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Degenerative myxomatous valvular disease (dmvd) in dogs: a new combined parameter dividing patients without pulmonary edema from those with pulmonary edema

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Abstract: *The current study compares the possibilities of some M-mode echocardiographic and radiographic dimensions to determine the extent of the progression of MVD. There is also a new LA/AO x VHS ratio that 100% separates the dogs included in the study in regard to the absence or presence of pulmonary edema, due to the development of decompensated heart failure. The size we are introducing LA / AO x VHS multiplies the heart enlargement from the X-rays and the M-mode ultrasound imaging. The mean value of this multiplication in group 1 was (16.3350 ± 2.7968) which is statistically significantly (0.0009) lower than the mean value in the edema group (26.0268 ± 5.8358).*

Keywords: *cardiography, DMVD, dogs, M-mode, VHS*

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I. Introduction

Degenerative mitral valve disease (DMVD) is the most common heart disease in dogs [1, 2]. Its distribution may reach 14-40% in small dog breeds, with even higher values in the elderly [3, 4, 5]. The progression of mitral regurgitation (MR) associated with chronic degenerative valve disease is the most important cause of heart failure in dogs [6]. The complexity of the problem with this cardiac disorder is determined by the variability of the pre- and post-loading, which is a limitation for ultrasonography in terms of accurate assessment of myocardial function.

The disease is characterized by a slow development of the clinical picture, sometimes for years. Many of the affected dogs, due to their late age and the poor progression of the disease, may not exhibit clinical signs until the end of their life [7].

It has been proven that treatment of animals with ACE inhibitors and other drugs that support weakened cardiac function has a positive impact on the quality of life of affected patients. On the other hand, the presence of MR and prolonged medical treatment for heart failure can negatively interact with other drugs administered to these patients for other diseases, and may prevent decision-making on surgical procedures or anesthesia [8]. It is these circumstances that determine the beginning of therapy as one of the most important moments after the diagnosis of MVD.

Driven by the idea of the multidimensionality of the aspects that determine the pre- and post-load in this heart disease, our team decided to combine ultrasound and X-ray studies in order to achieve a determinant value that reflects the onset of heart failure. This value could also be used in patients undergoing pretreatment with diuretics, where the absence of pulmonary edema in the X-ray does not mean a lack of cardiac decompensation.

II. Material and methods

Study design

In order to achieve this goal, dogs with left-sided apical systolic noise were examined radiographically and ultrasonographically. Based on the results of these studies, they were divided into two groups. First group- patients with MVD without pulmonary edema, and Second group - dogs with MVD with pulmonary edema.

The ultrasound was performed with a veterinary Doppler apparatus My Lab 70 vet XV apparatus (Esaote, Italia). Patients were evaluated with specialized cardiac phasometric transducers PA023E (at a frequency of 4-11MHz) and PA122E (with a frequency of 3-7 MHz), suitable for small dog breed cardiac patients in the right-sided parasternal position. Patients were examined in the right-sided parasternal sections - longitudinal (long axis) and transverse (short axis).

The radiographs of the thorax were performed with direct digital radiography (DR X-ray system) in LLR (left lateral), and VD (ventro-dorsal) projections.

In order to permit the comparison of echocardiographic measurements in patients of different sizes, the parameters were indexed according to the aortic size (Ao). The application of this ratio is better compared to the use of values, normalized according to body weight or body surface area, because the aorta does not change in size as a result of most cardiac disorders [9] and does not depend on the sex and nutritional status of the patients. The value of each index has a visual interpretation. According to Brown et al. [10] "How many aorta widths is the left ventricular size during diastole?"

The VHS was determined by the approved standard: the longitudinal axis of the heart was measured from the ventral border of the tracheal bifurcation to the most ventral part of the cardiac apex. Perpendicular to the longitudinal axis, the short axis was measured at the level of vena cava caudalis. These measurements were applied to the spine, from the beginning of the fourth thoracic vertebra. We then obtained a VHS, summing up the number of vertebrae on which the longitudinal and transverse dimensions were stretched.

