



# A Retrospective Study of Radiographic Measurements of Small Breed Dogs with Myxomatous Mitral Valve Degeneration: A New Modified Vertebral Left Atrial Size

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**Abstract** Vertebral left atrial size (VLAS) is an important indicator to predict myxomatous mitral valve degeneration (MMVD) in dogs. When the caudal margin of cardiac silhouette and the dorsal margin of caudal vena cava (CdVC) could not be seen exactly, another way to evaluate VLAS is needed. The objective of this study was to assess whether a new modified VLAS (m-VLAS) could be used as an indicator to predict MMVD in 57 small breed dogs with MMVD. The m-VLAS was also used to classify American College of Veterinary Internal Medicine staging groups and left heart enlargement confirmed with echocardiograph (EchoLHE) groups. The m-VLAS was measured as the distance from the ventral aspect of the carina to the dorsal aspect of the intersection of the cardiac silhouette and the farthest LA caudal margin, not the CdVC, followed by drawing the same line beginning at the cranial edge of T4. Based on VLAS values and m-VLAS values measured for dogs with MMVD, correlations between these values and left heart enlargement groups were then evaluated. There were significant differences in both the VLAS and the m-VLAS between EchoLHE groups. The AUC of the ROC curve of the m-VLAS to detect EchoLHE was higher than that of the VLAS. The optimal cutoff value for the m-VLAS was >2.7, which had a higher specificity (86.84%) than the VLAS specificity (71.05%). This study reveals that a new m-VLAS is a more specific indicator than the VLAS for predicting left side heart enlargement in small breed dogs. Therefore, the m-VLAS can be used as a clinically useful radiographic measurement alternative to or better than the VLAS.

**Key words** canine, small breed, myxomatous mitral valve disease, vertebral left atrial size, radiograph.

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## Introduction

Myxomatous mitral valve degeneration (MMVD), the most common cardiovascular disease in dogs, is characterized by degenerated mitral valve and remodeling of left side heart. MMVD in some dogs can progress to pulmonary artery hypertension and the development of a secondary disease such as pulmonary edema. It has been reported that MMVD is most commonly diagnosed in small to medium sized dogs over 10 years of age (2,6). The mean survival time of dogs with MMVD is 6.6 years (3). Evaluation of murmur is an important diagnostic assessment at the early stage MMVD. Thoracic radiography and echocardiography are gold standard methods for evaluating left side heart enlargement, especially the left atrium (LA) (6,17). Therefore, there are many radiography examinations (e.g., vertebral heart size (VHS) (1,4), radiographic left atrial dimension (RLAD) (23), value of tracheal bifurcation angle (16), bronchus to spine method (22) for predicting left heart size.

Recently, American College of Veterinary Internal Medicine (ACVIM) consensus has proposed vertebral left atrial size (VLAS), the measurement of LA enlargement in thoracic radiography, as a new radiographic measurement and a useful radiographic index for detecting LA enlargement in dogs (10,18). VLAS is the distance from the ventral aspect of the carina to the dorsal aspect of the intersection of the cardiac silhouette and caudal vena cava (CdVC) after drawing the same line beginning at the cranial edge of T4 (18). A study of VLAS in healthy adult dogs has revealed the median value of VLAS is 1.9 (1.4-2.2) (26). When VLAS values are equal to or larger than 3 ( $\geq 3$ ), it is possible to predict stage B2 without echocardiography (10). However, that study had a wide dog population ranging from small breed dogs to large breed dogs with variable weights. Differences in VHS between small breed and large breed dogs have been described in many studies (1,5,9,13,15,21). However, only a few studies on breed variation of VLAS in veterinary medicine have been reported (12,21,26). Therefore, we hypothesize that there would be differences in VLAS value if subjects are limited to small breed dogs.

Furthermore, cross point caudal margin of cardiac silhouette and dorsal margin of CdVC could not be seen exactly for many reasons (e.g., severe pulmonary pattern, no remarkable CdVC margin by dehydration, and mediastinal mass). Consequently, another way that is easy to evaluate VLAS using LA margin to replace the original method of measuring VLAS is needed. Such new method needs to be compared with the VLAS.

Therefore, our objectives of this retrospective study were as follows: 1) to compare VLAS, VHS, left atrial-to-aortic (LA/Ao) ratio, and normalized left ventricular internal dimension at end-diastole (LVIDDn) in small breed dogs on ACVIM 2019 Consensus; and 2) to evaluate the correlation between the modified VLAS (m-VLAS) and the VLAS in LA enlargement patients.

