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Article

The relationship between Stage B1 Myxomatous Mitral Valve Disease and Cardiac Weight in Dogs: a study on 19 patients

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Abstract: Myxomatous mitral valve disease (MMVD) is a prevalent heart condition in dogs, particularly affecting the mitral valve. Stage B1 of MMVD, as per the American College of Veterinary Internal Medicine (ACVIM) guidelines, encompasses asymptomatic dogs with structural heart disease. This stage is characterized by a range of radiographic and echocardiographic findings without significant cardiac remodeling. Despite its prevalence, the impact of MMVD Stage B1 on cardiac weight remains unclear. In this study, 28 dogs were examined to evaluate if MMVD Stage B1 correlates with abnormal increases in heart weight postmortem. Dogs were clinically examined, underwent echocardiography, and were divided into two groups based on MMVD staging. Heart weight relative to body weight (hW/bW) was assessed. Results revealed that MMVD Stage B1 had minimal impact on heart weight, with hW/bW ratios remaining within normal ranges. Notably, despite differences in breed, sex, and age, hW/bW ratios did not significantly deviate from normal values. This study provides valuable insights into the relationship between MMVD Stage B1 and cardiac weight in dogs, indicating the need for further investigations with larger sample sizes to validate these findings. Understanding cardiac weight alterations in MMVD can aid in refining diagnostic and management approaches for affected dogs.

Keywords: dog; MMVD stage B1; heart weight.

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1. Introduction

Approximately 10% of dogs presented to primary care veterinary practices are diagnosed with heart disease, with myxomatous mitral valve disease (MMVD) being the most common. In North America, MMVD accounts for approximately 75% of heart pathologies [1]. This pathology is known by various names in literature, including chronic valve disease, degenerative valve disease, endocardiosis, and chronic myxomatous valvular disease [2].

While MMVD primarily affects the mitral valve, it has been reported to affect the mitral valve alone in 62% of dogs, both the mitral and tricuspid valves in 32.5%, and the tricuspid valve alone in 1.3% [3]. The condition is approximately 1.5 times more frequent in males than in females, with higher prevalence observed in smaller dogs (<20 kg). Moreover, the prevalence of MMVD increases markedly with age, particularly in small breed dogs, with up to 85% showing evidence of valve lesions by 13 years of age [1].

Although the precise cause of MMVD remains unknown, it has been established that the disease has an inherited component in some breeds such as Cavalier King

Charles Spaniels [11] and Dachshunds [12]. Additionally, the severity of the disease may have a genetic component in other breeds [1].

The mitral valve leaflets consist of four distinct layers, and when the spongiosa layer thickens, it regains the appearance of mesenchymal tissue, hence the name "myxomatous" [14]. Within the spongiosa layer, myofibroblasts proliferate and form small nodules, which are characteristic of MMVD. Furthermore, endothelial dysfunction promotes thickening of the valve leaflets due to shear stress [2, 13], contrasting with normal atrioventricular valve leaflets, which appear as thin and translucent structures without nodules or thickening at the valve margins [3].

The course of the disease can have four stages of progression: 1) It can start at an older age, progress slowly and never end in heart failure; 2) It progresses slowly and then suddenly, after chordal rupture, progresses rapidly and ends in acute heart failure; 3) It progresses slowly and eventually ends in heart failure; 4) It can progress subclinically and end in sudden death [2].

The American College of Veterinary Internal Medicine (ACVIM) guidelines are commonly used for the clinical classification of dogs with MMVD which describes 4 basic stages of heart disease and heart failure: *Stage A,B,C* and *D* [1].

Stage B identifies dogs with structural heart disease and has 2 subcategories: stage B1 includes asymptomatic dogs that have no radiographic or echocardiographic evidence of cardiac remodeling in response to their MMVD, as well as those in which remodeling changes are present, but not severe enough to meet current clinical trial criteria for treatment initiating [1]; stage B2 refers to asymptomatic dogs that have more advanced mitral valve regurgitation that is hemodynamically severe and long-standing enough to have caused radiographic and echocardiographic findings of left atrial and ventricular enlargement that meet clinical trial criteria used to identify dogs that clearly should benefit from initiating pharmacologic treatment to delay the onset of heart failure [1].

