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Determination of left atrial volume in healthy dogs and dogs with myxomatous mitral valve disease[1]

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ABSTRACT.- Franco R.P., Zacche E., Camacho R.R., Sousa M.G. & Camacho A.A. 2016. **Determination of left atrial volume in healthy dogs and dogs with myxomatous mitral valve disease**. *Pesquisa Veterinária Brasileira 36(8):743-748.* Departamento de Ciências Agrárias e Veterinária, Universidade de Marília, Avenida Hygino Muzzi Filho 1001, Campus Universitário, Marilia, SP 17525-902, Brazil. E-mail: vetrpf@yahoo.com.br

The left atrial volume (LAV) can be obtained using the biplane Simpson's method via echocardiography. Although in medicine this parameter has been considered to be a prognostic marker of left atrial enlargement in several cardiac diseases, in dogs with myxomatous mitral valve degeneration (MMVD), a valvulopathy characterized by left atrial (LA) volume overload, atrial enlargement is usually assessed by the LA-to-Aorta ratio (LA:Ao). Therefore, the body surface area (BSA)-indexed LAV was measured in healthy dogs and in dogs with MMVD using the biplane Simpson's method. For this purpose, a total of 107 healthy dogs (control) and 81 dogs with MMVD in ACVIM stages B1, B2 and C were assessed, with LAV being calculated during atrial diastole (d) and systole (s) through the biplane Simpson's method. Two-dimensional apical four-chamber (4C) and two-chamber (2C) images were obtained in every dog through the left parasternal window. The values obtained from healthy dogs were correlated with body weight using Pearson's test. An analysis of variance (ANOVA) and Tukey's test were used to compare healthy and MMVD dogs, as well as to investigate differences according with MMVD stages. A strong positive correlation was documented between either LAVd ($r > 0.77$) or LAVs ($r > 0.73$) and body weight in healthy dogs. The BSA-indexed LAV calculated for MMVD dogs was significantly different ($p<0.01$) from that obtained for the control group. Also, LAV was significantly different ($P<0.05$) when stages B2 and C, and B1 and C were compared. In conclusion, this study provided a reference for left atrial volume and the applicability of this technique to assess atrial overload in dogs with varying-stage MMVD.

INDEX TERMS: Volume, left atrial, endocardiosis, dogs.

RESUMO.- [**Determinação do volume atrial esquerdo em cães sadios e portadores da degeneração mixomatosa da válvula mitral.**] A mensuração do volume atrial esquerdo (VAE) pode ser obtido pelo método biplanar de Simpson via ecocardiografia. Embora na medicina tal parâmetro venha sendo considerado um marcador prognóstico da sobrecarga atrial esquerda em várias cardiopatias, nos cães com degeneração mixomatosa da válvula mitral (DMVM), valvulopatia caracterizada pela sobrecarga do átrio esquerdo (AE), a avaliação da sobrecarga atrial é realizada rotineiramente apelas pela relação entre o diâmetro do AE e da artéria Aorta (Ao) (AE:Ao). Portanto, procurou-se mensurar os valores do LAV indexados à área de superfície corporal (ASC) em cães sadios e em portadores da DMVM utilizando-se do método biplanar de Simpson. Para tanto, foram avaliados 107 cães sadios (controle) e 81 portadores da DMVM nos estágios B1, B2 e C (ACVIM), sendo o VAE calculado nos momentos da diástole (d) e sístole (s) atrial utilizando o método biplanar de Simpson. Imagens bidimensionais apicais quatro (4C) e duas câmaras (2C) foram obtidas pela janela paraesternal esquerda em todos os cães. Os valores do LAV

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nos cães sadios foram correlacionados com o peso corporal utilizando o teste de Pearson. Para a comparação dos cães sadios com os portadores da DMVM, bem como para investigar diferenças atribuídas aos diferentes estágios da DMVM, empregou-se análise de variância (ANOVA) e o teste de Tukey. Uma correlação positiva forte foi identificada entre VAEd (r>0,77), VAEs (r>0,73) e o peso corporal dos cães sadios. O LAV indexado pela ASC calculado para os cães portadores de DMVM foi significativamente diferente (p<0,01) daquele obtido no grupo controle. Também foram observadas diferenças significativas (p<0,05) no VAE quando as classes B2 e C, e B1 e C foram comparadas. Em conclusão, este estudo fornece uma referência para o volume atrial esquerdo e a aplicabilidade dessa técnica para avaliação da sobrecarga atrial em cães com DMVM em diferentes estágios.

