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European Society of Veterinary Cardiology screening guidelines for dilated cardiomyopathy in Doberman Pinschers

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Abstract *Background:* Dilated cardiomyopathy (DCM) is the most common cardiac disease in large breed dogs and is inherited in Doberman Pinschers with a high prevalence (58%).
Objective: The European Society for Veterinary Cardiology convened a task force to formulate screening guidelines for DCM in Dobermans.
Recommendations: Screening for occult DCM in Dobermans should start at three years of age and use both Holter monitoring and echocardiography. Yearly screening over the life of the dog is recommended, as a one-time screening is not sufficient to rule out future development of DCM. The preferred echocardiographic method is the measurement of the left ventricular volume by Simpson's method

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of discs (SMOD). Less than 50 single ventricular premature complexes (VPCs) in 24 h are considered to be normal in Dobermans, although detection of any number of VPCs is cause for concern. Greater than 300 VPCs in 24 h or two subsequent recordings within a year showing between 50 and 300 VPCs in 24 h is considered diagnostic of occult DCM in Dobermans regardless of the concurrent echocardiographic findings. The guidelines also provide recommendations concerning ancillary tests, that are not included in the standard screening protocol, but which may have some utility when recommended tests are not available or financially untenable on an annual basis. These tests include assay of cardiac biomarkers (Troponin I and N-Terminal pro-B-type Natriuretic Peptide) as well as a 5-min resting electrocardiogram (ECG).
Conclusion: The current guidelines should help to establish an early diagnosis of DCM in Dobermans.
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Abbreviation table

cTnI	cardiac troponin I
DCM	dilated cardiomyopathy
ECG	resting electrocardiogram
EPSS	E-point to septal separation
LV	left ventricle
LVIDd	left ventricular internal diameter by M-Mode in diastole
LVIDs	left ventricular internal diameter by M-Mode in systole
NT-proBNP	N-terminal pro B-type natriuretic peptide
SI	sphericity index
SMOD	Simpson's method of discs
VPC(s)	ventricular premature complex(es)

Introduction

Cardiomyopathies are a heterogeneous group of diseases of the myocardium associated with mechanical and/or electrical dysfunction that usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilation [1]. Dilated cardiomyopathy (DCM) is defined by the presence of left ventricular dilation and contractile dysfunction, in the absence of abnormal loading conditions and severe coronary artery disease [2].

Dilated cardiomyopathy is one of the most common cardiac diseases in dogs and humans [1,3]. In the dog, it primarily affects large and giant breeds [3]. Some breeds, such as the Doberman, Newfoundland, Portuguese water dog, Great Dane, Cocker spaniel, and Irish wolfhound exhibit a higher prevalence of DCM [3—6].

Dilated cardiomyopathy in Dobermans is an inherited, slowly progressive disease [7—9]. The occult stage of the disease is characterized by evidence of morphologic or electrical derangement in the absence of clinical signs of heart disease [10—14]. The occult stage may last for several years, before clinical signs develop [8,12]. The morphologic abnormality consists of left ventricular (LV) enlargement in systole and later in diastole [15]. Ventricular premature complexes are a common finding in the occult stage of DCM in Dobermans [6,9,10,12—14,16—20]. Sudden death, caused by ventricular tachycardia-fibrillation, occurs during the occult stage in at least 25—30% of affected dogs [6,9,17]. These abnormalities, morphologic or electrical, may coexist or may be of predominantly one form at any time during the occult stage [6,10,17,21,22].

A recent study showed a high cumulative prevalence (58.8%) of cardiomyopathy in Dobermans in Europe [8], comparable to that reported in the United States and Canada (45 and 63%).[f] [21,23]. The early descriptions of DCM in Dobermans suggested that cardiomyopathy predominantly affected males [13] and was later confirmed, although females are also affected.[f] [11—13,17,21] One study showed that in Dobermans, approximately 50% of male dogs and 33% of female dogs develop DCM,[f] whereas another study found no gender difference [24]. The most recent study showed that the disease is equally distributed in male and female dogs in Europe [8]. The difference in reported gender distributions between earlier and later studies might be explained by the inconsistent inclusion of a 24-h electrocardiogram (Holter) or electrocardiogram

[f] O'Grady M.R., Horne R. The prevalence of dilated cardiomyopathy in Doberman Pinschers: A 4.5 year follow-up (abstract). J Vet Intern Med 1998; 12:199.

