

Prevalence of Dilated Cardiomyopathy in Doberman Pinschers in Various Age Groups

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Background: Dilated cardiomyopathy (DCM) in Doberman Pinschers is an autosomal dominant inherited disease. The prevalence of DCM in Doberman Pinschers of various age groups in Europe is currently unknown, but this information would be important to develop recommendations for screening programs.

Objectives: To evaluate the prevalence of cardiomyopathy in various age groups of Dobermans.

Animals: Seven hundred and seventy-five examinations in 412 Doberman Pinschers.

Methods: Dogs were included in a prospective longitudinal cohort study. Each examination included echocardiography and 24-hour ECG (Holter) examination. A cut-off value of > 100 ventricular premature contractions (VPCs) per 24 hours on Holter examination or abnormal echocardiography was considered diagnostic for cardiomyopathy. The cumulative prevalence included all dogs with DCM and healthy dogs > 7 years of age.

Results: DCM prevalence in various age groups was as follows: age group 1 (1 to < 2 years) 3.3%, age group 2 (2 to < 4 years) 9.9%, age group 3 (4 to < 6 years) 12.5%, age group 4 (6 to < 8 years) 43.6%, and age group 5 (> 8 years) 44.1%. The cumulative prevalence of Doberman Pinscher cardiomyopathy was 58.2%. There was an equal sex distribution, but male dogs showed earlier echocardiographic changes than did female dogs, which had significantly more VPCs.

Conclusions and Clinical Importance: The prevalence of Doberman cardiomyopathy is very high in Europe. Disease manifestation and progression are different between male and female dogs. Yearly screening for DCM by Holter examination and echocardiography is recommended, starting at 2 years of age.

Key words: Arrhythmia; Canine; Congestive heart failure; Dilated cardiomyopathy; Dogs; Sudden death.

Dilated cardiomyopathy (DCM) is a disease of the myocardium associated with dilatation and impaired contraction of the ventricles. In the dog, it primarily affects large and giant breeds with the Doberman Pinscher being one of the most frequently affected. Some breeds, such as Doberman Pinscher, Newfoundland, Portuguese Water Dog, Boxer, Great Dane, Cocker Spaniel, and Irish Wolfhound, exhibit a higher prevalence of DCM.¹⁻³ The high prevalence of DCM in specific breeds suggests a genetic background. Causal mutations have only been identified in Boxer dogs, but not yet in other breeds.^{1,4-10} There also seems to be a sex predisposition because male dogs are affected more often than female dogs, and in Great Danes, an X-linked recessive inheritance is likely.¹¹ In the Newfoundland and Boxer breeds, an autosomal dominant inheritance was found, whereas an autosomal recessive inheritance was described in Portuguese Water Dogs.^{1,4-6,12-15} DCM in Doberman Pinschers is a familial disease suspected to be inherited as an autosomal dominant trait.⁸ The genes responsible for this condition remain to be identified, despite the fact that several candidate genes have been evaluated.^{1,8-10,16-18} Extensive remodeling, in the form of a loss of collagen tethers, increased collagen synthesis, and alter-

Abbreviations:

Holter	24-hour ECG
CHF	congestive heart failure
DCM	dilated cardiomyopathy
LV	left ventricle
LVIDd	left ventricular internal end-diastolic dimension
LVIDs	left ventricular internal end-systolic dimension
VPCs	ventricular premature contractions

ations in collagen cross-links, occurs in the diseased myocardium. Changes in the collagenous matrix also are present in apparently normal Dobermans. These changes are likely to be involved in the progression of the disease.¹⁹