TERMOS DE INDEXAÇÃO: Volume, átrio esquerdo, endocardiose, cães.

INTRODUCTION

The left atrium (LA) is considered a blood vessel that guides the flow coming from the pulmonary veins into the left ventricle during the diastolic phase. Its remodeling is a chronic reflection of the overload caused by cardiovascular or hidden diseases, which may clinically characterize a significant risk of adverse consequences for the patient. Therefore, LA measurement is a key requirement in transthoracic echocardiography when conducting cardiological assessment in humans (Jiamsripong et al. 2008), especially in patients with atrial fibrillation, cardiomyopathies, valvular insufficiencies, and left ventricular diastolic dysfunction (Lang et al. 2005).

Two-dimensional (2D) methods have been used increasingly to assess LA diameter, due to its applicability in echocardiographic routine (Abhayaratna et al. 2006), noting that atrial dilation does not occur in an uniform fashion, with strong variations in its shape and size. Thus, alternatively to left atrial size one can measure its volume, a volumetric measurement obtained by measuring multiple plans aiming to detect atrial enlargement more precisely than by using parameters obtained by two-dimensional method, such as the ratio between the diameters of the LA and the Aorta (LA:Ao), which is a single linear atrial dimension (Hansson et al. 2002) used to indirectly assess left atrial enlargement in several heart diseases (Franco et al. 2011). The tests that accurately determine the values of the left atrial volume (LAV) and area, known as "gold standards", are: magnetic resonance imaging (MRI), computed tomography (CT) and 3D echocardiography (Poutanen et al. 2003). However, there are some differences regarding the atrial volumes obtained from these tests in comparison with two-dimensional (2D) echocardiography, which underestimates the values when compared to MRI and CT (Tsang et al. 2012).

The American Society of Echocardiography recommends the use of biplanar 2D echocardiography, using disks (modified Simpson's rule) or the area-length method to determine and assess LA volume and area (Lang et al. 2005). Simpson's technique can be used in either uniplanar or biplanar mode, and considers that the total volume of a figure is the sum of the volumes of its smaller parts. Also, because the results obtained by this method are not influenced by the geometric deformations of the LA, it is considered one of the most appropriate methods to calculate volumes from two-dimensional measurements (Boon 1998, Kienle & Thomas 2004).

In veterinary medicine, recent scientific studies that used the area-length biplane method have found left atrial volume values of 0.92 mL/kg in Beagle dogs and 1.1 mL/kg in other breed dogs, with variations been documented in relation to breed size, age and body weight (Wesselowski et al. 2014). Since myxomatous mitral valve degeneration (MMVD) is characterized by a chronic left atrial overload, besides being a highly prevalent cardiac disease in older dogs, the aim of this investigation was twofold: to calculate the left atrial volumes and area in healthy dogs and those with MMVD using Simpson's biplane method and to check whether a correlation exists between left atrial volume and body surface area.

MATERIALS AND METHODS

After granting approval from the institutional Animal Welfare and Ethics Committee (007820/13), this prospective cross-section observational investigation recruited supposedly healthy dogs (1-8 years old; 1-30 kg). When evaluating the dogs, healthy (normal) animals were those in which no alterations could be documented in clinical parameters, including heart rate, respiratory rate, rectal temperature, mucous membranes color, capillary refill time, cardiac auscultation, and systolic blood pressure (Camacho & Mucha 2004), the latter measured through a non-invasive method using a Doppler ultrasound device[5]. Unchanged blood count and serum biochemical tests (Thrall 2007), electrocardiographic tracing (Tilley 1992) and echocardiography (Boon 1998) were also considered, confirming the absence of any cardiac disease. Also, obese dogs and those with respiratory, endocrine, gastrointestinal or oncologic diseases were excluded from this study.

For the dogs with no cardiovascular impairment, the body surface area (BSA) was calculated and the echocardiographic assessment of left atrium included the calculation of LA area and volume using Simpson's biplane method. These results were subdivided in accordance with the animal's body weight,: **G1** was composed of dogs weighing up to 10 kg, **G2** was composed of dogs weighing between 10.1 and 15 kg, **G3** was composed of dogs weighing between 15.1 and 20 kg, and **G4** was composed of dogs weighing between 20.1 and 30 kg.

