Ability of a 5-Minute Electrocardiography (ECG) for Predicting Arrhythmias in Doberman Pinschers with Cardiomyopathy in Comparison with a 24-Hour Ambulatory ECG

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Background: Ventricular premature contractions (VPCs) are common in the occult stage of cardiomyopathy in Doberman Pinschers. Although the gold standard for detecting arrhythmia is the 24-hour ambulatory electrocardiography (ECG) (Holter), this method is more expensive, time-consuming and often not as readily available as common ECG.

Objectives: Comparison of 5-minute ECGs with Holter examinations.

Animals: Eight hundred and seventy-five 5-minute ECGs and Holter examinations of 431 Doberman Pinschers.

Methods: Each examination included a 5-minute ECG and Holter examination. A cut-off value of >100 VPCs/24 hours using Holter was considered diagnostic for the presence of cardiomyopathy. Statistical evaluation included calculation of sensitivity, specificity, positive predictive value, and negative predictive value.

Results: Holter examinations revealed >100 VPCs/24 hours in 204/875 examinations. At least 1 VPC during a 5-minute ECG was detected in 131 (64.2%) of these 204 examinations. No VPCs were found in the 5-minute ECG in 73 (35.8%) examinations of affected Doberman Pinschers. A 5-minute ECG with at least 1 VPC as cut-off had a sensitivity of 64.2%, a specificity of 96.7%, a positive predictive value of 85.6% and a negative predictive value of 89.9% for the presence of >100 VPCs/24 hours.

Conclusions and Clinical Importance: A 5-minute ECG is a rather insensitive method for detecting arrhythmias in Doberman Pinschers. However, the occurrence of at least 1 VPC in 5 minutes strongly warrants further examination of the dog, because specificity (96.7%) and positive predictive value (85.6%) are high and could suggest occult cardiomyopathy.

Key words: Arrhythmia; Dilated cardiomyopathy; Dogs; Electrocardiogram; Holter.

Ventricular premature contractions (VPCs) are a cardinal finding in the occult phase of dilated cardiomyopathy (DCM) in Doberman Pinschers.[a,1–13] Affected dogs in the occult phase are without clinical signs at this stage of the disease. Sudden death, caused by ventricular tachycardia and ventricular fibrillation, occurs during the occult phase in at least 25–30% of affected dogs.[3,7,8] The natural progression of DCM can be described by 3 distinct stages or phases.[2,9,10,11,13] Stage I is characterized by a morphologically and electrically normal heart and no evidence of clinical signs of heart disease. The occult stage of the disease, stage II, is characterized by evidence of morphologic or electrical changes in the absence of clinical signs of heart disease. The morphologic abnormality consists of left ventricular (LV) enlargement in both systole and diastole. The electrical abnormality consists of the presence of VPCs. These abnormalities, morphologic or electrical, may coexist or may be of predominantly 1 form at any time during this occult stage.[3,7,10,14,15] Stage III is characterized by the presence of clinical signs of heart failure and is known as the overt stage of DCM. Evidence of exercise intolerance usually is lacking until the onset of pulmonary edema and congestive heart failure.[3,7,10,14,15]

Abbreviations:

AUC	area under the curve
DCM	dilated cardiomyopathy
ECG	electrocardiography
Holter	24-hour ECG
LV	left ventricle
ROC	receiver operator curve
VPCs	ventricular premature contractions

The number of VPCs usually increases over time and eventually systolic dysfunction develops and dogs start to show clinical signs.[7–9,16] Therefore, most of the dogs are presented to veterinarians in advanced stages of cardiomyopathy. For diagnostic, prognostic, therapeutic, and breeding purposes it is essential to detect the early stages of the disease (ie, ventricular or atrial arrhythmias). In most clinical practices, in-hospital electrocardiographies (ECGs) are available for detecting arrhythmias, but the arrhythmias in Doberman Pinschers may not be equally distributed over a 24-hour time period and might be missed on an in-house ECG. The gold standard for detecting VPCs is a Holter examination.[3,7,8,17,18] Holter examinations, however, are not as readily available to the veterinarian, and are more expensive and time consuming to perform than in-house ECGs. One study in Boxer dogs showed that an in-house ECG is specific, but not sensitive enough for screening purposes and therapeutic evaluations in mature Boxers with ventricular arrhythmic disease.[18] However, no large study exists evaluating the use of an in-house ECG and comparing the results to the Holter recordings as a gold standard for detecting arrhythmias in Doberman Pinschers. Therefore, the aim of this prospective study was to

