

Chapter 2

Dilated cardiomyopathy in the Doberman dog: survival, causes of death and a pedigree review in a related line

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ABSTRACT

The objective of this study was to analyze clinical, electrocardiographic and echocardiographic characteristics, survival, cause of death and possible modes of inheritance of dilated cardiomyopathy (DCM) in Dobermanns (DO) and to compare the occurrence and survival with dogs of other breeds. Two cohorts of dogs were studied: 1. A consecutive series of 52 dogs of different breeds with DCM were included, 21 were Dobermanns and 31 dogs belonged to other breeds; 2. Twenty-eight asymptomatic Dobermanns, who were screened for DCM. Medical records of dogs with DCM were reviewed. Physical, electrocardiographic and echocardiographic examinations were performed on asymptomatic Dobermanns. Their pedigrees were reviewed.

Dobermanns survived on average 52 days (range <1-180), while dogs of other breeds survived significantly longer, i.e. 240 days (<1-1230). Survival of Dobermanns in congestive heart failure (mean 62, range <1-180) was not different from survival of Dobermanns with sudden death (mean 33, range <1-105). High prevalence, short survival time and the clinical course of DCM in Dobermanns showed similarities to previous studies. Twenty-one percent of asymptomatic Dobermanns had increased left ventricular end-systolic diameter and 14% developed DCM within a year. A line of Dobermanns with multiple members affected with DCM was identified by the review of their pedigrees. Exact mode of inheritance could not be established.

The prognosis of Dobermanns with DCM is poor. Further molecular genetic studies, which would enable detection and exclusion of disease carriers from the breeding, are necessary.

INTRODUCTION

Dilated cardiomyopathy is a well-known and common cause of congestive heart failure and sudden death in dogs. Dobermanns have been reported to be the most commonly affected breed (Lombard 1984; Calvert 1986; Calvert 1992; Monnet et al. 1995; Hammer et al. 1996). Frequent occurrence of the disease in some lines of Dobermanns has been observed (Calvert 1986; Calvert 1992; Hammer et al. 1996; Calvert 1982). Consequently, it was hypothesized, that the disease might have a genetic basis. The mode of inheritance of DCM in Dobermanns has not been fully elucidated. One abstract in the literature suggested that the mode of inheritance of DCM in Dobermanns is autosomal dominant with reduced penetrance (Hammer et al. 1996).

Genetic origin of the same disease has been suspected in other breeds (Staadén 1981; Gooding et al. 1986; Goodwin et al. 1995, Tidholm et al. 2000; Dambach et al. 1999). In addition, human studies have revealed a genetic component to DCM in a significant proportion of cases (Michels et al. 1985; Berko and Swift 1987; Emery 1987; Abelmann and Lorell 1998; Zeviani et al. 1991; Michels et al. 1992; Towbin et al. 1993; Goerss et al. 1995; Keeling et al. 1995).

The purpose of this study was to analyze the clinical, electrocardiographic, radiographic and echocardiographic characteristics of DCM and the cause of death in Dobermanns and to compare the occurrence and survival with cases of DCM in other breeds of dogs. Along with this DCM group of dogs (1st cohort), a small group of 28 asymptomatic Dobermanns (2nd cohort) were studied by means of physical examination, electrocardiography and echocardiography to determine the prevalence of DCM in these dogs. In order to evaluate the frequency of familial occurrence of the disease and to assess the mode of inheritance of the disease, pedigree review was performed.

MATERIALS AND METHODS

ANIMALS

Our study consisted of two cohorts of dogs. The first cohort consisted of 52 dogs (consecutive series) of different breeds with DCM (1st cohort) who were admitted to the outpatient department of the Clinic for Small Animal Medicine and Surgery, Veterinary Faculty of Ljubljana, Slovenia within a period of five years. The second cohort was comprised of 28 asymptomatic Dobermanns (2nd

cohort), whose owners participated in the DCM research, and were screened for any signs of heart disease.

PROCEDURES

The medical records of dogs with DCM were reviewed. In the 2nd cohort, a 3-minute ECG (standard leads) was recorded after a physical examination. Electrocardiographic parameters, (measured in lead II), were compared to the normal values (Tilley 1992). Thoracic radiographs were assessed subjectively (Suter and Lord 1984). Echocardiography (M - mode and two dimensional) was performed with a 5 MHz sector transducer using standard techniques (Thomas et al. 1993). Dogs were not sedated. They were examined in the right lateral recumbence on a plastic table with cutting outs to enable the transducer to be oriented from below. Simultaneous ECG was used to define timing of the measurements. Three measurements were averaged for each echocardiographic variable. M-mode was obtained from the left ventricular short axis view. In cases of atrial fibrillation we measured the beats, which occurred after longer diastolic filing and produced better contractility (Feigenbaum 1994). When PVC's were present, measuring the beats right before or after PVC's occurred was avoided.