Body surface are was also calculated for MMVD dogs, which were subdivided in accordance with the classification proposed by the American College of Veterinary Internal Medicine (ACVIM) in 2009. Therefore, LA area and volume were calculated for dogs with MMVD in stages B1, B2 and C. Stage B1 dogs were had a systolic murmur heard best over the mitral auscultatory area, were completely asymptomatic, and showed no evidence of cardiac remodeling either on chest radiographs or the echocardiogram. On the other hand, stage B2 dogs had a murmur heard best over the mitral area, were asymptomatic, but exhibited cardiomegaly on chest radiographs (VHS>10.5), as well as an increased LA-to-Aorta ratio (>1.5) and left ventricular remodeling on the echocardiogram. Finally, stage C dogs had a systolic murmur heard best over the mitral area, overt clinical signs of congestive heart failure (CHF), and cardiomegaly documented on chest radiographs and echocardiogram. All dogs that were later determined to be in stage D, to have any other cardiac disease or have been given any medication were excluded from the study.

[5] Doppler Flow Detector 811-B - Parks.

In either group, LA area and volume of dogs were determined using the Simpson's biplane method (Tsang et al. 2002), which is based on planimetry, as recommended by the American Society of Echocardiography (Lang et al. 2005). To do so, both apical four--chamber (4C) and two-chamber (2C) images were acquired from the left parasternal window. By rotating the transducer 90 degrees from the apical 4C image, an apical 2C image was produced and a larger area of the left atrium and ventricle became visible.

Once the mitral valve closure was identified on the apical 4C imagem, the entire atrial endocardial route was demarcated during atrial diastole (d) and systole (s). The diastole and systole phases were identified from a simultaneous electrocardiogram, where diastole is the period of left atrial distension at the end of ventricular systole, and atrial systole is the period of atrial contraction (active ventricular filling) identified in the electrocardiogram as final the duration of the wave P. Endocardial demarcation began in the septal leaflet towards the parietal leaflet of the mitral valve, with the exclusion of the left atrial appendage and the confluence of pulmonary veins. After demarcation, the length between the posterior wall of the left atrium and the closure of the mitral leaflets was measured. Once the apical 2C image was obtained, the area and volume of the left atrium were calculated again during the first atrial systole and diastole, as described before (Figure 1).

Based on the LA demarcation at the apical 4C and 2C views, the left atrial volume (mL) was measured during atrial diastole (LAVd) and systole (LAVs), and the difference between these values (DLAVd/s) was calculated. Also, the LA areas during diastole (LAd) and systole (LAs) were measured (cm^2) in both apical views (4C and 2C). Data concerning LA volume (mL) and area (m^2) were classified, analyzed and indexed in accordance with the BSA (m^2) of the dogs, therefore producing the following parameters: LAVd/BSA (mL/m^2), LAVs/BSA (mL/m^2), DLAVd/s-BSA (mL/m^2), LAd/BSA-4C (cm^2/m^2), LAs/BSA-4C (cm^2/m^2), LAd/BSA-2C (cm^2/m^2), and LAs/BSA-2C(cm^2/m^2).

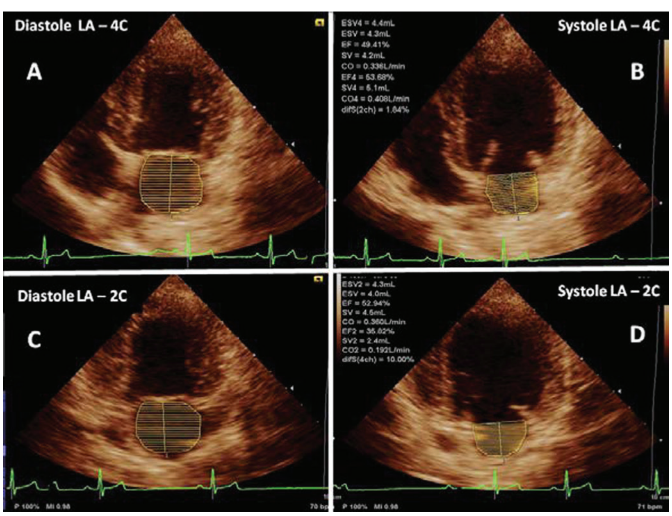

Fig.1. Sequence of images obtained from the left parasternal window in a 4.5 kg dog undergoing the measurement of left atrial volume using Simpson`s biplane method. (**A**) LA in diastole in an apical 4C view; (**B**) LA in systole in an apical 4C image; (**C**) LA in diastole in an apical 2C view; (**D**) LA in systole in an apical 2C image.