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## Materials and Methods

### Animals

Medical records of client-owned small-breed dogs ( $\leq 10$  kg) with MMVD examined at the Veterinary Medical Teaching Hospital between January 2018 and December 2019 were retrospectively reviewed. All dogs had to have undergone physical examination, blood analyses, thoracic radiography, and echocardiography. Dogs with heart murmur and mitral regurgitation confirmed by echocardiography were included even though they had no cardiovascular symptoms or radiographic findings of cardiomegaly. All dogs were reexamined for measurements of various values post MMVD diagnosis such as VHS, VLAS, m-VLAS, LA/Ao ratio, and LVIDDn.

Dogs were excluded if they had thoracic vertebral abnormalities, pericardial effusion, a cardiac mass, or if the cardiac silhouette could not be adequately visualized due to situations such as severe diffuse alveolar pulmonary pattern, pleural effusion, and peritoneal-pericardial diaphragmatic hernia. Dogs with tricuspid valve regurgitation were not excluded from this study. This is because clinically irrelevant tricuspid valve regurgitation is common in dogs. In addition, it does not affect the LA size.

### Thoracic radiography

A right lateral thoracic radiograph was used for measuring VHS, VLAS, and m-VLAS. VHS and VLAS were measured using a digital caliper in the right lateral view as described in the introduction. The VHS is the sum of measurements of cardiac silhouette length and width, followed by equating the sum of a dog's vertebrae starting at T4 (1). The VLAS is the distance from the ventral aspect of the carina to the dorsal aspect of the intersection of the cardiac silhouette and caudal vena cava (CdVC) after drawing the same line beginning at the cranial edge of T4 (18). The new method to evaluate VLAS is calculated after drawing a line from the ventral aspect of carina to the farthest LA caudal margin, not the CdVC (Fig. 1). An experienced veterinarian for radiology (ASY) performed all measurements of radiographic indices using a ZeTTA PACS Viewer 2001 (Taeyoung Soft, Korea).

### Echocardiography

All dogs underwent complete echocardiographic examinations, including transthoracic 2-dimensional, M-mode,



**Fig. 1.** Measurement of VLAS and modified VLAS (m-VLAS) demonstrated on right lateral inspiratory radiograph of a dog with myxomatous mitral valve degeneration. A line from the center of the ventral aspect of the carina to cross point of the caudal margin of cardiac silhouette and dorsal margin of caudal vena cava is drawn as a solid line. A line from the carina to the most caudal aspect of the left atrium is drawn as a dotted line. The same line that was equal in length was drawn beginning T4 parallel to the vertebrae.

spectral, and color-flow Doppler using an Aloka Arietta 70 ultrasound system (Hitachi Aloka, USA) with a sector probe (2-9 MHz, S31 sector probe, Hitachi-Aloka, USA) by radiologists. The LA/Ao ratio and the left ventricular internal diameter in diastole (LVIDd) value were obtained. The LA size was also determined from a right parasternal short-axis view (LA/AoSx) with a conventional method. Short-axis LVIDd was measured using M-mode at end-diastole. The LVIDd was normalized (LVIDDn) to body weight (kg) according to the following formula:  $LVIDDn (cm)/kg^{0.294}$ . MMVD stage B2 in ACVIM had the following criteria: murmur intensity  $\geq 3/6$ , LA/Ao ratio  $\geq 1.6$ , LVIDDn  $\geq 1.7$ , and VHS  $> 10.5$  (10). Dogs with current or past clinical signs of pulmonary edema were classified as ACVIM stage C-D. First, ACVIM criteria for cardiac remodeling were applied and divided by ACVIM stages in all dogs: stage B1, stage B2, and stage C-D (10). Second, all dogs included in this study were divided into two groups based on whether or not echocardiographic criteria for left heart enlargement (EchoLHE) were met: LVIDDn  $\geq 1.7$  and LA/Ao  $\geq 1.6$ . Dogs in group 1 (EchoLHE-no) failed to meet either or both EchoLHE criteria. Dogs in Group 2 (EchoLAE-yes) met both EchoLHE criteria (20).

