (Borgarelli and Buchanan, 2012). The etiology of DMVD is unclear. Most affected dogs are small breeds such as Cavalier King Charles spaniels, Poodles, Miniature pinchers, Dachshunds, Pomeranians, Chihuahuas and Shih tzus (Borgarelli and Buchanan, 2012). DMVD mostly affects old dogs particularly dogs more than 10 years old (Borgarelli and Häggström, 2010). Male is more prone to this disease, 1.5 times higher than female dogs (Atkins et al., 2009).

Dogs affected with DMVD can be diagnosed by auscultating murmur heart sound heard best at the left apical area, radiography determining cardiac remodeling and pulmonary edema secondary to heart failure condition, and echocardiography examining valve thickening and regurgitation as well as cardiac structural and function changes.

Blood pressure measurement is another diagnostic method recommended to perform in DMVD dogs (Atkins et al., 2009). High systemic blood pressure may affect the disease severity by augmenting afterload resulting in decreased forward stroke volume, increased regurgitant blood volume back into the left atrium, increased disease severity and risk for developing congestive heart failure (Gaasch and Meyer, 2008; Atkins et al., 2009; Suzuki et al., 2012). On the other hand, an increase in regurgitant volume back into the left atrium secondary to mitral valve regurgitation can cause decrease in forward stroke volume and a drop in blood pressure. According to Frank-Starling mechanism, the disease itself may enhance the force of contraction in response to an increase in the end diastolic volume in compensatory stage which may affect the systemic blood pressure. Changes of blood pressure in dogs affected with DMVD may occur even no clinical sign of heart failure develops.

To our knowledge, there is no published data of systolic blood pressure in newly diagnosed DMVD dogs in stage B ACVIM classification or dogs without clinical signs of heart failure. Therefore, this prospective observational study was primarily created to compare systolic blood pressure between normal and asymptomatic DMVD dogs for determining whether there are some changes in blood pressure in DMVD dogs even though the dogs have no clinical sign of heart failure. The second objective was to determine the relationship between echocardiographic values and blood pressure for evaluating the effect of blood pressure on echocardiographic changes.

Materials and Methods

All dogs enrolled in this study were patients of Small Animal Hospital, Faculty of Veterinary Science, Chulalongkorn University. The protocol used in the present study was approved by Chulalongkorn University Animal Care and Use Committee. The dogs were divided into two groups: control and DMVD

groups. All dogs were small breeds with age more than 6 years old and weight less than 10 kilograms. The control group consisted of The dogs in the DMVD group were newly diagnosed with stage B DMVD and had never received drugs that had effects on blood pressure such as angiotensin converting enzyme (ACE) inhibitors or steroids. The dogs in both groups had no disease affecting blood pressure.

Complete blood count and biochemistry profile including serum glutamic pyruvate transaminase (SGPT), alkaline phosphatase (AP), blood urea nitrogen (BUN) and creatinine were evaluated in all dogs to screen for diseased condition.

Echocardiography was performed by using ultrasound machine (Logic™ 5 Pro, GE medical) with multifrequency 6-10 MHz microconvex and 5-6 MHz phrase array transducers. DMVD was diagnosed by an increased thickness of valve leaflets with regurgitation. To determine the structural changes and systolic function, echocardiographic parameters including left ventricular internal diastolic diameter (LVIDd), left ventricular internal systolic diameter (LVIDs), left ventricular free wall thickness during diastole (LVWd) and systole (LVWs), ventricular septal thickness during diastole (VSd) and systole (VSs) and the ratio of left atrium to aorta dimension (LA/Ao) were measured from the right parasternal long axis views. To reduce effects of body weight variation, the value of chamber size and wall thickness were divided by body weight (Kg). Fractional shortening (%FS) was calculated by $\{(LVEDd-LVEDs)/LVEDd \times 100\}$.

Radiography was performed in the normal dogs to screen for abnormality within thorax and abdomen. Dogs in the DMVD group that had no pulmonary edema or no sign of heart failure on radiographic examination were included in the study.