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evaluate the usefulness of a 5-minute ECG for the purpose of detecting arrhythmias in Doberman Pinschers with cardiomyopathy.

Materials and Methods

Dogs

The presence of ventricular tachyarrhythmias was evaluated in 911 examinations of 447 (52.6% female, 47.4% male; mean age, 5.2 years; range, 1.3–12.8 years) client-owned Doberman Pinschers. Each examination included a physical examination, a 5-minute ECG, a 24-hour ambulatory ECG (Holter) examination and echocardiography, including M-Mode measurements, color and spectral Doppler examinations. The procedures implemented in this study were compliant with the Animal Use and Care Committee of the Ludwig Maximilians University of Munich. Written owner consent was obtained.

Inclusion Criteria. Enrollment was restricted to purebred Doberman Pinschers without evidence of systemic disease.

Exclusion Criteria. Dogs with concomitant congenital heart disease or evidence of mitral valvular disease (based on echocardiography) were excluded. Dogs with systemic diseases were not included. Dogs with 50–100 VPCs/24 hours were considered equivocal and not included in the study.

ECG. Dogs were positioned in right lateral recumbency. ECG was performed according to standard technique, and electrical activity was recorded for 5 minutes, with a 12-channel ECG machine.[b] The presence and number of VPCs were recorded.

Holter Examinations. Holter ECG was performed immediately after performing the in-hospital ECG. Each dog was released from the hospital to allow for monitoring of the dog's electrical activity in its normal environment. The monitor was removed after 25 hours. Analysis of the digitally recorded Holter ECGs was performed by veterinarians with experience in Holter analysis, with 1 of 2 available Holter analysis systems.[c,d] Manual adjustments and accuracy verification of the arrhythmias recognized by the software were performed. Any recordings that did not have at least 20 hours of readable data were excluded. Total numbers of VPC were tabulated. 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/24 hours were considered equivocal and not included in the study.

Statistical Analysis. The likelihood of observing VPCs during a 5-minute ECG was compared with the likelihood of observing >100 VPCs/24 hours during the Holter examination. Dogs were grouped according to the number of VPCs on the 5-minute ECG: no VPC, 1–2 VPCs, 3–5 VPCs, 6–10 VPCs, 11–20 VPCs, 21–50 VPCs, and >50 VPC/5 minutes. Receiver operator curve (ROC) analysis was derived to calculate the optimal cut-off value of numbers of VPCs per 5-minute interval to predict >100 VPCs on Holter examination. Sensitivity was calculated by dividing the number of dogs that had ≥1 VPCs observed on the 5-minute ECG by the total number of dogs that had >100 VPCs/24 hours observed on the Holter examination. Specificity was determined by dividing the number of dogs in which no VPC were observed on the ECG by the total number of dogs that had ≤50 VPCs/24 hours observed on the Holter examination. Positive and negative predictive value was determined for ECG results ≥1 VPC using the calculated prevalence from the dogs with >100 VPCs/24 hours on Holter examination and dogs with ≤50 VPCs/24 hours. Sensitivity, specificity, and positive and negative predictive values of ≥1 VPCs observed on the 5-minute ECG also were calculated with regard to different Holter groups (≤50 VPCs/24 hours, 51–100 VPCs/24 hours, 101–500 VPCs/24 hours, 501–2,000 VPCs/24 hours, and >2,000 VPCs/24 hours) by ROC and area under the curve (AUC) analyses. Pearson product moment correlation (for normally distributed residuals with constant variance) and simple linear regression analysis were used to identify and quantify correlations between numbers of VPCs detected in the 5-minute ECG and number of VPCs detected in 24 hours with the Holter examination. Commercially available software programs were used for analysis.[e,f]

