J Vet Intern Med 2010;24:1069–1076

Use of Simpson's Method of Disc to Detect Early Echocardiographic Changes in Doberman Pinschers with Dilated Cardiomyopathy

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Background: M-mode is the echocardiographic gold standard to diagnose dilated cardiomyopathy (DCM) in dogs, whereas Simpson's method of discs (SMOD) is the preferred method to detect echocardiographic evidence of disease in humans.

Objectives: To establish reference values for SMOD and to compare those with M-mode measurements.

Animals: Nine hundred and sixty-nine examinations of 471 Doberman Pinschers.

Methods: Using a prospective longitudinal study design. Reference values for SMOD were established using 75 healthy Doberman Pinschers >8 years old with <50 ventricular premature contractions (VPCs) in 24 hours. The ability of the new SMOD cut-off values, normalized to body surface area (BSA), for left ventricular end-diastolic volume (LVEDV/BSA >95 mL/m^2) and end-systolic volume (LVESV/BSA > 55 mL/m^2) to detect echocardiographic changes in Doberman Pinschers with DCM was compared with currently recommended M-mode values. Dogs with elevated SMOD values but normal M-mode measurements were followed-up using a prospective longitudinal study design.

Results: At the final examination 175 dogs were diagnosed with DCM according to both methods (M-mode and SMOD). At previous examinations, M-mode values were abnormal in 142 examinations only, whereas all 175 SMOD already had detected changes. Additionally, 19 of 154 dogs with >100 VPCs/24 hours and normal M-mode values had abnormal SMOD measurement. Six dogs with increased SMOD measurements remained healthy at several follow-up examinations (classified as false positive); in 24 dogs with increased SMOD measurements, no follow-up examinations were available (classified as unclear).

Conclusions and Clinical Importance: SMOD measurements are superior to M-mode to detect early echocardiographic changes in Dobermans with occult DCM.

Key words: Dilated cardiomyopathy; Dogs; Echocardiography; Occult.

Dilated cardiomyopathy (DCM) is an important cause of cardiac morbidity and mortality in dogs and is the most commonly acquired cardiac disorder in large and giant breed dogs.[1–3] Dobermans Pinschers are one of the most commonly affected breeds, and DCM in this breed is an inherited, slowly progressive primary myocardial disease.[1,4–7] The occult stage of the disease is characterized by evidence of morphologic or electrical derangement in the absence of clinical signs of heart disease.[1,6,8–10] The morphologic abnormality consists of left ventricular (LV) enlargement in systole and later in diastole. Ventricular premature contractions (VPCs) are a common finding in the occult phase of DCM in Doberman Pinschers.[1,4,5,8–16,a] Sudden death, caused by ventricular tachycardia-fibrillation, occurs during the occult phase in at least 25–30% of affected dogs.[4,11,15] These abnormalities, morphologic or electrical, can coexist or can be of predominantly one form at any time during this occult stage.[1,11,15,17,18] For diagnostic, prognostic, therapeutic, and breeding purposes it is essential to detect the occult phase of the disease. Diagnosis primarily depends on evidence of ventricular arrhythmias, detected by 24-hour ambulatory ECG (Holter) and echocardiographic evaluation of LV dimensions and function. Currently, M-mode is considered the gold-standard to diagnose echocardiographic changes in Doberman Pinschers with DCM.[a,b,4,5,11,16,18–22]

Abbreviations:

Holter	24-hour ambulatory ECG
ASE	American Society of Echocardiography
BSA	body surface area
CV	coefficients of variations
DCM	dilated cardiomyopathy
EF	ejection fraction
EDVI	end-diastolic volume index
ESVI	end-systolic volume index
LV	left ventricle
LVIDd	left ventricular internal end-diastolic dimension
LVIDs	left ventricular internal end-systolic dimension
ROC	receiver operator curves
SMOD	Simpson's method of disc
2D	two dimensional
VPC	ventricular premature contraction

Many echocardiography laboratories rely on M-mode measurements or linear dimensions derived from the two-dimensional (2D) image for quantification. Linear measurements from M-mode and 2D images have proven to be reproducible with low intraobserver and interobserver variability. However, M-mode is a 1D method that relies on geometric assumptions that may assess geometric changes occurring in diseases such as DCM less accurately. The Teichholz or Quinones methods of calculating LV volumes and ejection fraction (EF) from LV linear dimensions may result in inaccuracies as a result of the geometric assumptions required to convert a linear measurement to a 3D volume.[23–26] Accordingly, the American Society of Echocardiography (ASE) rec-

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Submitted February 1, 2010; Revised May 19, 2010; Accepted June 28, 2010.

10.1111/j.1939-1676.2010.0575.x

ommends not to use linear measurements to calculate LV volumes and EF for clinic practice.[26] The most commonly used 2D measurement for volume measurements in human beings is the biplane Simpson's method of discs (SMOD), currently the recommended method of choice according to the ASE.[25,26] Using SMOD, heart volume is measured as the summation of parallel cylinders, whose diameters are derived from endocardial border tracing performed on 1 or 2 orthogonal LV apical views. The principle underlying this method is that the total LV volume is calculated from the summation of a stack of elliptical disks. The height of each disk is calculated as a fraction (usually 1/20) of the LV long-axis based on the longer of the 2 lengths from the 2- and 4-chamber views. The cross-sectional area of the disk is based on the 2 diameters obtained from the 2- and 4-chamber views. When 2 adequate orthogonal views are not available, a single plane can be used, and the area of the disk is then assumed to be circular.[25,26] Recently, it has been recommended in human medicine to use the long-axis view instead of the 2-chamber view in combination with the 4-chamber view for accurate biplane LV volume and EF calculations.[27,28] The apical 2-chamber view is not a standard echocardiographic view in dogs and difficult to obtain, in contrast to the right parasternal long-axis 4-chamber view.[29] However, it has not been assessed in dogs if SMOD measurements from right parasternal long-axis view are comparable to measurements obtained from the left apical 4-chamber view. Furthermore, no SMOD reference values are published for Doberman Pinschers, and the ability of SMOD to detect echocardiographic changes in Doberman Pinschers with DCM has not been evaluated.

