P wave dispersion in obese dogs with and without mitral valve disease

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ABSTRACT: *Pwave dispersion (P_d) is an electrocardiographic index defined as the difference between the minimum and maximum Pwave duration in multiple leads. The augmentation of P_d reflects the discontinuous and inhomogeneous atrial depolarization resulting from cardiac and non-cardiac conditions. In humans, an increased P_d is associated with the development of cardiac arrhythmias, particularly atrial fibrillation. To investigate P_d in obese dogs, we enrolled 76 dogs, which were classified in four distinct categories according to body condition and the existance of valve insufficiency: obese dogs (O), dogs with both obesity and cardiac disease (O+CD), lean dogs with cardiac disease (CD) and healthy controls (H). To be included in the study, all dogs underwent an electrocardiographic and echocardiographic assessment. We reported significantly higher P_d in the animals included in categories O, O+CD and CD (18.0±7.6ms, 16.1±4.4ms, 12.1±4.3ms, respectively) as compared to the healthy subjects (7.3±2.2ms). Also, significant correlations between P_d and both the body mass index and body fat percentage were documented for the obese dogs. However, no association between P_d and LA/Ao could be identified in patients belonging to the O, O+CD and H categories. Thus, we have demonstrated that obese dogs, regardless of their valvular competency status, present high P_d values, suggesting an impaired propagation of atrial electrical impulse.*
Key words: *mitral degeneration, P wave indices, adiposity, obesity, left atrial size.*

Dispersão da onda P em cães obesos apresentando ou não doença valvar mitral

RESUMO: *A dispersão da onda P (P_d) é um índice eletrocardiográfico definido como a diferença entre as durações máxima e mínima da onda P em múltiplas derivações. O aumento da P_d reflete a despolarização descontínua e não homogênea resultante de condições cardíacas e não cardíacas. Em seres humanos, uma P_d aumentada está associada com o desenvolvimento de arritmias cardíacas, particularmente fibrilação atrial. Com o intuito de investigar a P_d em cães obesos, foram selecionados 76 cães, os quais foram classificados em quatro categorias distintas, de acordo com sua condição corporal e a existência de insuficiência valvar: cães obesos (O), cães com obesidade e doença cardíaca (O+CD), cães magros com doença cardíaca (CD) e cães saudáveis usados como controle (H). Uma vez selecionados para o estudo, todos os cães foram submetidos às avaliações eletrocardiográfica e ecocardiográfica. Os resultados mostraram maior P_d nos animais pertencentes aos grupos O, O+CD e CD (18.0±7.6ms, 16,1±4,4ms, 12,1±4,3ms, respectivamente) quando comparados aos cães saudáveis (7.3±2.2ms). Além disso, foram verificadas correlações significativas entre P_d e tanto o índice de massa corporal quanto o percentual de gordura corporal nos cães obesos. Entretanto, não se identificou associação entre P_d e a relação AE/Ao nos pacientes das categorias O, O+CD e H. Dessa forma, foi possível demonstrar que cães obesos, independentemente do estado de competência valvar, apresentam P_d elevada, fato que sugere comprometimento da propagação do impulso elétrico atrial.*
Palavras-chave: *degeneração mitral, índices da onda P, adiposidade, obesidade, tamanho atrial esquerdo.*

INTRODUCTION

P wave dispersion (P_d) is an electrocardiographic index defined as the difference between the minimum and maximum durations of P wave, which are obtained from different leads of the surface electrocardiogram (NOSZCZYK-NOWAK et al., 2008). An increased P wave lenght and dispersion may be the consequence of an abnormal atrial depolarization secondary to chronic injuries such as elevated atrial pressure, myocardial ischemia and metabolic stress (MAGNANI et al., 2009). In people, P_d was shown to consistently predict the development of atrial fibrillation and to be a prognostic surrogate (DILAVERIS & GIALAFOS, 2001; DOGAN et al., 2003; NIELSEN et al., 2015; LAZZERONI et al.,

