

Cardiomyopathy and Less Common Canine Heart Disease

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Dilated cardiomyopathy (DCM) is the second most common cause of congestive heart failure in the dog. Although congestive heart failure is the most commonly recognized complication of DCM, cardiac arrhythmias, episodic weakness, syncope, and sudden death are other recognized clinical manifestations.

Pathology - Dilated cardiomyopathy results in severe left and right ventricular and atrial enlargement (dilation of all 4 chambers) with modest thinning of the ventricular free walls and septum. The papillary muscles appear flattened, and the AV valve circumference increases due to cardiac dilation. Microscopic findings include mild endocardial fibrosis, mild interstitial fibrosis and edema, and focal areas of myocytolysis with a mild mononuclear infiltrate. Attenuated wavy fibers (i.e., myocardial cells < 6 μ m in diameter with a wavy appearance) have been described in dogs with DCM. Boxers with cardiomyopathy often develop fibrofatty replacement of the myocardium in the right ventricle and outflow tract and to a lesser degree the left ventricle, and this disease is currently termed arrhythmogenic right ventricular cardiomyopathy (ARVC). English bulldogs can also get ARVC.

Pathophysiology - DCM results in myocardial systolic dysfunction, although most cases also have significant diastolic dysfunction as well. Systolic pump failure leads to reduced cardiac output and results in activation of the neuroendocrine compensatory responses (sympathetic nervous system, renin-angiotensin system, etc.). Dilated cardiomyopathy leads to progressive cardiac dilation and AV valve dilation can lead to mitral or tricuspid valve incompetence. Congestive heart failure eventually results, although there seem to be differences in whether the predominant clinical manifestation will be cardiac arrhythmias, left-sided or right-sided heart failure.

Etiology - The disease is almost certainly a highly heterogenous condition. Clinical findings typical of DCM can be seen in a variety of other known causes of heart diseases in their advanced or late stages. In people, genetic causes have been identified for many families with DCM. Abnormalities in various cytoskeletal proteins appear to be the causes of the disease. In Boxer dogs with ARVC the defect is suspected to involve a specific genetic mutation, although reports vary relative to the frequency of this mutation in affected dogs, whether they get DCM or more arrhythmia, and there may be regional variations as well. At a minimum there appears to be more than one genetic mutation that might trigger ARVC in Boxer dogs. Similarly, there are at least 2 genetic mutations that might be associated with the development of DCM in Doberman pinschers. Taurine deficiency is a proven cause of DCM in the cat, and carnitine and taurine deficiency have been studied as potential causes or contributors to the development of DCM in dogs. Recently there has been interest in whether certain grain free diets that are high in legumes might cause DCM and/or contribute to taurine deficiency. In dogs with plasma or whole blood taurine deficiency, it appears that taurine supplementation can result in significant clinical improvement and longer than historically expected survival times in many dogs. Some dogs with DCM (esp. Cocker Spaniels, Newfoundland, Golden retriever) have been documented to have low plasma and whole blood taurine concentrations. It has been proposed that certain breeds of dogs, especially if fed certain lamb-based foods or high fiber/rice fiber foods or grain free diets, may

develop plasma or whole blood taurine deficiency. Post-viral inflammation, immune-mediated causes, and myocarditis-induced DCM have also been proposed as etiologies for the syndrome.

Signalment - Giant breed dogs such as Irish Wolfhound, Great Dane, St Bernard, Newfoundland, and German Shepherd Dogs are at risk. Doberman pinschers and Boxer are predisposed, and Cocker spaniels and Portuguese water dogs also have forms of the disease. Males predominate in many clinical surveys, although testing within a specific breed to search for frequency of DCM has often demonstrated an equal male/female distribution. An age range from 0.2-14 years has been reported, although onset of clinical signs between 4-8 years of age is typical for most breeds.

