Use of radiographic measurements to diagnose stage B2 preclinical myxomatous mitral valve disease in dogs

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OBJECTIVE

To investigate the usefulness of radiographic measures of the left atrium and ventricle as surrogates for echocardiographic criteria in identifying dogs with stage B2 preclinical myxomatous mitral valve disease (MMVD).

ANIMALS

56 client-owned dogs with preclinical mitral regurgitation attributed to MMVD examined between April 19, 2016, and November 22, 2017.

PROCEDURES

Medical records were retrospectively searched, and data collected included age, body weight, heart murmur grade, and echocardiographic and radiographic measurements. Dogs were grouped according to whether they did (case dogs) or did not (control dogs) meet echocardiographic criteria used to identify dogs with stage B2 MMVD. Measurements for lateral thoracic radiographic variables normalized to vertebral body units (VBUs) were obtained, and results were analyzed to identify variables that could best discriminate between case and control dogs.

RESULTS

Three radiographic variables of left atrial size (vertebral left atrial size [VLAS], left atrial width, and the combined variable of VLAS + left atrial width) most accurately distinguished control dogs from case dogs, and the VLAS was the simplest and fastest to perform in a clinical setting. The optimal cutoff for VLAS was 2.5 VBUs (sensitivity, 70%; specificity, 84%; and likelihood ratio, 4.38), with VLAS ≥ 2.5 VBUs for case dogs. The maximum specificity cutoff for VLAS was 3.0 VBUs (sensitivity, 40%; specificity, 96%; and likelihood ratio, 10.0), with VLAS ≥ 3.0 VBUs for case dogs.

CONCLUSIONS AND CLINICAL RELEVANCE

Results indicated that when echocardiography is unavailable, radiographic VLAS ≥ 3 VBUs could be used with minimal risk of false-positive diagnosis of stage B2 MMVD in dogs. (*J Am Vet Med Assoc* 2020;256:1129–1136)

Myxomatous mitral valve disease is the most common type of cardiac disease in dogs,[1] and a recent study[2] shows that signs of CHF developed later in dogs with preclinical MMVD treated with pimobendan versus a placebo. Identifying affected dogs that may benefit from treatment with pimobendan (stage B2 MMVD) can be challenging. Although radiographic examination (particularly including VHS to measure the extent of cardiac silhouette enlargement) is recommended for detecting and monitoring cardiac enlargement related to MMVD,[3-5] echocardiographic criteria (ie, LA:Ao [obtained from the right-sided short-axis view in early diastole] ≥ 1.6 and LVIDDN ≥ 1.7[6]) have been used as the gold standard for identifying dogs with stage B2 MMVD. Echocardiography, however, is not always available or feasible in general practice. Consequently, surrogate radiographic measurements that reliably identify patients that meet these echocardiographic criteria would be valuable in instances with limited echocardiographic access.

Development of a radiographic protocol to identify dogs with stage B2 MMVD may enable more detailed staging of the affected animals when echocardiography is unavailable. Radiographic VHS is a numeric score based on the sum measurement of cardiac silhouette length plus width, which is then normalized for body size by equating that sum distance to the number of the dog's vertebrae (starting at T4) that the distance spans. On the basis of angiographic images, the cardiac silhouette length measurement is

ABBREVIATIONS

CHF	Congestive heart failure
LA	Left atrium
LA:Ao	Left atrial diameter-to-aortic root diameter ratio
LA_{total}	Sum of the vertebral left atrial size and left atrial width
LA_{width}	Left atrial width
LV	Left ventricle
LVIDD	Left ventricular internal diameter in diastole
LVIDDN	Left ventricular internal diameter in diastole, normalized to body surface area
MMVD	Myxomatous mitral valve disease
MR	Mitral regurgitation
NPV	Negative predictive value
PPV	Positive predictive value
ROC	Receiver operator characteristic
VBU	Vertebral body unit
VHS	Vertebral heart size
VHS_{length}	Vertebral heart size length
VHS_{width}	Vertebral heart size width
VLAS	Vertebral left atrial size

thought to reflect the combined vertical dimension of the LA and LV.[7] More recently, a study[8] in dogs shows that the VLAS, which is a radiographic measurement in VBUs of the distance from the ventral aspect of the carina to the dorsal aspect of the intersection of the cardiac silhouette and caudal vena cava, has moderate to good correlation with the echocardiographic diameter of the LA. Especially pertinent is the relationship between the VLAS and the echocardiographic short-axis dimension of the LA, which was the echocardiographic measurement of LA size used in the study[2] mentioned earlier that shows that signs of CHF developed later in dogs with preclinical MMVD treated with pimobendan versus a placebo. No comparison between VLAS and size of the LV was reported in that study.[2]

The purpose of the study presented here was to investigate the usefulness of radiographic measures of the LA and LV as surrogates for echocardiographic criteria in identifying dogs with stage B2 MMVD. We hypothesized that ≥ 1 of the radiographic measurements would prove accurate for use in a general practice setting.