The aims of this study were therefore to (1) establish SMOD reference values using a large population of healthy Doberman Pinschers, (2) to compare the SMOD values obtained from the right parasternal long-axis view with the left apical 4-chamber view, (3) to determine the comparative within- and between-day variability of end-diastolic volume index (EDVI) and end-systolic volume index (ESVI), and (4) to compare the established SMOD cut-off values with currently recommended M-mode values in their ability to diagnose echocardiographic changes in a large population of Doberman Pinschers affected by DCM using a prospective longitudinal study design.

Material and Methods

Animals

The study population was 471 (249 female and 222 male) client-owned Doberman Pinschers that were prospectively selected according to the inclusion and exclusion criteria from a longitudinal cohort study starting in 2004. A total of 969 examinations from these 471 Doberman Pinschers met the selection criteria. Enrollment was restricted to purebred Doberman Pinschers without evidence of systemic disease. Written owner consent was obtained before enrollment. The dogs were examined at least once a year. Each examination included a thorough clinical examination, a Holter examination, and echocardiography. Body weight was recorded for calculation of body surface area (BSA) by the formula[30] $0.1 \times kg^{0.667}$.

Examinations

All dogs were examined without sedation in right and left lateral positions. Echocardiographic examinations were performed with a commercially available high frame rate ultrasound system equipped with a 2.0/4.3 MHz probe[c] with simultaneous ECG recording by the ultrasound machine. M-mode measurements were obtained from the right parasternal long-axis view. All valves were examined by color-Doppler. Velocities over the aortic and pulmonary valves were measured by continuous wave Doppler examinations and had to be below 2.2 m/sec. Twenty-four-hour Holter recordings were performed at each exam and analyzed by 1 of 2 commercially available software programs.[d,e] Manual adjustments and accuracy verification of the arrhythmias recognized by the software were performed by members (veterinarians) of the LMU cardiology team with extensive experience in Holter analysis and overseen by a Diplomate in cardiology (G.W.).

SMOD Measurements

SMOD measurements were done on (1) left apical 4-chamber view and (2) on the right parasternal long-axis 4-chamber view. Frame-by-frame analysis was performed, with selection of end-diastolic frames (corresponding to onset of QRS, ie, at the time of mitral valve closure) and end-systolic frames (corresponding to the last frame before mitral valve opening). The LV area was measured by tracing the endocardial border on each selected image; maximal LV length was measured from the middle of a line connecting the 2 mitral annuli to the endocardial border of the LV apex (Fig 1). LV volumes were then automatically calculated by the ultrasound machine. SMOD derived end-diastolic and end-systolic LV volumes were indexed to BSA (EDVI and ESVI, respectively). Reference values for EDVI, ESVI, and EF were established using 75 healthy Doberman Pinschers >8 years of age with <50 VPCs/24 hours and normal M-mode values.

Dogs were grouped into 3 different groups according to the results of the Holter and echocardiographic M-mode examinations at the last available examination:

(1) Control group: Dogs in this group had no clinical signs, <50 VPCs/24 hours, and normal echocardiographic measurements. M-mode values that were considered to be normal were as follows: left ventricular internal end-diastolic dimension (LVIDd) ≤ 47 mm and left ventricular internal end-systolic dimension (LVIDs) ≤ 38 mm.[5,11]
(2) VPC group: Dogs in this group had no clinical signs, >100 VPCs/24 hours on Holter examination, and normal echocardiographic M-mode measurements as described above. The dogs were in the occult phase of the disease.
(3) ECHO group: M-mode values that were considered abnormal and indicative of DCM were as follows: LVIDd ≥ 49 mm,[16,19] or LVIDs ≥ 40 mm,[5,7] or both measurements increased. The dogs were in the occult phase of the disease.

Exclusion Criteria

Dogs with evidence of systemic disease, concomitant congenital heart disease or evidence of primary mitral valve disease (based on echocardiography) were not included. Dogs that had between 50 and 100 VPCs/24 hours were considered "equivocal" and were not included in the study.