### Statistical analysis

Statistical analyses were performed with commercial soft-

**Table 1.** Descriptive data for 57 dogs with MMVD according to ACVIM staging group

Variable	Stage B1	Stage B2	Stage C-D
N	8	8	41
Age (year)	11.1 (3.6)	10 (3.3)	12.3 (2.5)
Weight (kg)	5.3 (1.9)	5.3 (2.8)	4.9 (2.2)
LA/Ao ratio	1.5 (0.3)	1.9 (0.4)*	2.0 (0.5)*
LVIDDn	1.3 (0.2)	1.5 (0.3)	1.6 (0.3)*
VHS (v)	10.6 (0.9)	10.7 (0.9)	10.9 (1.2)
VLAS (v)	2.4 (0.3)	2.6 (0.3)	2.5 (0.5)
m-VLAS (v)	2.4 (0.2)	2.5 (0.2)	2.6 (0.5)

MMVD, myxomatous mitral valve disease; ACVIM, American College of Veterinary Internal Medicine; LA/Ao, left atrial-to-aortic; LVIDDn, normalized left ventricular internal dimension at end-diastole; VHS, vertebral heart score; VLAS, vertebral left atrial size; m-VLAS, modified VLAS. \*Significant difference from ACVIM stage B1,  $p < 0.017$ .

ware programs (SPSS 25.0, IBM, SPSS, USA; MedCalc Statistical Software version 19.3.1, MedCalc Software Ltd, Ostend, Belgium; <https://www.medcalc.org>; 2020). Descriptive statistics were generated and the Kolmogorov-Smirnov test was used for normality testing of continuous data. In this study, values among three groups by ACVIM stage were compared using the Kruskal-Wallis test followed by the Mann-Whitney test for pairwise comparisons when necessary. The Bonferroni correction post hoc test was executed for multiple comparisons. A Mann-Whitney test was performed to compare values of EchoLHE-no groups and EchoLHE-yes groups. Receiver operator characteristic (ROC) curve analyses were performed to assess diagnostic accuracy, determine sensitivity and specificity percentages, and generate clinically relevant cutoffs for VHS, VLAS, and m-VLAS. The optimal cutoff value was defined as the point on the curve with the greatest Youden index (sensitivity - [1 - specificity]).

### Results

The sample population consisted of 57 small breed dogs with a mean age of 11.8 years (range: 5-17 years) and a mean weight of 5 kg (range: 1.6-9.8 kg). Analysis of clinical symptoms revealed that 21 dogs had cough, 5 had dyspnea, 13 had a case history of syncope, 2 had tachypnea, and 2 had depression. There were 14 asymptomatic dogs. Breeds included in this study were Maltese ( $n = 27$ ), Shih Tzu ( $n = 15$ ), Yorkshire terrier ( $n = 4$ ), Schnauzer ( $n = 3$ ), Pomeranian ( $n = 1$ ), Poodle ( $n = 1$ ), and mixed ( $n = 6$ ).

ACVIM stages B1, B2, and C-D groups comprised 8 dogs, 8 dogs, and 41 dogs, respectively. Groups B1, B2, and C-D had median ages of 11.1 years, 10 years, and 12.3 years with

median weights of 5.3 kg, 5.3 kg, and 4.9 kg, respectively. Descriptive data of radiographic and echocardiographic values in each group are summarized in Table 1. There were no significant differences in VHS, VLAS, or m-VLAS on thoracic radiographs between all ACVIM stage groups. However, LVIDDn and LA/Ao ratio on echocardiograph were significantly different between the B1 group and the C-D group. The LA/Ao ratio also showed significant differences between the B1 group and the B2 group.

The EchoLHE-no group ( $n = 38$ ) satisfied either LA/Ao ratio  $\geq 1.6$  or LVIDDn  $\geq 1.7$  or neither and the EchoLHE-yes group ( $n = 19$ ) satisfied both LA/Ao ratio  $\geq 1.6$  and LVIDDn  $\geq 1.7$  on echocardiographic measurements. Age and weight were not significantly different between the EchoLHE-no group and the EchoLHE-yes group. Radiographic index VHS and VLAS showed significant differences between the two groups. The mean value of the VHS in the EchoLHE-yes group was signifi-

cantly higher than that of the EchoLHE-no group ( $p < 0.001$ ). Values of VLAS and m-VLAS showed significant differences between the EchoLHE-no group and the EchoLHE-yes group. Mean values of VLAS and m-VLAS in the EchoLHE-yes group were significantly higher than those of the EchoLHE-no group ( $p < 0.001$ ). All clinical and radiographic data are displayed in Table 2.