2016). Also, an increased P_d was documented in subjects with arterial hypertension and diabetes, which are both recognized as independent factors for the development of atrial fibrillation (YAZICI et al., 2007; DAGLI et al., 2008). Other studies reported a direct relationship between augmented P wave indices and diseases that cause diastolic dysfunction, coronary syndromes and dilated cardiomyopthy (SENEN et al., 2004; GUNDUZ et al., 2005). Among several other conditions in people, obesity was shown to impair P wave indices, which are related with an increased risk for developing cardiac arrhythmias (MAGNANI et al., 2009). Studies have demonstrated an association between the increase of P_d in obese individuals and atrial arrhythmias (SEYFELI et al., 2006; KOSAR et al., 2008).

P_d values have been previously documented in healthy dogs, and in dogs with either chronic valvular disease or supraventricular conduction disturbances (NOSZCZYK-NOWAK et al., 2011). However, at least to the authors' knowledge, no information exists in literature concerning the role played by body condition, especially obesity, on both the duration and dispersion of P wave in dogs. Therefore, the aims of this study were two-fold: to investigate P wave indices in obese dogs and to determine whether these indices correlate with adiposity parameters and the left-atrial size.

MATERIALS AND METHODS

Seventy-six dogs of either sex were enrolled in this prospective observational study. Inclusion criteria included the animal's age ($\geq$4y) and body weight ($\geq$4 and $\leq$30kg)and meeting the selection characteristics for each of the studied categories (obese, obese+cardiac disease, cardiac disease, healthy). Having any cardiac alteration other than mitral valve disease was considered an exclusion criterion. Several breeds and crossbred dogs were admitted. All dogs underwent a thorough clinical examination and were assessed for body condition. Also, an electrocardiogram and an echocardiogram were performed. Prior to enrollment, the animals had blood aliquots drawn for laboratory analyses. Dogs which exhibited any abnormality in either CBC or bichemistry profile (albumin, alanine aminotransferase, alkaline phosphatase, blood urea nitrogen, creatinine, glucose, trigricerides, cholesterol, and free T4) were not admitted into the study.

The assessment of body condition included the determination of body condition score using the 1-9 scale, which is based on fat deposition over the costal and abdominal areas (LAFLAMME, 1997). Dogs were classified as either having a normal body condition score (4 or 5) or being obese (8 or 9). Also, two adiposity indices were obtained: the body mass index (BMI) described by MUELLER et al. (2008), and the body fat percentage (BF%) as proposed by BURKHOLDER & TOLL (2000).

Computed-based electrocardiographic tracings were recorded for a minimum of three minutes (ECGPC®, TEB, São Paulo, Brazil) with the dogs restrained in right lateral recumbency. Six limb leads (I, II, III, aVR, aVL and aVF) were recorded in all animals, while in 18 dogs the precordial leads (rV2, V2, V4 and V10) were obtained as well. All recordings were obtained with a speed of 50mm/s and a sensitivity of 1cm per millivolt. Each recorded lead was carefully assessed by a single experienced veterinarian to determine the duration of P wave, which was measured from its beginning (the start of either the positive or negative deflection at the isoelectric line) until its end (the return of the deflection to an isoelectric line). The minimum (P_{min}) and maximum (P_{max}) durations of P wave were documented. P wave dispersion was calculated as the diference between P_{max} and P_{min} ($P_d = P_{max} - P_{min}$). All parameters were considered as the average of three distinct measurements obtained from cardiac beats (cycles) of sinus origin.

All dogs underwent a transthoracic echocardiogram (Esaote® MyLab™ 30 Vet, Genova, Italy). That exam was the gold standard to confirm the diagnosis of degenerative mitral valve disease and to rule out any other cardiac anomaly. Also, using transverse views of the heart obtained from the right paraesternal window, the left atrial dimension and the aortic diameter were measured at the very beginning of diastole, which were later used to calculate the left atrium-to-aorta ratio (LA/Ao). In this study, we considered 1.37 as the cut-off for increased left atrium (PRADA et al., 2012).

