Use of the vertebral heart scale for differentiation of cardiac and noncardiac causes of respiratory distress in cats: 67 cases (2002–2003)

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Objective—To assess the effectiveness of the vertebral heart scale (VHS) system to differentiate congestive heart failure from other causes of dyspnea in cats.

Design—Retrospective case series.

Animals—67 cats with acute respiratory distress.

Procedures—Medical records of client-owned cats evaluated on an emergency basis because of acute respiratory distress during a 1-year period were reviewed. For study inclusion, cats must have undergone evaluation with echocardiography and thoracic radiography within 12 hours after hospital admission. The VHS was calculated for each cat by 2 investigators. Signalment, physical examination, and echocardiographic findings were reviewed for each patient.

Results—There was 83% agreement overall between the 2 investigators in assessment of cardiomegaly in cats with dyspnea ($\kappa = 0.49$). The VHS cutpoints were the same for both observers in terms of optimizing sensitivity and specificity. A VHS of > 8.0 vertebrae was the best cutpoint when screening for heart disease, whereas a VHS of > 9.3 vertebrae was very specific for the presence of heart disease. Measurements between 8.0 and 9.3 vertebrae suggested the cause of dyspnea was equivocal (ie, secondary to congestive heart failure or respiratory disease), in which case echocardiography would be most useful in providing additional diagnostic information.

Conclusions and Clinical Relevance—Results suggested that the VHS system may be a useful tool to help differentiate cardiac from noncardiac causes of respiratory distress in cats in an emergency situation when an echocardiogram is not available or is not plausible in an unstable patient. (*J Am Vet Med Assoc* 2013;242:366–371)

Identifying cardiac disease in cats can be challenging in a clinical setting. Historical data, physical examination findings, and biochemical analysis results are all important factors in determining the presence of underlying heart disease. However, several studies[1,2] have shown that cats with heart disease may not have murmurs on physical examination and, similarly, cats with murmurs may not have structural heart disease. Moreover, the early stages of HCM are extremely difficult to recognize without echocardiography because LVH results in chamber obliteration rather than an enlarged cardiac silhouette on radiographs. However, left atrial enlargement is closely related to severity and chronicity of left ventricular dysfunction in various types of heart disease.[3] Indeed left atrial enlargement is usually present in cats with CHF and has been associated with adverse clinical outcomes.[3–5]

Radiography is available in most clinical settings and serves as the best diagnostic tool for assessing the airway as well as cardiopulmonary changes consistent with CHF. Thoracic radiographs are useful for the assessment of pulmonary disease, mediastinal disease, and pulmonary vasculature abnormalities as well as cardiac size. Analysis of thoracic radiographs in light of historical findings and physical examination findings is often the only way to determine whether underlying cardiac disease is present when an echocardiogram is not available. Unfortunately, there are many variations in the radiographic appearance of cardiogenic pulmonary edema, which can make radiographic diagnosis challenging.[5] Yet, this determination is the most critical diagnostic step in a critically dyspneic cat because CHF occurs as a result of diastolic dysfunction in the most common forms of cardiomyopathy. Congestive heart failure secondary to diastolic dysfunction is initially addressed by means of preload reduction with diuretics (ie, furosemide).[6] Therefore, the most important urgent determination is whether dyspnea is due to CHF (rather than identifying the underlying type of heart disease). If cardiac disease is suspected, referral to a cardiologist can be pursued and echocardiography performed once the patient has been stabilized. However, it is often unclear whether thoracic radiographic findings are consis-

Abbreviations

AO	Aortic diameter at the sinus of Valsalva
CHF	Congestive heart failure
HCM	Hypertrophic cardiomyopathy
LA	Left atrial echocardiographic size in the short axis
LVH	Left ventricular hypertrophy
VHS	Vertebral heart scale

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tent with CHF. Therefore, an objective tool for assessing heart enlargement would be useful.