(ECG) as part of the standard diagnostic screening in earlier studies. This could explain the over-representation of dogs with morphological changes of the heart, detectable by echocardiography. Generally, male dogs are known to show structural changes earlier than female dogs, which are detectable with an echocardiogram. Males are therefore more likely to develop CHF at an earlier age than female dogs, and likewise succumb from it earlier [8]. Female dogs seem to have a more slowly progressive disease with ventricular premature complexes (VPCs) detected with a Holter as the only abnormality, even in older female dogs. However, most female Dobermans will develop the typical echocardiographically evident morphologic heart changes associated with DCM at an older age, compared with the male dogs [8].

The average age of detection of occult DCM is between 5 and 7 years, but some dogs are affected as young as 2 years of age. Therefore, it appears appropriate to start screening for occult DCM in Dobermans at three years of age and to use both Holter monitoring and echocardiography. Given that the disease can develop over time in combination with the known rate of progression over several years, screening should ideally be repeated on an annual basis [8,12]. In high-risk breeds, such as the Doberman, yearly screening over the life of the dog is recommended but can be cost prohibitive and requires a devoted owner.

However, early detection of occult DCM can facilitate timely removal of affected dogs from active breeding programs and early treatment for all affected dogs leading to an increase in symptom free and overall survival [22,25]. Removal of affected dogs from breeding programs should over time reduce the prevalence of DCM in Dobermans.

Recommendations

Screening age

Screening should be started at 3—4 years of age. A one-time screening is not sufficient to rule out future development of DCM, because the disease is acquired and may develop with increasing age.

Screening frequency

Yearly screening should be performed ideally in both male and female dogs. However, given male dogs involved in active breeding programs have the potential to pass on the disease to a greater number of progeny than female dogs if they are affected and not diagnosed, emphasis should be on annual screening of male dogs that are involved in active breeding programs. Female dogs involved in breeding programs, pets and non-breeding dogs could be screened once every two years if budgetary restrictions prevent annual screening.

Holter criteria

It is essential that the Holter recording be of sufficient duration (at least 23 h of readable recording), good quality and have an accurate analysis verified by a cardiologist. Holter reports generated by automated Holter analysis software are notoriously inaccurate and manual adjustments are always necessary. Inaccurate Holter reports can lead to both false positive and false negative results both of which can have a significant negative impact on breeders and pet owners.

Fewer than 50 single VPCs in 24 h are considered to be normal in Dobermans, although detection of any number of VPCs is cause for concern [6]. Greater than 300 VPCs in 24 h, or two subsequent recordings within a year showing between 50 and 300 VPCs in 24 h, is considered diagnostic of occult DCM in Dobermans regardless of the concurrent echocardiographic findings [26]. Many studies have used $>$ 100 VPCs in 24 h as the cutoff value for establishing a diagnosis of DCM, but the authors believe the results of the most recent study [26] should be the basis of current recommendations.

Comments on special situations:

1) Holter examination shows 1—50 VPCs/24-h: In Dobermans, detection of any number of VPCs is cause for concern, even if only a few VPCs are detected in 24 h ($<$50 VPC/24-hrs). In these cases, VPCs that have a short coupling interval (maximum velocity of beat to beat coupling interval $>$ 250/min) and complexity should also be considered as an additional diagnostic criterion, as couplets, triplets, or single short runs of VPCs with a fast instantaneous rate ($>$260/min) are potentially dangerous and are less likely to be caused by myocardial damage secondary to other systemic diseases. In these cases, DCM cannot be ruled out and a follow-up Holter examination should be performed within 3—6 months.
2) Holters showing between 50 and 300 VPCs in 24 h and a follow-up Holter within 12 months with $<$50 VPCs. Dogs in this category remain a challenge as DCM cannot be definitively ruled out. In these cases ongoing screening is strongly recommended.
3) It is also important to acknowledge, that some dogs will have normal echocardiograms but still have occult DCM diagnosed based on the Holter

results. Systemic diseases that could potentially cause VPCs should always be excluded. Ventricular escape complexes and accelerated idioventricular rhythms (ventricular rate < 160 bpm) are not considered to be diagnostic for DCM. The role of atrial premature contractions and atrial tachycardia (excluding atrial fibrillation) in the diagnosis of DCM in Dobermans is currently unknown.

4) The day-to-day variability of VPCs in Dobermans is currently unknown. In Boxer dogs and humans, an individual day-to-day variability of up to 85% was reported [27,28].