Stage B1 of myxomatous mitral valve disease (MMVD) encompasses a broad spectrum of radiographic and echocardiographic findings. This stage includes dogs with normal left atrial (LA) and left ventricular (LV) dimensions, normal LV systolic function, and normal radiographic vertebral left atrial size (VLAS). However, it also includes patients with echocardiographic or radiographic evidence of left atrial and ventricular enlargement that does not meet specific criteria, such as echocardiographic LA:Ao ratio in the right-sided short axis view in early diastole ≥1.6, left ventricular internal diameter in diastole normalized for body weight (LVIDDN) ≥1.7, and breed-adjusted radiographic vertebral heart score (VHS) >10.5 [1].

In most cases in the B1 ACVIM stage thoracic echocardiography often reveals remodeled, redundant valve tissue extending across the annulus into the left atrium during systole (3). This is accompanied by the presence of a turbulent jet flow at the level of the affected valve, clinicaly expres as a heart murmur with intensity ≥3/6.

Myxomatous degeneration transforms normal thin, translucent leaflets into opaque structures that become thickened in their distal third, progressing to diffuse valve thickening, nodularity, and deformation [3]. A simple classification scheme for grading the severity of gross, myxomatous lesions has been reported and is based upon the degree of leaflet nodularity, thickening, and deformity: Type I lesions represent valve leaflets that contain a few, small, discrete nodules in regions where leaflets contact each other, with areas of opacity in the proximal valve; Type 2 lesions represent leaflets with larger nodules which tend to coalesce at the edges of valve contact, and areas of diffuse opacity may be present; Type 3 lesions comprise larger nodules which have coalesced into irregular, plaque-like deformities, and extend to involve proximal portions of the chordae; Type 4 lesions denote gross distortion and ‘ballooning’ of the valve cusps, and the chordae tendineae are thickened proximally [3].

As part of a complete necropsy examination, a macroscopic and morphometric assessment of the canine heart is required. The first step of this examination involves weighing the heart. Ventricular wall thickness has shown a poor correlation with ventricular mass, so heart weight provides more valid information about possible ventricular hypertrophy, especially in cases of dilation and eccentric hypertrophy [7].

Due to the wide variety of dog somatotypes, accurately assessing cardiac mass requires a ratio of heart weight to total body weight. Few studies have mentioned the heart-to-body weight ratio, with similar results reported: 0.43% to 0.99% [7], 0.6% to 1.1% [5], 0.61% to 0.94% [6], and 0.66% to 1.20% [8]. A wider interval was reported by Ghoshal [9], with a heart-to-bodyweight ratio of 0.5% to 2.2% [5]. Schoning et al. [17]. published similar data for Greyhounds, with results of 1.3 ± 0.2% for females and 1.2 ± 0.2% for males. It is known that the heart-to-body weight ratio is higher in neonates than in adults and varies within species, being higher in more athletic animals (such as horses and dogs) [7].

All the mentioned studies are based on normal macroscopic hearts. In this context, the aim of this study was to evaluate if MMVD stage B1 (ACVIM) can be associated with an abnormal increase in heart weight after postmortem evaluation.

2. Materials and Methods

This research was conducted at the Department of Internal Medicine-Cardiology and Department of Animal Pathology, University of Agricultural Sciences and Veterinary Medicine, Cluj-Napoca, Romania. It involved 28 owner-owned dogs of various breeds, ages (over 1 year old), sexes, and body weights. All dogs underwent a comprehensive clinical examination including assessment of body weight, heart rate, and respiratory rate, followed by a thorough cardiac examination comprising thoracic palpation, auscultation, electrocardiography, and echocardiography. Transthoracic echocardiographic examinations were performed by the same examiner using an Esaote ultrasound (Esaote SpA, Genoa, Italy) equipped with phased-array transducers ranging from 2 to 8 MHz, along with simultaneous single-lead electrocardiography. Dogs were examined from both right and left parasternal positions, obtaining standard echocardiographic 2-dimensional, M-mode, and Doppler images without sedation. For the assessment of ACVIM stage B1, specific echocardiographic criteria were employed. These included the presence of mitral regurgitation (MR) with a mosaic pattern upon color flow Doppler, alongside a normal left atrium (LA) characterized by an echocardiographic LA:Ao ratio <1.6 in the right-sided short-axis view during early diastole. Additionally, normal left ventricular (LV) dimensions and systolic function despite the presence of MR were required. LV measurements, including interventricular septum (IVS), left ventricular internal diameter (LVID), and left ventricular posterior wall (LVPW), were determined in the right parasternal short-axis view using M-mode. Diastolic measurements were taken at the beginning of the QRS complex, while systolic measurements were timed at the shortest distance between the septum and the lateral wall. The leading-edge technique was used for all measurements, as described by Wyatt et al. (1983) [10].