Materials and Methods

Animals

The medical records of the Cardiology Service at the University of Wisconsin School of Veterinary Medicine were retrospectively searched to identify records of dogs in which MR attributed to MMVD was coded as the diagnosis and that were examined between April 19, 2016, and November 22, 2017. For inclusion in the study, dogs had to have had a heart murmur grade ≥ 3/6, hemodynamically substantial but preclinical MMVD with cardiac remodeling,[3] and body weight between 4.0 and 15.0 kg (8.8 to 33.0 lb) and had to have undergone full echocardiography and thoracic radiography within the same 24-hour period. Dogs were excluded if they had a heart murmur grade < 3/6, CHF, current transvenous pacing wires, or concurrent cardiac abnormalities other than myxomatous tricuspid valve disease (eg, severe pulmonary hypertension [estimated pulmonary arterial pressure > 75 mm Hg based on tricuspid regurgitation peak systolic velocity]). Also excluded were dogs that at the time of examination were being treated with pimobendan or furosemide and those with radiographic findings that prevented identification of the needed cardiac silhouette landmarks (eg, findings of tracheobronchial lymphadenopathy, heart-based mass, or cranial mediastinal mass) or that compromised reliability of vertebral length comparison (eg, findings of wedge or block vertebrae). Dogs with concurrent tricuspid regurgitation or nonpaced arrhythmias were not excluded. Age and body weight were recorded for each eligible dog.

Lateral thoracic radiographic measurements

Left and right lateral thoracic radiographic images of dogs were independently reviewed by a trained observer (MBR) who was not a board-certified veterinary cardiologist or radiologist and was blinded to the results of echocardiography. For each radiographic image, the VHS, VHS_{length}, VHS_{width}, VLAS, LA_{width}, and LA_{total} were determined. In addition, the sum of the VHS + VLAS and the sum of the VHS + LA_{total} were also calculated for each image and reflected the combined measurements of the LA and LV. Measurements for the same variables were obtained for each right or left lateral thoracic radiographic image. Each of these measurements was normalized to the imaged dog's body size by converting each distance measured to the number of thoracic VBUs (to the nearest 0.25 vertebrae), beginning at the cranial edge of T4 **(Figure 1)**.

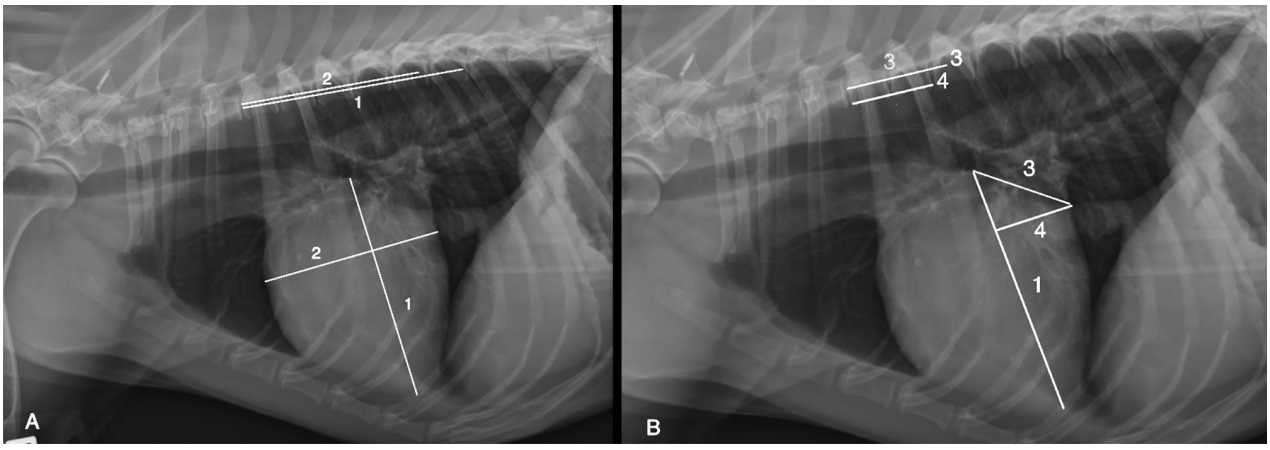

Figure 1—Representative left lateral thoracic radiographic images of 1 of 56 client-owned dogs with preclinical MR attributed to MMVD examined between April 19, 2016, and November 22, 2017, showing the lines used in measuring VHS (A) and LA size (B), with measurements compared with VBUs beginning at the cranial aspect of T4. A—The VHS is the VBU conversion of the sum of the VHS_{length} (1) measured from the ventral margin of the carina to the cardiac apex plus the VHS_{width} (2) of the cardiac silhouette maximum width measured perpendicular to VHS_{length}. B—The VLAS (3) is the VBU conversion of the distance from the ventral aspect of the carina to the dorsal aspect of the intersection of the cardiac silhouette and caudal vena cava, and the LA_{width} (4) is the VBU conversion of the distance of a line drawn perpendicular to the line of the VHS_{length} (1) and extending caudally to the dorsal aspect of the intersection of the cardiac silhouette and caudal vena cava.