Because the Doppler ultrasonic device and Oscillometer may provide different levels of blood pressure, both measurement methods were used in the present study. The measurement was performed according to the ACVIM Consensus Guidelines (Brown et al., 2007). The cuff size of at least 40% of limb circumferences was used. The dogs were in sternal recumbent position when blood pressure was measured at the left carpal joint. Blood pressure measurement was performed at least 5 times in each dog in quiet environment to reduce stress induced hypertension.

Data acquisition and statistical analysis: All data were reported and determined by descriptive analysis. Systolic blood pressure between the control and DMVD groups and between 2 measurement methods were analyzed by unpaired student's *t*-test. To determine the relationship between age or echocardiographic value and blood pressure, Pearson's correlation analysis was performed. *P*-value less than 0.05 was considered statistically significant.

Results

Forty-three dogs were enrolled in the study. Twenty-two dogs (8 males and 14 females) were in the control group and 21 dogs (13 males and 8 females) affected with DMVD stage B were in the DMVD group. In the

control group, 4 dogs had high alkaline phosphatase and blood pressure measurement using the oscillometric method was not achieved in 2 dogs. Therefore, 6 dogs were excluded from this group, making a total of 16 dogs which consisted of 6 Shih tzus, 6 Poodles, 2 mixed-breed dogs, 1 Yorkshire terrier and 1 Pomeranian. In the DMVD group, 2 dogs had high alkaline phosphatase and blood pressure measurement using the Doppler ultrasonic method was not achieved in 3 dogs. Thus, this group had a total of 16 dogs. Breeds of dogs in the DMVD group were 8

Poodles, 4 mixed-breed dogs, 2 Shih tzus, 1 Chihuahua, and 1 Miniature pincher. All dogs in the DMVD group had heart murmur and were diagnosed with DMVD by echocardiography. All dogs affected with DMVD were in stage B or asymptomatic and had no sign of pulmonary edema on radiographs. The dogs in the DMVD group were older than the dogs in the control group (Table 1). However, the weight of dogs in both groups was not statistically different. There was no correlation between age and systolic blood pressure in the whole population of dogs.

Table 1 Gender, age and weight of dogs in control and DMVD groups

Group	n	Male	Female	Age (year)	Weight (Kg)
Control	16	6	10	7.94±0.59	5.36±0.47
DMVD	16	9	7	11.25±0.82**	5.11±0.49

Data are reported as mean±SEM.