After the assessment was complete, the dogs were classified in four different categories:

Obese (O): dogs with body condition score indicative of obesity, but free from cardiac disease;

Obese + Cardiac Disease (O+CD): obese dogs which also had mitral valve disease documented in the echocardiogram;

Cardiac Disease (CD): lean dogs with documented mitral valve disease;

Healthy (H): lean dogs with no cardiac disease.

Dogs in either MMVD stage B2 or C were admitted into categories O+CD and CD, while B2 dogs had no clinical signs at all in spite of having cardiac remodeling. In stage C dogs were already symptomatic (ATKINS et al. 2009).

Statistical analyses were based on measures of central tendency and dispersion for heart rate, P_{min}, P_{max} and P_d. Normality of data was assessed with D'Agostino & Pearson test. Either an analysis of variance (ANOVA) followed by the *post hoc* Tukey test or the Kruskal-Wallis test followed by Dunn's test were used to compare groups in accordance with data normality. Also, Pearson's correlations were calculated between P_d and BMI, BF% and LA/Ao. All analyses were performed using the software GraphPad® Prism 5 (La Jolla, California, USA).

RESULTS

This study investigated 76 dogs, which were separated in four distinct categories. The obese group (O) included 18 dogs (15 female/3 male; 4-15 y; 17.5±5.2kg), while 19 animals (13 females/6 males; 9-20 y; 14.2±4.2kg) were enrolled into the obese with cardiac disease group (O+CD). In that group, 47% of the dogs (9/19) had an increased left atrium (LA/Ao>1.37) documented on the echocardiogram, i.e. belonged to either stages B2 (n=3) or C (n=6). For the lean and cardiac disease group (CD), another 19 dogs (6 females/13 males; 10-16 y; 7.4±2.3kg) were included, of which 58% (11/19) had left atrial enlargement, i.e. were classified as either stage B2 (n=3) or C (n=8). Finally, 20 dogs (14 females/6 males; 9-17 y; 7.3 ± 1.9kg) were assessed as healthy controls (H).

Table 1 brings the results obtained for heart rate, P_{min}, P_{max} and P_d in all four groups. A significant difference existed for P wave dispersion, which was higher in O, O+CD and CD dogs as compared to the healthy controls (P<0.0001).Also, P_{max} was higher in O in comparison with CD dogs (P=0.016). We documented no difference between males and females regardless of the category to which the subjects were

assigned (P=0.453), however our data derives from a small population of dogs. Figure 1 illustrates the individual and mean results of P_d for all groups.

For the dogs with mitral valve disease (groups O+CD and CD), we also compared the results of P_{min}, P_{max} and P_d between subjects with normal and remodeled left atria (LA/Ao>1.37) regardless of their body condition. While no difference existed for P_{min} and P_d (Table 2), dogs with an increased left atrium had a significantly greater P_{max}. However, when the role played by left atrium remodeling was assessed within CD and O + CD individually, a significantly higher P_d was documented for dogs with dilated left atria only in category CD (Figure 2).

When the correlations between P_d and body weight, BMI, BF% and LA/Ao were investigated, significant results were reported only between P_d and the adiposity indices for obese dogs (O) and obese dogs with cardiac disease (O + CD) (Figure 3). On the contrary, no correlations were shown to exist between P_d and both body weight and LA/Ao ratio for categories O, O + CD and H. However, specifically for CD results, significant correlations were documented between LA/Ao and P_d, P_{min} and P_{max} (Table 3).

The 18 dogs in which precordial leads were also recorded belonged to the four different categories of this study (O=4; O+CD=4; CD=5; H=5). No differences existed (P=0.847) when comparing P_d calculated in consideration of the precordial leads with the results obtained from the standard limb leads. Again, this data is fragile in view of the small number of dogs that have been assessed.

