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Correlation between Macruz Index and left atrial enlargement in dogs with myxomatous mitral valve disease

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The Macruz Index is a simple electrocardiographic methodology indicated in the evaluation of possible left atrial remodeling in human medicine. In dogs, the main cause of left atrial remodeling is mitral valve myxomatous degeneration, a degenerative valvulopathy with high occurrence in the routine of the veterinary clinic. Thus, the objective was to determine the values of the Macruz Index and correlate them with the echocardiographic variable left atrium/aorta ratio in dogs with valvulopathy. For this, 11 healthy dogs, male and female, aged between 2 and 8 years, weighing up to 10 kg were selected; together with 60 dogs with mitral valve myxomatous degeneration, small breed and ages 7 to 17 years, which were subdivided into groups according to the class of congestive heart failure - B1 (n=20), B2 (n=20) and C (n=20). All dogs in the present study underwent clinical cardiological, electrocardiographic and echocardiographic evaluation in order to obtain the values of the Macruz Index and the left atrium/aorta ratio. The results showed a significant difference ($p<0.05$) between the values of the Macruz Index of healthy dogs compared to the groups of dogs with the studied valvular disease (class B2 and C1). However, its correlation with the values of the left atrium/aorta ratio obtained in dogs with mitral valve myxomatous degeneration according to the congestive heart failure classes was low, positive and not statistically significant. Thus, we can conclude that the Macruz Index suggests left atrial remodeling in dogs with mitral valve myxomatous degeneration compared to healthy dogs. However, it does not correlate or evidence progressive left atrial remodeling between classes of congestive heart failure.

Key words: Atrium, endocardiosis, macruz index, echocardiography.

INTRODUCTION

Mitral valve myxomatous degeneration (MVMD) is characterized by a valvulopathy with a degenerative and

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progressive aspect, which promotes failure in the coaptation of the valve leaflets, leading to regurgitation of a ventricular volume towards the atrium in the systolic phase. As a result, due to its progressive nature, atrial remodeling is evidenced as a function of volume overload and an increase in left atrial pressure, with the activation of compensatory mechanisms of congestive heart failure (CHF). Left atrial remodeling is an indicator of the severity and chronicity of heart disease (Mazini and Prada, 2020) and a prognostic factor for the valvular disease in question (Mazini and Prada, 2020; Soto-Bustos et al., 2017).

The diagnosis of MVMD is performed through physical examination, chest radiography, electrocardiogram and echocardiogram (Junior et al., 2009); with the latter, responsible for qualifying and quantifying myocardial functions and cardiac remodeling. The linear measurement of the left atrial diameter (LA) and its relationship with the aorta (Ao) (Mazini and Prada, 2020) is a variable widely used to assess atrial remodeling in mitral valvulopathy. Computed electrocardiography has the purpose to identify changes in heart rhythm, when we observe the increase in P wave duration, we can suggest the occurrence of left atrial remodeling (Soto-bustos et al., 2017; Noszczyk-nowak et al., 2011). However, it has low sensitivity in dogs and cats (Xavier Junior et al., 2015; Mazini and Prada, 2020).

In 1958, the cardiologist and researcher Macruz (Macruz et al., 1958) proposed the use of a simple formula for the recognition of atrial enlargement in human medicine through electrocardiography, called the Macruz Index calculation. This index, used in human medicine, is obtained by dividing the P-wave duration value by the P-R segment value, showing positive values higher than1.6 in the D2 lead (Feldman and Goldwasser, 2004). Soto-Bustos et al. (2017) studied specific electrocardiographic variables for left atrial evaluation in dogs with MVMD that included the Macruz Index and concluded that the method has a low correlation with the LA:Ao ratio. However, De Oliveira (2019) using the method found a positive but low correlation between the increase in the Macruz Index and the LA:Ao ratio in dogs. However, when we talk about the Macruz Index and its applicability in veterinary medicine, the literature is still limited. Thus, we aimed to determine the values of the Macruz Index and correlate them with the echocardiographic variable left atrium/aorta (LA:Ao) in dogs with MVMD.