Results for the three radiographic measurements (VHS, VLAS, and m-VLAS) were identified by ROC curve as shown in Fig. 1. Discriminatory abilities of VHS, VLAS, and m-VLAS to detect EchoLHE were all clinically useful, with AUC values of ROC curves of 0.835 (95% CI, 0.713-0.920, Fig. 2A), 0.849 (95% CI, 0.729-0.930, Fig. 2B), and 0.868 (95% CI, 0.753-0.943, Fig. 2C), respectively. The highest AUC value was m-VLAS. Using Youden index, the optimal cutoff value was calculated as the highest clinically relevant one of the three criteria. The optimal cutoff value for VHS was  $\geq 10.2$ , which had a sensitivity of 100% and a specificity of 55.26%. The optimal cutoff value for VLAS was  $\geq 2.4$ , which had a sensitivity of 84.21% and a specificity of 71.05%. The optimal cutoff value for m-VLAS was  $\geq 2.7$ , which had a sensitivity of 68.42% and a specificity of 86.84%. The AUC, sensitivity, specificity, and cutoff value with 95% confidence intervals of selected values of VHS, VLAS, and m-VLAS are displayed in Table 3.

**Table 2.** Descriptive data for 57 dogs with MMVD according to echocardiographic criteria for EchoLHE

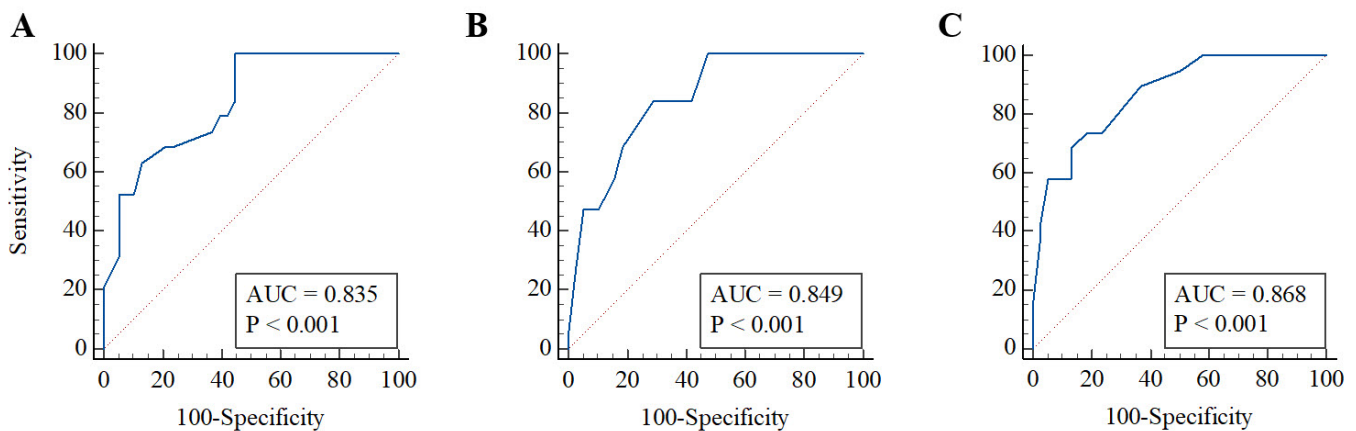
Variable	EchoLAE-no	EchoLAE-yes	p-value
N	38	19	-
Age (year)	11.84 (3.15)	11.68 (2.35)	0.621
Weight (kg)	5.3 (1.9)	4.26 (1.71)	0.115
VHS (v)	10.36 (0.83)	11.7 (1.16)	<0.001
VLAS (v)	2.31 (0.33)	2.82 (0.4)	<0.001
m-VLAS (v)	2.36 (0.33)	2.96 (0.41)	<0.001

EchoLHE-no, if LVIDDn  $< 1.7$  or LA/Ao  $< 1.6$ ; EchoLAE-yes, if LVIDDn  $\geq 1.7$  and LA/Ao  $\geq 1.6$  echoLHE criteria.

MMVD, myxomatous mitral valve disease; EchoLHE, left heart enlargement; VHS, vertebral heart score; VLAS, vertebral left atrial size; m-VLAS, modified VLAS.

## Discussion

The purpose of this study was to compare imaging indicators (VHS, VLAS, LA/Ao ratio, and LVIDDn) in small breed dogs with MMVD on ACVIM stage and the new method of measuring VLAS for assessing LA size on thoracic radiographs when the original method could not be used to



**Fig. 2.** Receiver-operating characteristic curve of radiographic vertebral heart score (A), vertebral left atrial size (B), and modified vertebral left atrial size (C). The area under the curve (AUC) values were 0.835, 0.849, and 0.868 for A, B, and C, respectively. AUC was evaluated with the following scales: excellent, AUC = 0.90-1.0; good, AUC = 0.80-0.90; fair, AUC = 0.70-0.80; poor, AUC = 0.60-0.70; and fail, AUC = 0.50-0.60.