The natural progression of DCM can be described by 3 distinct stages.²⁰⁻²⁴ Stage I is characterized by a morphologically and electrically normal heart and no evidence of clinical signs of heart disease. Stage II is characterized by evidence of morphologic or electrical derangement in the absence of clinical signs of heart disease. This stage has also been called "the occult stage" of DCM. The term "occult" refers to the owner's perspective. That is, from the owner's point of view, the dog appears normal despite evidence of abnormality on cardiac examination. The morphologic abnormality consists of left ventricular (LV) enlargement in systole, diastole, or both. The electrical abnormality consists of the occurrence of ventricular premature contractions (VPCs). These abnormalities, morphologic or electrical, may coexist or be of predominantly one form at any time during the occult stage.^{20,25-28} Stage III is characterized by the presence of clinical signs of heart failure and is referred to as the overt stage of DCM. Evidence of exercise intolerance usually is lacking until the onset of pulmonary edema and congestive heart failure (CHF).^{20,25-28}

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Existing prevalence information on cardiomyopathy in Doberman Pinschers is from dogs in the United States or Canada where prevalence ranges between 45 and 63%.^{27,29,30} The prevalence of DCM in Dobermans may be lower in Europe.³¹ To establish a screening program and be able to give recommendations as to when screening for DCM should be started, knowledge of the prevalence in various age groups is necessary. To the authors' knowledge, no such information exists for the European Doberman Pinscher population. Therefore, the aim of this study was to evaluate the prevalence of Doberman cardiomyopathy in a prospective study of various age groups and to estimate the overall prevalence of DCM based on this cohort of European Doberman Pinschers.

Material and Methods

Animals

The study population consisted of 412 (54.9% female, 45.1% male) client-owned Doberman Pinschers that were prospectively selected according to inclusion and exclusion criteria from a longitudinal cohort study starting in 2004. At the time of data analysis, 1014 examinations of Doberman Pinschers were available in the database. Seven hundred and seventy-five examinations from these 412 Doberman Pinschers met the selection criteria and were included. Excluded were dogs with other cardiac diseases ($n = 70$), dogs with only 1 examination, no follow-up, and 50–100 VPCs/24 hours ($n = 47$), and dogs with equivocal echocardiographic examinations between the normal and abnormal cut-off values without follow-up ($n = 46$) and dogs with systemic diseases ($n = 76$). Seven hundred and seventy-five examinations from these 412 Doberman Pinschers met the selection criteria and were included. Dogs were from Germany, the Netherlands, Austria, Switzerland, Italy, and some eastern European countries. Each dog was assessed by a 5-minute ECG, 24-hour ECG (Holter) examination, and echocardiography at each examination. The dogs were assigned to different age groups: age group 1 (1 to <2 years), age group 2 (2 to <4 years), age group 3 (4 to <6 years), age group 4 (6 to <8 years), and age group 5 (>8 years). Each dog was counted only once in each age group, even when the dog was examined several times. The last examination in the respective age group was used for analysis.

Inclusion Criteria

Enrollment was restricted to pure bred Doberman Pinschers. The dogs were assigned to 4 disease stages according to Holter and echocardiographic changes. Group 1 had only VPCs, group 2 had only echocardiographic changes, group 3 had VPCs and echocardiographic changes, and group 4 had clinically overt disease (decompensated). Groups 1–3 consisted of dogs in the occult disease stage. Occult DCM was present if the dogs met the Holter or echocardiographic criteria for cardiomyopathy or both, and had no clinical signs. Clinically, overt cardiomyopathy was considered present if the dog showed clinical signs (eg, syncope, exercise intolerance, coughing, dyspnea caused by CHF) and was electrocardiographically or echocardiographically abnormal, or both. Normal dogs (group 0) had to be normal on Holter and echocardiographic examination and no other systemic disease.

Exclusion Criteria

Dogs with concomitant congenital heart disease or evidence of mitral valvular disease (based on echocardiography) were excluded. Dogs that had between 50 and 100 VPCs/24 hours were considered

equivocal and not included in the study. Dogs that had echocardiographic measurements that fell between the criteria for normal and abnormal also were not included in the study.

Holter Examinations

Twenty-four hour Holter recordings were performed at each examination and analyzed by 1 of 2 commercially available software programs.^{a,b} Manual adjustments and accuracy verification of the arrhythmias recognized by the software were performed. A cut-off value of >100 VPCs/24 hours on Holter examination was considered diagnostic for cardiomyopathy. Fewer than 50 VPCs/24 hours were considered normal. Dogs with 50–100 VPCs or Holter data with <20 hours of analyzable data were excluded.

