Signalment, Survival, and Prognostic Factors in Doberman Pinschers With End-Stage Cardiomyopathy

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Congestive heart failure (CHF) was evaluated by retrospective review of case records of 66 Doberman Pinschers presenting with overt signs of 2 weeks' duration or less. Left-sided CHF was predominant, the majority of dogs were male, most were 5 to 10 years of age, and CHF tended to occur in females at an older age. Sudden death occurred in 13 dogs (20%). The mean and median survival times of all dogs were 9.65 and 6.5 weeks, respectively. Both atrial fibrillation and bilateral CHF at the time of presentation were associated with significantly shorter survival times.

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Dilated cardiomyopathy (DC) is the most common cardiomyopathy[1,2] in dogs, and of common breeds, the Doberman Pinscher in the United States and Canada has the highest prevalence.[1,2] Cardiomyopathy in the Doberman Pinscher is a chronic, slowly progressive disease characterized by ventricular tachyarrhythmias of progressive but variable severity and progressive myocardial failure.[3-6] The disease may terminate in sudden death before the development of congestive heart failure (CHF) or end-stage CHF.[3-6] After the onset of CHF, natural death usually results from pulmonary edema and cardiogenic shock or from sudden death as a result of ventricular tachycardia-fibrillation.[4-6]

Congestive heart failure in cardiomyopathic Doberman Pinschers develops after a period of gradually progressive left ventricular dysfunction.[5] Pulmonary edema is the most profound overt manifestation of CHF in this breed, although some dogs present with bilateral CHF characterized by pulmonary edema, ascites, and possibly pleural effusion or peripheral edema.[4,5] Atrial fibrillation is absent in most affected dogs.[4,5] The purposes of this study were to describe the age and gender distribution, survival times, and prognostic factors of Doberman Pinschers with advanced CHF.[7]

Materials and Methods

From March 1979 through June 1990, 66 Doberman Pinschers, without a prior diagnosis of cardiomyopathy, were presented to the University of Georgia Teaching Hospital with advanced CHF[7] of no more than 2 weeks' duration. Advanced CHF is characterized by immediately obvious clinical signs, including respiratory distress, profound exercise intolerance, and hypoperfusion at rest.[7] All of the dogs in this study had pulmonary edema documented by thoracic radiography. A right-sided component to the CHF was considered to be present if an abdominal fluid wave was balloted, there was loss of radiographic detail consistent with fluid accumulation in the abdomen, or ascites was documented. The patients' records were reviewed, and data pertaining to signalment, thoracic radiographs, electrocardiograms, body cavity effusions, drug therapy, survival times, and circumstances of death were tabulated.

The diagnosis of DC as the cause of CHF in the 66 dogs in this report was based on the radiographic diagnosis of cardiogenic, alveolar pulmonary edema with echocardiographic evidence of severe myocardial failure (left ventricular fractional shortening $<15\%$, E-point to septal separation >15 mm). Congestive heart failure was classified as left-sided if ascites and pleural effusion were absent or bilateral if, in addition to pulmonary edema, pleural effusion or ascites, or both were present. The presence or absence of ascites was determined by physical examination plus radiography or by abdominocentesis.

This study was not prospective, and patients were not randomized to receive specific drugs. Therefore, it was not intended to assess the efficacy of any particular drug or drugs. Medical therapy consisted variably of furosemide, dobutamine, digoxin, captopril, enalapril, hydralazine, milrinone, L-carnitine, and propranolol. In addition, acute therapy for some dogs included nitroglycerin (sublingual or topical or both), oxygen (intranasal or cage), and aminophylline. Terminally, some dogs received additional drugs not previously administered, or the dosages of drugs were increased.

Survival times were calculated from the time of presentation to the University of Georgia to death. Sudden death was defined as collapse and death within 1 minute of collapse in dogs with therapy-associated compensated CHF, death during sleep in the absence of overt CHF, collapse and death as a result of witnessed ventricular tachycardia-fibrillation, or collapse and death within 1 minute in the presence of overt CHF with a history of ventricular tachycardia.

Survival data were analyzed using the log-rank test (Mantel-Haenzel test for survivalship data).[8] A statistical significance level of .05 was used for analyses. Fisher's exact test was used to determine if the presence of atrial fibrillation decreased the risk of dying suddenly and if atrial fibrillation was more common in males. The Mann-Whitney test was used to determine if female dogs were older than male dogs and if survival of dogs with atrial fibrillation was shorter than in dogs without atrial fibrillation.