RESULTS

The data obtained in this study were statistically analyzed using a statistical analysis software called Minitab (version 14), calculating the repetitive averages, 95% confidence intervals, and positive Anderson-Darling Normality Test of the variables related to LA volume and area in dogs included in the control group. In addition, LAV and LA area variables were indexed by BSA using Pearson's correlation coefficient for the body weight of dogs included in the control group in relation to LAV and LA area. For dogs with MMVD according to CHF functional classes, the values of the evaluated echocardiographic variables were indexed by BSA and compared to those obtained from the dogs included in the control group, using the analysis of variance for repeated measures with grouping factor, comparing the arithmetic means by Tukey's test; where the differences between the values were considered significant when p<0.05.

A total of 107 healthy dogs were assessed and included in the control group. This total included 43 males and 64 females, aged 3.5 to 6 years, weighing on average 13.0±5.5 kg. Several breeds were represented, including Beagles (n=45; 42%), Poodles (n=12; 11.7%), Pinschers (n=10; 9.0%), Cocker Spaniels (n=6; 5.6%), Rottweilers (n=3; 2.8%), and Bull Terriers (n=1; 0.9%). mixed-breed animals (n=30; 28%) represented the second most prevalent population of healthy subjects in this study. Concerning the dogs with MMVD, of the 81 dogs enrolled into this investigation, 20 dogs were classified in stage B1 [7.5 to 9 years, 15.1±8 kg, 65% males (n=13) and 35% females (n=7)], 36 dogs in stage B2 [8.7 to 11 years, weighing 9.7±4.5 kg, 55.5% females (n=20) and 45.5% males (n=16)]; and 25 in stage C [11 to 15 years, 6.8±4.8 kg, 66% males (n=14) and 44% females (n=11)]. Breeds most represented in the MMVD group were Poodle (n=45; 56%), Pincher (n=17; 21%), Lhasa-

Table 1. Mean values and standard deviations of left atrial volume and area parameters obtained in healthy dogs (control group), subdivided in accordance with body weight

Parameter	G1: up to 10 kg (n=35)	G2: 10.1 to 15 kg (n=39)	G3: 15.1 to 20 kg (n=19)	G4: 20.1 to 30 kg (n=14)
LAVd (mL)	5.6±1.4^{A}	8.9±2.4^{B}	13.0±1.7^{C}	13.8 ±2.4^{C}
LAVs (mL)	2.8±0.9^{A}	5.5±1.7^{B}	7.8±0.6^{C}	7.7±1.0^{C}
DLAVd/s(mL)	2.8±0.9^{A}	3.3±1.4^{A}	6.0±1.3^{B}	6.3±1.9^{B}
LAd - 4C (cm2)	3.5±0.9^{A}	5.5±1.5^{B}	6.5±1.7^{B}	7.1±1.1^{C}
LAs - 4C (cm2)	2.2±0.8^{A}	4.0±0.9^{B}	4.7±1.2^{B}	5.4±1.3^{C}
LAd - 2C (cm2)	3.0±1.0^{A}	4.8±1.6^{B}	6.2±1.7^{C}	6.6±1.1^{C}
LAs - 2C (cm2)	1.9±0.6^{A}	3.7±1.2^{B}	4.5±2.6^{C}	5.1±1.3^{C}

LAVd = LA volume during diastole; LAVs = LA volume during systole; DLAVd/s = difference between diastolic and systolic volumes; LAd = LA area during diastole; LAs = LA area during systole; 4C = four-chamber view; 2C = two-chamber view. * Means followed by the same capital letters in the same row are not significantly different by Tukey's test.