History - Common historical complaints include dyspnea, cough, syncope, weight loss, lethargy, exercise intolerance, abdominal distention, and anorexia. Clinical signs may appear acutely, although in retrospect many owners notice that the dog has been "slowing down" for several weeks. In the author's practice, cough in a mature large breed dog with a bronchial and interstitial pattern is rarely due to bronchitis and is sometimes due to dilated cardiomyopathy with early heart failure.

Physical examination - Physical examination can be normal in the early (occult) stage of the disease. Common auscultatory findings include a soft (II-III/VI) systolic murmur of mitral or tricuspid valve regurgitation and/or a cardiac gallop, typically an S3 gallop. When CHF is present findings can include dyspnea, pulmonary crackles, jugular vein distention, hepatosplenomegaly, ascites, weight loss, and diminished heart and/or lung sounds if pericardial and/or pleural effusion is present. Mucous membrane pallor or cyanosis may be noted and arterial pulses are often weak. Cardiac arrhythmias with pulse deficits are often noted on physical examination.

Electrocardiography - The electrocardiogram can be normal, but some ECG abnormality is present in most animals. Common findings include evidence for left ventricular enlargement or biventricular enlargement, left atrial enlargement pattern (P-mitrale), and conduction disturbances like left bundle branch block. Common arrhythmias include atrial fibrillation, supraventricular depolarizations and ventricular depolarizations.

Thoracic radiographs - Generalized cardiomegaly is often present, usually with a VHS > 10.5v. Congestive heart failure can cause pulmonary venous distention and interstitial or alveolar pulmonary infiltrates (pulmonary edema). In some dogs, right heart failure or biventricular failure predominate and enlargement of the caudal vena cava, hepatomegaly, ascites, and/or pleural effusion are present.

Echocardiography -Classic echocardiographic findings include left ventricular dilation with thinned walls and atrophied papillary muscles and markedly diminished LV contractility (reduce fractional shortening to less than 25%). There is reduced thickening of the IV septum and the LV free wall, left atrial enlargement, increased E point to septal separation on M-mode, reduced aortic root motion, RV and RA dilation. A modified Simpsons approach to measuring the left ventricle can also be useful to document breed-specific normal vs abnormal findings.

Clinical pathology – Laboratory testing is often normal. Elevated BUN or creatinine (prerenal azotemia due to inadequate cardiac output, possibly diuretic/ACE inhibitor induced following initiation of therapy), elevated liver enzymes (chronic passive congestion), mild hypoproteinemia, and hypokalemia, hypochloremia, and metabolic alkalosis can be seen after high dose diuretic therapy. A mild increase in WBC count is often noted.

NT-proBNP testing can be helpful to identify affected dogs both at the time of CHF and possibly as a screening tool for certain breeds. There is a chance that NT-proBNP will start to rise in some dogs, even before the onset of overt cardiac dilation. Most dogs with DCM and CHF should have an NT-proBNP > 2000 pmol/L. In my view, all large breed dogs over 3-4 years of age that present with cough or collapse of undetermined origin should have an NT-proBNP performed, and if the value is elevated then an echocardiogram is indicated.

Treatment - The most common therapies include pimobendan, diuretics (furosemide), ACE inhibitors (lisinopril, benazepril, enalapril), moderation of dietary sodium, and exercise restriction. Some veterinarians will also include spironolactone in the list of medications to be started at the onset of CHF, while others might wait to add in this drug later. Antiarrhythmic medications are used as needed. Pimobendan can be a very useful to control clinical signs and improve survival times in dogs with DCM and CHF. Taurine and/or carnitine therapy has been used in some cases. Newer information indicates that if DCM is found in an asymptomatic stage that initiation of pimobendan can slow the progression towards CHF and prolong overall survival time.