Echocardiographic criteria

In general, the accuracy of the echocardiographic results will depend on the quality of the examination. A complete echocardiogram including color Doppler with a simultaneous ECG should be performed. Basic guidelines should be followed including all measurements being made in triplicate for volume and 5 sequential (if possible) cardiac cycles for M-Mode [29–31]. Congenital or acquired cardiac diseases other than DCM might also cause volume overload, systolic dysfunction or both, and need to be excluded accordingly. Examples are patent ductus arteriosus, ventricular septal defect, mitral valve dysplasia, or myxomatous mitral valve degeneration. Auscultation and color/spectral Doppler examinations should be used to exclude these and other diseases. Hypothyroidism [32–34] and DCM [8,35] are both common diseases in the Doberman. Recently, it was shown that Dobermans with DCM have a 2.26 fold increased risk to develop hypothyroidism [35]. However, hypothyroidism does not seem to play a role in the etiology or progression of DCM in this breed. In this study, hypothyroid dogs were receiving optimal thyroid supplementation, and there was no difference in cardiac size or number of VPCs between the healthy and hypothyroid group. Progressive increase in cardiac volume by Simpson's method of discs (SMOD) and the number of VPCs was not different between the groups [35].

Echocardiographic measurements

Left ventricular volume by Simpson's method of discs

Simpson's method of discs is more sensitive than M-Mode to detect early echocardiographic changes in Dobermans [15]. The LV volume determined by SMOD should be measured in the right parasternal long-axis 4-chamber view and in the left apical 4-chamber view (the aorta should not be visible in either view) by tracing the endocardial border on each selected image. The frame used to measure the end-diastolic volume is selected from the frames around the onset of the QRS complex, when the mitral valve is closed and the volume at its largest (which may not be exactly at onset of the QRS complex) and the frame used to measure the end-systolic volume is selected as the last frame before mitral valve opening, typically after the end of the T wave, where the volume is at its smallest (Fig. 1). Both right parasternal and left apical views should be measured and the larger volumes used, as this reduces potential underestimation of the volume. The tendency for apical foreshortening can easily lead to underestimation of both end-systolic volume and end-diastolic volume.

Cutoff values that indicate the presence of occult DCM based on LV volume estimates by SMOD are [15]:

$$\text{End-diastolic volume index} = \text{End-diastolic volume}(\text{ml})/\text{Body surface area}\,(\text{m}^2) :> 95\,\text{ml}/\text{m}^2$$

or

$$\text{End-systolic volume index} = \text{Ens-systolic volume}(\text{ml})/\text{Body surface area}\,(\text{m}^2) :> 55\,\text{ml}/\text{m}^2$$

Body surface area can be calculated from body weight (kg) using this formula [36]:

$$\text{Body surface area} = 0.101 \times \text{body weight}\,(\text{kg})^{2/3}$$

Left ventricular M-mode measurements

As M-mode is still commonly measured, the authors recommend use of the following reference values if volume measurements by SMOD are not available. However, if M-mode values are normal, but the volume index(s) is/are enlarged, the authors recommend that the results should be based on the volume index estimates, as they are more sensitive than M-mode.

M-mode reference values using the right parasternal long-axis view were obtained slightly differently in some studies [15,22]. Whereas the reference values from Wess et al. [15] were obtained from a right parasternal long-axis 4-chamber view, excluding the aorta (the same view as used for the SMOD measurements), the reference