The VHS was calculated as the VBU conversion of the sum of the VHS_{length} (measured from the ventral margin of the carina to the cardiac apex) plus the VHS_{width} (the cardiac silhouette maximum width measured perpendicular to VHS_{length}) as previously described.[7] The VLAS was the VBU conversion of the distance from the ventral aspect of the carina to the dorsal aspect of the intersection of the cardiac silhouette and caudal vena cava as previously described.[8] The LA_{width} was the VBU conversion of the distance of a line drawn perpendicular to the line of the VHS_{length} and extending caudally to the dorsal aspect of the intersection of the cardiac silhouette and caudal vena cava.[9] The LA_{total} was calculated as VLAS + LA_{width}.

Echocardiographic measurements

The previously recorded echocardiographic images[a] for each dog were reviewed by a board-certified veterinary cardiologist (RLS) blinded to dog identities and radiographic measurements. Cross-sectional M-mode images of the LVIDD and diameters of the aorta and LA in short-axis view were remeasured in triplicate, and the mean for each was recorded for each image. The LVIDDN was calculated with the formula[6] LVIDDN = LVIDD/(body weight [kg]$^{0.294}$), and the LA:Ao was calculated as previously described.[10] On the basis of an earlier study,[2] we grouped dogs according to whether they did (case dogs) or did not (control dogs) meet echocardiographic criteria (LVIDDN ≥ 1.7 and LA:Ao ≥ 1.6) used in identifying dogs with preclinical MMVD likely to benefit from treatment with pimobendan.

Statistical analysis

Statistical analysis was performed with available statistical software,[b] and values of $P < 0.05$ were considered significant for all analyses. Normality of data distribution was assessed with the D'Agostino and Pearson normality test, and parametric and nonparametric analyses were used as appropriate for the resulting distribution of data collected. Paired measurements obtained from right and left lateral radiographic views of all dogs were compared with a Student *t* test or Wilcoxon signed rank test as appropriate. The Pearson correlation coefficient or Spearman rank correlation coefficient was used to compare results for radiographic variables (VHS, VHS_{length}, VHS_{width}, VLAS, LA_{width}, LA_{total}, VHS + VLAS, and VHS + LA_{total}) with results for echocardiographic variables (LVIDDN and LA:Ao). Summary descriptive statistics were reported for each group (case dogs and control dogs), and results were compared between the groups with a Student *t* test or Mann-Whitney test.

Receiver operator characteristic curves and contingency analyses were used to obtain diagnostic test characteristics and determine optimal sensitivity and maximum specificity radiographic measurement cutoff values (in VBUs) for predicting group status. The optimal sensitivity cutoff values, used to minimize group overlap, were identified as those with the highest Youden index and calculated with the formula J = Se + Sp – 1,[11] where J was the Youden index, Se was the sensitivity, and Sp was the specificity. The maximum specificity cutoff values, used to minimize the likelihood of false-positive diagnosis of stage B2 MMVD, were chosen after review of the results of the ROC analysis.

Results

Animals

A search of the medical records identified 71 dogs with MR attributed to MMVD examined between April 19, 2016, and November 22, 2017. Of these, 15 did not meet the inclusion criteria because they did not have echocardiographic and radiographic examinations performed within a 24-hour period (n = 5) or had a transvenous pacing lead (6), misshapen thoracic vertebrae (2), or concurrent pulmonary hypertension (2). The remaining 56 dogs were included in the study.

Grouping by echocardiographic criteria

The echocardiographic criteria of LVIDDN ≥ 1.7 and LA:Ao ≥ 1.6 were present in 30 dogs (case dogs) and absent in 26 (control dogs). Of the 56 dogs, 15 (27%) had discordant echocardiographic results, with either the combination of LVIDDN ≥ 1.7 and LA:Ao < 1.6 (n = 11) or the combination of LVIDDN < 1.7 and LA:Ao ≥ 1.6 (4). These 15 dogs were included in the control group because they did not meet the combined echocardiographic criteria for inclusion in the case group. Neither the mean age nor mean body weight differed substantially between the control group (10.2 years and 8.4 kg [18.5 lb]) and the case group (10.5 years and 8.3 kg [18.3 lb]; **Table 1**).