Doberman pinscher cardiomyopathy: In Doberman pinschers, the disease is usually present for a significant period before any clinical signs are manifest, and this syndrome has been termed "occult cardiomyopathy". Many Doberman Pinschers have either ECG evidence of ventricular arrhythmias (via Holter monitor recording) or echocardiographic criteria indicative of early cardiomyopathy at a time when they are completely asymptomatic. It is recognized that a significant proportion of Doberman pinschers with DCM die suddenly, and this is part of the enthusiasm for identifying the disease in the occult phase. NT-proBNP testing may also help to identify early disease, as most healthy Doberman pinschers have an NT-proBNP concentration < 600 pmol/L – higher values may be a good trigger to recommend echocardiography. Once CHF develops the long term outlook is guarded, and survival beyond 12 months is generally considered a very good outcome.

Boxer ARVC/Boxer cardiomyopathy – The age of onset is 0.5 to 15 years (mean = 8 years), the male to female ratio is nearly equal, and the identification of an arrhythmia or the development of syncope are often the first manifestations of the disease. Ventricular arrhythmias common and can be refractory to antiarrhythmic therapy. Boxers often get rapid, sustained ventricular tachycardia at rates of 350-400/minute or faster, and the VPC morphology often has a LBBB pattern (positive QRS for the VPC in Lead II). Sudden death due to ventricular arrhythmias/ventricular fibrillation is common. Radiographs and echocardiograms may be normal in early disease. This disease has been noted to be associated with fibrofatty replacement of the right ventricular wall and to a lesser extent inflammation and fibrofatty changes in the left ventricle and is generally accepted to be best described as arrhythmogenic right ventricular cardiomyopathy (ARVC). English bulldogs can also get ARVC. Syncope is common in Boxers, and in very young boxers, cardiomyopathy must be differentiated from vasovagal syncope, a more benign cause of syncope. Holter monitor recording to search for ventricular arrhythmias is used to identify affected dogs, especially in dogs used for breeding, and is also useful as a screening tool for dedicated

owners. It has been proposed that unaffected Boxers should have less than 100 VPC in a 24-hour ECG recording, although the number needed to claim "affected with ARVC" might be less consistently agreed upon by cardiologists. Boxers with cardiomyopathy can eventually develop typical signs of cardiac dilation with reduced fractional shortening (e.g., classic DCM). Sotalol can be useful in controlling ventricular arrhythmias in these dogs, and another option is the combination of mexiletine and atenolol, or mexiletine and sotalol, or amiodarone. Carnitine may also be supplemented as carnitine deficiency was described in a family of Boxers with cardiomyopathy, although the majority of Boxer dogs in the author's practice area do not derive dramatic clinical benefit from this supplement.

English and American Cocker Spaniel Cardiomyopathy - The typical age at the time of diagnosis in 10 months to 13 years (average 6-10 years). Many affected Cocker spaniels have been documented to have low plasma or whole blood taurine concentrations. Following supplementation with taurine +/- carnitine, taurine concentrations have risen and some individual dogs have been documented to have appreciable echo improvements and have been able to be tapered from some, or sometimes all, cardiac medications.

Pericardial effusion

Pericardial effusion is most commonly seen in dogs, and it is one of the most common cardiac emergencies seen at Tufts University. The two conditions most commonly associated with pericardial effusion in the dog are cardiac neoplasia and idiopathic ("benign") pericardial effusion. The cardiac tumors most frequently reported are hemangiosarcoma originating in the right atrial wall or atrial appendage and heart base tumors (chemodectoma, aortic body tumor, thyroid carcinoma). Idiopathic pericardial effusion has also been described as benign pericardial effusion and idiopathic hemorrhagic pericardial effusion. Thickening of the parietal pericardium and epicardium with fibrosis and mild inflammation are the predominant histologic features of idiopathic pericardial effusion. Mesothelioma is another cause for pericardial effusion, and it can be very difficult to differentiate idiopathic pericardial effusion from mesothelioma. Lymphoma is an uncommon cause in dogs but is one of the most common causes of pericardial effusion in cats. Pericardial effusion has also been reported in cats in association with feline infectious peritonitis, congestive heart failure, renal failure, metastatic neoplasia, coagulopathies, and bacterial pericarditis. Primary cardiac tumors resulting in pericardial effusion are uncommon in the cat and idiopathic pericardial effusion is uncommon in this species.