Echocardiography

Echocardiography was performed in each dog in the right parasternal long-axis plane. M-mode values were considered normal when left ventricular internal end-diastolic dimension (LVIDd) was ≤ 47 mm and left ventricular internal end-systolic dimension (LVIDs) was ≤ 38 mm.^{25,32}

Values that were considered abnormal and indicative of DCM were LVIDd ≥ 49 mm^{29,33} LVIDs ≥ 40 mm or both.^{30,32} Animals with equivocal measurements were not included in the study.

Statistical Analysis

Comparisons of frequency of counts were performed by a 2-tailed Fisher's exact test. Analysis of variance (ANOVA) was used to analyze the influence of age and sex on the 4 disease stages and compare differences between the healthy and diseased groups. Bonferroni analysis was used as a posthoc test when ANOVA showed significance. A P -value < .05 was considered statistically significant. Statistical analysis was performed by a commercially available statistical software program.^c

Results

Seven hundred and seventy-five examinations were performed in 412 Doberman Pinschers. Each dog was counted only once per age group. Thus, 203 duplicate cases were identified in which dogs were examined several times in the respective age group (ie, the dog might have been examined at 2, 3, and 3.5 years of age, but only the last examination result was used for analysis). Duplicate cases were excluded from further analysis. Therefore, 572 examinations were used for further analysis.

Prevalence of cardiomyopathy was calculated separately for each of the 5 age groups. Each age group contained a minimum of 90 examinations. Ninety-two dogs were diagnosed with cardiomyopathy in various stages. To calculate the overall frequency of abnormalities, only the last examination of each dog was counted (Table 1). VPCs as the only abnormality were detected in 37.0% of the cases. Echocardiographic changes alone were found in some animals (13%), but not as commonly as VPCs (Table 1). Absolute numbers and percentages of dogs with DCM per age group are shown in Table 2. Clinical signs were rare in dogs younger than 6 years. The frequency of abnormalities per age group is shown in Figure 1. Ventricular arrhythmias were commonly the first abnormality found on examination, either alone or in combination with echocardiographic changes (Fig 1).

Table 1. Frequency of abnormalities detected in Dobermans with cardiomyopathy at the last examination.

Group	n	%	Male	Female
Only VPCs	34	37.0	12 (35.3%)	22 (64.7%)
Only echocardiographic changes	12	13.0	7 (58.3%)	5 (41.7%)
Occult echocardiographic changes and VPCs	27	29.3	18 (66.7%)	9 (33.3%)
Clinically overt	19	20.7	14 (73.7%)	5 (26.3%)
Total	92	100.0	51 (55.4%)	41 (44.6%)

“Only VPCs”, the dog had only VPCs, no echocardiographic changes and no clinical signs; “VPCs and echocardiographic changes”, the dog showed both abnormalities, but no clinical signs; “only echocardiographic changes”, the dog had only echocardiographic changes, but no clinical signs; “clinically overt”, the dog had echocardiographic changes, VPCs, and clinical signs of CHF. The number and percent of male and female dogs within the various disease groups are shown.

To calculate the cumulative prevalence of cardiomyopathy in Doberman Pinschers, 66 healthy Doberman Pinschers >7 years were compared with 92 dogs with cardiomyopathy (independent of age). Therefore, the cumulative prevalence of cardiomyopathy was 58.2%.

There was no significant difference with respect to sex between healthy dogs and dogs with DCM. This determination was made from the 158 dogs used for the calculation of the cumulative prevalence. However, multivariate analysis showed significant sex differences among the 4 disease stages, with females having VPCs more commonly and males showing echocardiographic changes with VPCs and overt DCM more commonly. Figure 2 shows the sex distribution in the different age groups and among the diseases stages. Although there was no overall difference in the occurrence of cardiomyopathy between male and female dogs, there was a difference between sex concerning disease manifestation. Female dogs had significantly more VPCs without echocardiographic changes than male dogs and this difference became more apparent with increasing age. On the other hand, male dogs developed earlier echocardiographic changes than did female dogs.