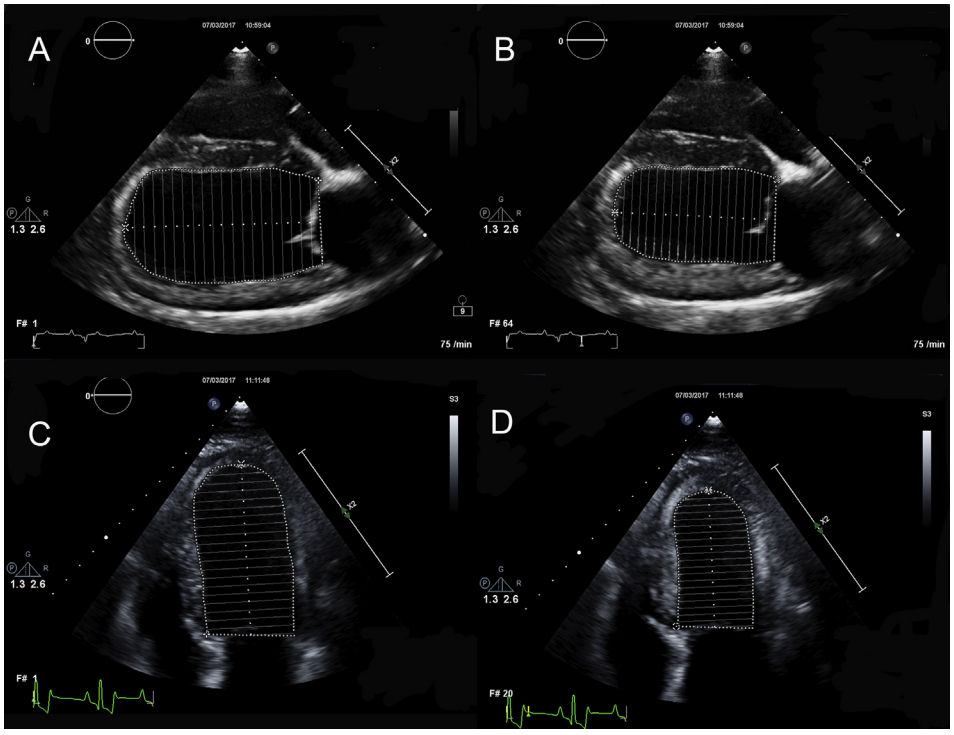

Figure 1 Left ventricular volume by Simpson's Method of Discs (SMOD). The SMOD should be measured in the right parasternal long-axis 4-chamber view (1A in diastole and 1B in systole) and in the left apical 4-chamber view (the aorta should not visible in either view; 1C in diastole and 1D in systole) by tracing the endocardial border on each selected image. The end-diastolic volume (EDV) is selected around the onset of the QRS complex, when the mitral valve is closed and the volume largest (which might not be exactly where the QRS complex starts (1A and 1C). The end-systolic volume (ESV) is selected typically near the end of the T wave, where the volume is smallest (1B and 1D).

values from O'Grady [22] were obtained from the right parasternal long-axis inflow/outflow view, with the aorta visible in the image (Fig. 2a and b). Others routinely use the right parasternal short-axis view at the level of the chordae tendineae to obtain M-modes of the left ventricle (Fig. 3), ensuring the M-mode cursor bisects the LV cavity. For all M-mode measurements, the left ventricular internal dimension in diastole (LVIDd) is obtained ideally at the onset of the QRS, and in the absence of an ECG, the largest LV internal dimension is selected. The left ventricular internal dimension in systole (LVIDs) is chosen at the nadir corresponding to the peak downward motion of the interventricular septum along a single cursor, typically near the end of the T wave. Care should be taken to minimize poor cursor alignment as this often leads to the overestimation of LVIDs. In dogs where it is difficult to achieve optimum alignment, a common complaint in Dobermans, and for which volume estimation is not possible, LVIDd and LVIDs can be acquired from 2 dimensional images, and this is preferred over a poor M-mode image. Although concurrent measurements from all views are most likely similar, there is currently no study available comparing all 3 methods. However, O'Grady adapted his long-axis derived M-mode reference range for LVIDs for the short-axis method and the short-axis cutoff value for LVIDs was used in the Protect study as an inclusion criterion. Therefore, when using M-mode reference values generated by different studies, the studies reported measurement method should ideally be used. One study did compare the accuracy of diagnosis of occult DCM in Dobermans using M-mode measurements and volume as estimated by SMOD and reported that SMOD (sensitivity 100%, specificity 99%) was superior to M-mode using both O'Grady's (sensitivity 89%, specificity 99%) and Wess's reported M-mode reference ranges (sensitivity 90%, specificity 89%) [15]. Both M-Mode measurements in that study were obtained from the right parasternal long axis using the right parasternal long-axis 4-chamber view, excluding the aorta.

Cutoff values that indicate the presence of occult DCM based on M-mode as described by Wess [15] (obtained from the right parasternal long-axis 4-chamber view, Fig. 2A):