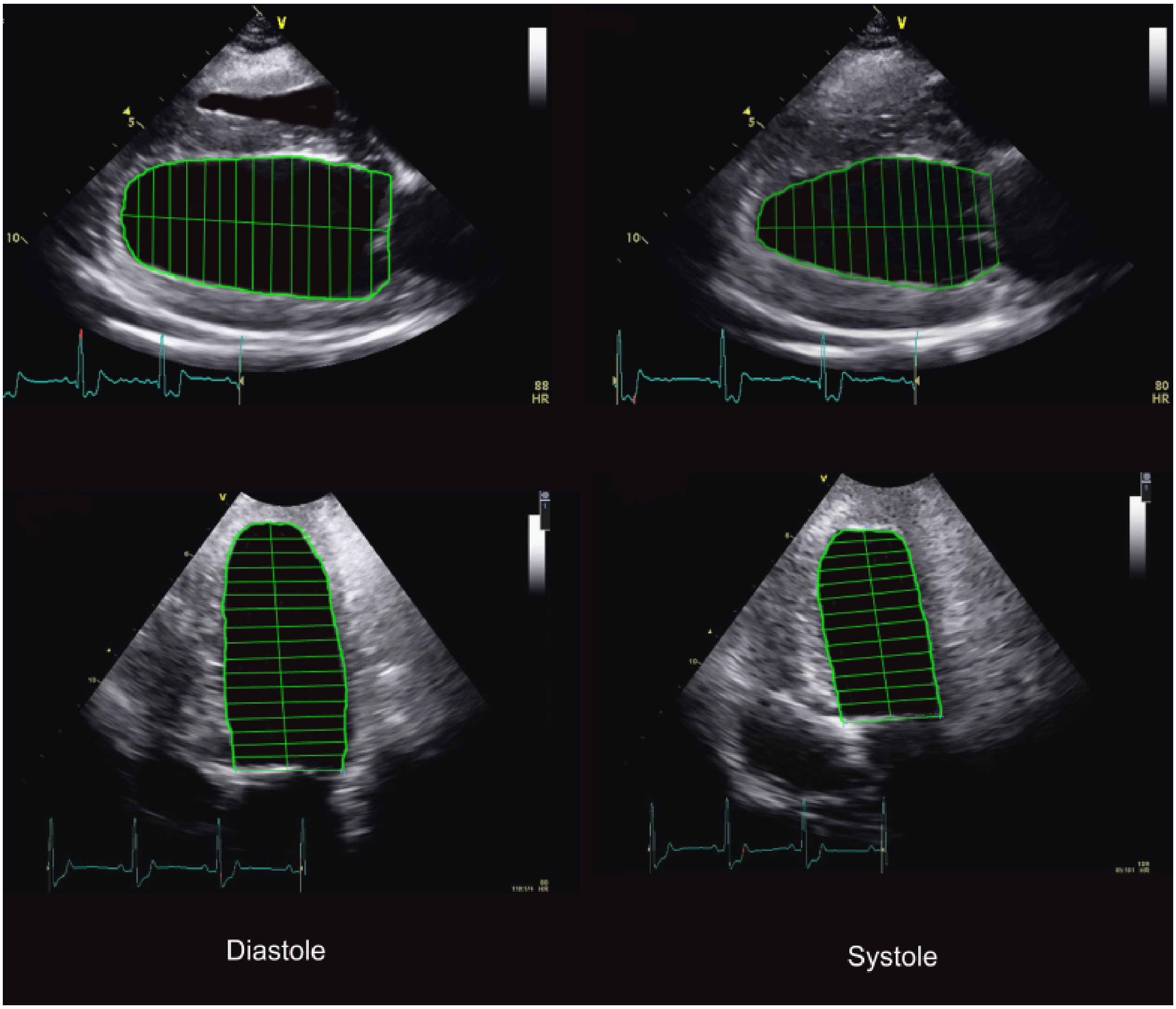

Fig 1. Simpson's method of disc measurements were performed on left parasternal apical 4-chamber view and using the right parasternal long-axis view. Left ventricular area was measured by tracing the endocardial border in end-systole and end-diastole and maximal LV length was measured from the mitral annulus to the endocardial border of the LV apex.

Follow-Up Examinations

After calculation of optimal cut-off values by receiver operating curves (ROC) (see "Results"), dogs with increased EDVI (>95 mL/m^2), or increased ESVI (>55 mL/m^2), or both were judged as correctly abnormal, if M-mode values were also abnormal (LVIDd $\geq$49 mm[16,19] or LVIDs $\geq$40 mm[5,7]) at the same examination, or if M-mode values became abnormal at a later examination. Cases in which only SMOD was abnormal and no follow-up examination was available were classified as unclear, or if M-mode measurements were in the gray zone (LVIDd 47.1–48.9 mm, or LVIDs 38.1–39.9 mm). Increased SMOD measurements were considered false positive, if M-mode values were still within the reference range after >1 year.

Measurement reliability was determined for EDVI and ESVI measurements and for both, the right parasternal long-axis view, and the left apical 4-chamber view. Ten echocardiograms were randomly selected to be subjected to 3 repeated analyses by 1 investigator (G.W.) to determine intraobserver measurement variability. The same 10 echocardiograms were subjected to independent repeated analyses by a 2nd investigator (J.S.) to determine interobserver measurement variability. Both investigators were unaware of the results of the prior echocardiographic analyses. The effect of image acquisition (intraechocardiographer and interechocardiographer effect) was tested by acquiring the right parasternal long-axis and left apical 4-chamber view on the same day on 2 different occasions (about 5 hours apart) of 10 Doberman Pinschers. The ultrasound examinations were performed by 2 echocardiographers (G.W. and J.S.) at each time point. The SMOD measurements were performed by 1 investigator (G.W.) by measuring each variable 3 times on 3 consecutive cardiac cycles by the recorded loops, and the mean value was used to determine the effect of intraechocardiographer and interechocardiographer variability.