DISCUSSION

Although simple, this study adressed a fairly "novel" electrocardiographic index in a population of obese dogs either with or without mitral

Table 1 – P wave parameters obtained in dogs. Results shown as the mean and standard deviation for heart rate, minimum and maximum P wave duration, and P wave dispersion.

	O	O+CD	CD	H	P value
HR (bpm)	140.4 ± 25.9[a]	128.4 ± 36.1[ab]	146.7 ± 32.3[a]	112.7 ± 14.1[b]	0.002
P_{min} (ms)	40.5 ± 5.4[a]	40.4 ± 3.5[a]	40.0 ± 4.8[a]	46.7 ± 9.8[a]	0.108
P_{max} (ms)	62.6 ± 8.1[a]	60.4 ± 5.4[ab]	55.5 ± 7.4[b]	55.9 ± 10.4[ab]	0.016
P_d (ms)	18.0 ± 7.6[a]	16.1 ± 4.4[a]	12.1 ± 4.3[a]	7.3 ± 2.2[b]	<0.0001

O: obese dogs (n=18); O+CD: obese dogs with mitral valve disease (n=19); CD: lean dogs with mitral valve disease (n=19); H: healthy control dogs (n=20); HR: heart rate; P_{min}: minimum duration of P wave; P_{max}: maximum duration of P wave; P_d: P wave dispersion. ([a,b]) different superscript letters indicate significant differences (P<0.05) between groups.
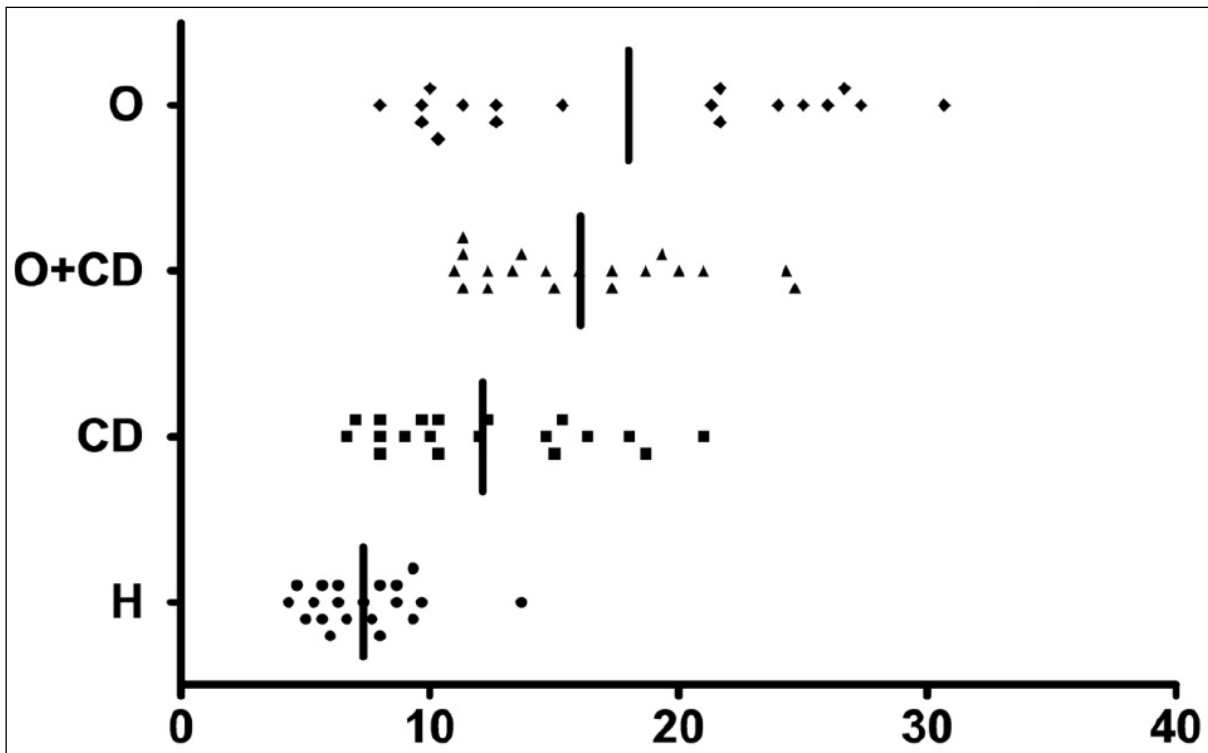
Figure 1 – Individual values and means of P wave dispersion (ms) obtained in dogs. (O: obese dogs; O+CD: obese dogs with mitral valve disease; CD: lean dogs with mitral valve disease; H: healthy control dogs).