Measurements

The mean ± SD LVIDDN and LA:Ao were significantly ($P < 0.001$) higher for case dogs (2.0 ± 0.2 and 2.0 ± 0.4, respectively) than for control dogs (1.7 ± 0.3 and 1.5 ± 0.2, respectively; Table 1). Similarly, the mean VHS_{length}, VHS_{width}, VHS, VLAS, LA_{total}, VHS + VLAS, and VHS + LA_{total} measurements were significantly ($P < 0.05$) higher for case dogs versus control dogs. Eight dogs in the control group and 3 dogs in case group had VHS measurements < 10.5 VBUs (reference range, approx 8.5 to 10.5 VBUs).

Two dogs had incomplete radiographic records available; 1 dog was missing a right lateral thoracic radiographic image, and 1 dog was missing a left lateral image. Therefore, these 2 dogs were excluded from analyses of measurements obtained from right versus left lateral thoracic radiographic images when images were paired. In the remaining 54 dogs (29 case dogs and 25 control dogs), no significant ($P = 0.252$ and 0.255, respectively) differences in the mean ± SD VHS and VLAS were identified in measurements obtained from paired left (11.3 ± 1.0 VBUs and 2.4 ± 0.5 VBUs, respectively) and right (11.5 ± 0.9 VBUs and 2.3 ± 0.4 VBUs, respectively) lateral radiographic images. No

Table 1—Summary of descriptive data for 56 client-owned dogs with preclinical MR attributed to MMVD examined between April 19, 2016, and November 22, 2017, grouped according to whether they did (case dogs [n = 30]) or did not (control dogs [26]) meet echocardiographic criteria (LVIDDN ≥ 1.7 and LA:Ao ≥ 1.6) used to identify dogs with MMVD that could likely benefit from treatment with pimobendan (stage B2 MMVD).

	Control group		Case group		
Variable	**Mean ± SD**	**Median (range)**	**Mean ± SD**	**Median (range)**	***P* value**
Age (y)	10.2 ± 2.5	10.0 (5.0–15.0)	10.5 ± 2.1	10.0 (7.0–15.0)	NS
Weight (kg)	8.4 ± 3.0	8.1 (4.2–15.0)	8.3 ± 2.6	7.7 (4.0–14.6)	NS
LVIDDN	1.7 ± 0.3	1.6 (1.2–2.2)	2.0 ± 0.2	2.0 (1.7–2.4)	< 0.001
LA:Ao*	1.5 ± 0.2	1.5 (1.1–1.8)	2.0 ± 0.4	1.9 (1.6–3.1)	< 0.001
VHS_{length}†	5.7 ± 0.6	5.3 (4.3–6.8)	6.0 ± 0.5	6.0 (5.3–7.0)	0.020
VHS_{width}†	5.3 ± 0.4	5.0 (4.5–6.0)	5.6 ± 0.6	5.5 (4.5–7.0)	0.045
VHS†	10.9 ± 0.9	10.8 (8.8–12.8)	11.6 ± 0.9	11.5 (10.0–13.5)	0.010
VLAS†	2.2 ± 0.3	2.3 (1.5–3.0)	2.7 ± 0.5	2.8 (1.8–3.5)	< 0.001
LA_{width}*†	1.7 ± 0.3	1.8 (1.3–2.0)	2.0 ± 0.3	2.0 (1.5–3.0)	< 0.001
LA_{total}†	3.8 ± 0.6	3.8 (2.8–5.0)	4.7 ± 0.8	4.5 (3.3–6.5)	< 0.001
VHS + VLAS†	13.1 ± 1.1	13.5 (10.5–15.8)	14.2 ± 1.3	14.1 (12.0–17.0)	0.001
VHS + LA_{total}†	14.8 ± 1.3	15.0 (12.0–17.8)	16.2 ± 1.6	16.4 (13.8–20.0)	< 0.001

Data were analyzed with the unpaired Student *t* test, except where indicated.
*Analyzed with the Mann-Whitney test. †Values reported to the nearest 0.25 VBUs as measured on left lateral radiographic images of 25 control dogs and 30 case dogs.
NS = Not significant.

other meaningful differences were identified when results of paired radiographic images were evaluated. In addition, when the mean of each radiographic variable according to laterality was assessed, no differences between corresponding means exceeded the preset precision threshold (> 0.25 VBUs). Given the statistical similarity between contralateral radiographic views, all subsequent analyses were performed with results for radiographic variables derived only from the left lateral view (n = 55 [25 control dogs and 30 case dogs]).