MATERIALS AND METHODS

The research in question was approved by the ethics committee on the use of animals under protocol 42/2021. For this purpose, seventy-one (n=71) adult dogs, male and female, of different breeds and ages, were included in the study after undergoing a complete cardiac evaluation, with physical examination, blood pressure measurement, electrocardiography and echocardiography in the period from August to October 2021. Dogs considered obese, with pathological arrhythmias, respiratory conditions, suspected infectious, endocrine or other diseases, under or without pharmacological therapy were excluded from the present study.. Thus, eleven (n=11) healthy dogs, free of cardiac affections, aged between 2 to 8 years and weighing from 2 to 11 kg, composed the control group (CG) and underwent computerized electrocardiogram (ECG - Agile/ INPULSE) to determine the values for the Macruz Index using the D2 lead of the electrocardiographic tracing. The sixty (n=60) dogs with MVMD were also submitted to computerized electrocardiography in order to obtain the values corresponding to the Macruz Index, with subsequent subdivision of the dogs according to their CHF classes:

1. Class B1 = dogs with MVMD - CHF class B1 (n = 20)
2. Class B2 = dogs with MVMD - CHF class B2 (n = 20)
3. Class C = dogs with MVMD - CHF class C (n = 20)

Classes are differentiated and classified mainly by symptomatic and asymptomatic animals. Thus, class B1 is classified by asymptomatic patients without left atrial remodeling or with mild remodeling; Class B2 is classified by asymptomatic patients with systolic murmur (>3/6), left atrial remodeling (AE:Ao ratio >1.6) and left ventricular (LVIDd) > 1.7 normalized), cardiomegaly on radiography (VHS>10 ,5). Class C patients are classified for being symptomatic in terms of CHF, systolic murmur (>3/6), left atrial remodeling (AE:Ao ratio >1.6) and left ventricular (LVIDd > 1.7 normalized), cardiomegaly in radiography (VHS>10.5) (Keene et al., 2019).

To obtain the values of the Macruz Index of the present study, the proposed methodology was described by RadiMacruz, Joseph Perloff and Robert Case (1958), using the conventional electrocardiography device. For this, the dogs were placed in left or right lateral decubitus without drug restraint, with the tracing obtained in leads D1, D2, D3, AVF, AVR, AVL and using lead D2 to obtain the values in milliseconds of the wave duration P and the PR segment; with subsequent calculation of the macruz index, according to the formula described in Figure 1.

All dogs underwent echocardiographic assessment (Sonosite Micro MAXX model, year 2014 - Sectoral Probe 5 to 9 MHz) and through the right parasternal window - cross section - Aortic Plan, measurements of the left atrial diameter and aorta artery were performed, with subsequent measurement of the LA:AO ratio, as recommended by Thomas et al. (1993) and shown in Figure 2. The data obtained were subjected to statistical analysis to verify the existence of the relationship between the increase in the Macruz Index in dogs with MVMD, as well as to correlate the values obtained with the LA:Ao ratio. The values obtained for age, sex and race were expressed as a percentage, with the median compared by the Kruscall-Wallis analysis and the correlation analysis by the Spearman method at 5% probability.

RESULTS

Regarding the control group, 36% were females (n=4) and 64% were males (n=7), being 18% Chihuahua (n=2), 9% Poodle (n=1), 9% Yorkshire Terrier (n=1) and 64% No Defined Breed (NDR) (n=7), with a mean body weight of 4.6 ± 1.7 kg. As for the dogs with MVMD, 47% were female (28 animals) and 53% were male (32 animals), being 33% Poodle (n=20), 15% No defined breed (n=9), 12% Shitzu (n=7), 10% Yorkshire (n=6), 10% Pinscher (n=6), 7% Lhasa Apso (n=4), 5% Maltese (n=3), 5%

