Clinical, electrocardiographic and echocardiographic profile of dogs with chronic degenerative mitral valve disease, treated at a private service of cardiology and respiratory diseases*

Perfil clínico, eletrocardiográfico e ecocardiográfico de cães com doença crônica degenerativa da valva mitral, atendidos em serviço particular de cardiologia e doenças respiratórias

Mário dos Santos Filho,** Alicia da Silva Bento,** Nathália Marques de Oliveira Lemos,** Karen Denise da Silva Macambira,** Bruno Ricardo Soares Alberigi,** Alexandre José Rodrigues Bendas,** Paulo de Tarso Landgraf Botteon**

Abstract

Chronic degenerative mitral valve disease is the most common acquired heart disease and the main cause of congestive heart failure (CHF) in middle-aged to elderly dogs, being more frequent in small and miniature breeds, being rare in breeds of medium to large size. This disease is characterized by nodular deformity of the valve leaflets, as well as thickening and, in some cases, distension of the chordae tendineae. Echocardiographic findings include cardiomegaly, thickening of the atrioventricular valves, valve insufficiency and myocardial dysfunction, which, in turn, become more common with the progression of the disease. According to the consensus of the American College of Veterinary Internal Medicine, endocardiosis can be classified into stages, according to its clinical evolution. The objective of the present study was to determine the clinical, electrocardiographic, radiographic and echocardiographic profile of dogs with chronic degenerative mitral valve disease in a cardiology service between the years 2017 to 2022. The selected animals were those whose diagnoses involved valve alteration with association with echocardiographic evaluation. The data obtained were compiled in Microsoft Excel® spreadsheets and evaluated using descriptive statistics and Pearson's correlation using the BioEstat® software. Through the observations and results obtained, it was possible to relate that the hypothesis of the correlation between the severity of clinical signs and the exacerbation of the structural alteration of the heart valves may be indicators of a worse prognosis for the evolution of chronic degenerative mitral valve disease.

Keywords: arrhythmia, echocardiogram, heart, murmur.

Resumo

A doença valvar degenerativa crônica de mitral (DVDCM) é a cardiopatia adquirida mais comum e principal causa de insuficiência cardíaca congestiva (ICC) em cães de meia idade a idosos, sendo mais frequente em raças de pequeno porte e miniaturas, sendo rara nas raças de médio a grande porte. Essa doença é caracterizada pela deformidade nodular dos folhetos valvulares, assim como espessamento e, em alguns casos, distensão das cordas tendíneas. Os achados ecocardiográficos incluem cardiomegalia, espessamento das válvulas atrioventriculares, insuficiência valvar e disfunção miocárdica que, por sua vez, tornam-se mais comuns com a progressão da doença. De acordo com o consenso do American College of Veterinary Internal Medicine, a endocardiose pode ser classificada em estágios, de acordo com a sua evolução clínica. O objetivo do presente estudo foi determinar o perfil clínico, eletrocardiográfico, radiográfico e ecocardiográfico de cães portadores de doença valvar degenerativa crônica de mitral em um serviço de cardiologia entre os anos de 2017 a 2022. Os animais selecionados foram aqueles cujos diagnósticos envolveram alteração valvar com associação a avaliação ecocardiográfica. Os dados obtidos foram compilados em planilhas do programa Microsoft Excel® e avaliados por meio de estatística descritiva e correlação de Pearson utilizando o software BioEstat®. Por meio das observações e resultados obtidos, possibilitou-se relacionar que a hipótese da correlação entre gravidade dos sinais clínicos com a exacerbação da alteração estrutural das valvas cardíacas podem ser indicadores de prognóstico pior para a evolução da doença valvar degenerativa crônica de mitral.

Palavras-chave: arritmia, ecocardiograma, coração, sopro.

Introduction

Chronic degenerative mitral valve disease (CDMVD) is the most common heart disease in dogs (CHAMAS et al., 2011; KOVACEVIC et al., 2019). One study suggests that there is a genetic predisposition for the manifestation of the disease (MUZZI et al., 2009). CDMVD is mostly found in dogs, small and miniature breeds, but it can affect dogs of any size and other species (CHAMAS et al., 2011).