A helpful tool for analyzing cardiac size from thoracic radiographs is the VHS system because it is easily performed, objective, and repeatable.[7] The VHS system allows objective measurement of the heart size scaled against the length of specific thoracic vertebrae.[8] This form of internal control reduces error associated with subjective interpretations and interpatient variability. Clinically normal cats have a VHS of < 8.0 vertebrae; in a case series of 100 clinically normal cats, the mean VHS was 7.5 ± 0.3 vertebrae.[8] Another study[9] obtained similar results in 50 clinically normal adult stray cats, although variability was somewhat higher. That study[9] found the VHS was 7.3 ± 0.49 vertebrae in the right lateral projection, 7.3 ± 0.55 vertebrae in the left lateral projection, 7.5 ± 0.68 vertebrae in the dorsoventral projection, and 7.5 ± 0.53 vertebrae in the ventrodorsal projection. The VHS reference range has also been reported for various breeds of dogs as well as growing puppies[10–16] and other species, including Japanese macaques (*Macaca fuscata*),[17] rabbits,[18] and ferrets.[19] The VHS system has also been studied with various forms of heart disease in cats and dogs.[7,20–24] In fact, 1 study[5] has shown that in cats with cardiogenic pulmonary edema, the VHS was increased above normal (8.1 vertebrae) in all cats in which cardiac borders were visible and the VHS could be measured.

The effectiveness of the VHS system to specifically differentiate cardiac versus noncardiac causes of respiratory distress in cats has not been evaluated. It appears likely that determination of the VHS may help determine whether respiratory distress is due to underlying cardiac disease in an emergency situation. Additionally, the VHS system may be a useful screening test to determine whether the additional cost of echocardiography is likely to be clinically beneficial in feline patients. If the VHS is normal, it may be reasonable to monitor heart size with serial radiographs and pursue echocardiography if or when heart enlargement occurs in a subset of feline patients (eg, if cardiology referral is not possible).

The purpose of the study reported here was to assess the ability of VHS to differentiate cardiac decompensation from other etiologies of respiratory distress in cats evaluated at an emergency service because of acute dyspnea. Our hypothesis was that the VHS would be a useful measurement in dyspneic cats to ascertain whether clinical signs were secondary to heart disease or extracardiac in origin.

Materials and Methods

Case selection—The medical records of client-owned cats evaluated at the emergency service of the Matthew J. Ryan Veterinary Hospital of the University of Pennsylvania because of acute respiratory distress from August 1, 2002, through August 1, 2003, were reviewed. To be included in the study, cats must have undergone evaluation with echocardiography and thoracic radiography within 12 hours after being admitted to the hospital.

Medical record review and echocardiography—Data collected from the records for analysis included sex, breed, age, presence of a murmur, echocardiographic parameters including left ventricular dimensions (in diastole and systole) obtained from M-mode or 2-D echocardiography, LA (short axis), left atrial size in the long axis, and AO. Left ventricular hypertrophy was defined as interventricular wall thickness or left ventricular free wall thickness ≥ 6 mm at end diastole, and left atrial enlargement was defined as an LA:AO ratio > 1.5.[2,3,25]

Thoracic radiography and VHS—For each cat, thoracic radiographs were reviewed by 2 investigators (one with 10 years of experience performing VHS measurements [observer 1; MMS] and the other with 1 year of experience [observer 2; RR]) in a blinded manner, and a VHS was assigned for each left lateral radiograph. Right lateral radiographs were used only when a left lateral projection was unable to be evaluated (n = 7).

For VHS determination, the long axis of the heart was measured on the lateral radiograph with a caliper extending from the ventral aspect of the left mainstem bronchus to the left ventricular apex. The caliper was repositioned along the vertebral column beginning at the cranial edge of the fourth thoracic vertebra, and the number of vertebrae within the long axis of the heart was recorded to the nearest 0.1 vertebrae. The maximal perpendicular short axis was measured in the same manner and likewise is quantified beginning at the fourth thoracic vertebra. These 2 values are then added to give the VHS (**Figure 1**).

Litster and Buchanan[8] reported a VHS of 7.5 ± 0.3 vertebrae for clinically normal cats. From this information, a reference range for VHS of the mean ± 2 SDs was proposed. These 2 values represented the outer points of the reference range. On the basis of this information, the upper limit of the reference range was 8.1 vertebrae, and 8.1 vertebrae was used as the reference cutoff value for normal versus cardiomegaly in the subsequent analysis in the present study.

Diagnosis of heart disease—Receiver operating characteristic analysis was used to determine the values with which a radiographic diagnosis of heart disease was established. Cats received a final cardiac diagnosis on the basis of echocardiographic data, thoracic radiographs, and response to treatment (ie, dyspnea improved with furosemide treatment). Multiple modalities were used to classify cats rather than radiographic findings alone because of the highly variable findings on thoracic radiographs of cats with heart failure.[5] Based on the response to furosemide treatment and the radiographic and echocardiographic findings, dyspnea was categorized as secondary to cardiac disease (left atrial enlargement present in conjunction with a radiographic pulmonary pattern consistent with CHF), secondary to respiratory disease (normal left atrial size and a radiographic pulmonary pattern consistent with primary respiratory disease), or equivocal in origin (normal left atrial size or mild left atrial enlargement and a mixed radiographic pulmonary pattern).