Results for LVIDDN were normally distributed; therefore, the Pearson correlation coefficient (*r*) was used to compare results for radiographic variables (VHS_{length}, VHS, VLAS, LA_{width}, LA_{total}, VHS + VLAS, and VHS + LA_{total}) with results for LVIDDN. However, results for LA:Ao were not normally distributed, and the Spearman rank correlation coefficient (ρ) was used to compare results for the radiographic variables with those for LA:Ao. Results for variables anticipated to have reflected LV size (VHS_{length} and VHS) were moderately and significantly ($r = 0.34$ and $P = 0.010$ and $r = 0.42$ and $P = 0.002$, respectively) correlated with results for LVIDDN but not correlated with results for LA:Ao **(Table 2)**. Results for variables anticipated to have had the greatest correlation with LA size (VLAS and LA_{total}) more closely correlated with results for LVIDDN ($r = 0.68$ and 0.65, respectively; $P < 0.001$) than with results for LA:Ao ($\rho = 0.46$ and 0.47, respectively; $P < 0.001$) and had higher correlation with results for LVIDDN than did findings for VHS_{length} and VHS. Results for LA_{width} correlated similarly with those for LA:Ao and LVIDDN.

Table 2—Results of analysis to identify potential correlations between results for selected radiographic variables as measured on left lateral thoracic radiographic images and echocardiographic variables for the 25 control dogs and 30 case dogs described in Table 1.

Echocardiographic variable	**Radiographic variable***	**Correlation coefficient (95% CI)**	***P* value**
LVIDDN	VHS_{length}	0.34 (0.09 to 0.56)	0.010
	VHS	0.42 (0.17 to 0.62)	0.002
	VLAS	0.68 (0.51 to 0.80)	< 0.001
	LA_{width}	0.54 (0.31 to 0.71)	< 0.001
	LA_{total}	0.65 (0.46 to 0.78)	< 0.001
LA:Ao	VHS_{length}†	0.23 (–0.05 to 0.47)	NS
	VHS†	0.24 (–0.03 to 0.48)	NS
	VLAS†	0.46 (0.21 to 0.65)	< 0.001
	LA_{width}†	0.54 (0.32 to 0.70)	< 0.001
	LA_{total}†	0.47 (0.23 to 0.66)	< 0.001

The Pearson correlation coefficient (*r*) is reported unless otherwise noted.
*Reported as VBUs to the nearest 0.25 vertebral body as measured on left lateral radiographic images of 25 control dogs and 30 case dogs. †Spearman rank correlation coefficient (ρ) is reported.
NS = Not significant.

Cutoff values

Receiver operator characteristic analysis was used to identify optimal cutoff values for radiographic variables used to predict group status (ie, whether a dog was assigned to the control dog group vs the case dog group). The optimal cutoff values (Youden index) and associated sensitivity, specificity, PPV, NPV, and likelihood ratio of each radiographic variable and the combined values of VHS + VLAS and of VHS + LA_{total} were calculated **(Table 3)**. Results for all radiographic variables had areas under the ROC curve > 0.65, with radiographic measurements of the LA (VLAS, LA_{width}, and LA_{total}) associated with the largest areas under the ROC curve (0.79, 0.78, and 0.81, respectively). Cutoff values associated with maximum specificity (fewest

Table 3—Results of ROC curve analysis to assess diagnostic accuracy of radiographic variables to predict group status (case group vs control group) as described in Table 1.

Radiographic variable	ROC curve analysis		Cutoff value*		Percentage sensitivity (95% CI)	Percentage specificity (95% CI)	Percentage PPV (95% CI)	Percentage NPV (95% CI)	LR	*P* value
	AUC (95% CI)	*P* value	Type	VBUs						
VHS	0.68 (0.54–0.82)	0.023	Optimal sensitivity†	12.00	37 (22–54)	92 (75–99)	85 (58–97)	55 (40–69)	4.58	0.024
			Maximum specificity‡	12.25	30 (2–48)	96 (80–99)	90 (60–99)	53 (39–67)	7.50	0.016
VLAS	0.79 (0.67–0.91)	< 0.001	Optimal sensitivity†	2.50	70 (52–83)	84 (65–94)	84 (65–94)	70 (52–83)	4.38	< 0.001
			Maximum specificity‡	3.00	40 (25–58)	96 (80–99)	92 (67–99)	57 (42–71)	10.0	0.003
LA_{width}	0.78 (0.66–0.90)	< 0.001	Optimal sensitivity†	2.00	63 (46–78)	76 (57–89)	76 (57–89)	63 (46–78)	2.64	0.006
			Maximum specificity‡	2.25	27 (14–44)	100 (87–100)	100 (68–100)	53 (39–67)	NA	0.006
LA_{total}	0.81 (0.69–0.92)	< 0.001	Optimal sensitivity†	4.50	70 (52–83)	84 (65–94)	84 (65–94)	70 (52–83)	4.38	< 0.001
			Maximum specificity‡	5.00	47 (30–64)	96 (80–99)	93 (70–99)	60 (45–74)	11.67	< 0.001
VHS + VLAS	0.74 (0.66–0.87)	0.003	Optimal sensitivity†	14.50	47 (30–64)	96 (80–99)	94 (70–99)	60 (45–74)	11.67	< 0.001
			Maximum specificity‡	14.75	43 (27–61)	96 (80–99)	93 (69–99)	59 (43–72)	10.83	0.001
VHS + LA_{total}	0.75 (0.62–0.88)	0.002	Optimal sensitivity†	16.25	53 (36–70)	92 (75–99)	89 (67–98)	62 (46–76)	6.67	< 0.001
			Maximum specificity‡	16.50	50 (33–67)	96 (80–99)	94 (72–99)	62 (46–75)	12.5	< 0.001

*Results reported for measurements obtained on left lateral thoracic radiographic images of 25 control dogs and 30 case dogs. †Cutoff value determined with the Youden index. ‡Cutoff value with near 100% specificity (least false-positive categorization).