The diagnosis of DCM was made either by echocardiography or by clinical findings with pathomorphologic/pathohistologic findings (Van Fleet and Feranns 1986; Everett et al. 1999; Tidholm et al. 1998; Calvert et al. 1997; Kittleson 1998a). Post mortem findings such as an enlarged heart with severe dilatation of left or all 4 heart chambers, with thin walls, dilated atrioventricular ring and no significant changes of the valvular apparatus or other heart structures were considered diagnostic of DCM. A finding of a mild AV valve myxomatous degeneration in older dogs was considered insignificant concurrent finding. Common simultaneous findings were pulmonary edema and liver congestion, in some cases accompanied by pleural or abdominal effusion.

In the 2nd cohort, dogs were assigned as having DCM on the basis of abnormal echocardiographic findings or at least one PVC recorded on the ECG (O'Grady and Horne 1995a). Echocardiographic diagnostic criteria for dogs of other breeds than Dobermanns were normal values referred by Bonagura et al. (1985), summarized in a table by Ware (1992). SF values $\leq 25\%$ were considered abnormal. The following echocardiographic variables of Dobermanns from the 1st cohort and from the 2nd cohort were considered abnormal: left ventricular fractional shortening (FS) < 25 , left ventricular end-diastolic diameter (LVEDD) > 46 mm in dogs weighing ≤ 42 kg and > 50 mm in dogs weighing > 42 kg, and left ventricular end-systolic diameter (LVESD) > 38 mm (Calvert 1982;

O’Grady and Horne 1995a; O’Grady and Horne 1995b; Calvert et al. 2000a; Sottiaux and Amberger 1997). Presented data are the results of the first examination.

Within the 1st cohort the percentage of different breeds, age at the time of diagnosis and length of survival in Dobermanns (DO 1st cohort) in comparison to other breeds (OB 1st cohort) were calculated. Survival times were calculated from the time of the 1st presentation (when DCM diagnosis was made) to the death or euthanasia. Treatment analysis was not included in the study. Medical therapy consisted of variable drugs used to treat CHF and arrhythmia. Therapeutics and number of dogs receiving each therapeutic are listed in Table 1. Asymptomatic dogs with evidence of DCM were not treated.

The cause of death was registered (congestive heart failure - CHF, sudden death - SD, other causes). We used published criteria for sudden cardiac death, i.e. dogs that were in heart or myocardial failure, must be stable one hour before death (Wilson et al. 1983).

The pedigrees of Dobermanns of both groups were reviewed to find relatives with DCM and to try to determine the mode of inheritance of the disease.

Table 1. Number of dogs of both groups receiving listed therapeutics

	OB n	DO	
		CHF n	SD n
Furosemide	29	11	3
Digoxin	28	11	3
ACE-I	18	9	2
Propranolol	4	1	1
Mexiletine	3		2
Lidocaine	2		1
Disopyramide	1		1
Propafenone			1
Dopamine HCl	1	1	
Spironolactone	1		
Hydrochlorothiazide	5		
Carnitine		2	
Taurine	1		
Low Sodium diet	2	1	
Peritoneocentesis	3		