Results

A total of 875 examinations, including a 5-minute ECG and Holter examination, were performed on 431 Doberman Pinschers and the results were analyzed statistically. More than 100 VPCs/24 hours were found in 204 Holter examinations (mean number of VPCs/24 hours, 4,511; median number of VPCs/24 hours, 910) and prevalence of arrhythmias was calculated to be 23.3% (of all 875 examinations). The 204 Holter examintations were from 77 dogs (mean age, 7.5 years; range, 1–12.8 years). The 5-minute ECG detected VPCs in 131 examinations (64.2%) of these 204 Holter recordings with >100 VPCs/24 hours. Absolute numbers and percentages of the 5-minute ECG results, grouped according to the 5-minute ECG into various VPC groups (no VPC, 1–2 VPCs, 3–5 VPCs, 6–10 VPCs, 11–20 VPCs, 21–50 VPCs, and >50 VPC/5 minutes) of the 204 positive Holter examinations are shown in Table 1. The 5-minute ECG examinations divided into different VPC groups, according to the number of VPCs per 5 minutes, of 875 Holter examinations with ≤50 VPCs or >100 VPCs/24 hours are shown in Figure 1. ROC curve analysis was performed to find the best cut-off value for the number of VPCs to predict >100 VPCs/24 hours, as this is the recommended cut-off value for detecting arrhythmias in Doberman Pinschers with cardiomyopathy.[17] The AUC of the ROC curve was 0.811 and ≥1 VPC/5 minutes was identified as the best cut-off value for detecting arrhythmias. For further analysis of sensitivity, specificity, and predictive values of the 5-minute ECG to predict Holter abnormalities, 2 groups, with no VPC and ≥1 VPC/5 minutes, were formed. The absolute numbers and percentages of these 2 groups in relation to the Holter results are shown in Table 2. Sensitivity was 64.4%, because 131 ECGs showed ≥1 VPC/5 minutes compared with 204 Holter examinations with >100 VPCs/24 hours. Specificity was high (96.7%) with 22 false positive ECG results showing ≥1 VPC/5 minutes when Holter analysis re-

Table 1. Number of examinations for different VPC groups (according to the 5-minute ECG) of 204 Holter examinations with >100 VPCs/24 hours.

VPCs/5 Minutes	n	Percent
0	73	35.8
1–2	34	16.7
3–5	15	7.4
6–10	9	4.4
11–20	14	6.9
21–51	29	14.2
>50	30	14.7
Total	204	100.0

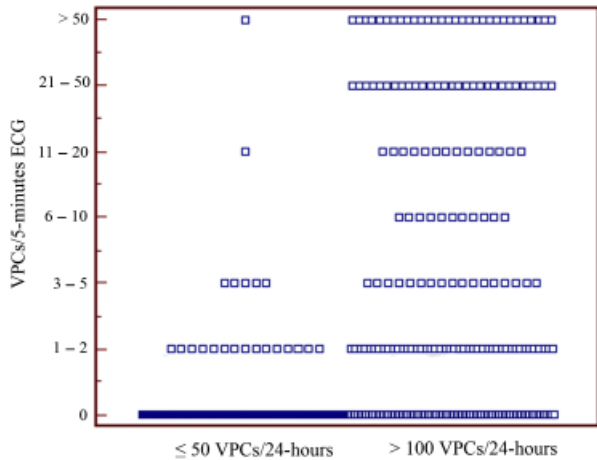VPC, ventricular premature contractions; ECG, electrocardiography.