Clinical signs of pericardial effusion include lethargy, weakness, abdominal distention, tachypnea, and collapse. Middle age to older dogs are predisposed to pericardial effusion, with the German shepherd dog and Golden retriever predisposed to both right atrial hemangiosarcoma and idiopathic pericardial effusion. Boxers, bulldogs, and Boston terriers have been reported to be predisposed to heart base tumors (chemodectoma). Physical exam findings can include muffled heart sounds, jugular venous distention, weight loss, ascites, pallor, tachycardia, cardiac arrhythmias, collapse, pallor, and pulsus paradoxus.

Laboratory testing may identify hypoproteinemia, mild anemia, leukocytosis, hepatic enzyme elevation or pre-renal azotemia, or anemia. High elevations of cardiac troponin I in dogs is associated with hemangiosarcoma.

Thoracic radiographs may show mild to severe globoid cardiomegaly with loss of cardiac chamber definition. The edges of the heart often look very well defined on the DV view due to lack

of cardiac motion. Enlargement of the caudal vena cava is variably noted, and pleural effusion may interfere with evaluation of the cardiac silhouette. Dogs with heart base tumors may have an increased soft tissue density at the heart base and/or tracheal displacement. Cats frequently demonstrate moderate cardiomegaly.

Electrocardiographic findings can include low voltage QRS complexes (< 1 mv in all leads in the dog), electrical alternans, ST segment elevation, or cardiac arrhythmias.

Echocardiography is the most sensitive and specific means for detection of pericardial effusion and is identified as an echo free space between the myocardium and the pericardium. This space is observed circumferentially with two dimensional echocardiography, and the heart may swing to and fro within the pericardial sac. Diastolic right atrial and ventricular collapse suggests cardiac tamponade. In animals with cardiac neoplasia or other mass lesions, the masses can be imaged directly, and the location of the mass (atrium or heart base) can often be identified. Echocardiography is currently the best test to determine whether neoplasia is present or not.

Pericardiocentesis is the preferred therapy for cardiac tamponade, providing prompt relief of clinical signs. Pericardiocentesis is performed with the patient in lateral or sternal recumbency. The right hemithorax is clipped, blocked, and aseptically prepared between the third and eighth intercostal space, from the sternum to above the costochondral junction. The fourth or fifth intercostal space is selected (guided by echocardiography if available) and a long (5 cm) large bore catheter is attached to polyethylene tubing, a three-way stopcock, and a large syringe. Under continuous ECG monitoring, the catheter and needle are cautiously advanced toward the heart and gentle suction is applied to the syringe. Once pericardial fluid is obtained, the catheter is advanced over the needle into the pericardial sac and as much fluid as possible is removed. Complications of pericardiocentesis can include coronary artery laceration, ventricular arrhythmias, and subsequent exsanguination into the pleural space in cases of active intrapericardial hemorrhage. Cytologic evaluation of the pericardial effusion is often consistent with a hemorrhagic effusion and thus can be unrewarding, however in dogs with infection or lymphosarcoma the cytology can be diagnostic. For this reason, we often submit the fluid for cytology, despite the relatively low diagnostic yield.

Dogs suspected of having idiopathic pericardial effusion are initially managed conservatively with pericardiocentesis. Approximately 50% of dogs will respond to one or two therapeutic pericardiocentesis. The remaining dogs will have recurrence several days to several years after pericardiocentesis. Anti-inflammatory drugs such as NSAID may be valuable, although there are no controlled studies to document this in dogs (NSAID are better than corticosteroids in people). Dogs that require frequent or repeated pericardiocentesis usually benefit from pericardiectomy. Many dogs remain asymptomatic after surgery, while others have recurrent pleural effusion. Thoracoscopy can be used as a minimally invasive surgical method to perform pericardiectomy.