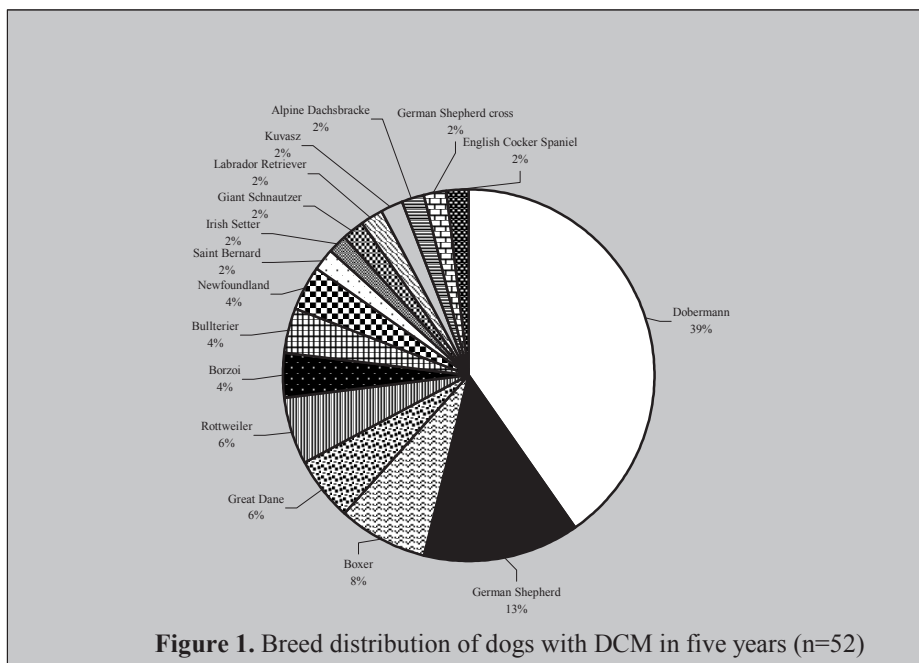
n - number, OB - other breeds, DO - Dobermanns, CHF - congestive heart failure, SD - sudden death, ACE-I - angiotensin converting enzyme inhibitor

STATISTICAL ANALYSES

The data was presented as the mean value, standard deviation and range. The two sample F test were used to detect significant differences in age of OB 1st cohort versus DO 1st cohort and age of DO 1st cohort that were dead because of CHF versus DO 1st cohort that died suddenly.

Survival was analyzed in OB 1st cohort vs. DO 1st cohort and in DO 1st cohort according to the mode of death (CHF vs. SD). In both analyses, Kaplan-Meier method was used for estimating survival curves, and Log Rank test was used for comparing survival between two groups of interest.

The F test was used to compare echocardiographic data of Dobermanns in the 1st cohort. The Chi - Square test was used to detect significant differences in the frequency of CHF dogs versus SD dogs within the group of Dobermanns from the 1st cohort. P values < 0.05 were considered statistically significant.



RESULTS

FIRST COHORT

OCCURRENCE OF DCM IN DOBERMANNS AND OTHER BREEDS, SURVIVAL AND CAUSES OF DEATH

According to the medical records, 52 dogs had a diagnosis of DCM. There were 21 Dobermanns (39 %) and 31 dogs (61 %) that belonged to other breeds (Fig. 1).

Gender, age and survival of dogs from the 1st cohort are presented in Tables 2 A & B and Fig. 2 & 3. A follow up analysis showed that all 21 Dobermanns (100%) and all dogs (100%) of other breeds were dead. Three dogs from OB group were censored in the survival analysis since they were lost for follow up. The survival time was significantly longer in dogs of other breeds (mean 240 days), versus Dobermanns (mean 52 days; Table 3 and Fig. 2).

Table 2A. Gender and age in cohort 1 (all, other breeds, Dobermanns)

	All	OB	DO	
male (n)	42	26	16	
%	80.7%	84%	76.2%	
female (n)	10	5	5	
%	19.2%	16%	23.8%	
age (years)				NS
mean ± STDEV		7.2±2.8	6.5±1.9	(0.10)

Table 2B. Gender and age in Dobermanns 1st cohort (CHF vs. SD)

	CHF DO	SD DO	P value (CHF vs. SD)
male n	11	5	
%	78.6%	71.4%	NS (0.86)
female n	3	2	
%	21.4%	28.6%	
age years (mean ± STDEV)	7.1±2.4	5.8±1.3	NS (0.43)

OB - other breeds, DO - Dobermanns, CHF - congestive heart failure, SD - sudden death, n - number of dogs, STDEV - standard deviation, NS - not significant; P value stays immediately after groups that are compared; age refers to the time of the 1st examination

Table 3. Survival times in days

Survival time	n	Mean	Median	Range
Dobermanns	21	52	39	<1-180
Other breed dogs	31	240	120	<1-1230
CHF Dobermanns	14	62	40	<1-180
SD Dobermanns	7	33	30	<1-105

SD - sudden death, CHF - congestive heart failure, n - number of dogs

Congestive heart failure (CHF) was the direct cause of death in seven of the 21 Dobermanns (33 %). Six dogs (29 %) were euthanised because of severe heart failure, seven Dobermanns (33 %) died suddenly and one (5 %) died due to gastric dilatation with mesenteric torsion. Autopsy was performed in ten Dobermanns with DCM, results are presented in Table 4.