Results

Signalment

Fifty-five of 66 dogs (83%) were males (Table 1). The mean and median ages ($\pm$SD) of all dogs were 7.6 ($\pm$2.5) and 7.5 ($\pm$2.5) years (range, 2–14 years), respectively. The mean and median ages of female dogs were 8.6 and 9.5 years as compared to 7.3 and 7.5 years for male dogs, respectively; however, these differences were not statistically significant ($P = .09$). Fifty-one (77%) of the dogs were 5 to 10 years of age, and 34 (51%) were 6 to 9 years of age.

Congestive Heart Failure and Atrial Fibrillation

Fifty of 66 dogs (76%) presented with left-sided CHF, and 20 of 66 dogs (30%) were in atrial fibrillation. Of these 20 dogs, 10 had left-sided CHF, and 10 had bilateral CHF. Seventeen of 55 male dogs (31%) and 3 of 11 female dogs

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Table 1. Gender and Age Distribution in Doberman Pinschers With End-stage Congestive Heart Failure

Age (years)	Male (n = 55)	Female (n = 11)
Mean	7.3	8.6
Median	7.5	9.5
Range	2–14	5–11
% >8 y	33	55
% >9 y	20	36
% >10 y	13	27

(27%) were in atrial fibrillation; the difference was not statistically significant.

Drug Therapy of Congestive Heart Failure

Survival of 1 week or less occurred in 6 of 66 dogs (9%). Treatment in these 6 dogs consisted of oxygen (n = 6), aminophylline (n = 4), nitroglycerin (n = 5), captopril (n = 1), furosemide (n = 6), and digoxin PO (n = 6).

Sixty of 66 dogs (91%) survived more than 1 week. Two initially received dobutamine (4 to 6 μg/kg/min, constant rate infusion) for 12 to 48 hours. All were treated with furosemide, 46 with digoxin, 25 with angiotensin-converting enzyme (ACE) inhibitors, 10 with milrinone, 8 with L-carnitine, 4 with hydralazine, and 5 with propranolol. The dosages were as follows: captopril (13 dogs), 0.5 mg/kg tid for 5 to 7 days followed by 1 mg/kg tid thereafter, and enalapril (12 dogs), 0.25 mg/kg sid for 5 to 7 days, followed by 0.5 mg/kg daily as a single or divided dosage. Furosemide alone was administered to 2 dogs; the rest received various combinations of drugs (Table 2).

Table 2. Summary of Medical Therapy in 60 Doberman Pinschers With End-Stage Cardiomyopathy

Drugs Used and Dosage (mg/kg)	No. Dogs Receiving Drugs
F (2–4 mg/kg bid)	2
F (2 bid), D (0.01 mg/kg daily)	16
F, D, H (0.5–1.0 mg/kg bid)	4
F, D, ACE*	10
F, D, ACE, Lt	8
F, D, P (10–20 mg bid–tid)	5
F, M (0.5 mg/kg bid)	6
F, ACE*	3
F, D, d (5 μg/kg/min)	1
F, M, ACE*	2
F, D, M, ACE*	2
F, d (5 μg/kg/min)	1

Abbreviations: F, furosemide; D, digoxin; H, hydralazine; ACE, angiotensin-converting enzyme inhibitor (captopril or enalapril); L, L-carnitine; P, propranolol; M, milrinone; d, dobutamine.

* Captopril (1 tid), 13 dogs. Initial dose was 0.5 mg/kg tid for 5–7 days. Enalapril (0.25 mg/kg bid or 0.5 mg/kg once daily), 12 dogs. Initial dose was 0.25 mg/kg once daily for 5–7 days.

† L-carnitine (2 g tid).

Table 3. Influence of Atrial Fibrillation on Sudden Death in 13 Dogs

	Atrial Fibrillation	
Sudden Death	Yes	No
Yes	2	11
No	18	33

Causes of Death

Sixty-four of 66 dogs died or were euthanized as a direct result of their disease. One dog was euthanized after 8 weeks following the discovery of cancer, and another was euthanized after 4 weeks because of renal failure. Of the 64 dogs whose deaths were directly attributable to DC, 34 died naturally, and 30 were euthanized. Euthanasia was performed because of failure of therapy either to relieve initially suffering because of pulmonary edema or to produce adequate stabilization to allow minimal exercise (9 dogs), or after the first (16 dogs) or second (5 dogs) relapse of overt CHF after initial resolution of pulmonary edema.