Fig 1. Five-minute electrocardiographic (ECG) examinations divided into different ventricular premature contraction (VPC) groups, according to the number of VPCs per 5 minutes, of 875 Holter examinations with ≤50 VPCs or >100 VPCs/24 hours.
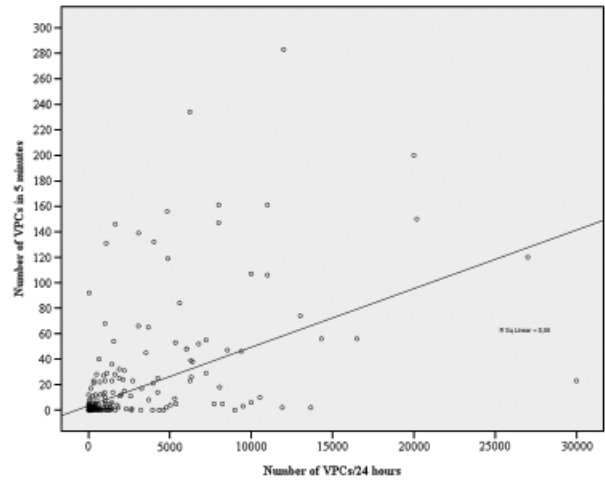

Fig 2. Scatter diagram of the regression analysis to compare the results of the 5-minute electrocardiography with the results of the Holter examination.

vealed ≤50 VPCs/24 hours (n = 671 examinations). The prevalence of >100 VPCs/24 hours was calculated to be 23.3% and this value was used to calculate positive and negative predictive values. The positive predictive value of a 5-minute ECG to detect >100 VPCs/24 hours was 85.6% and the negative predictive value 89.9% for the absence of >100 VPCs/24 hours.

There was a significant ($P < .001$) but only weak correlation ($R^2 = 0.56$) between the number of VPCs detected by the 5-minute ECG and the number of VPCs detected by Holter examination (Fig 2). To evaluate if higher numbers of Holter VPCs can be better predicted than lower VPC numbers, sensitivity, specificity, and positive and negative predictive values were calculated for different Holter groups using ≥1 VPC/5-minute ECG as a cut-off. The 5-minute ECG had a positive predictive value to predict >100 VPCs/24 hours that ranged from 59.3% to 73.8% and a negative predictive value of 92.5% to 99.1%. Sensitivity of the technique was 37.6% to 91.2% and specificity 96.7%. AUC ranged from 0.67 to 0.95 (Table 3).

Discussion

Cardiomyopathy in Dobermans Pinschers is a common, inherited, slowly progressive primary myocardial disease.[1,8,10,12,13,16] Ventricular premature contractions are a common finding in Doberman Pinschers with cardiomyopathy and may lead to sudden cardiac death in 25–30% of the cases in the occult phase of the disease.[3,7,8,16,17] Because of the high frequency of electrical abnormalities in this breed, Holter examination was suggested to be the best test for detecting early changes,[3,7,17] and thus Holter examinations have been evaluated and recommended in Doberman Pinschers as well as in other breeds for the purpose of diagnostic and therapeutic considerations.[3,7,17,19–25] However, availability of Holter recorders and expense of this technique may preclude its use in many dogs.[18,26] Consequently, many veterinarians currently base diagnostic and therapeutic decisions on lead II ECGs performed for only a brief period, while the dog is in the hospital. One study compared the results of an in-house ECG with that of a Holter examination in Boxer dogs and found that the ECG is an insensitive but very specific test to predict Holter results.[18] Arrhythmogenic right ventricular cardiomyopathy in Boxers and cardiomyopathy in Doberman Pinschers have similar disease progression, but they are different diseases, and the diagnostic value of a 5-minute ECG might be different in the different disorders.[27–34] However, the present study was able to show that the sensitivity, specificity, and positive and negative predic-

Table 2. Number of 5-minute ECG examinations with 0 or ≥1 VPC/5 minutes and the corresponding Holter examinations with ≤50 or >100 VPCs/24 hours.

ECG Exams with	< 50 VPCs/24 Hours		>100 VPCs/24 Hours		Group Total	
	n	%	n	%	n	%
0 VES/5 minutes	649	96.7	73	35.8	722	82.5
≥1 VPC/5 minutes	22	3.3	131	64.2	153	17.5
Group total	671	100.0	204	100.0	875	100.0

VPC, ventricular premature contractions; ECG, electrocardiography.