Table 4. Results of pathomorphologic and/or pathohistologic examination in DO 1st cohort

	n	%
4 chamber dilatation	5	62.5
pulmonary edema	6	75
pleural effusion	3	37.5
only LA, LV dilatation	1	12.5
Only right heart dilatation	2	25
pale heart muscle	2	25
mild AV valve degeneration	3	37.5
myocardial lipidosis	4	50
myocyte degeneration	2	25
myocardial fibrosis	2	25
myocardial vacuolar degeneration	1	12.5

6 dogs had pathomorphologic and pathohistologic examination done, 2 dogs had sole pathomorphologic and 2 dogs sole pathohistologic examination done; altogether 10 dogs. Severity of histologic lesions varied widely therefore gradation was not put in the table

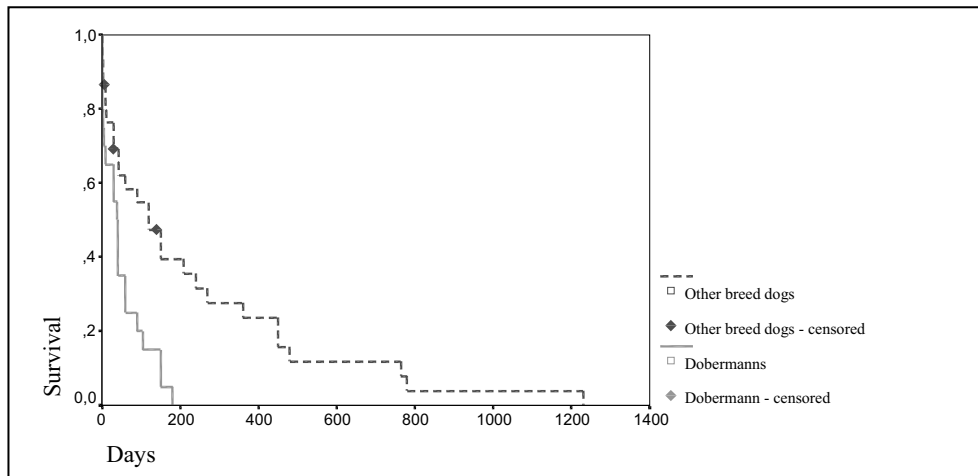


Figure 2. Survival curves comparing survival time in dogs of other breeds and survival time in Dobermanns. Dobermanns had significantly shorter survival time, ($p(\text{Log Rank}) = 0.0013$) than dogs of other breeds. Mortality in Dobermanns was the highest in the first 39 days (full color figure on page 181).

MEDICAL HISTORY, PHYSICAL EXAMINATION, ELECTROCARDIOGRAPHY, RADIOGRAPHY AND ECHOCARDIOGRAPHY OF DOBERMANNS WITH DCM (21 DOGS)

The group is divided into two categories: in the first one there are 13 dogs that died or were euthanised because of congestive heart failure and one dog which died due to gastric dilatation with mesenteric torsion but was also in heart failure prior to death. The second group included seven dogs that died suddenly. The results of medical history, physical examination, electrocardiography and radiography are summarized in Table 5, echocardiographic data are presented in Table 6. Four dogs that died suddenly, were not in congestive heart failure at the time of the 1st echocardiographic examination, the reason for examination was exercise intolerance in one, syncope in two, fast heart beat and vomiting in one, examination before anesthesia in one.