$$\text{LVIDd}(\text{male any weight}) > 48 \text{ mm}$$

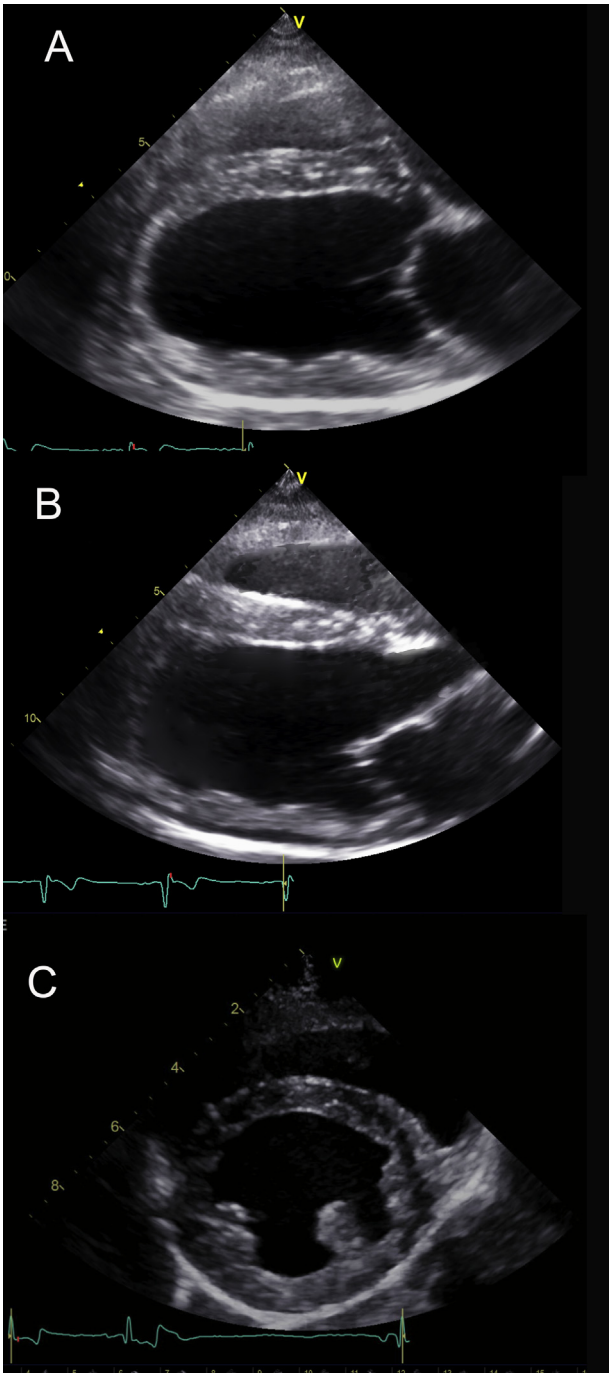

Figure 2 Different methods used to generate reference intervals for M-Mode: 2A: right parasternal long-axis 4-chamber view, excluding the aorta (the same view as used for the Simpson's Method of Discs measurements), as used for the reference values from Wess et al. [15]. 2B: right parasternal long-axis inflow/outflow view, with the aorta visible in the image, as used for the reference values from O'Grady [22]. 2C: right parasternal short-axis view at the level of the chordae tendineae to obtain M-modes of the left ventricle.

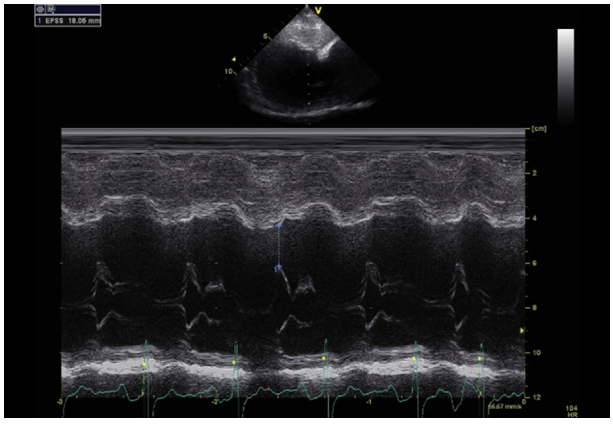

Figure 3 The E-point to septal separation (EPSS) measurement is obtained from the right parasternal long-axis view or short-axis view at the level of the tip of the septal mitral valve leaflet. It is the distance of the maximal motion (E-point) of the septal mitral valve leaflet to the interventricular septum during the rapid filling stage of diastole.

$$\text{LVIDd}(\text{female any weight}) > 46\ \text{mm}$$

or

$$\text{LVIDs}(\text{male and female any weight}) > 36\ \text{mm}$$

Comment: Although the diagnosis of DCM can be established if only one variable is above the reference values, the accuracy of diagnosis improves if both, diastolic and systolic measurements, are above the cutoff values.