Statistical analysis—Taking the upper cutpoint as > 8.1 vertebrae to provide the diagnosis of cardiomegaly, each observer's measurement was categorized into cardiomegaly or no cardiomegaly, and then these final diagnoses of heart size (cardiomegaly or not) for each

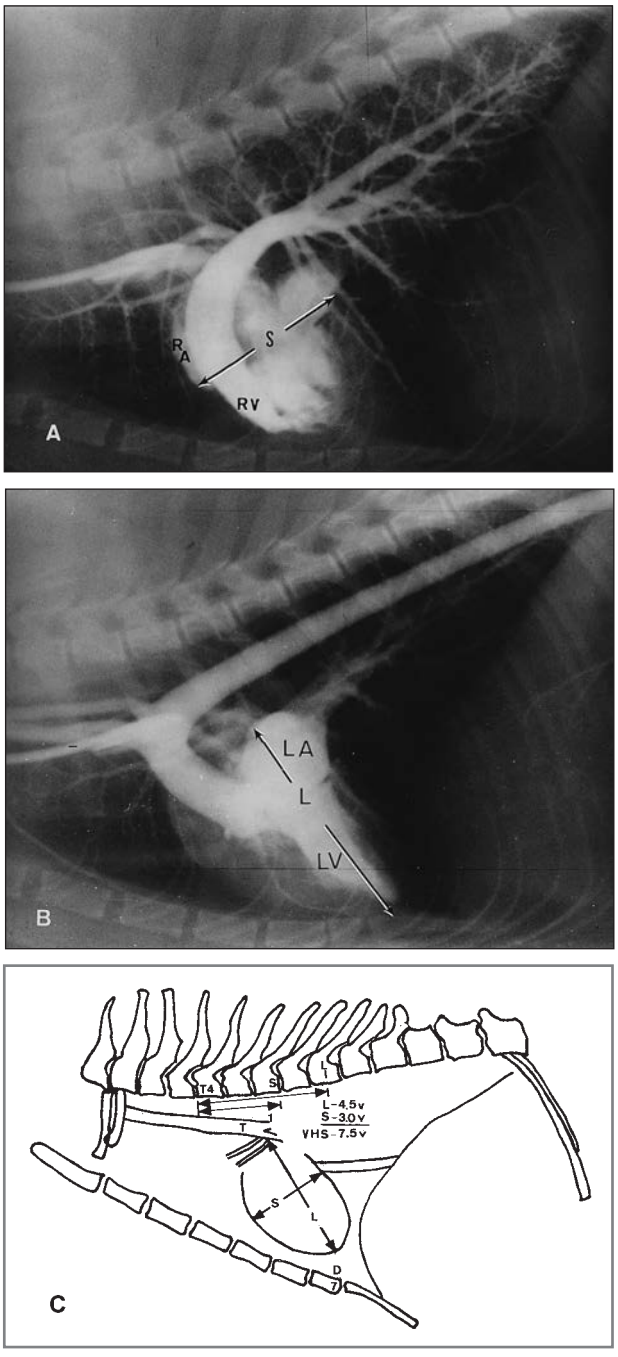

Figure 1—Lateral angiocardiographic views (A and B) of the thorax and diagram (C) of the thorax of a cat illustrating the VHS system. A—Notice the cardiac structures including the short axis (S) dimension of the VHS (left and right heart chambers at the level of the coronary groove). RA = Right atrium. RV = Right ventricle. B—Notice the cardiac structures included in the long axis (L) dimension of the VHS (combined length of the left atrium [LA] and left ventricle [LV]). C—The long axis and short axis dimensions of the heart are transposed onto the vertebral column and recorded as the corresponding number of vertebrae (V), as measured caudally from the cranial edge of T4. The values are then summed to obtain the VHS. D = Depth of thorax. 7 = Seventh sternebrae. T = Trachea. (From Litster AL, Buchanan JW. Vertebral scale system to measure heart size in radiographs of cats. *J Am Vet Med Assoc* 2000;216:210–214. Reprinted with permission.)

observer were compared with each other by means of a κ statistic to determine the level of agreement.