The disease is characterized by the deposition of collagen, mucopolysaccharides and glycosaminoglycans in the valve leaflets (SISSON et al., 1999). With this deposit, the valve apparatus begins to change its structure, compromising its coaptation function, allowing blood to flow back through the cardiac chambers, activating the renin-angiotensin-aldosterone system, which is responsible for the progression of the disease (KEENE et al., 2019). On physical examination, the main finding is the presence of systolic murmur in the mitral focus, diagnosed at the time of cardiac auscultation. Alterations in pulmonary auscultation can be perceived mainly in more advanced cases with the presence of fine discontinuous noises characteristic of pulmonary edema (ALMEIDA et al., 2021).

Clinical staging is based on clinical findings and the degree of cardiac remodeling and congestion in which the patient is, and can be classified into: (i) Stage A (includes predisposed races but still without valve alterations); (ii) Stage B, animals with a murmur but without clinical symptoms, being subdivided into B1 (without atrial remodeling or with mild remodeling) and B2 (animals with atrial remodeling that meet the EPIC criteria), (iii) Stage C (dogs that manifest current or past cardiac heart failure) and (iv) Stage D (end-stage CDMVD unresponsive to standard therapy) (KEENE et al., 2019).

The present work consists of a retrospective study, where the analysis of clinical, electrocardiographic, radiographic and echocardiographic alterations related to chronic degenerative mitral valve disease will be carried out.

Materials and methods

A retrospective study was carried out, looking for animals with systolic murmur in the mitral focus with a diagnosis of CDMVD confirmed by echocardiographic examination, seen between March 2017 and March 2022. CDMVD by echocardiographic examination. Forms with incomplete completion were not included.

In all patients, the evaluator was the same, using vascular Doppler to measure blood pressure, with the average of 10 measurements being taken, discarding extreme values (ACIERNO et al., 2018). As for the electrocardiograph equipment, digital equipment from the brand InPulse (Incardio©) was used, using electrodes soaked in alcohol to capture unipolar and bipolar leads, as recommended by Santilli (2020).

The classification of the murmur recommended following staging models, with a grade I-II/VI murmur classified as mild, a grade III-IV/VI murmur moderate, and a grade V-VI/VI murmur a severe murmur (GOMPF, 2002).

The electrocardiographic examination was performed according to Tilley's guidelines (2016). The echocardiogram followed the parameters and scale of BOON (2011).

Data from the animal review, staging of valve disease and echocardiographic changes were compiled in Microsoft Excel® spreadsheets to determine the frequency of echocardiographic changes in animals with murmurs on auscultation, and were evaluated using descriptive statistics using the BioEstat® software. The electrocardiographic findings were described in spreadsheets and recorded as a percentage.

Clinical findings were correlated with each other, considering the analytical statistical analysis of Pearson's correlation, in addition to the use of p-value for some parameters, with a probabilistic value of 0.05.

Results and discussion

After the initial screening of 387 clinical files of dogs and observing the inclusion criteria, 122 dogs were selected to compose the study sample. The average age of the treated animals was 100 ± 10 months, 60.5% females and 39.5% males. This value indicates a statistical difference ($p = 0.45, 0.05$), which may be justified by the fact that the greater number of females assisted is related to the high number of bitches assisted for preoperative examination for mastectomy, which today is one of the main conditions in this age group, which motivate the assessment by the cardiology service for purposes of surgical risk (BORGARELLI & BUCHANAN, 2012; MACHADO et al., 2022).

Approximately 15% of the animals (18/122) were mongrel dogs, followed by Poodle (16/122) and Shih-tzu (13/122). Yorkshire, Maltese and Pug followed, with the same absolute values (11/122). As for the weight, the average of the animals was 8.2 ± 6.1 kg, it being evident that the population is increasingly looking for smaller dogs, since with the verticalization of urban centers, the living spaces are getting smaller. . Data from the studied population are briefly presented in the table below (Table 1).

Table 1: Demographic data of dogs assisted by the private service of cardiology and respiratory diseases.

Total animals (*n*)	*n* sample = 122
average age	100±10 months
Sex	Females –73/122 (60.5%) Males – 49/122 (39.5%)
Breeds	Mixed breeds – 18/122 (15.0%) Poodle - 16/122 (13.0%) Shih Tzu – 13/122 (11.1%) Yorkshire Terrier – 11/122 (9.2%) Maltese – 11/122 (9.2%) Pug – 11/122 (9.2%) Others* – 42/122 (33.3%)

* -Bichon Frize, Boston Terrier, French Bulldog, Chihuahua, Cocker Spaniel, Fox Paulistinha, Jack Russel Terrier, Lhasa Apso, Pomeranian, Maltese, Pinscher, Schnauzer and West Highland White Terrier.