Discussion

DCM in Doberman Pinschers is a common, inherited, primary myocardial disease that usually has a late onset. The rate of progression of the disease from the occult phase to the overt stage usually is slow, but rapidly progressive once dogs reach the overt stage.^{20,21,29–32} The morphologic abnormality of DCM consists of LV enlargement in systole, diastole, or both. The electrical

Table 2. Prevalence of cardiomyopathy in Doberman Pinschers in various age groups.

Age groups	Healthy		Cardiomyopathy		Total n
	n	%	n	%	
1 to < 2	88	96.7	3	3.3	91
2 to < 4	154	90.1	17	9.9	171
4 to < 6	98	87.5	14	12.5	112
6 to < 8	53	56.4	41	43.6	94
>8	52	55.9	41	44.1	93
Table total	454	79.4	118	20.6	572

Each dog was only counted once per age group, even when several examinations had been performed, but could be part of several age groups.

abnormality includes VPCs or atrial fibrillation. These abnormalities, morphologic, or electrical, may coexist or may be of predominantly one form or the other at any time during the occult stage. Some studies have found that most Doberman Pinschers in the occult phase have evidence of both abnormalities.^{20,29} Other studies reported that VPCs are often the first evidence for cardiomyopathy in the occult phase.^{25,26,30,31,34} The present study shows that 37% of the dogs showed only VPCs without echocardiographic changes (Table 1) and that arrhythmias often were the first abnormality detected (Fig 1). Only a few dogs (13%) presented with only echocardiographic changes and no arrhythmias on Holter examination. The studies in which most dogs in the occult phase had both abnormalities might have included animals with more advanced disease, or Holter examinations were may not have been carried out in all dogs. Because of the high frequency of electrical abnormalities, Holter examination still remains the most sensitive test to detect occult DCM.

The prevalence of cardiomyopathy in Doberman Pinschers in the United States or Canada ranges between 45 and 63%.^{23,27,29,30} The prevalence of DCM in Dobermans in Europe may be lower.³¹ The present study shows that the prevalence of cardiomyopathy in Doberman Pinschers in Germany is as high as in the United States or Canada. Because not only dogs from Germany, but also those from the Netherlands, Austria, Switzerland, Italy, and some eastern European countries also were included in this study, the prevalence might actually be similar all over Europe.

The cumulative prevalence of cardiomyopathy was 58.2% in this study and was calculated from all dogs (at any age) with cardiomyopathy in comparison to healthy Doberman Pinschers >7 years of age. The reason for choosing 7 years of age as a cut-off for healthy Doberman Pinschers was that a dog at this age without electrical and echocardiographic abnormalities has a good chance to remain healthy. Some dogs might still develop disease at an older age, but in this case, the cumulative prevalence would be underestimated. A screening program for cardiomyopathy in Germany was stopped prematurely after 3 years by the breeding club because the prevalence was found to be very low according to their data. In this study, however, only dogs that had never been bred before were examined. Therefore, almost only young dogs <3 years of age were included, and this likely explains the low prevalence. This finding is