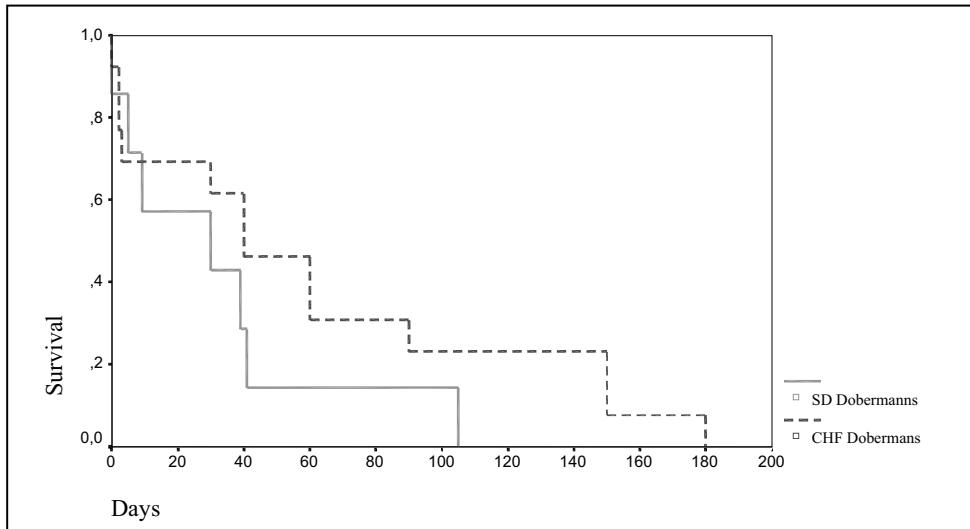


Figure 3. Survival curves in Dobermanns in CHF vs. Dobermanns with SD. Survival in the SD group was shorter but the test was not significant, p (Log Rank) = 0.2106 (full color figure on page 181).

SECOND COHORT

This cohort consisted of 16 male and 12 female Dobermanns that were screened for signs of occult DCM. They were from one to 11 years old (mean age: 6.1 years).

MEDICAL HISTORY, PHYSICAL EXAMINATION, ELECTROCARDIOGRAPHY AND ECHOCARDIOGRAPHY IN ASYMPTOMATIC DOBERMANNS (28 DOGS)

Results are presented in Table 5 and 6. One dog had PVC's during a 3 minute ECG recording. 16 dogs (57%) had increased LVEDD, six of these dogs (21%) had also increased LVESD and three of them (10,7%) had decreased FS. Within one year after the screening, four dogs developed DCM, three of them were in CHF and one died suddenly. Autopsy findings of the last dog were compatible with DCM. These four dogs had increased LVESD and LVEDD, three of them had also SF below 24% at the time of initial examination almost one year earlier. Among two other dogs with increased LVESD one died suddenly four years after examination and the other was euthanised for some other reasons, but no autopsy was undertaken in these two dogs.

Table 5. Clinical, electrocardiographic and radiographic findings in Dobermanns 1st cohort in congestive heart failure (CHF), sudden death (SD) and in DO 2nd cohort

Variable	DO 1 st cohort in CHF		DO 1 st cohort /SD		DO 2 nd cohort	
	n	%	n	%	n	%
Medical history	n=14		n=7		n=28	
cough	11	79	2	29		
exercise intolerance	6	43	1	14		
difficulty breathing	5	36				
not eating well	10	71				
vomiting	2	14				
fast heart beat	2	14	1	14		
abdominal swelling	1	7				
syncope	2	14	2	29		
no signs	0	0	2	29	28	100
Physical findings	n=14		n=6		n=28	
murmur	6	43	3	50	3	11
irregular pulse	6	43				
premature beats	2	14			1	4
tachycardia (>160 beats/min.)	6	43	3	50		
pulse deficit	5	36	2	33		
pulmonary crackles	3	21				
ascites*	2	14				
weak fem. pulse			3	50		
no signs	0	0			24	86
Electrocardiograms	n= 12		n=6		n=28	
sinus tachycardia	6	50	2	33		
atrial fibrillation	6	50				
QRS complex >0.06 s (lead II)	12	100	3	50		
ST slurring	8	67	2	33		
R wave >3 mV (lead II)	6	50				
P wave >0.04 s (lead II)	5	42	3	50		
P wave >0.4 mV (lead II)	4	33	2	33		
PVC's	4	33	2	33	1	4
sinus arrhythmia			2	33		
ventricular tachycardia			2	33		
left axis deviation			1	17	2	7
Normal					25	89
Thoracic radiographs	n=10		n=5			
generalized	6	60	1	20		
LA, LV enlargement	4	40	2	40		
pulmonary edema	10	100	3	60		
ascites	1	10				
pleural effusion	2	20				
RV enlargement			1	20		
Unremarkable findings			1	20		

*ascites was obvious by balloting, later also confirmed by ultrasound, MEA - mean electrical axis, LA - left atrium, LV - left ventricle, RV - right ventricle.

Table 6: Echocardiographic data of Dobermanns (DO 1st coh.) in congestive heart failure - CHF (n=11), sudden death - SD (n=6) and of DO 2nd cohort (n=28)