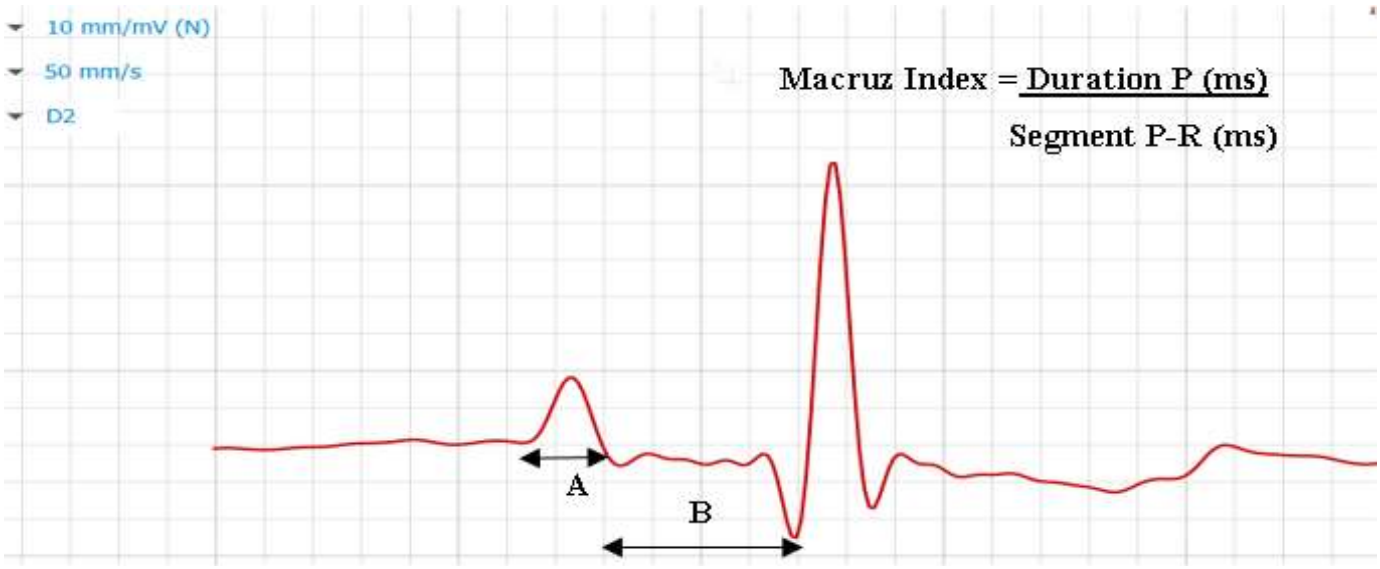

Figure 1. Measurement of P-wave duration (arrow A) and P-R Segment (arrow B), with subsequent obtainment of the Macruz Index.