Cutoff values that indicate the presence of occult DCM based on M-mode as described by O'Grady [22] (right parasternal long-axis M-mode using the inflow/outflow view, Fig. 2B):

$$\text{LVIDd} > 0.1749 \times \text{body weight}(\text{kg}) + 40.3\ \text{mm and/or}$$

$$\text{LVIDs} > 0.1402 \times \text{body weight}(\text{kg}) + 26.7\ \text{mm}$$

Cutoff values that indicate the presence of occult DCM based on M-mode as described by O'Grady and adapted for short axis [25] (right parasternal short-axis M-mode or 2 dimensional, Fig. 2C)

$$\text{LVIDs} > 0.1402 \times \text{body weight}(\text{kg}) + 35.3\ \text{mm}$$

Other secondary echocardiographic measures of systolic left ventricular function

E-point to septal separation (EPSS)

E-point to septal separation measurement is obtained from the right parasternal long-axis view

or short-axis view at the level of the tip of the septal mitral valve leaflet. E-point to septal separation is the distance of the maximal early diastolic motion (E-point) of the septal mitral valve leaflet to the interventricular septum (Fig. 3). A recent study evaluated EPSS in the role of detecting occult DCM in Dobermans and showed that EPSS >6.5 mm is a valuable additional variable for the diagnosis of DCM, which when added to M-mode measurements can improve sensitivity and specificity to levels that are similar to volume estimates by SMOD [37].

Sphericity index (SI)

The geometrical shape, i.e. the sphericity of the LV can be assessed by comparing left ventricular length in diastole obtained from a right parasternal long-axis or left parasternal apical 4-chamber view (obtained at end diastole as per the SMOD with caution to avoid apical foreshortening; Fig. 4) to the M-mode LVIDd. The SI is calculated by dividing the length of the LV in diastole by the width of the LV in diastole. An SI < 1.65 is associated with an increased sphericity and is considered abnormal according to the European Society for Veterinary Cardiology guidelines [38]. A study in Dobermans reported that an SI < 1.65 is also the best cutoff to identify occult DCM in Dobermans. However, because the sensitivity and specificity of SI alone was not very good (sensitivity 86.8%, specificity 87.6%) when compared to volume estimates using SMOD and EPSS, its inclusion as a recommended parameter in screening protocols for Dobermans is not warranted [37].

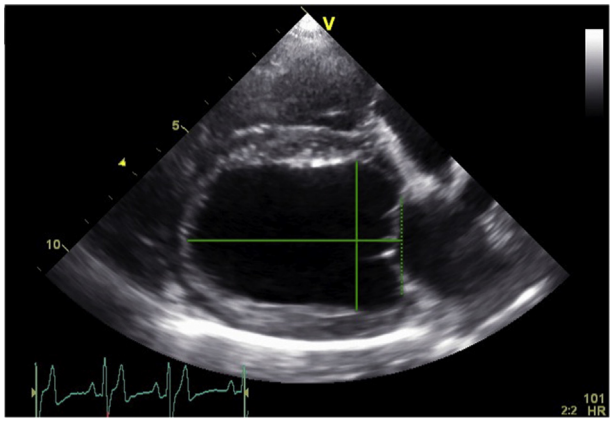

Figure 4 Sphericity index (SI). The geometrical shape "i.e. the sphericity of the left ventricle (LV)" can be assessed by comparing left ventricular length in diastole obtained from a right parasternal long-axis or left parasternal apical 4-chamber view (obtained at end diastole as per the SMOD with caution to avoid apical foreshortening) to the M-mode LVIDd. The SI is calculated by dividing the length of the LV in diastole by the width of the LV in diastole. SMOD, Simpson's Method of Discs; LVIDd, end-diastolic diameter of the left ventricle; LV, left ventricle.

Ancillary tests, currently not included as standard screening tests

The following tests are currently not recommended for screening purposes but may have some utility when recommended tests such as echocardiography and a Holter are not available or financially untenable on an annual basis.

Biomarkers such as cardiac troponin I (cTnI) [39] or N-Terminal pro B-type natriuretic peptide (NTproBNP) [40,41] might be abnormal in some dogs, in which Holter and echocardiography are still normal. But at this time, there is not sufficient evidence that they can replace Holter and or echocardiography, but they might be valuable additional tests. N-Terminal pro B-type natriuretic peptide values > 500 pmol/L can predict echocardiographic changes consistent with occult DCM and the corollary is also true in that Dobermans with an N-terminal pro B-type natriuretic peptide (NT-proBNP) < 500 pmol/L are unlikely to have contemporaneous echocardiographic evidence of occult DCM.