Statistical Analysis

All data were visually inspected and tested for normality by the Kolmogorov-Smirnov test. Statistical analyses were performed by computer software.[f,g] Data were normally distributed; therefore, comparisons between SMOD measurements obtained from (1) the right parasternal long-axis view and from (2) the left apical 4-chamber

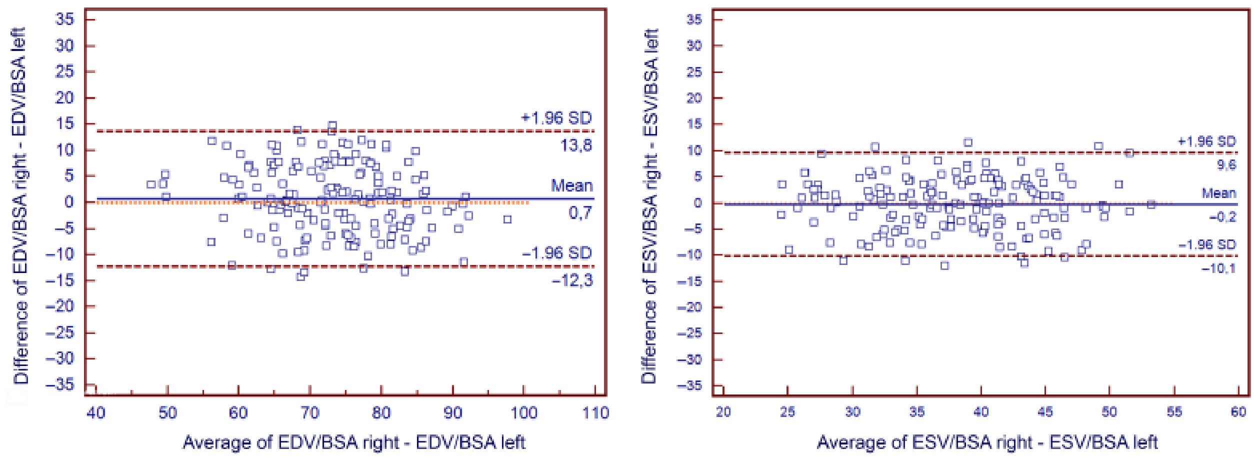

Fig 2. Bland and Altman scattergrams of end-diastolic volume index (EDVI) and end-systolic volume index (ESVI) of 969 Doberman Pinschers. The differences of the respective volume measurements, obtained from the right parasternal long-axis view and the left apical 4-chamber view, are plotted against average values of both views. The mean difference of two measurements and the limits of agreement (±1.96 SD of the mean) are shown as separate lines.

view were evaluated by a paired *t*-test. Limits of agreement were analyzed by Bland-Altman analysis.[31] Standard error and 95% confidence intervals were computed. ROC were used to calculate optimal cut-off values for EDVI and ESVI to detect echocardiographic changes. The intra- and interobserver coefficients of variations (CV) for EDVI and ESVI measurements were calculated by variance component analysis. The CV were obtained by dividing the root of the variance error by the mean of the repeated measurements and multiplying it by 100. A *P*-value $<.05$ was considered statistically significant.

Results

A total of 969 examinations of 471 (249 female and 222 male) Doberman Pinschers fulfilled the inclusion criteria.

There was no significant difference between the right parasternal long-axis view and the left apical 4-chamber for EDVI ($P = .49$) and ESVI ($P = .38$). The Bland and Altman scattergrams display the differences plotted against average values of the EDVI and ESVI obtained from the right parasternal long-axis view and the left apical 4-chamber view (Fig 2). The limits of agreement are shown as separate lines (±1.96 SD of the mean difference). The graphs show a good agreement between both views. As there was no difference between both views, modified biplane SMOD values for EDVI and ESVI were calculated for further analysis as mean of the right parasternal long-axis view and the left apical 4-chamber view SMOD measurements (modified biplane EDVI and ESVI). The reproducibility of SMOD measurements was very good for both intraobserver and interobserver measurements. The effect of image acquisition on SMOD measurements (intraechocardiographer and interechocardiographer CV) was similar to the effect of interobserver variability (Table 1).

For the calculation of SMOD reference values, 75 healthy Doberman Pinschers >8 years of age (mean age, 9.01 years; median age, 8.75 years; female, 43; male, 32) with <50 VPCs/24 hours (mean number VPCs/24 hours, 8; median number VPCs/24 hours, 3) and normal M-mode values were used. Only the last examination of each dog was included for this analysis, even if the dog had several examinations performed. Table 2 shows the mean, median, and percentiles for EDVI, ESVI, and EF for the modified biplane SMOD.

First, this older control population was used to calculate optimal cut-off values for EDVI (>95 mL/m^2) and ESVI (>55 mL/m^2) to detect echocardiographic changes in Doberman Pinschers with DCM by ROC analysis. The control group was then extended to include also younger healthy dogs for the calculation of sensitivity and specificity of these calculated cut-off values. Therefore, the final control group included 610 examinations of 317 healthy Doberman Pinschers (mean weight, 34.92 kg; mean age, 4.65 years, female, 186; male, 131)

Table 1. Intraobserver and interobserver, as well as intraechocardiographer and interechocardiographer coefficients of variation (CV) for end-diastolic (EDVI) and end-systolic (ESVI) volume measurements index to body surface area measured by Simpson's method of disc on the right parasternal long-axis view, and on the left apical 4-chamber view.