Table 3. Sensitivity, specificity, prevalence, and positive and negative predictive value of ≥1 VPC in 5-minute ECG recordings compared with different Holter VPC groups.

≥1 VPC/5 Minutes	Holter VPCs/24 Hours			
	< 50	100–500	501–2,000	> 2,000
n	671	84	52	68
Prevalence		11.2	7.2	9.2
Sensitivity		37.6	73.1	91.2
Specificity		96.7	96.7	96.7
PPV		59.3	63.3	73.8
NPV		92.5	97.9	99.1
AUC		0.67	0.86	0.95

Prevalence was defined as the percentage of dogs in the population with the given number of VPCs on the Holter examination.

PPV, positive predictive value; NPV, negative predictive value; AUC, area under the curve of the ROC analysis; VPC, ventricular premature contractions; ECG, electrocardiography.

tive values are almost identical in the ability to predict > 100 VPCs/24 hours in Boxers and in Doberman Pinschers. The study in Boxers included 188 examinations, whereas this study included 875 examinations in Dobermans Pinschers, yet the results are surprisingly similar. This leads to the conclusion that the sensitivity of an ECG is too low for screening purposes. However, specificities are very good if at least 1 VPC is seen on an in-house ECG for both breeds.

The presence of VPCs on ECG should be a strong indication for further evaluation of the dog with regard to a possible occult phase of cardiomyopathy. However, the absence of VPCs on a 5-minute ECG does not preclude the occurrence of VPCs during the rest of the day. Screening for cardiomyopathy should begin in Doberman Pinschers at 2 years of age.[1,8,10,16] Screening should include a Holter examination and echocardiography and should be repeated on a yearly basis.

Systemic diseases can cause VPCs, and therefore dogs with evidence of systemic diseases were excluded from the study. However, it may be possible that some dogs in the study had > 100 VPCs/24 hours because of undetected systemic diseases and not because they had occult cardiomyopathy. However, as the objective of this study was to evaluate the value of a 5-minute ECG to predict arrhythmias in Doberman Pinschers, a cut-off value of > 100 VPCs/24 hours was used for the detection of cardiomyopathy in Doberman Pinscher, as this is the recommended value and therefore the clinically most relevant information.[7,8,17] Sensitivity of the in-house ECG technique increased in Boxer dogs with higher number of VPCs on Holter examination (92% for dogs with > 3,000 VPC/24 hours compared with 68% for dogs with > 50 VPC/24 hours) or when dogs with syncope were evaluated (61% for dogs with syncope with > 50 VPC/24 hours).[18] The present study found similar results. Whereas sensitivity of ≥1 VPC/5 minutes as cut-off value to detect up to 500 VPCs was low (37.6%), sensitivity increased to 91.2% if the Holter examination showed > 2,000 VPCs/24 hours. It may be argued that the 5-minute ECG may be useful for screening dogs that are

severely affected, because these dogs might show more VPCs. However, it has not yet been demonstrated that the number of VPCs correlates with severity of disease or risk of unexpected death.[18]

A limitation of this study was that no attempt was made to evaluate the relationship between detection of VPCs by use of ECG and grade of arrhythmia (eg, couplets, triplets, paroxysms of VPC). However, the goal of this study was to compare 2 methods of arrhythmia detection as a screening test for cardiomyopathy.

In summary, this study showed a low sensitivity but high specificity of a 5-minute ECG to predict > 100 VPCs/24 hours, if at least 1 VPC is detected within 5 minutes. The absence of VPCs in the 5-minute ECG should not lead to the assumption that the dog is healthy, because false negative cases were found in 35.8% of the examinations. At least 1 VPC in a 5-minute ECG strongly warrants further examination, because specificity (96.7%) and positive predictive value (85.6%) are very high. Sensitivity increased with higher VPC numbers detected by the Holter examination. A 5-minute ECG cannot replace a 24-hour ECG examination for the purpose of detecting the occult phase of DCM in Doberman Pinschers. Performing a 24-hour ECG remains essential to screen for DCM in Dobermans.

Footnotes

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