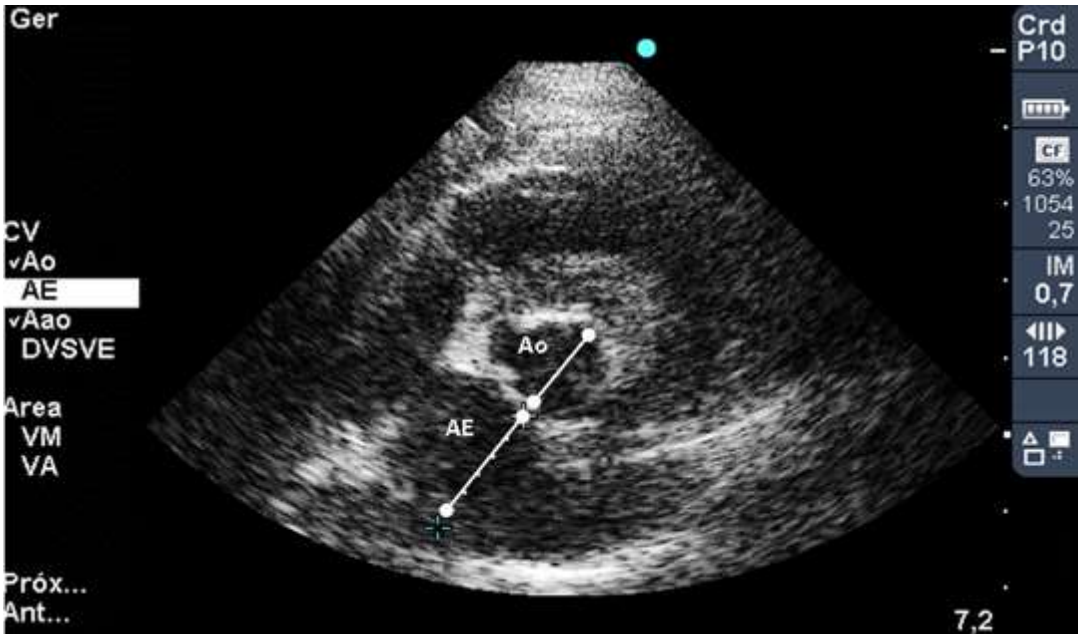

Figure 2. Measurement of the diameter of the left atrium (LA) measured on image A; measurement of the aortic diameter (AO) shown in image B; methodology performed to obtain the LA:Ao ratio in dogs with MVMD according to the CHF classes.

Dachshund (n=3) and 3% Pekingese (n=2). The average weight of the class B1 dogs was 7.34 ± 3.3 kg, the class B2 dogs were 6.7 ± 3.2 kg, and the class C dogs were 5.2 ± 2.0 kg. Regarding the age range of the animals with MVMD, 17% (n=10) of the dogs evaluated were between 7 and 10 years old, 51% (n=31) between 11 and 13 years old, and 32% (n=19) between 14 and 17 years old.

Regarding the Macruz Index, the median value obtained in the dogs of the control group was 0.77 ± 0.19, with a minimum value of 0.5 and a maximum value of 1.1. In the animals with MVMD the values obtained for the Macruz Index are described in Table 1, with the results showing a significant difference between dogs in the control group and dogs with MVMD. No significant difference was

Table 1. Representation of the Macruz Index results in the control group and in animals with myxomatous valve disease.

Group	Median	Minimum	Maximum
Control	0.77[c]	0.5	1.1
Class B1	1.21[ab]	0.47	2.7
Class B2	1.04[b]	0.6	2
Class C1	1.39[a]	0.72	2.5

B1, B2 and C1: Endocardiosis. Lower case letters different each other represent statistical difference at p<0.05

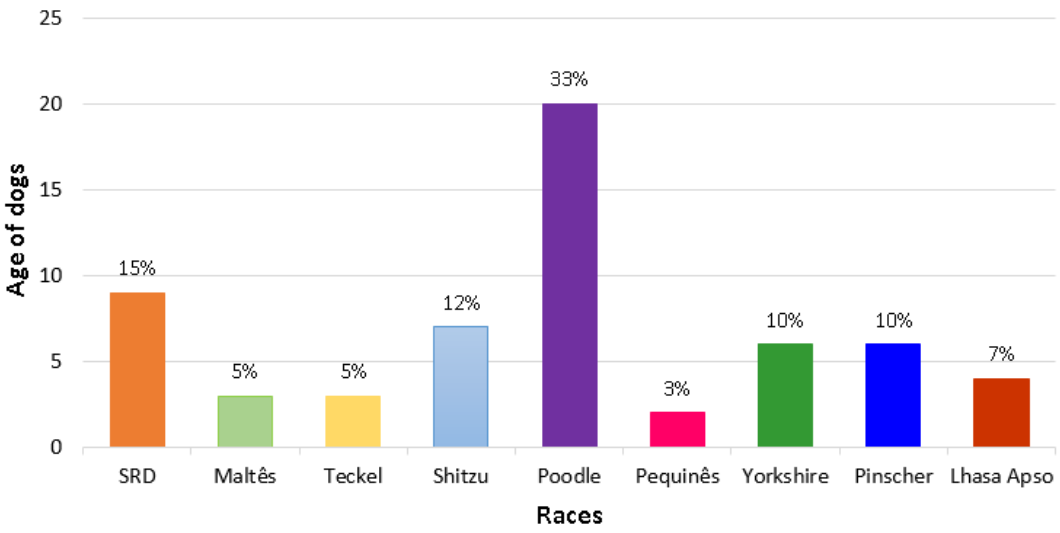

Figure 3. Graphic representation of dog breeds with MVMD in the study.

obtained when comparing the values between the CHF classes.