	CV (%) Intraobserver	CV (%) Interobserver	CV (%) Intraechocardiographer	CV (%) Interechocardiographer
EDVI right parasternal	2.7	5.2	6.2	6.5
ESVI right parasternal	3.6	5.3	6.1	5.7
EDVI left apical	3.1	4.9	5.6	5.8
ESVI left apical	3.3	5.9	5.1	5.4

Table 2. Modified biplane end-diastolic and end-systolic volume reference values, measured by Simpson's method of disc, index to body surface area (EDVI and ESVI) using 123 healthy Doberman Pinschers >5 years of age.

	EDVI (mL/m^2)	ESVI (mL/m^2)	EF (%)
Mean (±SD)	72 (8)	38 (6)	49 (6)
Minimum	56	24	27
Maximum	92	53	63
Percentiles			
25	66	33	44
50	72	37	47
75	79	41	54
95	88	48	60

SD, standard deviation; ESVI, end-systolic volume index; EDVI, end-diastolic volume index.

The modified biplane measurements were calculated as the mean of EDVI, ESVI, and ejection fraction (EF) measured in the right parasternal long-axis view, and the left apical 4-chamber view.

with normal M-mode and SMOD measurement. At the time of the data analysis, 175 Doberman Pinschers had abnormal M-mode and SMOD measurements. At previous examinations, evidence of DCM by use of M-mode was present in 142/175 dogs. Elevated SMOD measurement were present at the same previous examinations in all 175/175 dogs. Table 3 shows the frequency of EDVI and ESVI measurements that were abnormal at previous examinations, in which M-mode values were still within the normal range. Additional to the 142 dogs, in which both methods (M-mode and SMOD) were elevated, 30 dogs had elevated SMOD measurements while M-mode was normal (n = 15), or in the gray zone between normal and abnormal (n = 15). Follow-up examinations after 1–2 years in 6 of these dogs showed that these Doberman Pinschers did not deteriorate further on SMOD and still had no evidence of M-mode abnormality. These dogs were considered, therefore, as false positive results. Twenty-four dogs were considered "unclear" at the final examination for several reasons: 3 dogs with SMOD measurements above the SMOD cut-off values were in the M-mode gray zone, and in the remaining 21 dogs with elevated SMOD measurements no follow-up examination was performed. Additionally, 154 dogs were considered having "only VPCs," as M-Mode measurements were normal (n = 145) or in the M-mode gray zone (n = 9). However, SMOD measurements were abnormal in 19/154 dogs. Therefore, SMOD identified correctly early echocardiographic changes in 33 dogs that only at a later time point became abnormal according to M-mode measurements, and in additional 19 dogs that had VPCs but normal M-mode measurements (or M-mode values in the gray zone).

Table 4 shows the sensitivity, specificity, and area under the curve of the ROC-analysis for EDVI (>95 mL/m^2), ESVI (>55 mL/m^2), and M-mode measurements LVIDd and LVIDs to detect echocardiographic changes in Doberman Pinschers with DCM. For LVIDd and LVIDs 2 different cut-off values are given: (1) the cut-off values from the literature indicating clear echocardiographic changes (LVIDd > 49 mm, LVIDs > 40 mm) and (2) including the cases in the echocardiography gray zone (LVIDd > 47 mm, LVIDs > 38 mm). The ROC analysis was performed 2-fold: (1) including the unclear cases as healthy control, and (2) excluding those cases from analysis. Sensitivity was identical in both analyses, but specificity was higher when the unclear cases were excluded from analysis. The calculation of sensitivity and specificity revealed that SMOD measurements are more sensitive to detect early echocardiographic changes in Doberman Pinschers with DCM compared with M-mode, even when the cut-off values for LVIDd and LVIDs were lowered and when cases in the gray zone were included. Specificity was good for both methods (Table 4).

Discussion

The present study shows that the SMOD method to measure EDVI and ESVI is superior to conventional M-mode measurements in its ability to detect early echocardiographic changes in Doberman Pinschers with DCM. Echocardiography allows the noninvasive assessment cardiac function. Estimates of LV volumes can be determined from M-mode or 2D echocardiogram, and these data may be used to calculate EF and stroke

Table 3. Results of M-mode and Simpson's method of disc (SMOD) measurements at the final (last) examination, and at previous examinations.

		Previous Examinations				
		M-Mode and SMOD		M-Mode Normal and		
	Final Examination	Normal	Abnormal	EDVI and ESVI Abnormal	Only EDVI Abnormal	Only ESVI Abnormal
Control	616	610	0	1	5	0
DCM ECHO	175	0	142	23	6	4
VPCs only	154	135	0	9	8	2
unclear	24	0	0	10	10	4

VPCs, ventricular premature contractions; EDVI, end-diastolic volume indexed to body surface area (BSA); ESVI, end-systolic volume indexed to body surface area (BSA).

Cut-off values were >95 mL/m^2 for EDVI and >55 mL/m^2 for ESVI.

Table 4. Sensitivity and specificity of end-diastolic volume index (EDVI) and end-systolic volume index (EDVI), measured by Simpson's method of disc (SMOD), and left ventricular internal diameter in diastole (LVIDd) and systole (LVIDs), measured by M-Mode.

Parameter	Cut-Off	Sensitivity (%)	Specificity (%)	AUC
EDVI	> 95 mL/m^2	96.9	96.3 (98.7)	0.99
ESVI	> 55 mL/m^2	94.4	97.4 (99.5)	0.99
LVIDd	> 49 mm	71.6	100 (100)	0.97
LVIDs	> 40 mm	60.5	100 (100)	0.98
LVIDd	> 47 mm	84.6	99.0 (99.5)	0.97
LVIDs	> 38 mm	82.7	99.2 (99.7)	0.98

AUC, area under the curve.