valve disease. At least in people, P wave dispersion has been demonstrated to be associated with both cardiac and non-cardiac diseases (DOGAN et al., 2003; GOUDIS et al., 2015).

Our results showed no differences in P_d for males and females, which is likely supportive of its independency of gender. However, the effect of age on P_d could not be assessed in this study since only dogs aged at least four years were enrolled. Also, P_d

calculated from either six (I, II, III, aVR, aVL, aVF) or ten (I, II, III, aVR, aVL, aVF, rV2, V2, V4, V10) electrocardiographic leads was considered similar in this investigation. In a study that evaluated P_d in healthy dogs using six-lead electrocardiogram both unipolar and bipolar leads showed to be appropriate to calculate P wave dispersion, making uneccessary the use of precordial electrodes (NOSCZCZYK-NOWAK et al., 2008).

Table 2 – Comparison of P wave indices between dogs with mitral valve disease (groups O+CD and CD) presenting either normal or remodeled left atria. Means and standard deviations are shown.

	LA/Ao ≤ 1.37	LA/Ao > 1.37	P value
P_{min} (ms)	38.5 ± 3.7	41.5 ± 4.0	0.066
P_{max} (ms)	54.1 ± 6.0	60.0 ± 6.1	0.006
P_d (ms)	13.2 ± 4.5	14.8 ± 4.9	0.322