** indicates significantly different between control and DMVD groups ($p<0.05$).

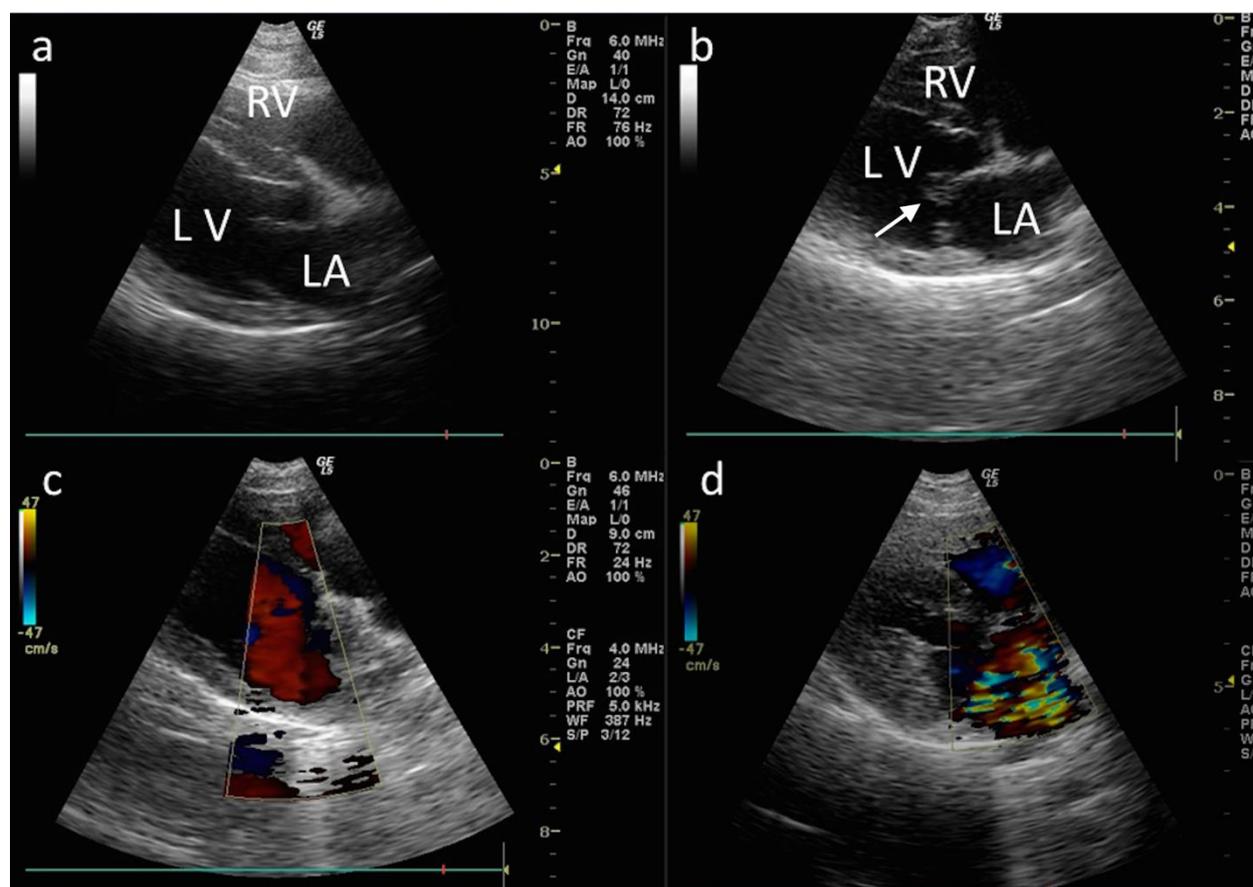


Figure 1 Two dimensional echocardiography, a. Normal mitral valves, b. Degenerative mitral valves (arrow). Color Doppler on 2 dimensional echocardiography, c. Normal valves without regurgitation, d. Degenerative mitral valves with regurgitation.

Echocardiography: All dogs in the control group had normal mitral valve appearance without valve regurgitation. The mitral valve of dogs in the DMVD group thickened. The mitral regurgitation was seen as mosaic color within the left atrium assessed by color Doppler echocardiography (Fig 1).

Four dogs in the DMVD group had left atrium enlargement. Two dogs had left ventricular

enlargement. Six dogs had both left atrium and ventricular enlargement and 4 dogs had normal heart size. Based on the echocardiographic examination, the means of LA/Ao ratio and LVIDd index were significantly higher in the DMVD group compared to the control group. The mean of %FS of the control group was less than that in the DMVD group. The other echocardiographic values including IVSd index,

IVSs index, LVPWd index, LVPWs index, and LVIDs index were not significantly different between the control and DMVD groups. The echocardiographic values are presented in Table 2.

Systolic blood pressure: Based on the oscillometric method, the systolic blood pressure in the DMVD group was significantly higher than that in the control group (Fig 2). On the other hand, the systolic blood pressure measured by the Doppler ultrasonic method in the DMVD group was higher but not significantly different from the control group (Fig 3). The average values of systolic blood pressure measured by the oscillometric and Doppler ultrasonic methods are presented in Table 3.