Inclusion criteria: Adult dogs (over 1 year old) with various pathologies, slated for euthanasia, without pre-existing cardiac diseases or with ACVIM stage B1 MMVD as determined by echocardiographic imaging.

Exclusion criteria: Presence of a heart murmur greater than 3/6 on auscultation; morpho-structural thoracic changes hindering quality echocardiographic imaging; administration of any cardio-vascular affecting substance within the previous 14 days; identification of congenital or acquired cardiac anomalies beyond ACVIM stage B1, as detected by 2D echocardiography, M-mode, and Doppler examinations.

Based on the provided criteria, the patients (n=19) were divided into two groups: group 1 (n=13), comprising patients without cardiac disease, and group 2 (n=6), comprising patients with MMVD stage B1 according to ACVIM.

In group 1, there were 7 females and 6 males, with body weights ranging from 7.9 to 65 kg and ages from 2 to 12 years old. The breeds represented were 4 mongrel dogs, 3 German Shepherds, and one each of Tosa Inu, Teckel, Labrador Retriever, Bichon Frise, Dogo Argentino, and Boxer.

In group 2, there were 2 females and 4 males, with body weights ranging from 8 to 43 kg and ages from 10 to 15 years old. Three of them were mongrel dogs, and one each of Golden Retriever, Irish Setter, and West Highland White Terrier.

All dogs from both groups exhibited normal body condition relative to their age and breed. No ECG modifications were observed during a five-minute recording with the patients in lateral recumbency.

The dogs were humanely euthanized (owner consent previusly obtained, in accordance with the national and interntional legislation) , and heart necropsy was performed. The necropsy examination was conducted with the dogs in lateral decubitus on the left side, with the abdomen dorsal. The entire cardiorespiratory system was dissected from the level of the tongue to the diaphragm. Initial inspection of the heart was done together with the lungs before separation. The pericardium was removed for proper macroscopic examination. Residual blood clots and large vessels were eliminated, and the heart was weighed using the same scale, with the weight noted in grams.

3. Results

The results of the study are presented in Tables 1 and 2. The relationship between heart weight and body weight (hW/bW) was assessed individually, indicating that the heart weight represented 0.44% to 1.11% of the animal's body weight for group 1 and 0.51% to 0.93% for group 2.

Table 1. Results obtained from group 1 (free of cardiac pathologies)

No.	Breed	Age (years)	Sex	Weight (kg)	Cardiac murmur	Cardiac pathology	hW/bW ratio
1	Tosa Innu	8	F	26	No	No	0,79
2	Teckel	4	F	9,8	No	No	0,85
3	Mongrel dog	2	F	26,3	No	No	0,66
4	Mongrel dog	10	M	30,7	No	No	0,86
5	Labrador Retriever	7	F	36	No	No	0,57
6	German Shepard	8	M	38,7	No	No	0,77
7	Bichon Frise	5	M	7,9	No	No	0,94
8	German Shepard	12	F	18,1	No	No	1,03
9	Mongrel dog	3	M	40	No	No	0,68
10	Dogo Argentino	2	M	40	No	No	0,7

11	German Shepard	6	F	23,6	No	No	1,11
12	Mongrel dog	6	M	65	No	No	0,44
13	Boxer	5	F	27	No	No	0,74

bW= body weight; hW= heart weight.

Table 2. Results obtained from group 2 (with MMVD stage B1).

No.	Breed	Age (years)	Sex	Weight (kg)	Cardiac murmur	Cardiac pathology	hW/bW ratio
1	Mongrel dog	10	F	8	Yes	Yes	0,78
2	Mongrel dog	15	M	30	Yes	Yes	0,55
3	Mongrel dog	13	F	21,4	Yes	Yes	0,85
4	Golden Retriever	10	M	23,2	No	Yes	0,93
5	Irish Setter	13	M	43	No	Yes	0,51
6	West Highland White Terrier	12	M	9,8	No	Yes	0,88

4. Discussion

Cardiac diseases often manifest through changes in the size and weight of specific heart components, with the degree of change typically proportional to the severity of the disease, as seen in hypertrophic and dilated cardiomyopathies [5, 18].

Stage B1 (ACVIM) represents perhaps the most common yet underdiagnosed form of MMVD, characterized by the absence of clinical signs. In this stage, the heart murmur may be of low intensity and even be missed by the examiner during cardiac auscultation. Additionally, ECG and thoracic radiographs may show no significant changes, further complicating diagnosis. Consequently, Stage B1 represents a gray area in MMVD, where pathology exists but without clinical signs and without the need for treatment at this stage.