AUC = Area under the curve. LR = Likelihood ratio.

false-positive categorizations) were slightly higher than the optimal cutoff values (values that best distinguished between the 2 groups).

Results for the 3 radiographic variables pertaining to the size of the LA (VLAS, LA_{width}, and LA_{total}) were identified as the most accurate in identifying case dogs. Of these 3 variables, the VLAS was the simplest and fastest to perform in a clinical setting. The optimal cutoff value for VLAS was 2.5 VBUs, which had a sensitivity, specificity, and likelihood ratio of 70%, 84%, and 4.38, respectively, for identifying case dogs (VLAS ≥ 2.5 VBUs). The maximum specificity cutoff value for VLAS was 3.0 VBUs, which had a sensitivity, specificity, and likelihood ratio of 40%, 96%, and 10.0, respectively, with the lowest risk of false-positive categorization as case dogs (VLAS ≥ 3.0 VBUs). In addition, the combined variable of VHS + VLAS at the cutoff with maximum specificity in the dogs of the present study was 16.5 VBUs and had a PPV of 94%.

Discussion

Recent recommendations for initiating treatment with pimobendan in dogs with preclinical MMVD are based on findings from a clinical trial[2] that shows signs of CHF developed later in dogs with preclinical MMVD treated with pimobendan versus a placebo. The clinical criteria used for patient selection in that study[2] (murmur intensity ≥ grade 3/6, LA:Ao [obtained from the right-sided short-axis view in early diastole] ≥ 1.6, LVIDDN ≥ 1.7,[6] and VHS > 10.5) have been generally recommended to identify dogs that might benefit from pimobendan administration prior to the onset of CHF.[12,c] The most recent MMVD consensus statement[12] has designated dogs with these findings as stage B2 MMVD patients.

The dogs in the present study represented a specific cohort of clinical patients: small-breed dogs with preclinical MMVD that closely matched selection criteria for a recent clinical study[2] in which certain echocardiographic criteria (LVIDDN ≥ 1.7 and LA:Ao ≥ 1.6) were found useful in identifying dogs most likely to benefit from pimobendan administration. This combination of cohort composition and balance of the number of dogs with and without the specific echocardiographic criteria allowed us to evaluate our findings for the dogs in the present study; however, our findings should not be assumed to apply to all dogs with MMVD.

Measurements of VHS obtained from right versus left lateral thoracic radiographic images have been investigated, with some studies[13–15] showing small but significant differences in VHS values obtained from right versus left lateral images, whereas another study[7] shows no meaningful difference. Although the present study indicated minimal difference in VHS on the basis of laterality, consistent patient positioning is recommended for consistent serial monitoring of cardiac status in clinical patients.

Dogs in the present study met inclusion criteria if their clinical assessment was designated as meeting stage B2 MMVD criteria,[12] which includes radiographic assessment of cardiac enlargement. However, 3 dogs assigned to the case group on the basis of echocardiographic criteria had retrospective VHS measurements (recorded at time of the study) that were < 10.5 VBUs. This finding highlighted interobserver variability (in this case, between the attending clinician and our trained observer) in VHS measurement that might affect clinical assessment of some animals.[16]

In the present study, results for variables that we anticipated to reflect LA size (VLAS, LA_{width}, and LA_{total}) more closely correlated with results for LVIDDN than did results for variables we anticipated to reflect LVIDDN directly (VHS and VHS_{length}). Vertebral heart size has long been recognized as a measure of general cardiac size and incorporates measures of left