Death occurred suddenly from 2 to 26 weeks after the onset of CHF in 13 of 64 dogs (20%) whose deaths were directly attributable to DC. The mean and median survival times of these 13 dogs was 10.8 and 9 weeks, respectively (range, 2 to 26 weeks). The mean survival time of 51 dogs that died of CHF was 9.7 weeks (range, 21 to 60 weeks). The mean survival time of 48 dogs that lived for 2 or more weeks and then died of CHF was 10.2 weeks (range 2 to 60 weeks). The presence of atrial fibrillation was not significant to the risk of sudden death (Table 3). Overt CHF was absent at the time of sudden death in 11 of 13 dogs. In 9 of the 13 dogs, 1 or more episodes of ventricular tachycardia were documented by Holter recordings (n = 5) or cage-side monitoring (n = 4); ventricular tachycardia was sustained in 4 dogs. Ventricular tachycardia-fibrillation was observed during cage-side monitoring at the time of death in 3 dogs. One dog had severe pulmonary edema and severe ventricular tachyarrhythmias observed by cage-side monitoring that terminated in ventricular tachycardia-fibrillation. One dog whose CHF had been stabilized and had a history of multiple episodes of nonsustained ventricular tachycardia detected by Holter monitoring collapsed and died in less than 1 minute within 24 hours after the reoccurrence of coughing (presumed CHF) and within minutes of moderate exertion. Death occurred during or soon after exertion in 6 dogs, in the morning soon after arising in 3 dogs, during sleep in 2 dogs, and under other circumstances in 2 dogs.

Survival Times

The mean and median survival times of all dogs were 9.7 and 6.5 weeks (range 1 day to 60 weeks) (Table 4). Overall mortality at 2, 4, and 8 weeks was 17/66 (26%), 26/66 (40%), and 42/66 (64%), respectively. Five of 66 dogs (8%) survived 6 months or longer, and 2 of 66 (3%) survived more than 1 year.

Dogs presenting with atrial fibrillation or bilateral CHF

Table 4. Survival Times of Dogs with Left-Sided or Bilateral CHF With or Without Atrial Fibrillation

		Survival Time (weeks)		
Parameters	N	Mean	Median	Range
Left-sided CHF	50	11.0	7.5	<1–60
Bilateral CHF	16	5.7	2.8	<1–22
AF	20	4.1	2.9	<1–13
AF and bilateral CHF	10	3.8	2.0	<1–13
All dogs	66	9.7	6.5	<1–60

Abbreviations: CHF, congestive heart failure; AF, atrial fibrillation.

had significantly shorter survival times (Figs 1, 2). Of the 66 dogs, the 46 dogs that did not experience atrial fibrillation had significantly ($z = 3.45$, $P = .0003$) longer survival times than those that did. Atrial fibrillation was associated with greater than 50% mortality during the first 2 weeks. Of 50 dogs that presented with left-sided CHF (without ascites or pleural effusion), 10 were in atrial fibrillation. The 40 dogs in this subset without atrial fibrillation also lived significantly ($\chi^2 = 7.35$, df = 1, $P < .01$) longer than those with atrial fibrillation. Within the subset of dogs with bilateral CHF (16), 10 had atrial fibrillation. There was no significant difference in survival time associated with atrial fibrillation in this subset.

The survival times of 50 dogs presenting with overt left-sided CHF were compared with those of 16 dogs presenting with bilateral CHF. Left-sided CHF was associated with a significantly ($\chi^2 = 3.98$, df = 1, $P < .05$) longer survival when compared to bilateral CHF. There was an increased frequency of death during the first 2 weeks in dogs with bilateral CHF; subsequently, mortality was similar (Fig 2).

Discussion

Cardiomyopathy is extremely common in the Doberman Pinscher.[1,2,9-13] Sudden death or CHF is the fate of most affected dogs, although, in our experience, some live to old age and die of unrelated problems, often without the presence of cardiomyopathy being detected.

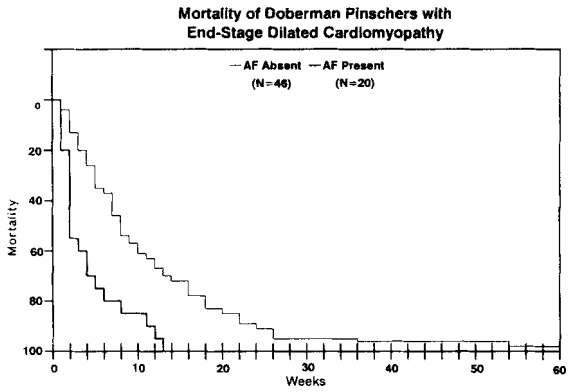

Fig 1. Survival curves comparing the influence of atrial fibrillation (AF) versus predominant sinus rhythm on survival. The presence of AF was associated with significantly shorter survival time ($P < .001$). Greater than 50% mortality occurred in the former group by 2 weeks; afterwards the curves are similar.