The result acquired when correlating Macruz Index value and LA:Ao ratio value in dogs with MVMD obtained by echocardiography showed a low but positive statistical correlation between the data (rho = 0.16; p-value=0.20) as shown in Figure 3.

A non-significant increase in the correlation coefficient was evidenced between the overall data (all CHF groups) and classes B1 and B2. Class C dogs show a negative correlation in the present study.

DISCUSSION

The Macruz Index obtained from the control group was 0.77 ± 0.19, data that resembled the study by Soto-Bustos et al. (2017), where they used a Philips Envisor CHD brand image manipulation software to detect the accuracy of all P-wave related electrocardiographic parameters in dogs with mitral valve endocardiosis, including the Macruz Index measurement (Cardioline Mod AR1200view brand), with values obtained from the median of 0.94, with a minimum of 0.35 and a maximum of 1.85 in healthy animals.

The values obtained for the Macruz Index in dogs with MVMD had a mean value of 1.21 for class B1, mean value of 1.04 for class B2 and mean value of 1.39 for class C, showing a significant difference between dogs of the control group and dogs with MVMD, which may suggest left atrial enlargement in dogs with the disease. However, when comparing the values of the Macruz index between the ICC classes, no significant difference was identified. This result can be explained by the low sensitivity of the electrocardiogram in detecting cardiac chamber remodeling (Xavier Junior et al., 2015) and high sensitivity in capturing the heart rhythm. In addition, the left atrium presents chronic, progressive three-dimensional remodeling, and echocardiography is indicated for its evaluation (Mazini and Prada, 2020). Soto-Bustos et al. (2017) also did not show significant differences between the ICC classes in relation to the Macruz Index, only between the control group and dogs with class B2. Similar facts were also evidenced in the

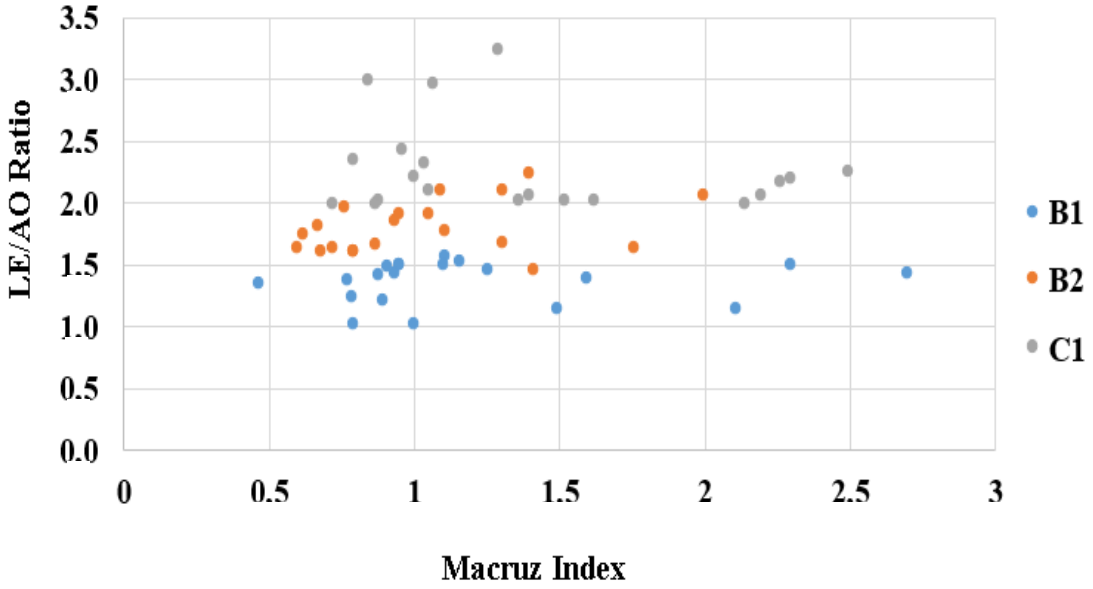

Figure 4. Correlation between the Macruz Index and the LA:Ao ratio in dogs with MVMD.