LA/Ao: left atrium-to-aorta ratio; P_{min}: minimum duration of P wave; P_{max}: maximum duration of P wave; P_d: P wave dispersion.
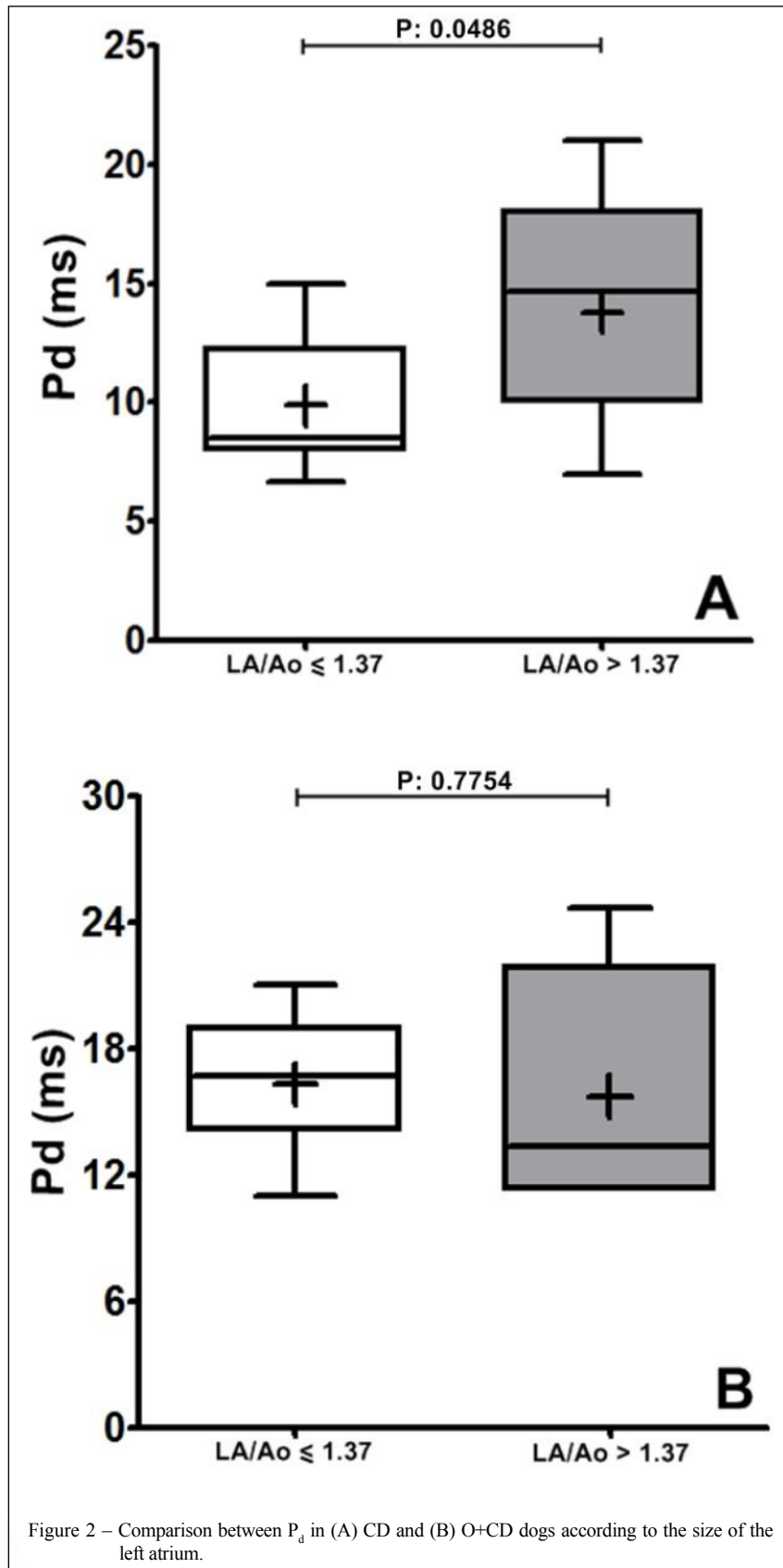