Statistical analysis

All indicators presenting the echocardiographic M-mode and radiographic dimensions in patients with pulmonary edema and those without pulmonary edema were determined by a computer program (Statistica, v. 6.0.), using the nonparametric method (Mann Whitney U-test) and the parametric method (One-way ANOVA) with LSD post hoc analyses and represented as an average mean – its average arithmetic standard deviation (SD). The differences were considered statistically significant at $P< 0.05$. The linear regression analysis was performed with computer program Statistica, v. 6.0.1.

III. Results and Discussion

The first group (Table 1) consisted of 7 patients (4 male and 3 female) at an age between 7 and 11 years, with a body weight between 4.3 and 12.5 kg. The breed composition of the group was as follows: 1 dog from the breeds Shih Tzu, Bichon frize, Pinscher, Maltese, Dachshund, Poodle, and 1 patient from a mixed breed. Of those there were 3 with mitral prolapse and 4 without mitral prolapse. Flail leaflet was established in 3 patients. For one of the dogs there was data of broken secondary chords.

Table 1. Individual values of the dogs with MVD without pulmonary edema

Dog № (sex)	Indicator				
	LA/AO	LVD /AO	LC/AO=LA/AO +LVD/AO	VHS	LA/AO x VHS
1 (F)	1.176	2.082	3.258	11.0	12.980
2 (M)	1.160	1.911	3.071	11.5	13.340
3 (M)	1.686	2.571	4.257	11.0	18.590
4 (M)	1.587	1.825	3.412	11.5	18.285
5 (F)	1.264	1.943	3.207	11.0	13.860
6 (M)	1.765	2.429	4.194	11.0	19.360
7 (F)	1.630	2.310	3.94	11.0	17.930

LA– left atrium; AO – aorta; LVD-d – left ventricul diameter – diastole; LC (Index of Le Bobinnec) = LA+ LVD;
VHS – vertebral heart rate; LA/AO x VHS – combined (echocardiographic and radiographic) indicator; M – male; F – female

The second group (Table 2) was formed of 11 dogs (8 male и 3 female) at an age between 8 and 15 years, with body weight between 4.5 and 10 kg. The breed composition of the group was as follows: 1 dog from the breeds Dachshund, Shi Tzu, Cavalier King Charles, 2 of the Pekingese breed and 6 mixed breed dogs. All dogs in the second group had mitral prolapse, Flail leaflet and data of broken secondary chords.

Table 2. Individual values of the dogs with MVD with pulmonary edema

Dog № (sex)	Indicator				
	LA/AO	LVD /AO	LC/AO=LA/AO +LVD/AO	VHS	LA/AO x VHS
1 (M)	2.212	2.577	4.789	11.5	25.415
2 (F)	2.268	2.123	4.391	12.0	27.24
3 (M)	1.541	1.44	2.981	13.0	20.02
4 (M)	2.075	2.625	4.7	13.0	27.04
5 (M)	1.688	2.567	4.255	12.0	20.28
6 (F)	2.155	2.558	4.713	11.5	24.84
7 (M)	2.030	2.611	4.641	13.0	26.39
8 (M)	2.880	3.031	5.911	14.5	41.76
9 (M)	1.950	2.858	4.808	13.0	25.35
10 (F)	1.970	2.234	4.204	11.0	21.67
11 (F)	2.390	2.68	5.07	11.0	26.29

LA– left atrium; AO – aorta; LVD-d – left ventricul diameter – diastole; LC (Index of Le Bobinnec) = LA+ LVD;
VHS – vertebral heart rate; LA/AO x VHS – combined (echocardiographic and radiographic) indicator; M – male; F – female.

After extensive echocardiographic and radiographic examinations of the patients, only the dimensions that most closely reflected the changes in cardiac structures in case of MVD were selected and reflected in tables.