Reference point to determine if a dog had echocardiographic changes consisted with dilated cardiomyopathy (DCM) was the final examination. Unclear cases without follow-up examination, but abnormal SMOD results were (1) included in the control group (false positive cases), or (2) excluded from analysis (specificity in parenthesis). Sensitivity did not change excluding the unclear cases.

volume. Whereas M-mode methods of volume determination sometimes have a poor correlation with noninvasive methods and may not be clinically useful in the presence of heart disease, volume determinations by 2D echocardiography images seem to be more accurate, because they involve more direct measurements and fewer geometric assumptions.[26,32,33] The ASE currently recommends the SMOD method as the preferred method of calculating LV volume in humans.[26] Ideally, paired orthogonal left apical views should be used. When 2 views are not possible, a single apical plane may be used.[26] The use of 1 plane in veterinary medicine is potentially more accurate than in humans as regional myocardial dysfunction secondary to myocardial infarcts is less common in dogs compared with humans. Surprisingly, there are only a few studies by SMOD measurements in veterinary medicine, probably because of the lack of published reference values for this method.[32,34] Only a small study using 23 dogs had previously compared right and left cardiac windows using the area-length method to obtain LV volume measurements.[35] Therefore, the present study is the 1st comparing SMOD measured from the right parasternal long-axis view with the left apical 4-chamber view in a large study population. The present study shows that LV volume can be measured in dogs either from right parasternal long-axis view or from left-apical view, the right view being technically less demanding. The conformation of the canine thorax permits excellent right parasternal long-axis images that appear to optimize LV lengths and volumes. However, it is important to optimize the right parasternal long-axis 4-chamber view in order to include the anatomical LV apex, which occasionally might be technically challenging. The anatomical LV apex in a dog is diaphragmatically located, and it is not imaged from the left-apical view unless a modified view is used and the length and the volume from this view may be underestimated, particularly during diastole, especially in broad, shallow chested dogs.[35] In deep, narrow-chested dogs like Dobermans this is less of an issue.[35] However, from a technical perspective, it is technically more demanding to have the transducer in good contact with the thoracic wall close to the sternum in deep, narrow-chested dogs like the Doberman in order to image the LV from the felt apical window. Less experienced echocardiographers might tend to go dorsally (away from the sternum) to have a better contact with the chest and have then the problem that they truncate the LV apex. Nevertheless, SMOD should best be measured using both views. Results from both views should then be compared and either the higher value should be used (as an overestimation of SMOD is not possible), or the mean of both views can be calculated to obtain a modified biplane result and used for assessment of the case. Intraobserver and interobserver, as well as intraechocardiographer and interechocardiographer reproducibility of the SMOD method were very good and comparable to a previous veterinary study reporting intraobserver reproduciblity.[32]

Using a longitudinal study with follow-up examinations enabled a unique study design, by providing follow-up examinations in most dogs in which EDVI, ESVI, or both were above the calculated cut-off value, while M-mode values still were normal. Usually, if a new test is evaluated against the current gold standard (in the case of cardiomyopathy in Doberman Pinschers, echocardiography and Holter examinations), it can only be as good as the gold standard, but it cannot perform better than the current test. A positive result using the new test in a patient that is classified by the current gold standard as "healthy" would be considered false positive, even if the patient has the disease (but the gold standard was unable to diagnose it at this time point). The present study could prove that most abnormal SMOD measurements became clearly abnormal according to M-mode measurements at a later time. Six cases were considered as false positive results, as M-mode did not become abnormal within 1–2 years. However, it might be possible that some of these cases may not have been followed for long enough and that they might show abnormal M-mode values at a later time point, which would increase the specificity of SMOD measurements.

There are different M-mode cut-off values to diagnose DCM in Doberman Pinschers available in the literature, but most studies are in accordance with the cut-off values used in the present study to define DCM and to characterize the control group.[4,7,11,18–20,36,h] For the purpose of a scientific study, usually only clearly normal and clearly abnormal dogs are included. However, a gray zone between the defined normal and abnormal cut-off values often exists. The present study shows that the sensitivity of M-mode measurements using the cut-off values of LVIDd > 49 mm and of LVIDs > 40 mm was only 71.6 and 60.5%, respectively, to detect early echocardiography changes. By decreasing the cut-off values to LVIDd > 47 mm and LVIDs > 38 mm, an increased sensitivity to 84.6 and 82.7%, respectively, could be reached, while specificity remained very high. However, SMOD EDVI and ESVI were clearly more sensitive than M-mode, even when the lower M-mode cut-off values were used. Interestingly, SMOD was also abnormal in 19 dogs that were considered to only have VPCs, as M-mode values were either normal or in the echocardiographic gray zone. In the proposed guidelines for the diagnosis of canine idiopathic DCM by the European society of veterinary cardiology, SMOD measurements have been mentioned as a method to measure LV volumes, but no clear cut-off values were reported in that manuscript. The report stated that an ESVI $> 80\,\mathrm{mL/m^2}$ would be clearly abnormal, and an ESVI $< 30\,\mathrm{mL/m^2}$ has been suggested as normal.[37] The ESVI cut-off values established in the present study are higher than the (unreferenced) $30\,\mathrm{mL/m^2}$, but lower than the $80\,\mathrm{mL/m^2}$. It might be therefore possible that either normal ESVI measurements in Doberman Pinschers are higher compared with other breeds, indicating an impaired systolic function,[38] or that the suggested ESVI $< 30\,\mathrm{mL/m^2}$ is too low. Further studies establishing SMOD reference values in different breeds should be performed, as currently no published reference values are available.