Hemangiosarcoma is typically incurable, has already metastasized by the time of diagnosis and surgical attempts to remove the mass are associated with short survival times. However survival with surgery plus chemotherapy (doxorubicin) is reportedly better than survival without surgery (3-6 months vs days to 1 month). Heart base tumors are slower growing and less likely to metastasize, and though they are difficult or impossible to excise, pericardiectomy is frequently useful to relieve cardiac tamponade and surgery has been shown to prolong survival compared to conservative management. Palladia may also be useful in dogs with chemodectoma. Animals with lymphosarcoma may be treated with chemotherapy.

Active pericardial hemorrhage, for example due to coagulopathy or secondary to left atrial tear, represents the exception to the rule that pericardiocentesis is always indicated with cardiac tamponade. If tamponade is life threatening, pericardiocentesis is performed with the realization that further pericardial hemorrhage may result in reoccurrence of tamponade and/or exsanguination into the thorax.

- 1) In dogs with dilated cardiomyopathy, an S3 gallop might be noted. This sound is due to:
 - a. A leak at the mitral valve
 - b. Mitral valve prolapse
 - c. Oscillation of the heart at the end of rapid ventricular filling
 - d. An atrial premature depolarization
- 2) Doberman pinschers often have a long asymptomatic period and this phase is often referred to as:
 - a. Occult cardiomyopathy
 - b. Obliterative cardiomyopathy
 - c. Arrhythmogenic Phase
- 3) Dilated cardiomyopathy with congestive heart failure is often associated with:
 - a. Systolic dysfunction
 - b. Diastolic dysfunction
 - c. Both
- 4) An NT-proBNP value above 2,000 pmol/L in a large breed dog with cough should trigger concern for a diagnosis of:
 - a. Chronic bronchitis
 - b. Congestive heart failure
 - c. Aspiration pneumonia
 - d. Pneumothorax
- 5) Serious ventricular arrhythmias in a Boxer dog should trigger concern for a diagnosis of:
 - a. Arrhythmogenic right ventricular cardiomyopathy
 - b. Arrhythmogenic left ventricular cardiomyopathy
 - c. Hemangiosarcoma
 - d. Pulmonary neoplasia
- 6) An NT-proBNP concentration > 600 pmol/L in an otherwise healthy Doberman pinscher might trigger a decision to:
 - a. Recommend echocardiography to look for occult cardiomyopathy
 - b. Recommend echocardiography to look for obliterated cardiomyopathy
 - c. Recommend a urinalysis to look for proteinuria
 - d. Recommend a thyroid test to search for hyperthyroidism
- 7) Pimobendan might be recommended to treat:
 - a. Congestive heart failure
 - b. Pre-clinical dilated cardiomyopathy
 - c. Pulmonary hypertension
 - d. Pre-clinical degenerative mitral valve disease
 - e. All of the above
- 8) Dogs with pericardial effusion and a heart base mass:
 - a. Have a longer survival time if they go to surgery for a pericardiectomy
 - b. Rarely get recurrent pericardial effusion after pericardiocentesis
 - c. Usually die from metastatic disease
- 9) Cardiac tamponade due to pericardial effusion can be identified as:
 - a. Collapse of the right heart on echocardiography
 - b. A globoid shaped cardiac silhouette

- c. Electrical alternans on the ECG
 - d. An elevated NT-proBNP concentration above 3000 pmol/L
- 10) Standard therapy for CHF in dogs with dilated cardiomyopathy usually includes:
- a. Pimobendan, spironolactone and thyroxine
 - b. Pimobendan, and ACE inhibitor, and a diuretic**
 - c. An ACE inhibitor, diuretic, and a calcium channel blocker
 - d. A diuretic, a calcium channel blocker, and thyroxine