Receiver operating characteristic curve analysis was then performed on each observer's measurements, and the areas under the curves were calculated via the trapezoid method. Additionally, these curves were used to determine the optimal cutpoints for each observer in determining which cutpoints are best for overall accuracy, optimizing sensitivity (sensitivity, 100%), and optimizing specificity (specificity, 100%). The values developed were subjectively compared between the 2 observers. After these comparisons were performed, VHS measurements were then subjectively categorized as indicating definitely no cardiac disease (very low VHS) or definitely cardiac disease (very high VHS); VHS measurements in a midrange, for which diagnoses were likely to be inconsistent, indicated that patients should be referred for echocardiography.

All continuous variables were evaluated for normality via the Shapiro-Wilk test. Nonnormally distributed continuous variables are described with median (range), and normally distributed continuous variables are described with mean ± SD. The Spearman rank method was used to assess correlation of VHS with diastolic left atrial size in terms of diameter (short- and long-axis dimensions), LA:AO ratio, and left ventricular diastolic dimension. For all analyses, a value of $P < 0.05$ was considered significant.

Results

Descriptive findings—Sixty-seven cats were evaluated. Cats ranged in age from 8 months to 19 years (median, 10 years). There was no significant ($P = 0.26$) correlation between age and type of heart disease. There were 23 (34%) female cats and 44 (66%) male cats in the study. Three of the females and 1 male were sexually intact, and all others were neutered. Thirty-eight of 67 (57%) cats were determined to have heart disease (CHF) as the underlying cause of dyspnea. In 17 cats, there was no evidence of heart disease and respiratory distress was determined to be primarily respiratory in origin. The remaining 12 cats had evidence of primary heart and respiratory disease, and dyspnea was categorized as equivocal in origin. The 12 cats with dyspnea of equivocal origin had LVH without left atrial enlargement.

Of the 50 cats with primary heart disease, 34 (68%) were male and 16 (32%) were female. Final echocardiographic diagnosis for 50 cats with echocardiographic abnormalities included dilated cardiomyopathy (4/67 [6%]), LVH (21/67 [31%]; 9 of which were found to have HCM, whereas the cause of LVH was uncertain in 12), unclassified cardiomyopathy (10/67 [15%]), and restrictive cardiomyopathy (8/67 [12%]); 7 of 67 (10%) had other forms of cardiac disease (eg, endomyocarditis or congenital heart disease). Left ventricular hypertrophy was presumed to be due to HCM; however, from the available medical records, it was impossible to definitively rule out secondary causes of LVH (systemic hypertension and hyperthyroidism) in all 21 cats with LVH. None of the cats had evidence of pericardial effusion on echocardiography. Among all cats with CHF, 11 (29%) were female and 27 (71%) were male.

Of the 17 cats without evidence of heart disease, 9 had heart murmurs and 8 did not. Of the 50 cats with heart disease, 22 (44%) had heart murmurs and 28 (56%) did not. Pleural effusion was present in 7 cats.

Level of agreement between observers—Each observer identified 36 of 46 (78%) cats that had a VHS of

> 8.1, although they were not in complete agreement on a cat-by-cat basis. There was 83% agreement overall between the 2 observers in assessment of cardiomegaly ($\kappa = 0.49$; $P < 0.001$). There were 7 cats with pleural effusion in which one observer gave measurements and the other did not; these measurements were not included in the κ analysis. In every case, observer 2 did not think that a measurement could be made for the 7 cats. Area under the curve for each receiver operating characteristic curve was 0.91 (95% confidence interval, 0.82 to 1.0) and 0.93 (95% confidence interval, 0.86 to 1.0) for observers 1 and 2, respectively. Area under the curve was not significantly different between observers.

The VHS cutpoints for optimizing sensitivity, specificity, and overall accuracy for detection of heart disease for each observer were determined. The VHS cutpoints were the same for both observers in terms of optimizing sensitivity and specificity of VHS for detection of heart disease, although there was some difference between observers for VHS cutpoints that optimized overall accuracy. On the basis of this information, a VHS of > 8.0 vertebrae was the best cutpoint when screening for heart disease, whereas a VHS of > 9.3 vertebrae was highly specific for the presence of heart disease. Measurements between 8.0 and 9.3 vertebrae suggested the cause of dyspnea was equivocal and echocardiography would be needed to distinguish whether heart disease is present. There were 7 cats with pleural effusion for which a VHS was not obtained by 1 of the 2 observers. In 2 of these cats, the pleural effusion was associated with CHF, and in 5, it was extracardiac in origin.