**Table 3.** Diagnostic accuracy of VHS, VLAS, and m-VLAS for predicting left side heart enlargement

	ROC						
	AUC (95% CI)	Cutoff value	Cutoff type	Sensitivity (%)	Specificity (%)	Youden index	p-value
VHS	0.835 (0.713-0.920)	≥10.2	Maximum sensitivity	100	55.26	0.5526	<0.001
		≥10.2	Clinically relevant	100	55.26		
		≥12	Maximum specificity	21.05	100		
VLAS	0.849 (0.729-0.930)	≥2.2	Maximum sensitivity	100	52.63	0.5526	<0.001
		≥2.4	Clinically relevant	84.21	71.05		
		≥3.2	Maximum specificity	5.26	100		
m-VLAS	0.868 (0.753-0.943)	≥2.2	Maximum sensitivity	100	42.11	0.5526	<0.001
		≥2.7	Clinically relevant	68.42	86.84		
		≥3.2	Maximum specificity	15.79	100		

VHS, vertebral heart score; VLAS, vertebral left atrial size; m-VLAS, modified VLAS.

measure VLAS (10). Our study results indicated that useful indicators in small breed dogs on the ACVIM stage were LA/Ao ratio and LVIDDn and that m-VLAS values were useful for differentiating the presence or absence of LA enlargement in echocardiography. The m-VLAS could be used to complement limits of the original VLAS measurement method, and considering the three-dimensional shape of LA enlargement, m-VLAS is also considered valuable as an additional indicator.

A recent retrospective study of 168 small breed dogs with MMVD showed that MMVD occurred at a mean of 10.8 years in dogs with a mean weight of 5.2 kg (11). Our study revealed that the mean age was 11.8 years and the mean weight was 5 kg in dogs with MMVD, similar to results obtained from the previous study. Previous studies have reported a possible influence of body condition score on VHS (9). However, the possible influence of body condition score on VLAS was not evaluated in our study.

To predict cardiac disease, VHS was the most widely used and useful radiographic measurement. However, VHS has been recognized as a measure of general cardiac size, not only LA enlargement. A previously published study has reported that the mean value of VHS is 9.7 v (9.2-10.2 v) in normal dogs (4). In our study, total mean VHS was 10.8 v (9.0-15.2 v). In addition, the VHS was not over 10.2 v in 21 of 57 dogs. Another study has shown that VHS values of ACVIM stage B1, stage B2, and stage C-D were 10.0 v (9.7-10.5 v), 10.7 v (10.6-11.1 v) and 11.8 v (11.0-12.3 v), respectively (12). VHS values of ACVIM stage B1, stage B2, and stage C-D in this study were 10.6 v (9.5-12.0 v), 10.7 v (9.1-11.7 v), and 10.8 v (9.0-15.2 v), respectively. These results showed that values of VHS were increased with increasing ACVIM stage, similar to findings of previous studies (12,14,19).

Recently, the ACVIM 2019 consensus for the evaluation of

cardiac remodeling and classifying MMVD stage is that VLAS value > 3 can predict stage B2 without echocardiography (10). Moreover, a recent study has shown the possibility of predicting ACVIM stage B2 using VLAS > 2.3 in 183 dogs (7). The present study showed that values of VLAS and m-VLAS for dogs with MMVD of ACVIM stage B2 were 2.5 v (1.6-3.8 v) and 2.6 v (1.6-3.8 v), respectively, similar to results of previous studies (7,12,14,19). Previous studies have revealed a correlation of MMVD progression with VLAS level (12,19,24), similar to our result. In contrast to previously published studies (7,12,18-20,24), our study revealed no correlations for VLAS ( $p = 0.44$ ) or m-VLAS ( $p = 0.28$ ), but the LVIDDn and LA/Ao ratio of echocardiographic value showed a significant ( $p < 0.001$ ) correlation among ACVIM groups. The mean value of LVIDDn in stage B2 was 1.5 (1.2-1.9) and the LA/Ao ratio was 1.9 (1.6-2.8). These results were similar to stage B2 criteria of ACVIM consensus, LVIDDn  $\geq 1.7$  and LA/Ao ratio  $\geq 1.6$ . Especially, the LA/Ao ratio showed significant differences between the B1 group and the B2 group or the C-D group.