Three dogs in the DMVD group had systolic blood pressure measured by the Doppler ultrasonic method higher than 160 mmHg. None of the dogs in the DMVD group had systolic blood pressure higher than 160 mmHg when measured by the oscillometric method. All of the dogs in the control group had systolic blood pressure less than 160 mmHg measured by both techniques. Comparing the systolic blood pressure measured by the 2 methods, the average value from the Doppler ultrasonic method was significantly higher than that from the oscillometric method (Table 4). All echocardiographic values in the DMVD group did not correlate with the systolic blood pressure measured by both methods.

Table 2 Echocardiographic values in control and DMVD groups

Parameter	Control (n=16)	DMVD (n=16)	p-value
IVSd index (mm/Kg)	1.49±0.17	1.48±0.12	0.965
LVIDd index (mm/Kg)	4.25±0.32	5.70±0.52	0.026*
LVPWd index (mm/Kg)	1.36±0.13	1.29±0.13	0.733
IVSs index (mm/Kg)	1.96±0.17	2.12±0.20	0.572
LVIDs index (mm/Kg)	2.70±0.21	3.14±0.33	0.274
LVPWs index (mm/Kg)	1.84±0.18	1.97±0.20	0.634
LA/Ao	1.34±0.03	1.68± 0.09	0.002**
%FS	37.69±2.00	45.06±2.40	0.027*

Data are presented as mean±SEM; *indicates significantly different $p<0.05$; **indicates significantly different $p<0.01$. DMVD, degenerative mitral valve disease; IVSd, interventricular septal thickness at end-diastole; LVIDd, left ventricular end-diastole dimension; LVPWd, left ventricular posterior wall thickness at end-diastole; IVSs, interventricular septal thickness at end-systole; LVIDs, left ventricular end-systole dimension; LVPWs, left ventricular posterior wall thickness at end-systole; LA/Ao, left atrial to aortic root ratio; %FS, fractional shortening

Table 3 Comparison of systolic blood pressure between control and DMVD groups measured by oscillometric and Doppler ultrasonic methods

Parameter	Control (n=16)	DMVD (n=16)	p-value
Oscillometer (mmHg)	105.9±2.5	113.0±2.0	0.035*
Doppler (mmHg)	129.8±3.4	139.9±8.3	0.270

Data are presented as mean±SEM.
* indicates significantly different $p<0.05$.

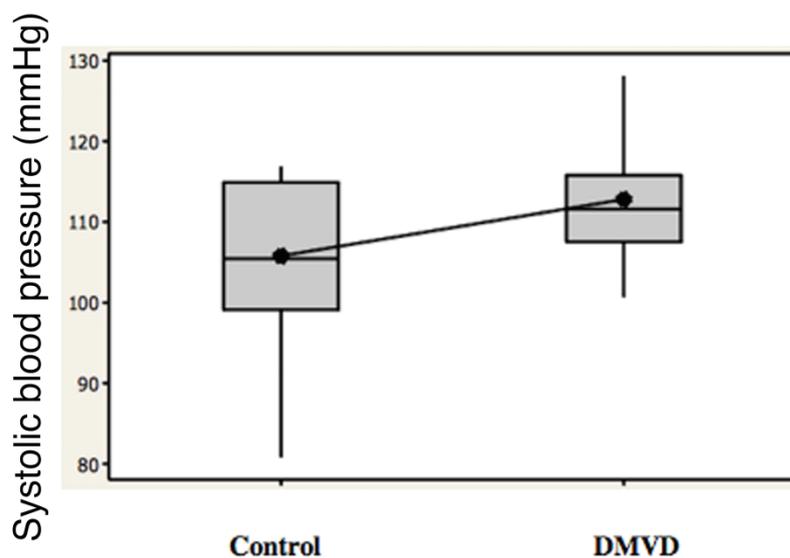


Figure 2 Boxplot of systolic blood pressure (mmHg) in control and DMVD groups measured by oscillometric method. The line within the box represents the mean value; the limits of the box represent the 25th and 75th percentile value.