Numerous studies have been conducted to determine a single ultrasound parameter that could predict the onset of heart failure in MVD. In this connection, Borgarelli et al. in a study conducted with a large number of animals, demonstrated that as a predictor of survival, when only cardiac-related deaths were included in dogs with MVD, only the LA/Ao ratio maintained statistical significance. The left atrial enlargement reflects the degree of severity and the chronic nature of mitral regurgitation [11]. In our study, the detailed analysis of this ratio (Tables 1 and 2) shows that in 4 patients from the first group (= 57%) and in 2 dogs from the second group (= 18%), values overlap from 1,541 to 1,765. Below these values, the patients are without pulmonary edema, and above these values they have pulmonary edema. In this regard, we believe that LA/AO can be used as an important indicator in the interpretation of data in group studies, but it cannot conclusively demonstrate the need for a medical intervention in the individual.

In order to enhance the predictive effect of the LA/AO ratio, Le Bobinnec, [12] introduces a new index that includes the left ventricular diastolic score. MVD has a very variable evolution, and the unresolved issue in this disease is still: when should we start treatment?

It is already proven that ACE inhibitors improve the clinical condition and extend the life span of dogs with symptomatic MVD, but unfortunately they have no preventative effect in the asymptomatic stages. Therefore, we obviously need a "key" to make it possible to predict the risk and the time until the beginning of CHF. The author believes that this will allow premature interventions that will improve the outcome of the treatment. He steps on previous studies of NT-proBNP and M-mode echocardiographs and introduces a new set of indexes (LC/Ao) = LA/Ao + LVD/Ao), giving values for the individual classes of MVD – for Class 1a: 3.12; Class 1b: 4.01; Class 2: 4.59; Class 3a: 5.04. Based on this, the author claims that if an asymptomatic MVD is detected with LC/Ao > 4.5, treatment with ACE inhibitors, pimobendan or spironolactone can be initiated immediately. A detailed analysis of this ratio in our study (Tables 1 and 2) showed that using the value of 4.5 given by Le Bobinnec, G., [12], which determines in which dogs it is necessary to start treatment for heart failure, independently of the presence or absence of pulmonary edema, in group 1 there are no patients in need of drug therapy since the maximum LC/Ao ratio is 4.257. In the 2-nd group, 4 dogs (=36%) were below 4.5 and despite the radiographically diagnosed pulmonary edema, according to the individual LC/Ao values, they did not require any treatment. This gives us reason to assert that this indicator, similar to the LA/AO ratio, is appropriate for group studies, but can be misleading in the individual assessment of cardiac activity.

Standard summarized statistical data for Group 1 – dogs with MVD with pulmonary edema were compared with those in Group 2 – dogs with MVD without pulmonary edema in Table 3, where the mean and standard deviation of the investigated ratios were shown.

Table 3. Echocardiographic M-mode and radiographic dimensions, depending on the absence and presence of pulmonary edema

Indicator	Without pulmonary edema (n = 7)		With pulmonary edema (n = 11)		Statistical significance
	Mean	SD	Mean	SD	
LA/AO	1.4669	0.2575	2.1054	0.3554	** ♦♦♦
LVD/AO	2.1530	0.2860	2.4822	0.4263	*
LC/AO=LA/AO +LVD/AO	3.6199	0.4973	4.0058	0.7058	** ♦♦
VHS	11.143	0.244	12.318	1.079	* ♦♦
LA/AO x VHS	16.3350	2.7968	26.0268	5.8358	** ♦♦♦

Statistically significant difference between data on dogs with and without pulmonary edema using nonparametric method – Mann Whitney U-test: * - $p < 0.05$; ** - $p < 0.01$; and parametric method – one way ANOVA: ♦ - $p < 0.05$; ♦♦ - $p < 0.01$; ♦♦♦ - $p < 0.001$

The mean LA/AO ratio in the non-edema group was (1.4669 ± 0.2575) which is statistically significantly lower (Table 3) than the mean for the edema group (2.1054 ± 0.3554) (Table 3).

The mean value of the indexed size LVD/AO in the group without edema (2.1530 ± 0.2860) is statistically with lower significance (Table 3) according to the nonparametric method – Mann Whitney U-test, and statistically insignificantly lower than the mean value in the group with edema (2.4822 ± 0.4263) according to the parametric method – one way ANOVA.