Table 2. Confidence intervals, mean values, and percentiles of the body-weight indexed left atrial volume and area parameters obtained in healthy dogs (control group)

Parameter	95% CI	Mean	25th Percentile	75th Percentile	Normality
LAVd/BSA (mL/m2)	15.6-16.9	16.3+/-3.4	13.6	19.0	0.88
LAVs/BSA (mL/m2)	8.6-9.5	9.1 +/-2.9	7.5	10.8	0.77
DLAVd/s BSA (mL/m2)	8.5-9.5	7.9 +/-2.5	7.2	10.7	0.88
LAd/BSA - 4C (cm2/m2)	9.08-10.1	9.5 +/-2.3	7.9	11.3	0.18
LAs/BSA - 4C (cm2/m2)	8.01-8.9	8.4 +/-2.1	7.8	0.1	0.64
LAd/BSA - 2C (cm2/m2)	6.3-7.1	6.7 +/-2.0	4.9	8.02	0.84
LAs/BSA - 2C (cm2/m2)	7.7-8.7	8.2 +/-2.5	6.3	10.2	0.23

LAVd = LA volume during diastole; LAVs = LA volume during systole; DLAVd/s = difference between diastolic and systolic volumes; LAd = LA area during diastole; LAs = LA area during systole; 4C = four-chamber view; 2C - two-chamber view. *p<0.005 represent the values outs.de the normal distribution.

Table 3. Mean values and standard deviations of body-weight-indexed left atrial volume and area parameters in healthy (control group) and varying stage MMVD dogs

Parameter	Control Group (n=107)	95% CI	B1 (n=20)	B2 (n=36)	C (n=25)	*P*
LAVd/BSA (mL/m2)	16.3 ± 3.4^{A}	15.4-19.9	18.8 ± 2.4^{Aa}	21.7 ± 4.0^{Ba}	60.2 ± 10.1^{Bb}	0.0001
LAVs/BSA (mL/m2)	9.1 ± 2.9^{A}	8.6-9.5	11.8 ± 3.8^{Aa}	14.4 ± 2.2^{Ba}	37.3 ± 8.1^{Bb}	0.0001
DLAVd/s-BSA (mL/m2)	7.2 ± 2.5^{A}	8.5-9.5	7.7 ± 2.6^{Aa}	7.1 ± 3.5^{Aa}	23.1 ± 9.4^{Bb}	0.005
LAd - 4C/BSA (cm2/m2)	9.5 ± 2.6^{A}	9.1-10.2	9.9 ± 1.1^{Aa}	12.3 ± 4.2^{Ba}	27.1 ± 2.3^{Bb}	0.0001
LAs - 4C/BSA (cm2/m2)	8.4 ± 2.1^{A}	7.1-8.2	7.4 ± 1.5^{Aa}	9.2 ± 2.9^{Aa}	19.9 ± 6.9^{Bb}	0.0001
LAd - 2C/BSA (cm2/m2)	6.7 ± 2.0^{A}	6.3-7.12	10.1 ± 1.5^{Ba}	14.3 ± 2.7^{Bb}	18.2 ± 2.9^{Bc}	0.005
LAs - 2C/BSA (cm2/m2)	8.2 ± 2.5^{A}	8.7-9.3	7.2 ± 1.3^{Aa}	7.9 ± 3.5^{Ba}	19.5 ± 4.9^{Bb}	0.005

LAVd = LA volume during diastole; LAVs = LA volume during systole; DLAVd/s = difference between diastolic and systolic volumes; Lad = LA area during diastole; LAs = LA area during systole; BSA = body surface area; 95% CI = 95% confidence interval p<0.05 present a significant difference at 5%; p<0.01 present a significant difference at 1; * Comparison between healthy and diseased animals: means followed by the same capital letters in the same row are not significantly different by Tukey's test; ** Comparison between stages in MMVD dogs: means followed by the same lowercase letters in the same row are not significantly different by Tukey's test.

-Apso (n=3; 4%); Shih-Tzu (n=3; 4%), Cocker Spaniel (n=2; 2%), as well as mixed-breed dogs (n=11; 13%).

Data obtained in the control group subdivided in accordance with body weight indicated a progressive and significant increase in left atrial values as the canine body weight increased (Table 1), except for groups G3 (15.1 to 20 kg) and G4 (20.1 to 30 kg), which attained no differences in five out of seven parameters. The results were confirmed by the significant correlation between both LA volume and LA area and the body weight of the assessed dogs [LAVd (r=0.77), LAVs (r=0.73), DLAVd/s (r=0.65), LAd-4C (r=0.69), LAs-4C (r=0.59), LAd-2C (r=0.52) and LAs-2C (r=0.55)]. Therefore, all parameters related to LA volume and area were indexed to BSA, all of which presented a normal statistical distribution (Table 2).