(length) and right (width) chambers of the heart. Because VHS renders a more global assessment, it is likely to be less sensitive in detecting LV enlargement specifically. In a previous study[17] of large-breed dogs, results for VHS and VHS_{length} had better correlation with echocardiographic LVIDD (r = 0.81 and 0.79, respectively) than results for these variables in the present study correlated with LVIDDN (r = 0.42 and 0.34, respectively). Also, in that earlier study, [17] bilateral atrial and ventricular dilation was noted as a result of chronic pacing, suggesting greater VHS accuracy in dogs with global cardiac enlargement because VHS assesses bilateral chamber size.[7] Dogs with concurrent tricuspid regurgitation that may have resulted in cardiac enlargement affecting the right side of the heart were not excluded from the present study, and the prevalence of bilateral valvular regurgitation was not assessed; however, the VHS in those dogs could have been a less accurate reflection of LVIDDN because of cardiac enlargement affecting both sides of the heart. In another study[5] of dogs of various breeds with MR, results for VHS correlated with results for LA:Ao but not with results for LVIDD divided by body surface area, in contrast to the findings of the present study, in which VHS moderately correlated (r = 0.42 and P = 0.002) with LVIDDN. Complete assessment of the LA is difficult with 2-D radiography because of the irregular shape of the LA, variable patient positioning, and variability associated with breed and body conformation.[4] Measurements of the LA in the present study (VLAS, LA_{width}, and LA_{total}) could have encompassed portions of the cardiac silhouette that overlapped with the LV, especially with enlargement of the LV.[7] A correlation between VLAS and LA:Ao in dogs with MMVD has been reported,[8] and our results suggested that VLAS could have reflected both LA and LV size in dogs of the present study.

Because the purpose of our study was to investigate the usefulness of radiographic measures of the LA and LV as surrogates for echocardiographic criteria (LVIDDN ≥ 1.7 and LA:Ao ≥ 1.6[2]) in identifying dogs with stage B2 MMVD, dogs were grouped according to whether they met both echocardiographic criteria (case dogs) or did not meet 1 criterion or both criteria (control dogs). Fifteen of 56 (27%) dogs overall had discordant echocardiographic results (one or the other echocardiographic criterion was not met) and were therefore included in the control group. The relatively common occurrence of this phenomenon with differential enlargement of the LV and LA in dogs of the present study likely reflected a common situation in practice, and results for these dogs were not excluded from our statistical analyses. Therefore, veterinarians should be aware that dogs with discordant echocardiographic results may comprise a clinically substantial portion of the population and that use of the radiographic criteria indicated in the present study may not accurately identify all dogs with stage B2 MMVD. Further studies are required to determine whether dogs with solitary enlargement of either their LV or their LA would benefit from pimobendan treatment.

Identification of optimal cutoff values for use in clinical circumstances requires analysis of the relative risks and benefits of positive test results. In the present study, the optimal cutoff values that we identified were ones that best distinguished between the control and case groups and that provided a balance in minimizing false-positive and false-negative diagnoses of stage B2 MMVD in dogs. The associated PPV and NPV could be applied in a clinical setting to judge the likely reliability of the group categorization (ie, dogs that likely would vs likely would not benefit from treatment with pimobendan). In contrast, use of the cutoff associated with maximum specificity and PPV provides higher certainty that false-positive diagnoses would be minimal and, in the present study, lessened the chance that a dog that did not meet the echocardiographic criteria for treatment with pimobendan would have been prescribed the drug. In patients for which treatment is too expensive or associated with increased risks of adverse effects, a clinician may prefer to use a cutoff value that maximizes specificity and PPV, recognizing that the tradeoff is an increased likelihood of miscategorizing some patients (increased number of false-negative categorization) and thereby denying treatment to those miscategorized patients. Because the treatment option contemplated (initiating lifelong treatment with pimobendan in a dog without current clinical signs of MMVD) involves costs to owners and risks of adverse effects in patients, we identified maximum specificity cutoffs, which were values that maximized the probability that disease was present.

Results indicated that the radiographic variable that most reliably distinguished control dogs from case dogs in the present study was VLAS ≥ 2.5. Results for the LA_{total} had similar diagnostic characteristics but had the disadvantage of requiring more measurements (LA_{width} and VLAS) and the identification of the VHS_{length} line, which increased the time needed to obtain the measurement and the chances that ≥ 1 measurement may not be correct or discernable in a given patient. Results indicated that the composite variable of VHS + VLAS could also be useful because many patients will already have a VHS measurement as part of their radiographic evaluation and therefore would require only 1 additional measurement, the VLAS. The combined variable VHS + VLAS may be best used at the cutoff with maximum specificity, which in the dogs of the present study was 16.5 VBUs and had a PPV of 94%.

The present study design had strengths and weaknesses. Although the sample size was small, it included multiple dog breeds, allowing for generalization of results to a diverse clinical population but potentially confounding findings with breed differences in radiographic measurements.[4,18] The diverse study population mirrors that from another study[2] that shows benefits of pimobendan treatment

of MMVD prior to the onset of CHF in dogs, and we believe that our results would likely be applicable to similar clinical patients. To make the present study as applicable to general practice as possible, we had radiographic measurements performed by a nonspecialist in a fashion mimicking a clinical situation in which experienced practitioners may be trained but do not routinely perform these measurements. However, dogs in the present study may not have been representative of those in general practice, given the expected differences in referral hospital populations and proportion of animals affected in the population assessed by the present study.