Variable	DO 1st cohort. in CHF		Difference	DO 1st cohort /SD *		DO 2nd cohort	
	n	Mean ± stdev (Range)		n	Mean ± stdev (Range)	n	Mean ± stdev (Range)
Weight (kg)*	11	36.4±4.3 (27.2-42.0)	NS	6	36.6±3.1 (33-42)	28	35.8± 5.4 (28-47)
LVEDD (mm)	11	70.5±9.0 (54-83)	NS	6	55.1±9.8 (45-67.5)	28	49.1± 5.3 (40-62)
LVESD (mm)	11	64.6±9.8 (44-79)	NS	6	46.6±10.6 (35-60)	28	34.1± 4.5 (28-47)
FS (%)	11	8.5±5.7 (14-18)	NS	6	16±7.3 (8-27)	28	30.1± 5.3 (18-44)
LVPWd (mm)	10	8.4±1.3 (7.0-11)	NS	5	8.76±2.5 (5-11.5)	23	8.6± 1.3 (6-11)
LVPWs (mm)	7	10.2±2.2 (6.0-12.6)	NS	5	10.1±3.2 (6-14)	18	11.8± 1.4 (9-14)
IVSd (mm)	10	8.8±2.2 (6.0-12.3)	NS	5	8±1.8 (5-9.5)	25	8.9± 1.6 (5-12)
IVSs (mm)	7	11.2±3.4 (6-16.0)	NS	5	11.4±2.1 (8-13)	14	12.6±2.3 (8-17)

LVEDD - left ventricular end-diastolic diameter, LVESD - left ventricular end-systolic diameter, FS - fractional shortening, LVPWd - left ventricular posterior wall in diastole, LVPWs - left ventricular posterior wall in systole, IVSd - interventricular septum in diastole, IVSs - interventricular septum in systole, NS - not significant, P value<0.05, stdev - standard deviation; * 4 of dogs from SD group were not in CHF at the time of echocardiographic examination

PEDIGREE REVIEW

We obtained 38 pedigrees - 13 from DO 1st cohort and 25 from DO 2nd cohort. Review of the pedigrees showed that within the 1st cohort, 9 dogs (numbers 1 to 9 in Fig. 4) were members of one line with a high incidence of heart disease and sudden death.

Within the 2nd cohort, 22 DO (78 %) have relatives in the last three generations who died suddenly or due to heart disease. In figure 4, only 15 DO 2nd cohort (A1-A15) are presented, since the data of the ancestors from the rest of the dogs was scarce and presenting them in this pedigree would be non informative.

The constructed pedigree with multiple affected members demonstrates that this particular line of Dobermanns in Slovenia was subjected to strong inbreeding, which probably enabled the diseased gene to be propagated. The exact inheritance pattern could not be determined due to incomplete data (the status of parents and siblings was frequently unknown).