The most prevalent valve disease was the mitral 61.4% (n=75 animals), followed by the association between mitral and tricuspid valve disease with 19.6% (n=24 animals) and only tricuspid valve disease with 19 % (n=23 animals). According to Borgarelli

and Buchanan (2012) it is an acquired disease, degenerative of the mitral valve, which leads to heart failure, characterized by a thickening of the ends of the valve. And from the statistical point of view, 60% of the cases affect the mitral valve, in 30% the two atrioventricular valves and in 10% of the cases only the tricuspid valve, with values close to the data collected by several epidemiological studies in the area being observed (BORGARELLI & BUCHANAN, 2012; KEENE et al., 2019).

On clinical examination, 34% (n=42/122) of the animals presented some degree of murmur on auscultation, however, without hemodynamic alterations on Doppler echocardiographic examination and, therefore, not evaluated regarding the degree of manifestations and their severity, since found hemodynamically compensated and without clinical symptoms related to the disease, being included in stage B1, according to Keene et al. (2019).

Among the animals that had a murmur with hemodynamic repercussions, 65% were identified (n=80/122). Among this group of animals, 25% (20/80) had mild-grade murmur (I-II/VI), 40% (n= 32/80) had moderate-grade murmur (III-IV/VI), and 35% (n= 28/80) had a severe murmur (V-VI/VI). Also discriminating signs such as: cough, cyanosis, and easy tiredness, among the above groups, the patients described with moderate to severe murmur, represent 85% of the findings of these manifestations, making up a marked degree of nosological association for the prognosis and worsening of the disease in cases of greater intensity also described by Häggström et al. (1995) and Bright and Mears (1997). Other authors reported that, with the progression of the murmur, there is an increase in the chances of greater blood reflux and consequent greater congestive condition and more intense clinical manifestations, as in the animals above cited, with chronic valve disease (BORGARELLI; BUCHANAN, 2012).

Mean systemic systolic blood pressure values of the 122 animals was 129±19 mmHg. There was a strong positive correlation between the patient's age and blood pressure (0.752, p=0.041, 0.05%). However, when comparing weight with blood pressure (0.120, p=0.021, 0.05%) and weight with age (0.115, p=0.089, 0.05%), the correlation was negligible. These data are in line with what was previously described relating degenerative kidney diseases, with age as a predisposing factor for the occurrence of chronic kidney disease and endocrinopathies, triggering factors for systemic arterial hypertension in small animals. However, not expected in patients in advanced stages of CDMVD, since a decrease in systemic systolic blood pressure values is commonly reported in these patients (BRIGTH; MEARS, 1997.; PEDERSEN et al., 1999).

The age of the patients in the total sample (n=122) had a moderate correlation with the degree of the murmur (0.678, p=0.034, 0.05%). However, when comparing the mean ages of the animals up to 7 years of age and the degree of the murmur, there is no correlation. This may be related to the cases reported separately, in which older patients with a low degree of murmur may have a slower disease course than compared to "younger" animals within the senile range, where audible murmurs in these patients denote prognosis. and more progressive and rapid progression of the disease. Aspects already described showed that the occurrence of CDMVD mainly affects small breed and male dogs of advanced age, correlating and reinforcing the data shown above (ETTINGER; FELDMAN, 1999; BORGARELLI; BUCHANAN, 2012).

The correlation of the degrees of murmur with blood pressure in the studied population of 122 animals took place gradually, according to the intensity of the murmur, where the following were observed: strong positive correlation of pressure vs light murmur (0.752, p=0.045, 0.05%), moderate correlation with pressure vs moderate murmur (0.655, p=0.034, 0.05%) and strong negative correlation of pressure vs major murmur (-0.812, p=0.065, 0.05%). These data reinforce the information mentioned above, in the context of blood pressure vs age, since what can be observed, in this case, is that with the evolution of the congestive condition, due to the intensity of the murmur being more severe, the greater the drop in blood pressure, resulting from the loss of compensatory mechanisms, which in this context begin to become deleterious (KITTLESON 2005; CASTRO 2009).

The most prevalent finding on respiratory auscultation was increased expiratory noise with 54.1% (n = 65), followed by increased expiratory noise associated with fine discontinuous noise 19.9% (n=24), continuous inspiratory noise 16.8% (n= 19) and fine discontinuous 9.2% (n= 14). Considering the average age of the included dogs, this finding is not surprising, as they are frequent findings in dogs with senile bronchial disease or brachycephalic dog syndrome (CARVALHO et al., 2022).