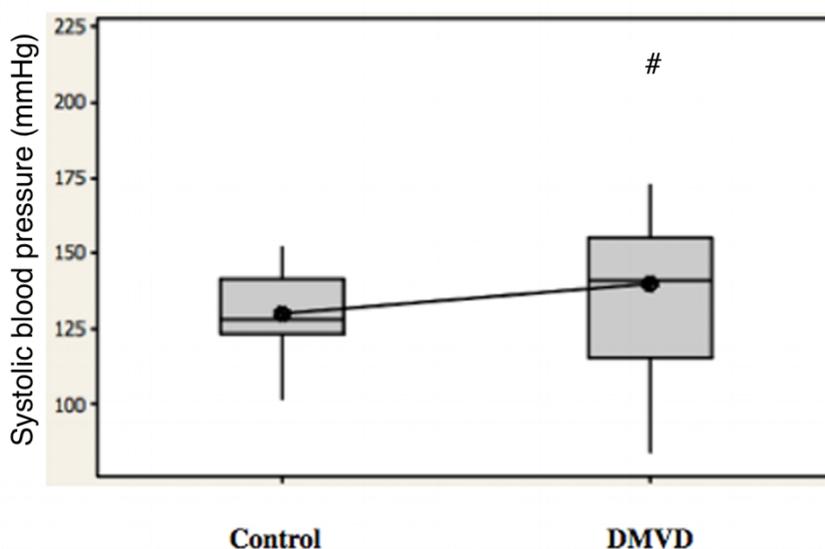


Figure 3 Boxplot of systolic blood pressure (mmHg) in control and DMVD groups measured by Doppler method. The line within the box represents the mean value; the limits of the box represent the 25th and 75th percentile value. The outlier value (>1.5 interquartiles) is shown as #.

Table 4 Comparison of systolic blood pressure measured by oscillometric and Doppler ultrasonic methods in control and DMVD groups

Group	Oscillometer (mmHg)	Doppler (mmHg)	p-value
Control (n=16)	105.9±2.5	129.8±3.4	0.0001**
DMVD (n=16)	113.00±2.0	139.9±8.3	0.006**

Data are presented as mean±SEM.
** indicates significantly different $p < 0.01$.

Discussion

The main finding of this study was that the asymptomatic DMVD dogs had a slightly higher systemic blood pressure than the normal dogs; however, it was considered clinically insignificant. Some dogs with asymptomatic DMVD might have

systemic hypertension. In addition, there was no correlation between the blood pressure levels and echocardiographic values.

DMVD is the most common cardiac disease in dogs. It is currently the number one cause of mitral valve regurgitation and left sided congestive heart failure. Once the valves degenerate, the leaflets thicken

and cannot close properly resulting in mitral valve regurgitation and congestive heart failure in the late stage of disease (Carr and Egner, 2009). Systemic blood pressure has effects on disease severity, and vice versa. An increase in systolic blood pressure can worsen the disease severity by increasing afterload, reducing forward stroke volume and increasing regurgitant blood flow back to the left atrium (Gaasch and Meyer, 2008; Atkins et al., 2009; Suzuki et al., 2012). On the other hand, an increase in regurgitant volume back to the left atrium can reduce the forward stroke volume and cause blood pressure to drop. Considering the roles of blood pressure on the disease status, ACVIM encourages monitoring blood pressure levels in dogs affected with DMVD (Atkins et al., 2009). Petit et al. (2013) reported systolic blood pressure in dogs with degenerative mitral valve disease under medical treatment for heart failure. However, the data of blood pressure level in newly diagnosed DMVD dogs particularly stage B or asymptomatic DMVD dogs are still lacking.

Normal reference values of blood pressure in dogs are different depending on size, measurement methods, and animal handling condition (Brown et al., 2007). Moreover, there are several factors that have effects on the blood pressure level including age, weight, and breeds. The present study was created by controlling all of those factors by matching age, weight and breeds of dogs in the control and disease groups. Unfortunately, the age of dogs in the DMVD group was significantly higher than that in the control group. However, this age difference was not considered clinically meaningful because all dogs in both groups were older than 6 years and categorized as senior or geriatric dogs (AAHA, 2005). The correlation between age and systolic blood pressure was not found in the population of dogs in the present study.