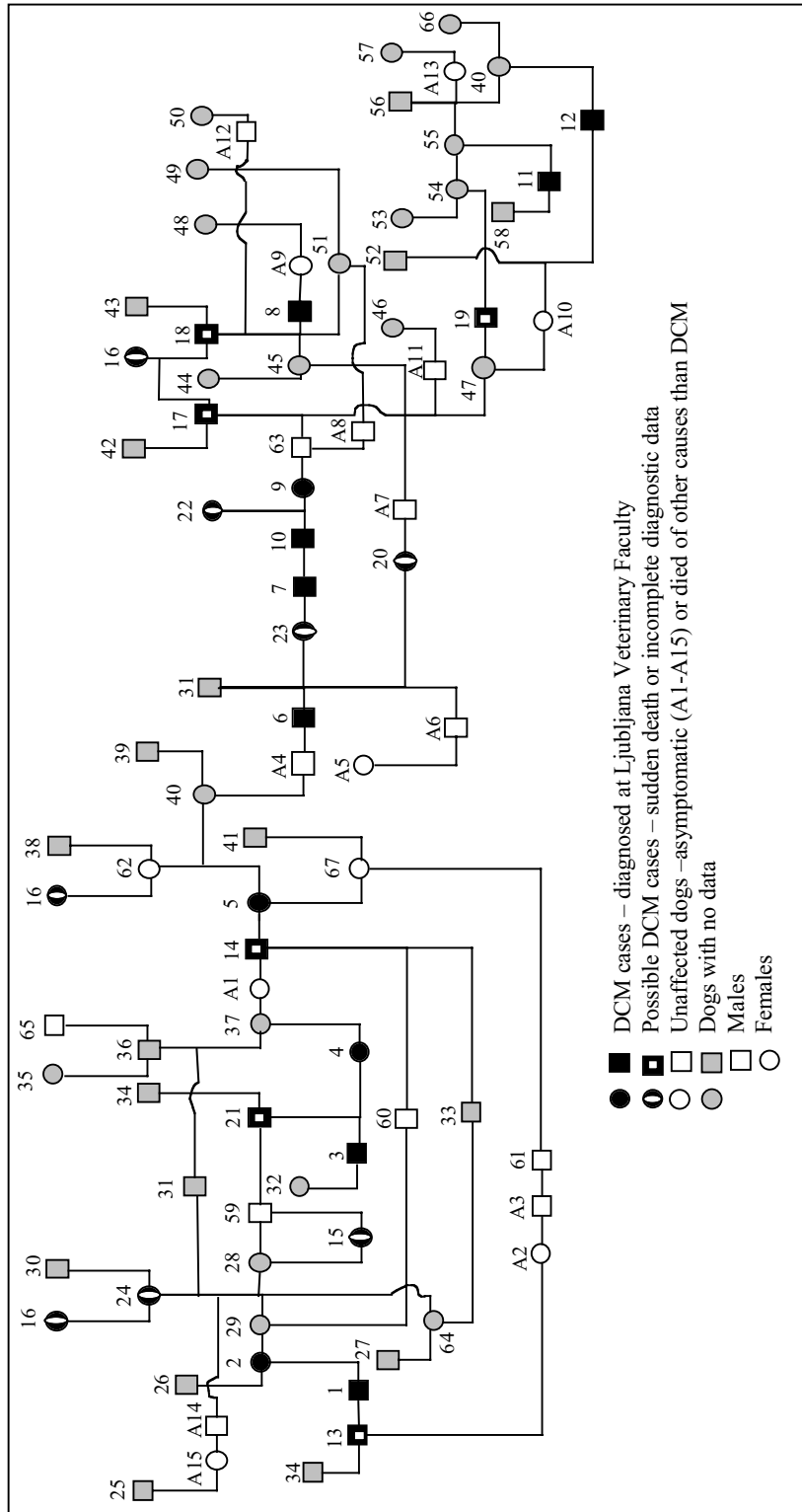


Figure 4. Pedigree of a family of Dobermanns

DISCUSSION

In a consecutive series of 52 dogs, who were evaluated for DCM at our institution, 39 % were Dobermanns. The second most common breed affected with this disease was the German shepherd (13%), followed by the German boxer (8 %), the Great Dane (6%), the Rottweiler (6%), and others (refer to Fig. 1). Other authors reported that Dobermanns are among the three most commonly affected breeds (Calvert 1992; Kittleson 1998a; Sisson and Thomas 1995). According to the literature, the German shepherd is not so commonly affected. The high incidence in German shepherds may just be a reflection of the high popularity of this breed in Slovenia.

In our study males predominated in all groups (OB, DO, DO with CHF and DO with SD). Male predominance was found also by Calvert with coworkers (Calvert 1982; Calvert et al. 1997). In contrast, O'Grady and Horne (1995a) had not found a gender predisposition. The age difference of dogs of OB and DO with DCM was not significant. Dobermanns in CHF were not significantly older at the time of diagnosis than dogs that died suddenly. Calvert et al. (1997) found out that dogs dying suddenly are approximately one year younger than dogs developing CHF. An explanation for younger age in SD group of DO would be that some dogs with arrhythmias died due to arrhythmias early in the course of the disease. Congestive heart failure seems to be a more frequent outcome than sudden death in our Dobermanns, but the difference was not significant.

From our pedigree review it was evident that the majority of the DO 1st cohort and the DO 2nd cohort belonged to one family line, which represented a limited gene pool. We found out that the incidence of DCM and SD in this family line of Dobermanns was high.

The survival time of our Dobermanns with DCM 1st cohort was significantly shorter than survival time of other breeds. It had been reported by Calvert (1992) that Dobermanns with CHF have shorter survival in comparison to other breeds. They die suddenly or as a consequence of heart failure. In our study Dobermanns in CHF did not live significantly longer (mean 62, range <1-180) than Dobermanns that died suddenly (mean 33, range <1-105). Veterinary and human studies reported the occurrence of sudden death to be between 10 and 64 % (Calvert 1992; Calvert et al. 1997; Calvert et al. 2000a; Wilson et al. 1983; Sisson and Thomas 1995; Hofmann et al. 1988). Incidence of sudden death in our Dobermanns was 33%. The data obtained by medical history, physical examination, thoracic radiographs and electrocardiogram are similar to those reported by others (Lombard 1984; Calvert 1986; Calvert 1992; Calvert et al. 1982; Calvert et al. 1997; Calvert and Brown 1986). We found greater end-

diastolic and end-systolic diameter and lower fractional shortening in Dobermanns who died due to congestive heart failure in comparison to those who died suddenly. The differences did not reach the level of statistical significance. The explanation for these differences in end-diastolic and end-systolic diameters would be that the 4 dogs that died suddenly were in an earlier stage of the disease. This finding was made also by other investigators (Calvert et al. 1997).