Cough was present in 85% of the patients, after performing the reflex test, being classified according to the intensity from 1 to 4. There is an evident and remarkable percentage of cough manifestation in the listed patients, requiring more detailed and comparative studies with patients in different degrees, with healthy control group. In addition, excluding pulmonary causes, for this manifestation and, thus, reaching values closer to the expected percentage for dogs with heart disease, even knowing that cough is the main and most related finding by the tutors. In a study comparing the clinical manifestations of dogs with heart disease with dogs infected with *Dirofilaria immitis*, no difference was observed between the groups, with cough being a frequent finding in dogs with heart disease, and common in other diseases, being a nonspecific and frequent sign in dogs (CARVALHO et al., 2022; LEMOS et al., 2022).

Thus, for quantitative correlation purposes, lung sounds were transformed into numerical values regarding findings and intensity, from 0 to 4, and their comparison parallel to cough intensity, making a moderate positive correlation with cough (0.565, p= 0.028, 0.05%). Although the noises may be normal or reveal diffuse crackles, depending on the stage of the disease (PEDERSEN et al., 1999.; WARE 2015; CARVALHO et al., 2022), it was found that the more severe the pulmonary patterns evidenced on auscultation, the more intense and frequent was the manifestation of cough, emphasizing the fact that none of the patients included used antitussive or steroid anti-inflammatory drugs, which could, in a way, mask the values regarding the presentation of this clinical sign (ATAIDE, 2020.; SILVA et al., 2022).

The pulmonary pattern obtained in the analyzes of the radiographic images reports were: bronchial and interstitial pattern 38.5% (n= 47 animals), bronchial, alveolar and interstitial pattern 22.1% (n= 27 animals), bronchial and vascular pattern 18 % (n= 22 animals), interstitial pattern 8% (n= 10 animals) and no change or compatible with senility 13.4% (n= 16 animals). In a comparative way, it was observed that the patterns had a higher incidence and greater severity compared to the animals

with greater clinical alterations, such as the intensity of the cough and lung noise, making up a moderate positive correlation (0.614, p= 0.034, 0.05% and 0.514, p= 0.037, 0.05%, respectively). Bright & Mears (1997) reported that variations in the degree of pulmonary edema may occur according to the stage of the disease, leading to dyspnea and orthopnea. In advanced stages of chronic valve disease, increased pressure in the left atrium can trigger complications such as pulmonary congestion, and it is possible to observe signs of left CHF, such as interstitial and alveolar pulmonary edema (ETTINGER; FELDMAN, 1999.; SOARES et al., 2005.; CARVALHO et al., 2022).

As for electrocardiographic findings, sinus tachycardia was the most frequent finding with 24.5% (n=30 animals), followed by sinus rhythm 21.5% (n=26 animals), sinus arrhythmia 21.5% (n= 26 animals), premature atrial complexes 18% (n=22 animals) and atrial tachycardia 14.8% (n=18 animals). Corroborating results obtained in a study by Muzzi et al. (2009) who observed a predominance of sinus arrhythmia and sinus and atrial tachycardia in dogs with CDMVD. This can be evidenced in cases of compensatory mechanisms in the decrease of cardiac output, where very often the heart rate tends to increase, in an attempt to maintain the volume per minute (PEDERSEN et al., 1999.; SISSON et al., 1999; SYDNEY; FOX, 1999.; KITTLESON, 2005.; RASMUSSEN, 2012).

Thus, 78% of the evaluated animals (Table 2) presented rhythm disorders associated with tachyarrhythmias, with a percentage of 22% of the animals without alterations, denoting a strong positive correlation (0.789, p=0.0101, 0.05%), between valve disease and electrocardiographic alterations, compatible with findings of some authors who evaluated dogs in routine consultations (CASTRO, 2009.; MACHADO et al., 2021.; SILVA et al., 2022).

This study underscores the importance of periodic cardiological evaluation of elderly female dogs of small breeds, seeking the early diagnosis of this prevalent disease. The course of the disease is generally slow and insidious, with a poor prognosis.

Alterations of heart failure are often associated with diseases of mitral origin, with chronic valve disease being the main related disease and the findings of systemic systolic blood pressure, cough, cyanosis and easy tiredness being listed as the main manifestations involved in the present study.

These data reinforce the idea that the clinician of small animals should be aware of the possible findings of the physical examination, history and anamnesis to support their medication conduct, individually, but, even so, following the guidelines of the consensus established by the entities.