All dogs in this study were small breeds. The most represented breed of dogs in the DMVD group was Poodle (8/16). This is different from other DMVD studies in Europe and USA in which the most common breeds were Cavalier King Charles spaniels and Dachshunds (Häggström et al., 2004; Häggström et al., 2005). It is probably because Poodle is the most popular breed in Thailand particularly in the metropolitan area. Although the present study included several breeds of dog, the breed variation did not affect the result because in both study groups all dogs were small breeds predisposed to DMVD. The weight of dogs is another factor that can affect blood pressure. Obese dogs may have higher blood pressure than dogs in normal weight range (Brown et al., 2007). The weight effect in the present study was also excluded by matching the same weight range in the two studied groups.

There are two methods of blood pressure measurement, direct and indirect methods. The *direct method* is a gold standard technique measuring blood pressure from the peripheral artery directly. On the other hand, the *indirect method* is performed by using a device to measure blood pressure outside the vessels. Presently, there are 2 methods of the indirect techniques: oscillometric and Doppler ultrasonic methods. The oscillometric method detects the vibration of artery wall secondary to blood flow, but

the Doppler ultrasonic method detects blood flow by ultrasound transducer. Unlike the Doppler ultrasonic device, which can measure only systolic blood pressure, the Oscillometer can measure systolic, diastolic and mean arterial blood pressure. In terms of accuracy, the value of blood pressure from the Doppler ultrasonic method is closer to the direct method than the Oscillometric method (Haberman et al., 2004; Harberman et al., 2006). The present study showed that the systolic blood pressure measured by the Doppler ultrasonic method was significantly higher than that measured by the oscillometric method in both control and DMVD groups. This finding suggests that blood pressure measurement should be performed by the same method when values need to be compared such in the case of monitoring the result of treatment because values of blood pressure from different types of devices could be different. In this study, the failure of measurement was found more often with the oscillometric method than the Doppler ultrasonic method secondary to the movement of the dogs. In addition, the variation of blood pressure level was also higher in the measurements from the oscillometric method compared to those from the Doppler ultrasonic method.

Presently, there is no consensus for the treatment of DMVD dogs in stage B. As mentioned previously, an increase in blood pressure may affect the disease severity. The prescription of anti-hypertensive or afterload reducer drugs such as angiotensin converting enzyme inhibitor in dogs affected by DMVD in stage B may slow down the disease progression. However, the blood pressure between normal and stage B DMVD dogs has never been compared. The result of this study showed that the systolic blood pressure of the DMVD dogs was higher than that of the normal dogs similar to a previous study by Petit et al. (2013). An increase in blood pressure may be secondary to the compensatory mechanism of the heart to deal with volume overload within cardiac chambers by increasing the force of contraction. An increase in fractional shortening, i.e. increase in contractility, was also noted in the DMVD dogs. However, because the average blood pressure in the DMVD dogs was higher than in the normal dogs only around 10 mmHg, this was considered clinically insignificant. In addition, the average blood pressure level of the DMVD dogs was still in the normal limit (<160 mmHg) (Brown et al., 2007; Henik and Brown, 2008).

Systemic hypertension can be divided into 3 categories: 1) white coat hypertension which is not true systemic hypertension occurring secondary to sympathetic nervous system stimulation arising from fear, nervousness, stress or pain; 2) secondary hypertension which is hypertension secondary to diseases such as kidney disease, diabetes mellitus, hyperadrenocorticism, pheochromocytoma, and hypothyroidism or drug induction such as glucocorticoids, mineralocorticoids, and non-steroidal anti-inflammatory drugs (Brown et al., 2007); and 3) primary or idiopathic hypertension which is hypertension occurring spontaneously by itself with unknown causes. To minimize the white coat effect, all dogs in the present study were allowed to relax for at

least 10-15 min in a quiet room before the blood pressure measurement. Unfortunately, 3 dogs in the DMVD group had blood pressure higher than 160 mmHg, i.e. systemic hypertension.