In group 2, all patients showed no clinical signs attributable to cardiac pathology, had normal ECG readings, but exhibited an audible heart murmur ranging in intensity from 1/6 to 3/6.

The likelihood of ACVIM stage B1 of MMVD affecting total cardiac weight is diminished, given that the valvular apparatus is the primary element impacted. This fact is corroborated by the results obtained in this study. However, significant weight variations may occur from ACVIM stage B2 onwards, indicating substantial cardiac remodeling as identified by echocardiography. Exploring the correlation between left ventricular mass and total body weight across different ACVIM MMVD stages could be a promising avenue for future research. Such a study could reveal more notable differences in values due to the nature and progression of the pathology, which affects the left ventricle in 62% of cases [3].

An overview of the age distribution among the patients involved in the study reveals a higher average age for the dogs included in group 2, supporting the hypothesis of a higher incidence of cardiac pathology in geriatric patients [1]. MMVD is widely recognized as a disease of the aging heart, as extensively described by

Connell et al. [4]. Despite two patients being classified as large breed dogs, specifically a Golden Retriever and an Irish Setter, it can be inferred that the remainder of patients in group 2 are predominantly medium to small-sized dogs, which is also a risk factor and predictor for cardiac pathology. It's commonly observed that small dogs tend to live longer on average than large dogs, potentially contributing to the development of MMVD in smaller breeds [3].

The hW/bW ratio results in both groups were within normal ranges, with only 4 values falling below the minimum range, set at 0.6%. However, when compared to Ghoshal's findings (9), which reported a wider range of 0.5% to 2.2%, only one value fell below the lower limit. This value, at 0.44%, was observed in a noncardiac mongrel dog (male) weighing 65 kg. Values below 0.6% were observed in both groups. Among the cardiac patients, an Irish Setter exhibited a ratio of 0.51%, and a 30 kg male mongrel dog had a ratio of 0.55%. The noncardiac patient, a female Labrador Retriever weighing 36 kg, had a ratio of 0.57%.

Only two values exceeded 1%, both found in female German Shepherds without cardiac diseases. In group 2, no value reached 1%, and none of the patients reached the maximum value of 2.2% reported by Ghoshal [9]. Consistent with other studies, neither breed, sex, nor age of adult dogs influenced the hW/bW ratio [5, 6, 17].

An important factor that should not be overlooked and can significantly influence the hW/bW ratio investigated in this study is the patient's body condition score (BCS). BCS is a numeric evaluation system commonly used to assess body fat accumulation [15], with the 9-point scale being most frequently employed in dogs [16]. Utilizing this scale helps reduce subjectivity in the assessment. Excessive body fat accumulation leading to overweight or obesity in dogs may result in a low or normal hW/bW ratio. Conversely, various pathologies can induce cachexia in a patient, potentially leading to a falsely higher ratio than the normal range. Therefore, evaluating BCS before or during necropsy examination is becoming increasingly essential. Although the dogs involved in this study were neither obese nor emaciated, a formal BCS assessment was not performed.

Additionally, previous studies [5-8, 17]. considered dogs to have normal weight based on subjective assessments. Overweight dogs could provide a valid explanation for the lower results observed in this study. For instance, the values of 0.44% and 0.51% were obtained from dogs with the highest weights, 65 kg and 43 kg, respectively. However, the value of 0.44% may still be considered normal according to references provided by some authors [7].

The novelty of this study lies in its comprehensive approach, which involves both pre- and post-necropsy examinations of the heart, a methodology not previously employed in existing studies [5-9]. Previous studies typically examined dogs without the clinical examination being complemented by ultrasound, and the heart was considered normal based solely on macroscopic examination during necropsy.

Estimating cardiac hypertrophy at necropsy is typically attempted through various methods, including gross observation of cardiac structure, measurements of ventricular wall thickness, and weighing of the heart in relation to body weight [5]. However, the variations in heart weight depending on cardiac pathology remain largely unknown, as there are no published studies of this nature. Therefore, this study fills an important gap in the literature by providing a more detailed and nuanced understanding of cardiac pathology and its impact on heart weight.

5. Conclusions

The ACVIM stage B1 of MMVD has a minor effect on heart weight, keeping the hW/bW ratio within the normal range. Further research is needed due to the limited patient pool. These findings provide a foundation for calculating this ratio across different ACVIM stages. Results for noncardiac patients align with past studies.

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