NT-proBNP

Screening for occult disease is one of the most promising areas of blood sample-based biomarker research. In one study including 328 Dobermans, plasma NT-proBNP concentration was significantly higher in Dobermans with DCM, including those with occult DCM, diagnosed by echocardiography alone or both echocardiography and a Holter, than in healthy dogs [40]. The NT-proBNP assay was not clinically useful to detect disease in dogs presenting only with ventricular arrhythmias. In this study, the best cutoff value for the prediction of echocardiographic abnormalities indicative of DCM was >550 pmol/L (sensitivity 78.6%, specificity 90.4%). Reduction of the cutoff value to >400 pmol/L increased the sensitivity to 90.0%, whereas specificity decreased to 75.0%.

In a second study, the combined use of an NT-proBNP cutoff value >457 pmol/L and a Holter recording led to detection of occult DCM with a sensitivity of 94.5%, specificity of 87.8%, and overall accuracy of 91.0% [41]. Similar to the aforementioned study [40], NT-proBNP concentration was most accurate for the detection of occult DCM when Dobermans had echocardiographic changes

indicative of occult DCM but had poor accuracy for the identification of dogs that had only ventricular arrhythmias. Both of these studies were performed using the first-generation assay without the use of the protease inhibitor tubes for sample collection (but immediately frozen at −80 °C and then sent frozen for batch analysis). N-Terminal pro B-type natriuretic peptide values degrade over time, if the samples are not frozen and shipped cooled. This is especially important if the first-generation assay is used. One laboratory is offering now a second-generation assay, which does not require protease inhibitor tubes and can be posted unfrozen. As this assay was designed to give similar results to the first-generation assay and was utilized in one study of 449 Dobermans screened with a combination of echocardiography and a 3-min ECG.[g] This study reported that a cutoff of >548 pmol/L had a sensitivity of 100% and a specificity of 80% to detect the characteristic echocardiographic morphologic changes of DCM with or without concurrent evidence of VPCs on a 3-min ECG. These findings are not significantly different from those reported on earlier generations of this assay and together emphasize the role of NT-proBNP testing in the Doberman.[g]

Despite its reported usefulness, the NT-proBNP assay does not replace recommended gold standard diagnostic procedures such as echocardiographic examination, for which the sensitivity and specificity of detecting left ventricular dysfunction can be as high as 97% [15].

One study reported a longitudinal design that included follow-up examinations allowing the retrospective identification of a group of dogs (last normal) that were determined to be normal according to gold standard diagnostic methods (echocardiogram and Holter) at the time of NT-proBNP sample collection but went on to develop DCM within 1.5 years of this evaluation [40]. Plasma NT-proBNP concentrations were significantly increased in this group, compared with concentrations in the control group, suggesting that DCM was detected in this group by NT-proBNP measurement earlier than was possible with a combination of echocardiography and a 24-h Holter [40]. Validation of these results in other studies would be needed to make screening recommendations solely on blood-based testing.

[g] Gordon S.G., Estrada A.H., Braz-Ruivo L., Drourr L., Morris N., O'Grady M.R., Boggess M.M. Evaluation of NTproBNP, High Sensitivity Troponin I and PDK4 for the Detection of Occult DCM: A Prospective Study in 449 Doberman Pinschers. (Abstract ECVIM Forum 2015) J Vet Intern Med 2016; 30:365.

NT-proBNP recommendations

N-terminal pro B-type natriuretic peptide appears to be especially useful to predict echocardiographic changes in Dobermans, and it might be reasonable to screen dogs >3−4 years using the NT-proBNP test. This type of testing could be considered when the owner cannot afford the expense of echocardiography and Holter recording. There is not sufficient evidence to support NT-proBNP testing alone in screening Dobermans when the other established tests are available and affordable. In addition, it cannot be used alone to establish a diagnosis on which to base a recommendation to begin therapy [42].

As with any diagnostic test, certain limitations and considerations must be recognized when using the NT-proBNP assay. Circulating NT-proBNP concentration can be affected by concurrent disease processes such as renal dysfunction, pulmonary hypertension, sepsis, or systemic hypertension as well as incorrect blood sample handling or use of the assay in inappropriate patients. Finally, if repeated sampling is done as a part of a screening protocol, normal day-to-day variation should be taken into account [43].