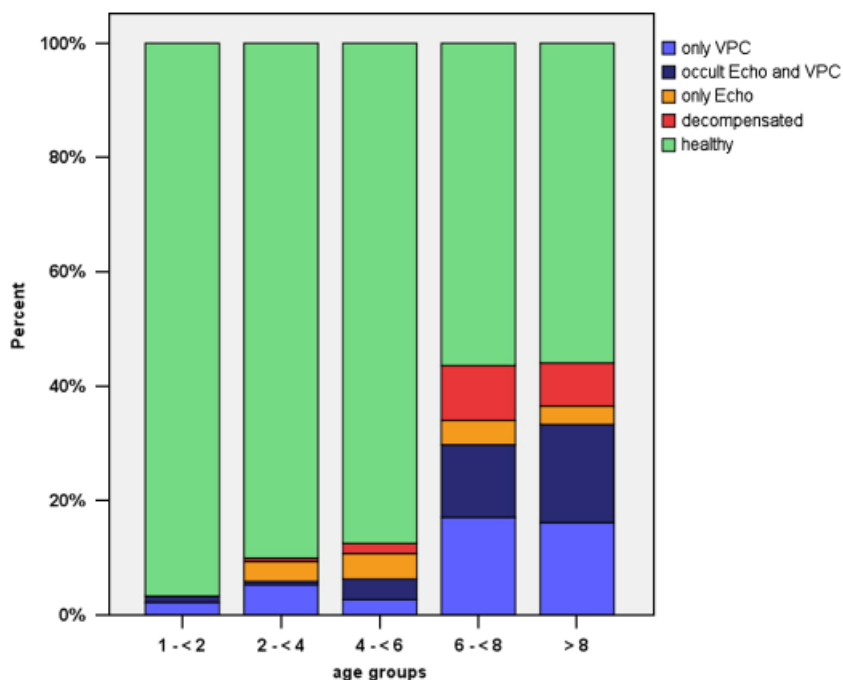


Fig 1. Percentage of abnormalities detected in various age groups in comparison to healthy Doberman Pinschers (n = 572 examinations of 412 dogs). “Only VPCs” = the dog had only VPCs, no echocardiographic changes and no clinical signs; “occult Echo and VPCs” = the dog showed both abnormalities, but no clinical signs; “only Echo” = the dog had only echocardiographic changes, but no clinical signs; “decompensated” = the dog had echocardiographic changes, VPCs, and clinical signs of congestive heart failure. VPCs, ventricular premature contractions.

similar to the prevalence in the present study in the age group 1 to <2 years. However, because the disease manifests itself more with increasing age, and because the prevalence was very high in the present study, a screening program should be established. A genetic test would be desirable, but is not yet available. Even if the chance to detect cardiomyopathy in young dogs before breeding is not very high, approximately 10% of the dogs could be excluded from breeding. Screening for breeding purposes should be continued on a yearly basis as long as the dog remains in the breeding program. Screening for health purposes should be recommended for all Doberman Pinschers, because the chance that the dog will develop the disease is very high. Recommendations concerning screening for the disease based upon this study and in accordance with other studies are that screening for cardiomyopathy in Doberman Pinschers should be started at an age of 2 years.^{20,30–32} Screening should include a Holter examination and echocardiography and should be repeated on a yearly basis.

The early descriptions of DCM in Doberman Pinschers suggested that cardiomyopathy was primarily a disorder of males.²³ More recent work continues to demonstrate that male dogs are more frequently affected than female dogs but that the disorder is much more prevalent in female dogs than previously suspected.^{21–23,25,27,29} One study showed that in Doberman Pinschers, approximately 50% of male dogs and 33% of female dogs develop DCM,²⁹ whereas another study found no sex difference.⁸ The present study found an equal sex distribution, which would support the suspected autosomal dominant mode of inheritance reported in 1 study.⁸ The

different findings concerning the sex distribution may be explained by the results of the present study that showed an equal sex distribution but different disease progression between male and female dogs. Female dogs seem to experience a more slowly progressive disease with VPCs as the only abnormality found even in the older age groups. Male dogs, on the contrary, showed echocardiographic changes earlier than did female dogs. These changes are easier to detect because no Holter examination is necessary, and male dogs therefore are also more likely to develop CHF at an earlier age than female dogs and also die earlier from their disease. From a clinical perspective, it is important that despite the fact that female dogs are more likely to show only VPCs as an abnormality, a Holter examination also should be performed in every male dog, because the risk of sudden death is high in all dogs with VPCs.^{24–26,32,34}

A limitation to this study is that it is an ongoing longitudinal study and animals included as healthy might develop cardiomyopathy at a later stage. However, this study included the largest Doberman Pinscher cohort examined prospectively so far, and all dogs were examined at least once a year with Holter examination and echocardiography. Therefore, the number of affected dogs might be even higher than detected in this study. Additionally, only dogs with clear abnormalities according to the selection criteria were included and some of the excluded dogs, especially those with 50–100 VPCs/24 hours or equivocal echocardiographic examinations may develop DCM at a later stage. Because no follow-up examinations were available in those dogs at this time,