Vertebral heart scale was found to correlate with several echocardiographic measurements, including the diastolic left atrial diameter obtained from the long axis (Spearman $\rho = 0.492$; $P = 0.009$), the left atrial diameter obtained from the short axis (Spearman $\rho = 0.403$; $P = 0.001$), and the LA:AO ratio (Spearman $\rho = 0.341$; $P = 0.029$). The left ventricular internal dimension in diastole was not significantly correlated with VHS (Spearman $\rho = 0.217$; $P = 0.095$). No other correlations were noted between VHS and echocardiographic measurements.

Discussion

The diagnosis of cardiac disease in cats can be challenging in a clinical setting. For example, the presence of a heart murmur in an otherwise clinically normal cat may not be indicative of primary cardiac disease, whereas a considerable proportion of cats with cardiomyopathy do not have cardiac murmurs. In a study[1] evaluating subclinically affected cats, heart murmurs were detected in 16% of the 103 cats; two-thirds of these cats had no abnormalities on echocardiography, and one-third had cardiomyopathy. In contrast, 11 of the 16 cats with cardiomyopathy in the same study[1] did not have heart murmurs. In another study[2] of subclinically affected cats that compared variable criteria for LVH, 18% to 62% of cats with murmurs had hypertrophy. Our findings are similar to those other reports,[1,2] with 37% of cats with heart disease having normal cardiac auscultatory findings. Likewise, in the study reported here, 53% of cats without heart disease had murmurs. Thus, the presence or absence of a heart murmur in a cat neither confirms nor disconfirms the presence of cardiac disease.

Although there remains some controversy regarding the best echocardiographic method to assess left atrial enlargement[3,25] and LVH,[2] echocardiography remains the gold standard for assessment of cardiac structures in veterinary clinical practice. However, echocardiography may not be available in the emergency setting and it may be cost prohibitive in some situations. The VHS has been shown to be a reasonably specific, albeit less sensitive, marker of left atrial enlargement in cats.[3] Our data corroborate these results, with VHS correlating with the echocardiographic left atrial diameter and LA:AO ratio. When one considers the cardiac structures included in the VHS measurement (Figure 1), it is not surprising that the VHS is closely correlated to left atrial size.

Our results further suggest the VHS system is a useful screening technique to guide therapeutic decisions for dyspneic feline patients. Echocardiographic assessment is essential for diagnosing cardiac disease, but this requires an ultrasound machine as well as a skilled ultrasonographer. Moreover, although echocardiography is the gold standard for assessing cardiac structure and function in a clinical setting, it is not without limitations. In some cases, even when complete echocardiography is performed, a clear-cut diagnosis of heart disease is not possible. For example, dehydration and volume depletion can cause an (false) LVH appearance with increased left ventricular wall thickening and a reduction in the left ventricular chamber diameter.[26] This scenario is particularly likely in the emergency setting when furosemide is administered to a dyspneic animal without heart disease. Thus, in an emergency situation, the most critical question is whether to treat the patient for CHF (with diuretics) or for respiratory disease (with bronchodilators and anti-inflammatories). Moreover, because there was no significant difference in VHS measurements among observers in our study (regardless of the degree of experience), the VHS system should prove to be a useful tool for practitioners with various amounts of experience in interpretation of feline thoracic radiographs. The κ value of 0.49 is consistent with moderate agreement between the observers. This finding highlights results from a study[27] of Cavalier King Charles Spaniels that showed the amount of experience of observers was not a factor in determining VHS measurements but that some individual observers may select variable reference points, which could alter the results. Therefore, consistent selection of radiographic reference points is an important factor to ensure the most accurate measurement of VHS.

From our results, a VHS of 8.0 vertebrae or less indicates that underlying heart disease is highly unlikely to be the cause of dyspnea and an echocardiogram is unlikely to be a cost-effective diagnostic tool. A VHS of > 9.3 vertebrae indicates that underlying heart disease is highly likely to be present and an echocardiographic evaluation is warranted to determine the type of cardiac disease present (although it is not necessary prior to beginning treatment for CHF). For VHS values between 8.0 and 9.3 vertebrae, echocardiographic assessment will add supportive information regarding whether heart disease is present and the type of cardiac disease. However, a reasonable therapeutic approach

in this population of dyspneic cats would be to begin treatment for CHF, recognizing that primary respiratory disease remains plausible.