Intraobserver repeatability was not assessed in the present study but has been considered to be good in previous similar studies.[8,16] Although subject miscategorization was possible with altered hydration status between measurements, this risk was minimized in the present study by our inclusion criteria that dogs had to be clinically normal, not be receiving cardiac medications, and have ≤ 24 hours between echocardiographic and radiographic examination.

Radiographic and echocardiographic measures like the ones in the present study are 2-D representations of 3-D anatomy, and appreciation of cardiac chamber enlargement is therefore restricted to the incident angle of x-ray beams or ultrasound waves, respectively. As such, cardiac chamber measurements are highly influenced by diagnostic imaging view and patient positioning, including obliquity. Because of the 2-D nature of these diagnostic imaging modalities, they neither account for unassessed anatomic planes or directional views nor represent the true size of the LA but only assess diameter of the chamber in 1 plane and are limited by the angle at which the atrium is imaged. Consequently, the present study was designed to allow differentiation of individuals on the basis of previously published and commonly used techniques, rather than identifying true 3-D LA diameter or volume measurements.

Vertebral size–based radiographic measures of the cardiac silhouette may be affected by vertebral body aberrations (eg, wedge or butterfly vertebrae), border effacement of vertebral end plates or cardiac silhouette margins, phase of respiration, and patient obliquity. Intervertebral disk space width also influences measurements of these variables, with narrowed spaces giving the false impression of an enlarged cardiac silhouette.[16] Each of these factors may contribute to imprecise estimation of cardiac silhouette size with respect to VBU measurements. In contrast to other studies[4,7,18] in which VBU was measured in 0.1 vertebrae, the present study used measurements rounded to the nearest 0.25 vertebrae. Although use of larger units may increase variability owing to rounding error, it might also minimize the influence of altered intervertebral disk spacing and vertebral body aberrations.

Findings of the present study supported the use of radiographic variables to identify dogs with stage B2 MMVD. Specifically, when echocardiographic criteria of a previous study[2] were used in the present study as the gold standard to identify dogs with stage B2 MMVD, 3 radiographic variables (VLAS, LA_{width}, and LA_{total}) were identified as the best discriminators of group status, with VLAS being the simplest and fastest to perform in a clinical setting. Because of the complexity of evaluating 3-D anatomy, echocardiography remains the preferred method of identifying dogs with stage B2 MMVD. The cutoff values for radiographic variables reported here, used as surrogates for the echocardiographic variables, may provide guidance when considering the initiation of pimobendan treatment, especially when cutoff values associated with the highest specificity and PPV are used to further help minimize risks of false-positive diagnosis of stage B2 MMVD in dogs.

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Footnotes

a. Vivid E95 echocardiographic system, GE Healthcare, Wauwatosa, Wis.
b. Prism 7, version 7.0d for Mac OS X, GraphPad Software, San Diego, Calif.
c. Keene BW. Guidelines for the diagnosis and treatment of chronic valvular heart disease in dogs (oral presentation). Am Coll Vet Intern Med Forum, National Harbor, Md, June 2017.

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From this month's *AJVR*

Evaluation of subcutaneously administered electrolyte solutions in experimentally dehydrated inland bearded dragons (*Pogona vitticeps*)

Lily A. Parkinson and Christoph Mans

OBJECTIVE
To evaluate the effects of 3 electrolyte solutions administered SC to experimentally dehydrated inland bearded dragons (*Pogona vitticeps*).

ANIMALS
9 inland bearded dragons.

PROCEDURES
In a randomized, complete crossover study, experimental dehydration was induced by means of furosemide (10 mg/kg, SC, q 12 h for 4 doses), and then lactated Ringer solution, Plasma-Lyte A, or reptile Ringer solution (RRS; 1:1 mixture of 5% dextrose solution and isotonic crystalloid solution) was administered SC in a single 50-mL/kg dose in 3 treatments sessions separated by a minimum of 14 days. Food and water were withheld during treatment sessions. Plasma biochemical values, PCV, blood total solids and lactate concentrations, and plasma osmolarity were measured prior to (baseline) and 4 and 24 hours after fluid administration.

RESULTS
Administration of RRS resulted in severe hyperglycemia (mean ± SD plasma glucose concentration, 420 ± 62 mg/dL), compared with baseline values (190 ± 32 mg/dL), and this hyperglycemia persisted for at least 24 hours. It also resulted in significant reductions in plasma osmolarity and sodium and phosphorus concentrations, which were not observed after administration of the other 2 solutions. Administration of lactated Ringer solution caused no significant increase in blood lactate concentration.

CONCLUSIONS AND CLINICAL RELEVANCE
The changes in plasma glucose, sodium, and phosphorus concentrations and plasma osmolarity observed after SC administration of a single dose of RRS suggested this type of electrolyte solution should not be used for rehydration of bearded dragons. Rather, lactated Ringer solution or Plasma-Lyte A should be considered instead. (*Am J Vet Res* 2020;81:437–441)

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