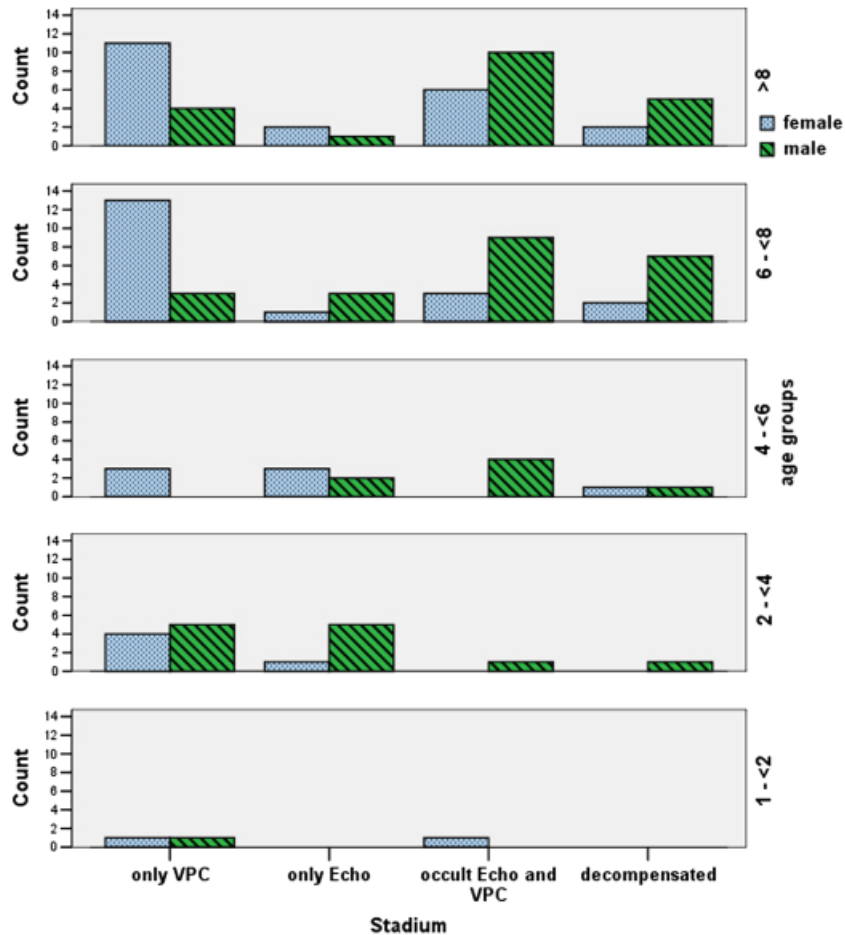


Fig 2. Sex distribution at various age groups and separated for each of the disease groups.

they were not included in the study. Another concern might be that this study was biased toward dogs that might have been referred because of a suspicion of cardiomyopathy. However, dogs were included prospectively and most owners were not aware of any clinical signs when cardiomyopathy was diagnosed. Many dogs developed the disease while in the longitudinal study. Thus, a bias is not very likely.

This study showed a high prevalence of cardiomyopathy in Doberman Pinschers in Europe, comparable to that reported in the United States and Canada. The disease is equally distributed in male and female dogs, but there appears to be different disease manifestations between sexes. Female dogs have significantly more often VPCs detected as the only abnormality, whereas male dogs show echocardiographic changes earlier than do female dogs. Screening for occult cardiomyopathy should be started in Dobermans at 2 years of age and include Holter monitoring and echocardiography. The screening should be repeated on a yearly basis.

^bAmedtech ECGpro Holter software, EP 810 digital Recorder, Medizintechnik Aue GmbH, Aue, Germany
^cSPSS for Windows, Version 13.0, SPSS Inc, Chicago, IL

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Footnotes

^a Custo tera, Arcon Systems GmbH, Starnberg, Germany

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