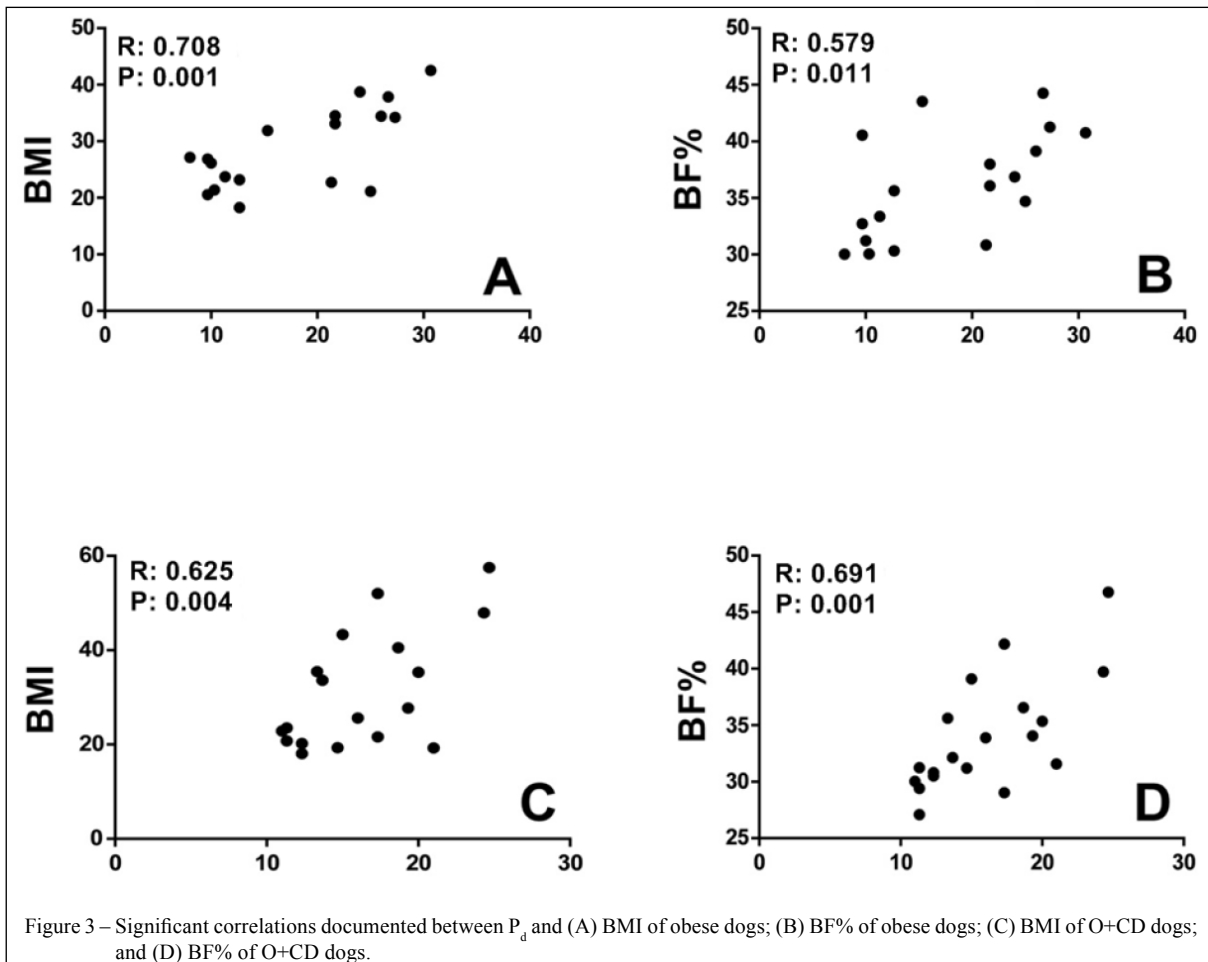
Figure 2 – Comparison between P_d in (A) CD and (B) O+CD dogs according to the size of the left atrium.