Tachyarrhythmias were present in 78% of the animals that were diagnosed with CDMVD, suggesting that this arrhythmia may be strongly associated with this disease and also with compensatory heart rhythm disturbances.

Table 2: Relation between the number of animals that presented changes in vagal exacerbation associated with respiratory disease.

Electrocardiographic finding	Animals with Valve Disease	RF(%)
sinus tachycardia	30	24,5%
sinus rhythm	26	21,5%
Respiratory Sinus Arrhythmia	26	21,2%
PACs*	22	18%
Atrial Tachycardia	18	14,8%
Total	122	100%

*Premature Atrial complexes; RF= Relative Frequency.

Conclusion

Based on the research and the results obtained, it can be assumed that there was an association between the evolution of the valve disease with the evolution of the reported clinical findings, in cases of greater murmur intensity, pulmonary patterns and degree of congestive insufficiency, these being, somehow, contributing to the previous history of those denoted in the literature, which does not prevent clinical and controlled studies from being recommended for a better elucidation of these occurrences, considering that the studied population reflects only one group of animals.

References

ACIERNO, M.J.; BROWN, S.; COLEMAN, A.E.; JEPSON, R.E.; PAPICH, M.; STEPIEN, R.L.; SYME, H.M. 2018. ACVIM consensus statement: Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats. *Journal of Veterinary Internal Medicine,* v.32, n.6, p.1803-1822. doi: 10.1111/jvim.15331.

ALMEIDA, C.D.O.S. 2021. Degeneração mixomatosa da valva mitral em cães: Revisão. *Pubvet,* v.15, n.208, p.1-17. doi:10.31533/pubvet.v15n07a863.1-10.

ATAIDE, W.F. 2020. Estudo retrospectivo dos procedimentos cirúrgicos realizados em cães e gatos em um Hospital Veterinário Universitário na Região Centro-Oeste do Brasil. *Brazilian Journal of Development,* v. 6, n. 6, p. 35413-35422.

BOON, J. A. 2011. *Acquired valvular disease.* In BONN, J.A. (Ed.), Veterinary echocardiography. 2nd ed. Hoboken: Wiley-Blackwell. p.267-333.

BORGARELLI, M.; BUCHANAN, J.W. 2012. Historical review, epidemiology and natural history of degenerative mitral valve disease. *Journal of Veterinary Cardiology,* v.14, n.1, p.93-101.

BRIGHT, J.M.; MEARS, E. 1997. Chronic heart disease and its management. *Veterinary Clinics of North America: Small Animals Practicers,* v.27, n.6, p.1305-1329. Doi: https://doi.org/10.1016/S0195-5616(97)50128-8

CARVALHO I.C.; SANTOS FILHO, M.; HAINFELLNER, D.C.; VEIGA, C.C.P.; MACAMBIRA, K.D.S.; MENDONÇA, D.A.; KNACKFUSS, F.B.; BENDAS, A.J.R.; ALBERIGI, B.R.S. 2022. Brachycephalic Syndrome in Dogs - Endoscopic Findings in the Airways. *Acta Scientiae Veterinariae,* n.50, n.1859, p. 1-11.

CASTRO, M. G. 2009. Estudo retrospectivo ecodopplercardiográfico das principais cardiopatias diagnosticadas em cães. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia,* v. 61, p. 1238-1241.

CHAMAS, P.P.C.; SALDANHA, I.R.R.; COSTA, R.L.O.; NORONHA, N.P. 2011. Prevalência da doença degenerativa valvar crônica mitral em cães. *Revista de Educação Continuada em Medicina Veterinária e Zootecnia,* v.9, n.2, p.44-45.

ETTINGER, S.J.; FELDMAN, E.C. *Doenças valvulares e endocárdicas adquiridas.* In: ETTINGER, S.J.; FELDMAN, E.C. (eds.) Tratado de Medicina Interna Veterinária. Rio de Janeiro: Elsevier. 1999. p. 7543-7841.

KEENE, B.W.; ATKINS, C.E.; BONAGURA, J.D.; FOX, P.R.; HAGGSTROM, J.; FUENTES, V.L. 2019. ACVIM consensus guidelines for the diagnosis and treatment of myxomatous mitral valve disease in dogs. *Journal of Veterinary Internal Medicine,* v.33, n.3, p.1127-1140. doi: 10.1111/jvim.15488.