All our postmortem results revealed lesions described as typical and most commonly present in DCM (Van Fleet and Feranns 1986; Everett et al. 1999; Calvert et al. 1997). Attenuated wavy fibers of myocardium which were described by Tidholm and others were not described pathohistologic lesions in our cases (Tidholm et al. 1998). The severity of lesions was not consistent with the diagnosis of DCM since it is known, that there are no differences in histologic lesions or lesion severity in dogs with mild or severe disease (Calvert et al. 1997; Kittleson 1998a).

Only one dog in the group of 28 asymptomatic Dobermanns showed ventricular ectopy. This may be due to the fact that only a short ECG recording was obtained. This dog was already 11 years old at the time of examination and was 2 years later euthanised for some other reason. The relevance of this arrhythmia is unknown. Holter recording would probably detect significantly more arrhythmias as reported by Calvert et al (2000a). They detected PVC's in 52% of asymptomatic Dobermanns and consider this as an indicator of developing of DCM even before echocardiographic changes appear (Calvert et al. 2000a; Calvert et al. 2000b). O'Grady and Horne (1995) found out that 15 DO that demonstrated at least one PVC during a short ECG recording, died. Hence, finding a PVC on an ECG recording in a dog may be suspicious of DCM and associated with a higher risk of sudden death.

Increased LVESD which is a consistent echocardiographic change in DCM, was found in 6 dogs (21%) in DO 2nd cohort (Kittleson 1998b). Four dogs in this group developed DCM within a year, three of them were in CHF and one died suddenly. One dog among these six was euthanised for other reason and one died suddenly after four years. O'Grady and Horne (1995a) performed an extensive screening on DCM in asymptomatic DO and they found out that 28.2% of DO in a group of 103 asymptomatic DO developed DCM within the period of 28.3 months. In a group of 30 asymptomatic DO, Sottiaux and Amberger (1997) found 28% of dogs with increased LVEDD and/or LVESD.

Pedigree review demonstrated one line in which multiple family members were affected with DCM or sudden death, suggesting a genetic basis of the disease. Since DCM appears late in life, it was difficult to determine which dogs are unaffected. Dogs that died young and dogs in which no signs of asymptomatic DCM were found at screening could not be treated as unaffected, since the disease

could become apparent later in life. This, coupled with incomplete data of several family members, prevented us from determining the mode of inheritance.

In dogs, DCM has been suggested to be familial in Dobermanns, Boxers, Cocker Spaniels, Newfoundlands and Portuguese water dogs on the basis of frequent occurrence of the disease in certain lines (Calvert 1992; Goodwin et al. 1995; Tidholm et al. 2000; Dambach et al. 1999). Data about inheritance patterns in dogs are scarce; autosomal dominant inheritance was suggested in a family of Dobermanns and in English Cocker Spaniels (Hammer et al. 1996; Staaden 1981). Research regarding the dystrophin and α -cardiac actin gene had been done in Dobermanns, but no disease mutations were found so far (Meurs et al. 2001; Schatzberg et al. 1999).

For human familial DCM, nine disease genes were identified to date: seven (α -cardiac actin, desmin, lamin A/C, δ -sarcoglycan, α -tropomyosin, cardiac β -myosin heavy chain and cardiac troponin T) for the most common autosomal-dominant form and two (dystrophin and tafazzin) for the X-linked form (Olson et al. 1998; Li et al. 1999; Fatkin et al. 1999; Tsubata et al. 2000; Ortiz-Lopez et al. 1997; D'Adamo et al. 1997; Kamisago et al. 2000; Olson et al. 2001). With the exception of tafazzin, whose function is not currently known, these genes encode for the proteins of the cell cytoskeleton, which transmit mechanical and chemical stimuli within and between cells and contribute to the cell stability (Seidman and Seidman 2001; Chen and Chien 1999; Hein et al 2000; Towbin 1998). DCM in dogs closely resembles the human form of the disease. It is expected that cytoskeletal proteins may play a significant role in the canine DCM as well and are therefore excellent candidate genes. Identification of the DCM gene in dogs would enable early specific diagnosis and detection of carriers. This could consequently reduce the incidence of DCM in predisposed breeds through selective breeding. Since DCM is common in Dobermanns, they could be an ideal breed for such a study.

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