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Dilated Cardiomyopathy in Dogs: Diagnosis and Treatment

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Introduction
Dilated cardiomyopathy (DCM) is prevalent in certain breeds of dog and is rare in cross breeds. Indeed, DCM contributes to a large proportion of the overall mortality in certain large breed dogs <10 years of age. Population based European actuarial data shows that out of the 12 breeds with the highest cardiac mortality, 11 were breeds prone to develop DCM (Irish wolfhound, Great Dane, St. Bernard, Newfoundland, Leonberger, Doberman, Finnish hound, boxer, giant schnauzer, English cocker spaniel, and flat-coated retriever). The impact of DCM on mortality is striking in affected breeds; the mortality ranges from 3.6% per year at risk (Irish wolfhound). This cause-specific mortality can only be matched by myxomatous mitral valve disease in cavalier King Charles spaniels (2.5% per year at risk). DCM is most common in large breed dogs, but not all large breeds are affected. For instance German shepherds and Labrador retrievers have cardiac mortality comparable to the ‘average breed’ in the European actuarial data. DCM is uncommon in small-bred dogs and findings indicative of DCM in such dogs should always be questioned. The prognosis after diagnosis of symptomatic DCM is poor and the median survival time ranges between 27 to 140 days, but there may be breed differences. For the pet owner with a dog with DCM, it is important that the clinician establish an accurate diagnosis to allow adequate therapy to improve the dog’s quality of life and improve survival.

Presentation
DCM is defined as a primary myocardial disease characterized by cardiac enlargement and impaired systolic function in the absence of other cardiac or non-cardiac causes. The clinical presentation may be subtle and include the gradual development of exercise intolerance and weight loss. However, more commonly, these early indications are overlooked and the diagnosis of DCM is not established until congestive heart failure (CHF) develops and the patient is presented for coughing, dyspnea, tachypnea, wasting, arrhythmia and sometimes ascites. For the symptomatic patient, it is important for the clinician to rule out other possible causes for the clinical signs, such as pericardial effusion, pneumonia, neoplastic disease, undiscovered congenital heart disease. For the asymptomatic patient, the challenge lies in differentiating normal variation and cardiac or non-cardiac pathologies from DCM.

In a proportion of boxers and Dockermans (not all), ventricular tachyarrhythmias may cause fainting and weakness, whereas the cardiac dilation and systolic dysfunction is not apparent. Histopathological characterization of dogs with DCM has shown that there are two histopathological phenotypes that presumably precipitates different clinical presentations. The Dobermans and boxers presenting with ventricular tachyarrhythmias have myocardial lesions that include myocytolysis, myofibre degeneration, vacuolization and myocyte atrophy with extensive fibrosis and fatty infiltration. presenting with systolic dysfunction. Cardiac dilation may also present with an arrhythmia, most commonly atrial fibrillation, but the histopathological findings include myocytes that are thinner than normal with a wavy appearance that are separated by a clear space, indicating edematous fluid that is generally free from cellular infiltrates; there may also be diffuse infiltration of subendocardial fibrosis.

Diagnosis
Although DCM is currently believed to be a genetic disease, there are currently no genetic tests available for establishing early diagnosis and the diagnosis is, therefore based on phenotype characterization. Because of the two histopathological phenotypes, dogs of different breeds are screened differently for preclinical disease. Most breeds are screened using echocardiography, whereas Dobermans and boxers are also screened with 24-h (Holter) recordings because a single ECG trace is not useful, since it corresponds to a small fraction of the dog’s rhythm over a 24 hour period, and identification of abnormalities may be entirely fortuitous. Evidence of ventricular arrhythmia precedes echocardiographic evidence of DCM in the Doberman by some months or even years. Guidelines for diagnosing DCM were suggested in 2003 by the European Society of Veterinary Cardiology (ESVC) Taskforce Group. The echocardiographic diagnosis of DCM is based on the identification of myocardial (predominantly but not solely systolic) dysfunction with the active exclusion of other acquired or congenital cardiac disease. Evaluation of diastolic function may be valuable for determining prognosis as it has been shown in dogs that a restrictive pattern on mitral inflow and a short E wave deceleration time (<80 milliseconds) were significantly associated with a poor prognosis. However it appears that abnormalities...
in diastolic function do not appear to precede the systolic dysfunction or changes in chamber dimensions in dogs developing DCM, which makes it less informative in screening for DCM.

The suggested criteria for diagnosing DCM are likely to be changed in the future as new findings and new techniques become available to a broader veterinary community. New techniques that appear particularly promising are the Tissue-Doppler Imaging (TDI) and Tissue Tracking Imaging (TTI) techniques. These techniques allow characterization of global and regional myocardial function, which not only gives insight to the pathophysiology and characterization of myocardial disease in dogs, but appears to allow identification of diseased individuals before conventional echocardiography. Furthermore, the biomarker N-terminal pro-Brain Natriuretic Peptide (NT-proBNP) appears very promising in correctly identifying dogs with preclinical DCM.