Following, the results obtained in the control group were compared with those of dogs with MMVD, indicating a significant differences to exist between them. In addition, significant differences were found when the parameters obtained in dogs in either stage B1 or stage B2 were compared with those in stage C, as shown in Table 3.

DISCUSSION

Simpson's biplane method allows the calculation of LA volume and area. It is recommended that these results be indexed by BSA to be used as a prognostic factor in patients with MMVD (Pritchett et al. 2003, Tourneau et al. 2010). The acquisition of data in this investigation followed the recommendation from the American Society of Echocardiography to calculate LAV by Simpson's biplane method using apical images obtained from the left parasternal window (Tsang et al. 2002, Lang et al. 2005).The results obtained are similar to those reported in people by Maréchaux et al. (2010), who considered Simpson's technique as an appropriate method to determine LA overload in patients with MMVD, as well as by Tsang et al. (2012), that recommended using a two-dimensional-derived volumetric method to assess left atrial overload instead of standard linear measurements.

Because the healthy dogs recruited for this study were divided into subgroups in accordance with body weights, a progressive increase in LA volume and area could be demonstrated. The indexation of these two parameters by BSA was already considered appropriate (Gaasch & Zile 2004), and was performed and confirmed by the results of this study. However, differences were not observed for any parameter in the group of dogs that weighed 15 to 30 kg. This interesting finding might be explained because only a few dogs were included in that group as compared to the others.

On the subject of LAV indexation, Pritchett et al. (2003) reported results similar to those obtained in this study, indicating that body weight is the most appropriate method to regulate the relationship between LAV and the patient's body. This information is corroborated by Gottdiener et al. (1997), who described the influence of body weight on left atrial diameter in people with no cardiovascular diseases. Recently, Höllmer et al. (2013) studied the LAV in healthy dogs using the two-dimensional area-length method, and observed significant differences among the assessed dog breeds. These results were also observed by Wesselowski et al. (2014) who reported a change in the LAV of 0.45mL/kg in normal dogs and also among executors upon measuring echocardiographic values. These results reinforce the recommendation to index the studied variables by BSA in order to obtain consistent values, as conducted in this research.

LA remodeling is a chronic reflection of volume overload caused by cardiovascular or hidden diseases, and may clinically represent a significant risk of adverse consequences for the patient. In veterinary medicine, assessment of left atrial overload is performed by measuring the diameter of the LA and the LA-to-Ao ratio, obtained by either through two-dimensional or M-mode echocardiography (Rishniw & Erb 2000). However, these parameters only represent an indirect and subjective assessment, as it determines the incomplete atrial size, since only a single extension of the atrial body is measured, which underestimates the obtained values. Therefore, it is recommended to study LAV and LA area using Simpson's biplane method.

In this study, the obtained results were not compared with the standard values from the tests considered to be "gold standard" for LA volume measurement, such as MRI and CT. These comparisons would indicate real LAV values and differences from volumes obtained by 2D echocardiography. In human beings, reported lower LA volumetric values when comparing 2D and 3D echocardiography with MRI. Thus, further research should be conducted in order to clarify the possible variations, always aiming to improve the MMVD prognosis using volumetric methods in transthoracic echocardiography (Jiamsripong et al. 2008).

In dogs with MMVD, the conventional assessment of LA, which includes the calculation of LA-to-Ao ratio using either two-dimensional or M-Mode echocardiography, allows a subjective differentiation among CHF functional classes (Franco et al. 2011, Prada et al. 2012). In turn, measuring LA volume and area through the method indicated in this study allows a more precise assessment of LA overload in dogs with MMVD, as it calculates the area and volume of the left atrial chamber. That is different than conducting a linear and single measurement of the inner diameters of LA and aorta, or the LA-to-Ao ratio (Hansson et al. 2002). Wesselowski et al. (2014) confirmed the low predictive correlation of left atrial overload among the LA-to-Ao ratio values and the atrial volume measured by the biplane area-length method in dogs with MMVD, noting that the values of mild LA volumetric overload are higher in comparison with those identified via the LA-to-Ao ratio.