Although it is always optimal to obtain 2 orthogonal radiographic views for diagnostic purposes, the VHS measurements used in this study were obtained from the lateral radiographic views. In a dyspneic cat, obtaining 1 lateral projection rather than lateral and ventrodorsal projections is likely to be safer and appears to result in useful diagnostic information in an emergency setting. Taking this a step farther, it is possible a VHS obtained from 1 dorsoventral projection would be even better tolerated and yield similar results; however, an additional study would be necessary to evaluate this hypothesis.

The population characteristics of our study cats are similar to those in a previous study,[2] in which a higher proportion of male than female cats had underlying heart disease. In the cats with CHF, the proportion of cats with HCM (9/67 [13%]) was similar to the number of cats with restrictive cardiomyopathy (8/67 [12%]) and unclassified cardiomyopathy (10/67 [15%]). When including subclinically affected cats, 21 of 67 cats in our study had evidence of LVH (however, secondary causes of LVH such as systemic hypertension could not be ruled out in all of these cases). Most previous studies have shown a greater percentage of cats with HCM than the other forms of cardiomyopathy in cats. However, 2 of these previous studies[1,2] evaluated subclinically affected cats, in contrast to our study. Conversely, 1 study[28] identified a substantial proportion of cats with myocardial diseases other than HCM, with 21% having restrictive cardiomyopathy, 10% having dilated cardiomyopathy, and 10% having unclassified cardiomyopathy. These variations may reflect our lack of knowledge of the natural history of myocardial disease in cats[2] or may reflect variability in the populations being studied.

The retrospective nature of this study provides some limitations. In most cats, the left lateral view was used for VHS measurement, although in a few cats, only the right lateral view was available. Two studies[14,29] in dogs revealed that the VHS was larger in right lateral projection, compared with the left lateral projection. This discrepancy was determined to be clinically unimportant in the initial description of the VHS system.[10] Moreover, the difference between VHS obtained from right and left lateral projections in 50 adult cats was not significant.[9] Blood pressure data and thyroid function status were not available in many of the cats in the study reported here. It is most likely that HCM was present in those with CHF; however, it is impossible to be certain because secondary causes of LVH were not ruled out in all cases. Not surprisingly, the presence of pleural effusion obscures the cardiac silhouette, preventing accurate measurements of cardiac dimensions with the VHS system. Pleurocentesis prior to evaluation of radiographs may help make determination of the VHS more accurate; however, if the cardiac silhouette remains obscured, an echocardiographic evaluation of these animals would be necessary to determine whether heart disease is present. In this study, enough pleural effusion was present to preclude cardiac measurement in 7 (10%) cases. Despite these limitations, the VHS system appears to be a useful screening technique in dyspneic feline patients to develop an initial therapeutic plan, particularly if echocardiography is not available. Additionally, it will allow clinicians to better assess the cost-to-benefit ratio regarding echocardiography in feline patients.

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From this month's *AJVR*

Evaluation of vincristine-associated myelosuppression in Border Collies

Denise L. Lind et al

Objective—To determine whether Border Collies (ATP binding cassette subfamily B1 gene [ABCB1] wildtype) were more likely than other breeds to develop vincristine-associated myelosuppression (VAM) and, if so, whether this was caused by a mutation in ABCB1 distinct from ABCB1-1Δ.

Animals—Phase 1 comprised 36 dogs with the ABCB1 wildtype, including 26 dogs with lymphoma (5 Border Collies and 21 dogs representing 13 other breeds) treated with vincristine in a previous study; phase 2 comprised 10 additional Border Collies, including 3 that developed VAM and 7 with an unknown phenotype.

Procedures—For phase 1, the prevalence of VAM in ABCB1-wildtype Border Collies was compared with that for ABCB1-wildtype dogs of other breeds with data from a previous study. For phase 2, additional Border Collies were included. Hematologic adverse reactions were graded with Veterinary Co-operative Oncology Group criteria. Genomic DNA was used to amplify and sequence all 27 exons of the canine ABCB1 gene. Sequences from affected dogs were compared with those of unaffected dogs and dogs of unknown phenotype.

Results—3 of 5 Border Collies with the ABCB1 wildtype developed VAM; this was significantly higher than the proportion of other dogs that developed VAM (0/21). A causative mutation for VAM in Border Collies was not identified, although 8 single nucleotide polymorphisms in ABCB1 were detected.

Conclusions and Clinical Relevance—Breed-associated sensitivity to vincristine unrelated to the ABCB1 gene was detected in Border Collies. Veterinarians should be aware of this breed predisposition to VAM. Causes for this apparent breed-associated sensitivity should be explored. (*Am J Vet Res* 2013;74:257–261)

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