The mean value of the ratio LC/Ao in the group without edema was (3.6199 ± 0.4973) which is statistically significantly (Table 3) lower than the mean value in the group with edema (4.0058 ± 0.7058).

The mean value of VHS in the group without edema was (11.1429 ± 0.2440) which is statistically significantly (Table 3) lower than the mean value in the group with edema (12.3182 ±1.0787). The size we introduce LA/AO x VHS multiplies the heart enlargement from the radiographic and M-mode ultrasound examination. The mean value of this multiplication in the first group was (16.3350 ± 2.7968) which is statistically significantly (P<0.01) lower than the mean value in the group with edema (26.0268 ± 5.8358).

The detailed analysis of the LVD/AO ratio (Tables 1 and 2) shows that there is a 100% overlap in both groups. The values in the group without pulmonary edema range from 1.825 to 2.429, while in the group with pulmonary edema they vary from 1.44 to 3.031. Similar is the situation with the radiographically determined VHS, where the detailed analysis (Tables 2 and 3) shows that there is a 100% overlap in both groups. VHS values in the group without pulmonary edema range from 11.0 to 11.5, whereas in the group with pulmonary edema they are between 11.0 to 14.5.

The size we introduce LA/AO x VHS multiplies the heart enlargement from X-ray and M-mode ultrasound imaging. The detailed analysis of the multiplication (Tables 1 and 2) shows that there is a 100% difference in the values in the two groups, and in the group without edema they range from 12.98 to 19.36, while in the group with edema they range from 20.02 to 41.76. Additional studies with a larger number of patients would indicate the potential of this ratio to be predictive of cardiac decompensation.

Tables 4 and 5 clearly show the amplifying for some and balancing for other indicators, character of the new echocardiographic indicator. This is particularly evident from the size that has no common elements with it – LVD/Ao, where there is a lack of a reliable correlation with VHS. The new echocardiographic parameter compensates for this, at the expense of LA/AO's correlation credibility. In cases of MVD, the proposed combined (echocardiographic and radiographic) indicator LA/AO x VHS reduces the reliability of the correlation where it is in surplus and increases it where it is insufficient.

Table 4. Results from the linear analysis of the new ratio LA/AO x VHS

Ultrasound size	LA/AO x VHS (n = 18)			
	Coefficient of determination	**Correlation coefficient**	**Model selection criterion**	**R^2**
LA/AO	0.912	0.955	2.213	0.912
LVD/AO	0.451	0.672	0.378	0.451
LC/AO=LA/AO +LVD/A	0.792	0.890	1.350	0.792
VHS	0.538	0.733	0.551	0.538

LA/AO x VHS – independent; LA/AO, LVD/AO, LC/AO, VHS – dependent.

Table 5. Values for the reliability of the cross linear regression in dogs with MVD

Indicator				
LA/AO	*LA/AO*			
LVD /Ao	0.0012	*LVD /Ao*		
LC/AO=LA/AO +LVD/Ao	2.356E-008	1.242E-007	*LC/AO*	
VHS	0.0297	0.1835	0.0541	*VHS*
LA/AO x VHS	7.070E-010	0.0023	7.482E-007	0.0005

IV. Conclusion

The combined size LA/AO x VHS, compared to other investigated echocardiographic and radiographic values in dogs of different breeds, sex, weight and age, most reliably shows the rate of development of MVD. This value can be used in patients undergoing pre-diuretic therapy where the absence of pulmonary edema in the radiographic examination does not mean a lack of cardiac decompensation. Proving the possibility that the value of this coefficient can be a prognostic factor for the onset of heart failure and a marker for the initiation of treatment in patients with myxomatous valve degeneration needs further examination with a larger number of patients.

The ratios LA/AO; LC/AO and the values of VHS, despite the statistically significant differences between the two treatment groups, cannot be used as a marker to initiate therapy in patients with MVD, due to the overlapping values obtained in this study.

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