A limitation of this study is that follow-up examinations were not available in all dogs with elevated SMOD measurements. These dogs were therefore included in the control group (as false positive results) for the purpose of sensitivity and specificity calculations, which explains why the specificity was "only" 96.4% for EDVI and 97.4% for ESVI. However, as some dogs may actually have "true" early echocardiographic changes, these unclear cases without follow-up examination were excluded in a 2nd statistical analysis and specificity increased to 99.0 and 99.2%, respectively. The calculation of SMOD reference values included only dogs >5 years of age with <50 VPCs/24 hours on Holter examination. The reason to include only older dogs was that DCM usually has a late onset and chances that the dogs are truly healthy become higher with increasing age. However, it cannot be excluded that some of the dogs in the control group will develop DCM at a later time. Additionally dogs were deemed to be free of systemic disease based upon thorough physical examination and unremarkable history, but no blood work was obtained. Therefore, some dogs might have had undetected systemic disease.

In conclusion, this study shows that the right parasternal long-axis view can be used interchangeably or in combination with the left apical 4-chamber view to obtain SMOD measurements. Intraobserver and interobserver respectabilities are very good for both EDVI and ESVI measurements. Using $>95\,\mathrm{mL/m^2}$ for EDVI and $>55\,\mathrm{mL/m^2}$ for ESVI as cut-off values, SMOD measurements are superior to conventional M-mode measurements to detect early echocardiographic changes in Doberman Pinschers with DCM.

Footnotes

[a] O'Sullivan ML, O'Grady MR, Minors SL, et al. Occult dilated cardiomyopathy in the Doberman Pinscher, a retrospective study of prognosis in 163 cases. J Vet Intern Med 2005;19:406 (abstract)

[b] O'Grady MR. Echocardiogarphic findings in 51 normal Doberman Pinschers. J Vet Intern Med 1995;9:202 (abstract)

[c] Vivid 7 dimension, General Electric Medical System, Waukesha, WI

[d] Custo tera, Arcon Systems GmbH, Starnberg, Germany

[e] Amedtech ECGpro Holter software, EP 810 digital Recorder, Medizintechnik Aue GmbH, Aue, Germany

[f] SPSS for Windows, Version 13.0, SPSS Inc, Chicago, IL

[g] MedCalc, Version 8.1, Mariakerke, Belgium

[h] O'Grady MR, Minors SL, O'Sullivan ML, et al. Evaluation of the efficacy of pimobendan to reduce mortality and morbidity in Doberman Pinschers with congestive dilated cardiomyopathy. J Vet Intern Med 2003;17:440 (abstract)

Acknowledgments

This work was partly funded by the European Commission (LUPA, GA-201370).

References

1. O'Grady MR, O'Sullivan ML. Dilated cardiomyopathy: An update. Vet Clin North Am Small Anim Pract 2004;34:1187–1207.
2. Tidholm A, Haggstrom J, Borgarelli M, et al. Canine idiopathic dilated cardiomyopathy. Part I: Aetiology, clinical characteristics, epidemiology and pathology. Vet J 2001;162:92–107.
3. Vollmar AC. The prevalence of cardiomyopathy in the Irish wolfhound: A clinical study of 500 dogs. J Am Anim Hosp Assoc 2000;36:125–132.
4. Calvert CA, Meurs K. Cardiomyopathy in Doberman Pinschers. In: Bonagura JD, Twedt DC, eds. Current Veterinary Therapy. St Louis, MO: Saunders Elsevier; 2009:800–803.
5. Calvert CA, Brown J. Influence of antiarrhythmia therapy on survival times of 19 clinically healthy Doberman Pinschers with dilated cardiomyopathy that experienced syncope, ventricular tachycardia, and sudden death (1985–1998). J Am Anim Hosp Assoc 2004;40:24–28.
6. Calvert CA, Chapman WL Jr, Toal RL. Congestive cardiomyopathy in Doberman Pinscher dogs. J Am Vet Med Assoc 1982;181:598–602.
7. Calvert CA, Meurs K. CVT update: Doberman Pinscher occult cardiomyopathy. In: Bonagura JD, Kirk RW, eds. Kirk's Current Veterinary Therapy. Philadelphia, PA: Saunders; 2000: 756–760.
8. Calvert CA, Hall G, Jacobs G, et al. Clinical and pathologic findings in Doberman Pinschers with occult cardiomyopathy that died suddenly or developed congestive heart failure: 54 cases (1984–1991). J Am Vet Med Assoc 1997;210:505–511.
9. Calvert CA, Pickus CW, Jacobs GJ, et al. Signalment, survival, and prognostic factors in Doberman Pinschers with end-stage cardiomyopathy. J Vet Intern Med 1997;11:323–326.
10. Petric AD, Stabej P, Zemva A. Dilated cardiomyopathy in Doberman Pinschers: Survival, causes of death and a pedigree review in a related line. J Vet Cardiol 2002;4:17–24.
11. Calvert CA, Jacobs G, Pickus CW, et al. Results of ambulatory electrocardiography in overtly healthy Doberman Pinschers with echocardiographic abnormalities. J Am Vet Med Assoc 2000;217:1328–1332.
12. Calvert CA, Jacobs GJ. Heart rate variability in Doberman Pinschers with and without echocardiographic evidence of dilated cardiomyopathy. Am J Vet Res 2000;61:506–511.
13. Calvert CA, Jacobs GJ, Kraus M. Possible ventricular late potentials in Doberman Pinschers with occult cardiomyopathy. J Am Vet Med Assoc 1998;213:235–239.
14. Calvert CA, Jacobs GJ, Kraus M, et al. Signal-averaged electrocardiograms in normal Doberman Pinschers. J Vet Intern Med 1998;12:355–364.
15. Calvert CA, Jacobs GJ, Smith DD, et al. Association between results of ambulatory electrocardiography and development

of cardiomyopathy during long-term follow-up of Doberman Pinschers. J Am Vet Med Assoc 2000;216:34–39.