By comparing the healthy and MMVD dogs, this study found LA overload to increase as CHF syndrome intensifies, characterizing the progressive nature of the valvulopathy and contributing to the deterioration of the clinical prognosis. In a study in which 492 individuals were enrolled, Tourneau et al. (2010) documented the inverse correlation between LAV/BSA and the survival of patients with MMVD, which reinforce the need to incorporate volumetric methods in the standard echocardiographic assessment.

With the indexation of the obtained values by BSA, we excluded the effect of body weight variation among the assessed dogs, seeking to indicate LA remodeling in accordance with the varying disease stages regardless of body weight. Thus, the results of this study confirm the variation in LA as MMVD progresses, corroborating the findings of Borgarelli et al. (2008) and Franco et al. (2011), who assessed LA-to-Ao ratio in dogs with MMVD and found that parameter to indicate the progression of such disease. However, we emphasize that the LA-to-Ao ratio refers to subjective values which might fluctuate in accordance with the technique used for its calculation. Also, it is solely indicated to monitor the progression of the valvulopathy instead of being used as a predictive and prognostic surrogate.

By comparing the values of LA volume and area among MMVD in stages B1, B2 and C, our results point to the activation of compensatory CHF mechanisms chronically as the severity of the disease increases and clinical signs become overt. In stage C dogs, LA volume and area were approximately three-fold higher than in control group, and two-fold higher than stage B1 and B2 dogs. Similar results were found by Tanabe et al. (2007) when studying LAV as a predictor of atrial fibrillation in patients with severe MMVD. They indicated that LAV and LA area in people with sinus rhythm were two-fold lower than in patients with atrial fibrillation. When using the biplane area-length method, Wesselowski et al. (2014) also documented a significant increase in left atrial volume in MMVD stage C dogs.

Chronic left atrial overload is, in fact, frequent and progressive in MMVD, where atrial complacency becomes an adaptive response to the increasing preload, seeking to minimize the increase in atrial and pulmonary pressure. This fact justifies the progressive and insignificant increase in LAV and LA area valuesobserved by comparing stage B1 and stage B2 dogs. In stage C dogs, which already present clinical signs of CHF, the LAV and LA area are significantly increased when compared with the other disease stages investigated herein. Similar data was described by Tanabe et al. (2007), who reported a LAV/BSA above 75 mL/m^2 as a surrogate for the occurrence of left atrial fibrillation in human beings, while a value of 32 mL/m^2 was documented for healthy men and women, and 60 mL/m^2 for MMVD patients in sinus rhythm. These results were consistent with Wesselowski et al. (2014), who found a weak correlation between LAV and LA/Ao in dogs with no or mild left atrial remodeling (stages B1 and B2), whereas a significant correlation was documented when data from stage C dogs were considered. Nevertheless, using either Simpson's biplane method or the area-length method to obtain LA volumetric measurements shows a greater accuracy in estimating LA overload as compared to the techniques commonly used, therefore providing relevant information concerning clinical management of patients with cardiac diseases (Jiamsripong et al. 2008, Wesselowski et al. 2014).

Unfortunately, LAV parameters obtained in this study using Simpson's biplane method were not compared with results obtained through "gold standard" methods. That would have provided a better identification of similarities, correlations or differences between techniques, as previously documented in people (Kircher et al. 1991, Jenkins et al. 2005). Therefore, it is clear that further studies are necessary in this area. Also, Simpson's biplane method may indicate subjective values, as it manually determines the volume of an irregular and three-dimensional area. However, because the results are not affected by irregularities found in heart chambers (Filho 2006), it is considered to be an appropriate technique to measure LAV in patients with cardiac diseases. Thus, incorporating this methodology in routine echocardiography would likely result in a greater and more reliable assessment of CHF progression.

CONCLUSIONS

Based on the conditions in which the different steps of this assay were conducted, we conclude that Simpson's biplane method may be used to determine left atrial volume in dogs.

In healthy dogs, the mean LAV in diastole was 16mL/m^2, while in systole it was 9mL/m^2.

In MMVD dogs this technique was able to differentiate animals in accordance with the progression of such disease, with the increase in left atrial volume being consistent with the disease functional stages.

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