present study. Another argument for the non-correlation of the increase in the macruz index and the left atrial increase in relation to the ICC classes is the smaller number of animals studied, it is suggested that if the number of animals studied were higher, there could be a greater correlation between the data obtained.

In human medicine Balci et al. (2016) evaluated the Macruz Index before and after valvuloplasty in women and men with mitral stenosis, showing significant differences between patients with higher values for those who did not undergo valvuloplasty. This result was justified by the significant reduction in left atrial volume and pressure as well as pulmonary systolic pressure after the procedure. This does not occur in dogs with MVMD, due to the fact that valvuloplasty is not performed in the veterinary clinical routine in Brazil and because it is a degenerative and progressive valvular process..

The values of the Macruz Index were correlated with the values of the LA:Ao ratio obtained in dogs with MVMD through echocardiography, with the results showing a low and positive statistical correlation between the data (rho = 0.16; p-value = 0.20) as shown previously in Figure 4. This fact shows the non-monitoring of the increase in the values of the LA:Ao ratio as the CHF table progresses with the values of the Macruz Index obtained in dogs with MVMD. The justification for the described result is the applicability and purpose of the different diagnostic methods used; the echocardiogram aims to analyze the heart anatomically and functionally, and the electrocardiogram captures the cardiac electrical impulses (Hansson et al., 2002; Arnolds et al., 2011).

The increase seen between the overall data and classes B1 and B2 was not significant. However, it should be noted that class B1 patients have no left atrial remodeling on echocardiography and class B2 dogs have an increase in LA:Ao ratio above 1.6 and in the left ventricle (Ziegler et al., 2018); facts that demonstrate the inability of the studied index to evidence the progression of left atrial remodeling, as described by Tsao et al. (2008) when they studied human patients and did not reliably recommend the identification of atrial enlargement by the Macruz Index. However, Soto-Bustos et al. (2017) observed a positive and low correlation between Macruz Index increase and left atrial enlargement in dogs with MVMD, noting that normalized Macruz Index values will not exclude left atrial enlargement in these dogs. Recently, De Oliveira (2019) studied the mean values of the Macruz Index in dogs with and without an increase in the LA:Ao ratio, with the results showing a low and positive correlation between the Macruz Index and the increase in the LA:Ao ratio, corroborating with the research performed by Soto - Bustos et al. (2017) and the present research.

The negative correlation of Class C animals is justified by the large variation between the values of the LA:Ao ratio and, consequently, of the Macruz Index in the dogs studied. This is because dogs with class C MVMD are characterized by animals that show clinical signs of CHF and significant left atrial and ventricular remodeling (Mazini and Prada, 2020; Soto-bustos et al., 2017; Keene et al., 2019). Furthermore, left atrial remodeling is not two-dimensional, as obtained in the echocardiographic method studied, but three-dimensional. This justifies the oscillations in the LA:Ao ratio values and possibly in the

Macruz Index values, leading to the formation of a negative line in the correlation graph (Poutanen et al., 2003).

Conclusion

After analyzing the data, we can conclude that the values of the Macruz Index were higher when comparing healthy dogs in relation to those obtained in patients with DMV. However, it was not possible to observe the progression of values and their correlation with the progression of left atrial remodeling identified in dogs with VMD, according to ICC classes. It is suggested that to confirm the progression of cardiac remodeling between the classes of CHF with the Macruz Index, further studies with a greater number of animals in function on the results presented.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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