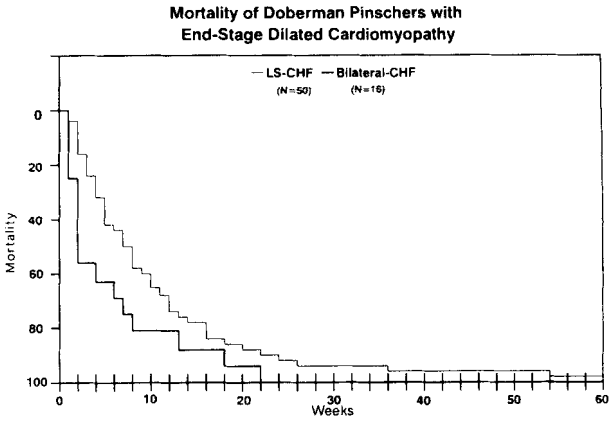

Fig 2. Survival curves comparing the influence of bilateral congestive heart failure (CHF) versus left-sided (LS) CHF on survival. The presence of bilateral CHF at the time of presentation was associated with significantly shorter survival time ($P < .05$); increased mortality occurred during the first 2 weeks. Thereafter, the mortality of both groups was similar.

As previously reported,[3-5] the majority of the patients in this study were male. O'Grady and Horne,[9] however, observed a more nearly equal gender distribution among Doberman Pinschers with occult or latent cardiomyopathy. Among the dogs in our study, there was a wide range of ages, but approximately three fourths were 5 to 10 years of age, and one half were 6 to 9 years of age. The mean and median ages of the female dogs were 1.3 and 2.0 years greater than those of the male dogs, but this was not statistically significant.

The data indicate and our current experience is that medical treatment of CHF in Doberman Pinschers is usually unsatisfactory when initiated after the onset of pulmonary edema. Although remission of pulmonary edema can usually be accomplished, sudden death or relapsing pulmonary edema usually occurs within 6 months. Recurring episodes of CHF become increasingly difficult to control and, barring sudden death, the patient enters a state of intractable CHF. Close observation, attention to detail, extensive client education, and periodic temporary or permanent drug and dosage adjustments may be important to maximizing survival.

In our experience, a second episode of CHF often proves fatal, and those dogs whose pulmonary edema is subsequently resolved are always functionally impaired. Survival and stabilization of a third episode is unlikely. Ascites, pleural effusion, and peripheral edema tend to develop in dogs surviving 2 episodes of CHF. Latent atrial fibrillation heralds a relapse of CHF, weakness or syncope, and functional deterioration.

In this study, survival times were short. Approximately 25% of the dogs were dead within 2 weeks of the onset of signs of CHF, approximately 1 of every 3 was dead in 1 month, and approximately 2 of every 3 were dead in 2 months. Only 5 dogs (7.5%) survived 6 months, and 2 sur-

vived 1 year. Patients initially presenting with generalized CHF or atrial fibrillation were difficult to stabilize, usually remained weak and unthrifty, and had short survival times in most instances. The onset of atrial fibrillation or ascites during the course of therapy correlated with clinical deterioration, and the subsequent survival time was usually short.

The short survival times in these dogs can be attributed to several factors. The prognosis is poor for most dogs with CHF resulting from DC, and our experience is that it is particularly bad for Doberman Pinschers. The vast majority of the dogs in this study were referred, often without a diagnosis, and prior therapy was generally inadequate. Furthermore, some of the dogs that died less than 1 week after presentation to the University of Georgia might have benefited from more aggressive therapy, such as dobutamine, amrinone, milrinone, or nitroprusside.

Both bilateral CHF and atrial fibrillation were negative prognostic factors. Both of these abnormalities may simply reflect more severe cardiac dysfunction. Also the loss of atrial contraction constitutes the loss of an important contribution to ventricular performance, not to mention the detrimental influence on hemodynamics of an irregular, rapid heart rate. The survival curves comparing dogs with and without atrial fibrillation reflect greater than 50% mortality in the former group by 2 weeks. Afterwards the curves appear similar, although some divergence favoring dogs with sinus rhythm continues (Fig 1). This same pattern of early death in dogs with bilateral CHF is seen in Fig 2. Subsequently the curves are similar with the exception of 3 relatively long survivors in the left-sided CHF group.

In studies comprised partially of human patients with DC, enalapril has been shown to exert a favorable influence on survival of CHF.[14,15] A multicenter, placebo-controlled enalapril study of heart failure concluded that the time to treatment failure was improved in cardiomyopathic dogs receiving enalapril.[16] Perhaps initiating treatment earlier in the course of the disease will improve survival times. The point in the evolution of the disease at which medical intervention is indicated remains to be determined.

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