GOMPF, R.E. 2002. *Diagnóstico das cardiopatias: a história e o exame físico,* In: TILLEY, L.P.; GOODWIN, J.K. (eds). Manual de Cardiologia para Cães e Gatos. 3ª ed. Roca, São Paulo, 2022, p. 3-14.

KITTLESON, M.D. *Therapy of Heart Failure.* In: ETTINGER, S.J.; FELDMAN, E.C. (eds.). Textbook of Veterinary Internal Medicine. St. Louis, Missouri, USA. Saunders, 2005. p.713-736.

KOVACIC, J.C.; DIMMELER, S.; HARVEY, R.P.; FINKEL, T.; AIKAWA, E.; KRENNING, G.; BAKER, A.H. 2019. Endothelial to mesenchymal transition in cardiovascular disease: JACC state-of-the-art review. *Journal of the American College of Cardiology,* v.73, n.2, p.190-209. doi: 10.1016/j.jacc.2018.09.089.

LEMOS, N.M.O.; ALBERIGI, B.; LABARTHE, N.V.; KNACKFUSS, F.B.; BALDANI, C.D.; SILVA, M.F.A. 2022. How does *Dirofilaria immitis* infection impact the health of dogs referred to cardiology care. *Brazilian Jornal of Veterinary Medicine,* v.44, n.e002622. doi: 10.29374/2527-2179.bjvm002622.

MUZZI, R.A.L.; MUZZI, L.A.L.; ARAÚJO, R.B.; LÁZARO, D.A. 2009. Valvopatia mitral crônica em cães: avaliação do estágio clínico funcional e medida ecocardiográfica da valva mitral. *Arquivos Brasileiros de Medicina Veterinária e Zootecnia,* v.61, n.2, p.337-344.

PEDERSEN, H.D.; HAGGSTROM, J.; FALK, T.; MOW, T.; OLSEN, L.H.; IVERSEN, L.; JENSEN, A.L. 1999. Auscultation in mild mitral regurgitation in dogs: observer variation, effects of physical maneuvers, and agreement with color Doppler echocardiography and phonocardiography. *Journal of Veterinary Internal Medicine,* v.13, n.1, v.56-64. Doi: https://doi.org/10.1111/j.1939-1676.1999.tb02166.x

RASMUSSEN, C.E. 2012. Heart rate, heart rate variability, and arrhythmias in dogs with myxomatous mitral valve disease. *Journal of veterinary internal medicine,* v. 26, n. 1, p.76-84.

SANTILLI, R.; MOISE, N.S.; PARIAUT, R.; PEREGO, M. Eletrocardiografia de Cães e Gatos: diagnóstico de arritmias. 2ª ed. Medvet, São Paulo, 2020. p.358.

SISSON, D.; KVART, C.; DARKE, P.G.G. *Acquired valvular heart disease in dogs and cats.* In: FOX, P.R.; SISSON, D.; MOISE, N.S. (eds.) Textbook of canine and feline cardiology. 2.ed. Philadelphia: W.B. Saunders. 1999, p.536-565.

SILVA, J.; GONÇALVES, B.P.; MACHADO, E.O.S.L.; PAIVA, B.A.S.; CARVALHO, E.B.; SANTOS FILHO, M. 2022. Electrocardiographic findings in dogs with obstructive airway diseases. *Acta Veterinaria Brasilica,* v.16, n.2, p.166-171. doi:/10.21708/avb.2022.16.2.10838

SOARES, E.C.; LARSSON, M.H.M.A.; YAMATO, R.J. 2005. Valvulopatia crônica: correlação entre aspectos clínicos, eletrocardiográficos, radiográficos e ecocardiográficos em cães. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia,* v.57, n.4, p.436-441.

SYDNEY, N.M.; FOX, P. 1999. *Echocardiography and doppler imaging.* In: FOX, P.; SISSON, D.; SYDNEY, N.M. (eds.) Textbook of canine and feline cardiology. W.B.: Saunders, p.130–171.

TILLEY, L. P.; SMITH JR, F. W. K. 2016. *Electrocardiograph.* In: SMITH, JR.; TILLEY, L. P.; OYAMA, M.; SLEEPER, M. (Eds.). Manual of canine and feline cardiology, 5th ed. St. Louis: Elsevier, p.49-76.

WARE, W. A. Doença valvar endocárdica adquirida. In: NELSON, R.W.; COUTO, C.G. (eds.). *Medicina interna de pequenos Animais.* Rio de Janeiro, Brasil.: Elservier, 2015. p. 113-126.