**Treatment**

**Preclinical cases**

There are very few studies addressing the potential benefit of treating preclinical DCM. In dogs with cardiac dilatation, ACE-inhibitors (0.5 mg/kg q12-24h is the usual dose for most of the ACE-inhibitors) and/or the inodilator pimobendan (0.25 mg/kg q12h) are often introduced. Although reasonable, there is very little evidence that these drugs are beneficial at this stage. Many experts initiate antiarrhythmic therapy once an arrhythmia, such as atrial fibrillation or ventricular tachycardia, is discovered. In the case of ventricular tachycardia in boxers or Dobermans, commonly used antiarrhythmics include sotalol (2 mg/kg q12h), amiodarone (8-10 mg/kg q12h and reduce to 5 mg/kg q24h after 6 months; should be used with caution due to irreversible hepatotoxicity), or a combination between mexiletine (5-8 mg/kg q8h) and a low dose atenolol. A significant (85%) reduction of number of ventricular complexes is considered a therapeutic success, but it is not proven that this leads to improved survival. In the case of atrial fibrillation, therapy is usually aimed at reducing ventricular rate by introducing digoxin (0.22 mg/m² q12h or lower), or a beta-blocker (carvedilol (maximum dose 0.5 mg/kg q12h), metoprolol (maximum dose 1 mg/kg q8h), atenolol (maximum dose 1 mg/kg q12h), or propranolol (maximum dose 1 mg/kg q8h)). Caution should be used when introducing an antiarrhythmic drug with negative inotropic actions (such as beta-blockers) in a dog with a hypocontractile heart or in a dog with fluid retention (heart failure). The dose should be slowly titrated upwards starting with approximately 1/4 to 1/2 of the recommended dose.

**Symptomatic cases**

The minimal database required for managing the symptomatic DCM patient includes, in addition to echocardiography, a complete case history (including previous diagnostic tests and previous/current medication), a thorough physical examination, thoracic radiographs (to identify cardiomegaly and pulmonary edema and exclude other disease), abdominal radiographs and ultrasound examination in case of ascites, ECG recording (to identify and characterize an arrhythmia), and routine hematological tests and urinalysis (to exclude other disease and identify prerenal azotemia and disturbances in the fluid electrolyte balance). Therapy should be started once a tentative diagnosis has been established.

**Moderately to severely symptomatic dogs** should preferably be hospitalized and subject to intensive therapy that includes; minimizing stress, absolute rest, oxygen supplementation, intravenous injections of furosemide at a comparably high dose (initially 2-6 mg/kg, and then 2-3 mg/kg q1-2 h until pulmonary edema has improved). Severely symptomatic patients may require, in addition to the measures listed above, nitroglycerine ointment, pimobendan, or infusions of sodium nitroprusside and/or dobutamine (the latter two requires careful monitoring in a specialized clinic). Mildly symptomatic dogs or those with stabilized CHF may be managed at home. Successful CHF therapy is always based on a good collaboration between pet owner and veterinarian. It is important that the owner is educated on the following issues: how to monitor heart rate and respiratory rate at home; importance of regular habits and medication; the possibility to modify diuretic dose within a fixed range; avoid strenous exercise; diet; possible complications; and importance of rechecks. Chronic medical therapy includes diuretic therapy (furosemide) at a dose of 1-4 mg/kg q8-24h. Spironolactone at a dose of 2 mg/kg q12-24h and/or hydrochlorothiazide at a dose of 2-4 mg/kg q12h may be added in cases where the fluid retention is refractory to furosemide alone. Pimobendan and/or an ACE-inhibitor are often added to the diuretic therapy once the diagnosis of DCM has been established. Many dogs with DCM are tachycardic and may potentially benefit from heart rate control by adding digoxin or a beta-receptor blocker. However, introduction of a beta-receptor blocker should be done with care to avoid adverse side reactions and the dose should preferably be titrated upwards slowly. The above mentioned drugs are often added stepwise as the severity of clinical signs progress. Neutraceuticals such as taurine/L-carnitine and omega-3 fatty acid supplementation may be considered.

The strength of evidence for clinical efficacy of different heart failure drugs in canine DCM is not strong owing to
few published clinical trials. ACE-inhibitors have shown to improve quality of life variables in two clinical trials comprising clinical (symptomatic) DCM cases, but they have never been shown to improve survival. Pimobendan has been shown to improve quality of life variables and survival in a population of different breeds and in Dobermans when compared to placebo. The combined alpha- and beta-receptor blocker carvedilol was recently studied in DCM, but the authors could not detect any clinical or laboratory effect of the drug. Furthermore, the median survival time in propranolol treated DCM dogs was recently reported similar to DCM cases without beta-receptor blockade.

Summary
Dilated cardiomyopathy is a common disease in some large breed dogs, in which the disease leads to increased mortality. There are at least two distinct phenotypes of DCM: one that is characterized by systolic dysfunction and histopathological evidence of attenuated wavy fibers; and one characterized by ventricular tachyarrhythmias and histopathological evidence of myocyte degeneration, fibrosis and fatty infiltration. In the absence of genetic tests, dogs are currently screened for DCM in affected breeds using echocardiography and/or 24h-Holter ECG recordings. Suggested criteria for diagnosing DCM has been suggested, but these are likely to be changed in the future as new diagnostic techniques are developed. There is very little published evidence that any type of therapy has a prophylactic effect in preclinical DCM, even in arrhythmic patients. Therapy of symptomatic dogs varies in composition and intensity depending on severity of clinical signs and presence of arrhythmia, but chronic therapy should preferably include furosemide and pimobendan ± ACE-inhibitor.

Selected references