The cardiac wall thickness assessed by echocardiography can increase secondary to systemic hypertension (Chetboul et al., 2003). None of the dogs in this study had the left ventricular wall thickness higher than the normal limit. In addition, there was no correlation between the systemic blood pressure and echocardiographic values. This is probably because most of the dogs had blood pressure within the normal range. The afterload was probably not high enough to affect the cardiac structural remodeling.

In conclusion, the systolic blood pressure of dogs affected with stage B DMVD is higher than of normal dogs around 10 mmHg which is clinically insignificant. Some dogs in this stage of disease can have high blood pressure. Blood pressure measurement should be monitored in all dogs affected with DMVD, even though the dogs have no clinical signs. Antihypertensive drugs or afterload reducers such as angiotensin converting enzyme inhibitors should be supplemented on a case by case basis to slow down the disease progression and control the systemic hypertension.

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บทคัดย่อ

การเปรียบเทียบระดับความดันโลหิตในช่วงหัวใจหดตัวในสุนัขพันธุ์เล็กปกติและที่เป็นโรคหัวใจไมทรัลเสื่อม

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โรคหัวใจไมทรัลเสื่อมเป็นสาเหตุหลักของการเกิดภาวะลิ้นหัวใจรั่วและหัวใจล้มเหลวในสุนัข ภาวะลิ้นหัวใจรั่วที่เกิดขึ้นอาจส่งผลกระทบต่อความดันโลหิตโดยไม่มีผลต่ออาการแสดงทางคลินิก วัตถุประสงค์ของการศึกษานี้ เพื่อเปรียบเทียบความดันโลหิตในช่วงหัวใจหดตัวระหว่างสุนัขปกติและสุนัขที่ป่วยเป็นโรคหัวใจไมทรัลเสื่อมแต่ยังไม่แสดงอาการ (กลุ่มบี แบ่งโดย ACVIM) และเพื่อศึกษาความสัมพันธ์ระหว่างค่าที่ได้จากการวัดด้วยวิธีคลื่นเสียงสะท้อนความถี่สูงและระดับความดันโลหิต ทำการวัดความดันโลหิตในช่วงหัวใจหดตัวในสุนัขพันธุ์เล็กที่น้ำหนักน้อยกว่า 10 กิโลกรัม โดยเป็นสุนัขปกติ 22 ตัว และสุนัขที่ป่วยด้วยโรคหัวใจไมทรัลเสื่อมแต่ยังไม่แสดงอาการ 21 ตัว พบว่าค่าเฉลี่ยความดันโลหิตในช่วงหัวใจหดตัวที่วัดจากเครื่องดอปเพลอร์และออสซิลโลมิเตอร์ในกลุ่มสุนัขที่เป็นโรคหัวใจไมทรัลเสื่อมมีค่าสูงกว่าสุนัขปกติ สุนัข 3 ตัวในกลุ่มที่เป็นโรคหัวใจไมทรัลเสื่อมมีระดับความดันโลหิตในช่วงหัวใจหดตัวมากกว่า 160 มิลลิเมตรปรอท ค่าที่ได้จากการวัดด้วยวิธีคลื่นเสียงสะท้อนความถี่สูงไม่มีความสัมพันธ์กับระดับความดันโลหิต โดยสรุปความดันโลหิตในสุนัขที่เป็นโรคหัวใจไมทรัลเสื่อมแต่ยังไม่แสดงอาการอยู่ในระดับที่ไม่ต่ำกว่าปกติ สุนัขบางตัวที่เป็นโรคหัวใจไมทรัลเสื่อมอาจมีระดับความดันโลหิตในช่วงหัวใจหดตัวที่สูงกว่าปกติได้

คำสำคัญ: ความดันโลหิต โรคหัวใจไมทรัลเสื่อม สุนัข

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