Troponin I

Circulating cardiac troponin I has been demonstrated to be a highly specific and sensitive marker for myocardial cellular damage in humans and animals. The primary value of cTnI as a cardiac biomarker in humans is to detect myocardial infarcts [44]. It is reported to be significantly elevated in Dobermans with DCM [39]. Dogs with more advanced stages of the disease had the highest concentrations of cTnI. It was not only elevated in Dobermans with echocardiographic changes but also in dogs that had only VPCs. This study also reported that cTnI was elevated in a very early stage of the disease ("last normal group" or "incipient group" as discussed above). Dogs in the "last normal" or "incipient" group had significantly higher cTnI values compared with control dogs. The best cutoff for cTnI to predict DCM using the Immulite assay was >0.22 ng/mL (sensitivity 79.5% and specificity 84.4%) and therefore, as for NT-proBNP, it is a valuable additional diagnostic test to screen for cardiomyopathy in Dobermans when the gold standard is not available. It likewise suffers from similar limitations as outlined previously for NT-proBNP [39]. However, there is not sufficient evidence to support that this test could replace conventional methods such as echocardiography

and Holter examinations [39]. Finally, cTnI concentrations have also been shown to have an additional value for risk assessment of sudden cardiac death in Dobermans with an enlarged heart, using a cutoff value of >0.34 ng/mL [45].

It is important to realize that cTnI may be increased in dogs with systemic conditions or myocarditis and the cardiomyocyte injury indicated by increased cTnI is not specific for DCM [39,46–52]. Therefore systemic diseases should be excluded if increased cTnI levels are detected.

There are different cTnI assays available and the test results might not be completely comparable. Ultrasensitive tests may detect even earlier changes compared with this study and may lead to lower cutoff values. This needs to be investigated in future studies. One study in 449 Dobermans reported a cTnI cutoff off >0.139 ng/mL (ADVIA Centaur CP Ultra-TnI; lower limit of detection of 0.006 ng/mL) had a 100 sensitivity and 79% specificity to detect the characteristic echocardiographic morphologic changes of DCM with or without concurrent evidence of VPCs on a 3-min ECG.[g]

In-house ECG

An in-house ECG cannot be used to replace a Holter examination. However, > 1 VPC/5 min is highly suggestive that >100 VPCs will be recorded in 24 h if a Holter is performed [53]. Therefore, when Holter and/or echocardiography are not available, or an owner wants to first have other tests performed, to be more convinced that further examinations (Holter, echocardiography) are necessary a combination of the following tests should be performed. However, it should be emphasized that these tests are not validated as sole screening tests, do not represent the gold standard screening tests, and cannot be used to establish a diagnosis with which to make recommendations to begin treatment.

Clinical examination

A systolic murmur over the left apex, an audible gallop sound on auscultation, weak pulse quality, an arrhythmia or pulse deficits are all suspicious findings in Dobermans and represent a strong indication to proceed with additional tests.

Biomarker

NTproBNP result > 500 pmol/L
cTnI > 0.22 ng/mL

ECG: 1 VPC/5 min (or more) or atrial fibrillation are considered abnormal.

If any of the above tests are abnormal, a further work-up including Holter examination and echocardiography is strongly recommended.

Genetic tests for DCM in Dobermans

The genetic test based on the 16-bp deletion in the canine pyruvate dehydrogenase lipoamide kinase isozyme 4 (PDK4) might be useful in the USA [54] but may not be useful in Europe, as one study showed no association between PDK4 and DCM in a European study [7].

The results of genetic tests should not be used in place of standard screening. The absence of a genetic mutation known to be associated with a heritable disease such as DCM in Dobermans does not ensure the dog will never go on to develop DCM. In addition, the identification of a genetic mutation does not guarantee the dog will go on to develop DCM, and should not be considered a death sentence, but should be followed up with screening as outlined above. It is also clear that there may be important regional differences even within a single breed and single disease. The real value of identifying genetic markers associated with heritable diseases may be to take them into consideration when selecting breeding pairs. Identification of genetic markers of heritable diseases in dogs and cats remains an active area of investigation.

Conclusions

Yearly screening over the life of the dog is recommended, as a one-time screening is not sufficient to rule out future development of DCM. Screening for occult DCM in Dobermans should start at three years of age and use both Holter monitoring and echocardiography. The preferred echocardiographic method is the measurement of the left ventricular volume by SMOD. Greater than 300 VPCs in 24 h, or two subsequent recordings within a year showing between 50 and 300 VPCs in 24 h is considered diagnostic of occult DCM in Dobermans regardless of the concurrent echocardiographic findings. Ancillary tests, including biomarkers (cTnI and NT-proBNP) as well as in-house ECG recordings could be helpful in situations where the standard recommended tests are not available.

Conflicts of Interest Statement

The authors do not have any conflicts of interest to disclose.

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