Figure 3 – Significant correlations documented between P_d and (A) BMI of obese dogs; (B) BF% of obese dogs; (C) BMI of O+CD dogs; and (D) BF% of O+CD dogs.

It has been well accepted that obese people have an increased P wave dispersion, which seems to be a risk factor for developing cardiac arrhythmias, especially atrial fibrillation (DOGAN et al., 2003; GOUDIS et al., 2015). In veterinary medicine, no information exists concerning the association of obesity and changes in P wave duration and dispersion. Our results demonstrated, for the first time, that obese dogs, either with or without valvular disease and atrial remodeling, have an increased P_d in comparison with healthy animals. Although, no significant difference was documented, a trend of increase in P_{max} was observed in the obese animals (categories O and O+CD) as well. The effect of obesity in the P wave indices was already demonstrated in human beings. These studies showed a significant increase in P_{max} and P_d, which could be fully

Table 3 – Correlation coefficients obtained between P wave indices and the LA/Ao ratio for each of the studied categories.

	O	O+CD	CD	H
P_{min} (ms)	R: -0.030 P: 0.904	R: 0.090 P: 0.713	R: 0.561 P: 0.012	R: -0.119 P: 0.618
P_{max} (ms)	R: 0.047 P: 0.852	R: -0.002 P: 0.993	R: 0.778 P:<0.0001	R: -0.040 P: 0.867
P_d (ms)	R: 0.110 P: 0.664	R: -0.043 P: 0.860	R: 0.606 P: 0.006	R: 0.305 P: 0.190

O: obese dogs (n=18); O+CD: obese dogs with mitral valve disease (n=19); CD: lean dogs with mitral valve disease (n=19); H: healthy control dogs (n=20); HR: heart rate; P_{min}: minimum duration of P wave; P_{max}: maximum duration of P wave; P_d: P wave dispersion.

reversed after weight loss (DURU et al., 2006; SEYFELI et al., 2006; KOSAR et al., 2008; FALCHI et al., 2014). Moreover, in obese subjects a positive correlation between those indices and the BMI was shown to exist. In people, increases in duration and dispersion of P wave is associated with prolonged atrial conduction, left atrial remodeling and the predominant sympathetic tone, which impair the velocity of impulse propagation. Also, there are evidences of structural cardiovascular alterations and impairment of myocardial electrical conduction attributable to obesity (ABEL et al., 2008; ADOLPHE et al., 2014).

In our study, obese dogs and dogs with chronic valvular disease had similar results for P_d. NOSZCZYK-NOWAK et al. (2011) reported an increased P_d in dogs with valvular disease as compared with healthy subjects, which is similar to our own findings. Chronic valvular disease results in inhomogeneous propagation of electrical impulses within the atria, which together with atrial remodeling cause the increase of such index. Nevertheless, it is not completely clear whether P_d might be an independent index to evaluate both inter-and intra-atrial electrical conduction.

We reported a correlation to exist between P_d and the adiposity indices in obese dogs, which is similar to the findings of Kosar et al. (2008). In their study, a significant correlation between P_d and BMI was documented in obese people. In our study, P_d increased in parallel with the adiposity indices of the obese dogs. This finding suggested that obesity may indeed play a role in atrial electrical activity.

P wave indices were also investigated in view of atrial remodeling regardless of body condition. In that sense, a significant correlation was found between P_{max} and LA/Ao ratio only for dogs with left atrial dilatation. Hence, it is reasonable to speculate that the larger the electrically excited atrial tissue, the longer the duration of P wave as suggested by SURAWICZ (1986). Moreover, once specifically Pd was compared between dogs with remodeled and non remodeled left atria, a significant difference was documented only for the experimental group CD. A reasonable explanation for the contrasting results between CD and O + CD in this regard lies on the conflicting population of stage B1 (larger in O + CD) and stage C (larger in CD) in these two groups. Curiously, the duration of P wave was already shown to be poorly related to left atrial size in dogs, with just a mild correlation with LA/Ao. For instance, SAVARINO et al. (2012) showed that P wave duration is not a reliable surrogate for left atrial remodeling. Concerning P_d, no correlation existed with LA/Ao, which is similar to the findings of NOSZCZYK-NOWAK et al. (2011). We speculated that P_d may be more dependent on inter-

and intra-atrial conduction disturbances as well as an inhomogeneous conduction of electrical impulses than the degree of left atrial dilatation itself.

Among the limitations of this study are the small number of dogs enrolled in each category, as well as the absence of stages B1 and D of MMVD. Although measurements of P wave duration seem quite easy to accomplish, we neither evaluated intra- and inter-observer repeatability for measurements of P wave duration, nor assessed how the level of training would interfere with the results of that parameter, i.e. an experienced veterinarian versus a resident or student. Finally, assessing how P wave dispersion might predict the development of supraventricular arrhythmias in either lean or obese dogs was not the purpose of this investigation.

CONCLUSION

P wave dispersion was higher in obese dogs, either presenting or not mitral valve insufficiency. Our results are indicative of the role played by excess of weight and the accumulation of fat on the canine cardiovascular system. Further studies might add information on the prognostic aspect of P wave dispersion.

DECLARATION OF CONFLICTING INTERESTS

The authors declare no conflict of interest. The founding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results.

AUTHORS' CONTRIBUTIONS

The authors contributed equally to the manuscript.

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