Only assessing the LA with radiographic measurement is difficult because of a three-dimensional shape of the LA, patient positioning, breed, and body conformation (15,24). Therefore, we divided dogs into two groups using echocardiographic criteria (7,20,24). The group that satisfied EchoLHE (both LVIDDn  $\geq 1.7$  and LA/Ao ratio  $\geq 1.6$ ) and the group not satisfying EchoLHE (LVIDDn  $\geq 1.7$  or LA/Ao ratio  $\geq 1.6$ , or neither) were classified and radiographic measurements were compared between the two groups. Previously published studies showed that there were significant differences in values of VHS and VLAS between classified echocardiographic criteria groups (7,20). In this study, significant differences were confirmed on VHS, VLAS, and m-VLAS ( $p < 0.0001$ ) between EchoLHE-no and EchoLHE-yes groups. Moreover,

many earlier studies have shown that VLAS is a useful radiographic measurement for detecting enlargement of the left side heart on echocardiography (7,12,19,20,26). A previous study has shown that VLAS can reflect LA size in dogs (19). Another study has shown that the VHS represents the LA size as VLAS (20). Although we did not evaluate correlations between single radiographic values and echocardiographic values, we revealed that not only the VHS, but also the VLAS could be a sensitive marker of left side heart enlargement. Therefore, we suggest that both VHS and VLAS should be measured for predicting left heart sizes of dogs.

A recent study showed that the diagnostic accuracy of VLAS with AUC value of 0.890 for detecting both LA/Ao ratio  $\geq 1.6$  and LVIDDn  $\geq 1.7$  was significantly ( $p = 0.003$ ) greater than VHS with AUC value of 0.81 (7). Another previous study showed that VHS and VHS + VLAS to detect both LA/Ao ratio  $\geq 1.6$  and LVIDDn  $\geq 1.7$  were clinically useful, with AUC values  $> 0.800$  (20). The present study showed that discriminatory abilities of VHS, VLAS, and m-VLAS to detect left side heart enlargement were clinically useful, with AUC values  $> 0.800$  in all three measurements. Our results showed that VLAS was a significantly more accurate predictor of EchoLHE than VHS. Moreover, the AUC value of m-VLAS was the highest at 0.868 (AUC value of the VHS: 0.835; AUC value of the VLAS: 0.849). Therefore, m-VLAS can be a useful radiographic measurement for detecting left side heart enlargement under silhouetted CdVC situations.

A previous study has reported that the optimal VLAS cutoff for predicting EchoLHE is  $\geq 2.3$  v with a sensitivity of 69% and a specificity of 85.7% (7). Our study found that the optimal cutoff value was  $\geq 2.4$  v for VLAS (sensitivity: 84.2%; specificity: 71.0%) and  $\geq 2.7$  v for m-VLAS (sensitivity: 68.4%; specificity: 86.8%). The specificity of the m-VLAS cutoff was significantly higher than that of the VLAS cutoff, although the sensitivity of the m-VLAS cutoff was lower than that of the VLAS cutoff. This result means that using m-VLAS has the lowest risk of false-positive categorization in case dogs.

This study has a few limitations. First, the sample size in our study was small, especially ACVIM stage B1 group. Second, values of normal dogs were not collected. Comparisons between control group and ACVIM staging groups or EchoLHE groups might obtain different results. Third, although radiographic measurements were evaluated by only one radiologist, all echocardiographic measurements were performed by many radiologists in Veterinary Medical Teaching Hospital. Therefore, measurement variability might exist in this study. Fourth, our chosen criteria on EchoLHE were linear methods in echocardiography. The LA is a three-dimensional structure that dilates with an asymmetric shape. The volume based

echocardiographic method is more precise than the LA/Ao ratio in previous studies (8,25). A further study is needed to evaluate the correlation between VLAS and volume based methods to achieve higher accuracy.

In conclusion, VLAS is a clinically useful radiographic measurement to quantify LA enlargement size in small breed dogs with MMVD. Additionally, our results confirm that m-VLAS is a more specific indicator of left side heart enlargement than VLAS and that it is helpful for measuring VLAS when it is impossible to use the CdVC point. A further study is needed to evaluate the clinical significance using m-VLAS in a large population of dogs with MMVD and normal dogs.

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## Conflicts of Interest

The authors have no conflicting interests.

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