16. O'Grady MR, Home R. The prevalence of dilated cardiomyopathy in Doberman Pinschers: A 4.5 year follow-up. J Vet Intern Med 1998;12:199.

17. Hazlett MJ, Maxie MG, Allen DG, et al. A retrospective study of heart disease in Doberman Pinscher dogs. Can Vet J 1983;24:205–210.

18. O'Grady MR, O'Sullivan ML, Minors SL, et al. Efficacy of benazepril hydrochloride to delay the progression of occult dilated cardiomyopathy in Doberman Pinschers. J Vet Intern Med 2009;23:977–983.

19. O'Grady MR, Minors SL, O'Sullivan ML, et al. Effect of pimobendan on case fatality rate in Doberman Pinschers with congestive heart failure caused by dilated cardiomyopathy. J Vet Intern Med 2008;22:897–904.

20. Calvert CA, Brown J. Use of M-mode echocardiography in the diagnosis of congestive cardiomyopathy in Doberman Pinschers. J Am Vet Med Assoc 1986;189:293–297.

21. Kraus MS, Thomason JD, Fallaw TL, et al. Toxicity in Doberman Pinchers with ventricular arrhythmias treated with amiodarone (1996–2005). J Vet Intern Med 2009;23:1–6.

22. O'Grady MR. DCM in Doberman Pinschers: Lessons learned in the first decade of study. Proceedings 20th annual ACVIM Forum, Denver, CO, 2002.

23. Quinones MA, Waggoner AD, Reduto LA, et al. A new, simplified and accurate method for determining ejection fraction with two-dimensional echocardiography. Circulation 1981;64:744–753.

24. Teichholz LE, Kreulen T, Herman MV, et al. Problems in echocardiographic volume determinations: Echocardiographic-angiographic correlations in the presence of absence of asynergy. Am J Cardiol 1976;37:7–11.

25. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification. Eur J Echocardiogr 2006;7:79–108.

26. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: A report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440–1463.

27. Malm S, Sagberg E, Larsson H, et al. Choosing apical long-axis instead of two-chamber view gives more accurate biplane echocardiographic measurements of left ventricular ejection fraction: A comparison with magnetic resonance imaging. J Am Soc Echocardiogr 2005;18:1044–1050.

28. Nosir YF, Vletter WB, Boersma E, et al. The apical long-axis rather than the two-chamber view should be used in combination with the four-chamber view for accurate assessment of left ventricular volumes and function. Eur Heart J 1997;18:1175–1185.

29. Thomas WP, Gaber CE, Jacobs GJ, et al. Recommendations for standards in transthoracic two-dimensional echocardiography in the dog and cat. Echocardiography Committee of the Specialty of Cardiology, American College of Veterinary Internal Medicine. J Vet Intern Med 1993;7:247–252.

30. Kirk RW. Current veterinary therapy. Small Anim Pract 2000;XIII:800–803.

31. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307–310.

32. Serres F, Chetboul V, Tissier R, et al. Comparison of 3 ultrasound methods for quantifying left ventricular systolic function: Correlation with disease severity and prognostic value in dogs with mitral valve disease. J Vet Intern Med 2008;22:566–577.

33. Takemoto Y, Tanabe K, Chandrasekaran K, et al. Single-plane and biplane echocardiography: Use of targeted scan planes improves the estimates of left ventricular volume and shape for analysis of postinfarction remodeling. J Am Soc Echocardiogr 2003;16:448–456.

34. Serres F, Pouchelon JL, Poujol L, et al. Plasma N-terminal pro-B-type natriuretic peptide concentration helps to predict survival in dogs with symptomatic degenerative mitral valve disease regardless of and in combination with the initial clinical status at admission. J Vet Cardiol 2009;11:103–121.

35. Dukes-McEwan J. Comparison between right and left cardiac windows to determine left ventricular volumes and ejection fraction in six dog breeds with differing somatotypes. Eur J Ultrasound 2002;27:S4–S5.

36. O'Sullivan ML, O'Grady MR, Minors SL. Assessment of diastolic function by Doppler echocardiography in normal Doberman Pinschers and Doberman Pinschers with dilated cardiomyopathy. J Vet Intern Med 2007;21:81–91.

37. Dukes-McEwan J, Borgarelli M, Tidholm A, et al. Proposed guidelines for the diagnosis of canine idiopathic dilated cardiomyopathy. J Vet Cardiol 2003;5:7–19.

38. Smucker ML, Kaul S, Woodfield JA, et al. Naturally occurring cardiomyopathy in the Doberman Pinscher: A possible large animal model of human cardiomyopathy? J Am Coll Cardiol 1990;16:200–206.