Degenerative Mitral Valve Disease in Dogs

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Introduction

Degenerative Mitral Valve Disease (DMVD) is the most frequent heart disease in the dog, and the most common cause for congestive heart failure (CHF). Knowing the stage of disease has implications for cardiac therapy, anesthesia, fluid administration, and for prognosis. This session will review the disease and present some information on newer tests and interventions.

Overall Incidence

The incidence of DMVD is reported as being between 11% (clinical determination) and 42% (necropsy determination) depending on the age of the dog and method of examination. The mitral valve is most commonly affected, and many dogs have some disease in both the mitral and tricuspid valves. The aortic and pulmonic valves may be affected but clinical disease in small animals is unlikely. The disease is primarily a non-inflammatory, myxomatous degeneration of the atrioventricular valves that is commonly referred to as **endocardiosis**.

Signalment

DMVD is most common in small to medium sized breeds of dogs, and the incidence of CHF is increased in male dogs relative to females (1.5 to 1.0). DMVD is slowly progressive with lesions sometimes beginning early in life (e.g., by 2 to 3 years microscopically), but overt clinical disease is unlikely before middle age. Cardiac decompensation and CHF typically occurs in later life (e.g., 5 to 14 years of age or older). Up to 90% of Cavalier King Charles spaniels can be affected and the disease is common in miniature poodles, Dachshunds, Shi Tzu dogs, and many other small breed dogs. The disease is less common in large breed dogs but ca be seen in German shepherd dogs, Doberman pinschers, Weimaraner, and other breeds.

Etiology

The etiology for chronic valvular heart disease is unknown. A genetic tendency to develop the disease has been proved in the Cavalier King Charles Spaniel. Serotonin levels may be elevated in some affected dogs or at certain stages of the disease. The exact interplay of genetics, diet, exercise, or other risk factors is uncertain at this time.

Clinical Syndromes

A wide range of clinical presentations are possible for dogs DMVD. Many dogs will be presented for routine examination and at that exam a cardiac murmur, mid-systolic click, or arrhythmia will be noted. Baseline testing can be offered to the owner and is often helpful for comparison at subsequent examinations or for determination of whether early therapy is indicated. In dogs with a III/VI or louder murmur, therapy to delay the onset of CHF might be available and baseline thoracic radiographs and echocardiography are recommended. Alternatively, signs resulting from congestive heart failure may be the cause for presentation with intermittent cough, nocturnal dyspnea or altered sleep habits, abdominal distention and exercise intolerance being presenting complaints. Syncope or collapse may be the trigger for a veterinary exam, and collapse is common in dogs at the first onset of CHF, most likely due to a vagally-mediated event.

Physical examination

Auscultation of a cardiac murmur is a classic finding in DMVD, and an extra systolic sound known as a mid-systolic "click" has been associated with early disease, due to mitral or tricuspid valve prolapse. A third heart sound, typically an S3 gallop, can develop at the time of CHF. In dogs with DMVD there is a tendency for the intensity of the murmur to be roughly correlated with the severity of cardiac dysfunction, and most dogs with CHF have at least a IV/VI systolic murmur over the left cardiac apex.

Dogs with CHF may have tachypnea, dyspnea, orthopnea, or anxiety with a reluctance to lie down. A cough may be noted or elicited by tracheal palpation. Cough may end in swallowing or the production of a white foam; in advanced cases, a blood tinged froth is produced. Mucous membranes are pink in early stages, but may progress to a muddy to somewhat cyanotic color with severe pulmonary edema due to left-sided CHF. Pulmonary auscultation may also reveal increased respiratory sounds which progress to "crackles" with the onset of alveolar edema. Hepatomegaly and ascites may be evident in dogs with RCHF from advanced disease and/or significant tricuspid regurgitation, and in these cases the jugular veins are typically distended. The femoral pulses are often normal in dogs with DMVD, unless severe decompensation has developed. Cardiac arrhythmias, when noted, are more likely to be supraventricular premature depolarizations, although other arrhythmias are possible.

Thoracic Radiography

Cardiomegaly, especially left atrial enlargement, is identifiable in most dogs with DMVD. On the lateral projection, the left atrium is visualized at the caudal-dorsal aspect of the cardiac silhouette and can be seen to enlarge with disease progression. On the DV view the LA bulge is noted at the 2:00 to 3:00 location. Left atrial and left ventricular enlargement result in elevation of the trachea and carina. The left mainstem bronchus may become elevated (compressed) in cases of marked left atrial enlargement and cause cough related to airway compression. Pulmonary venous dilation occurs as dogs get closer to CHF, but dogs with acute rupture of a chordae tendinae might not have as much atrial enlargement and may lack pulmonary vein distention. Early pulmonary edema is seen as a diffuse increase in interstitial density in the hilar or caudal lung fields, progressing to fluffy densities and air bronchograms (alveolar pattern) with the onset of alveolar edema. Ascites, hepatomegaly +/- splenomegaly may be present in dogs with concurrent tricuspid valve disease.

Studies that have followed dogs longitudinally have identified that dogs with a VHS of > 11.5v are at increased risk for development of CHF in the next 6 to 12 months.

Cardiac Biomarkers – BNP and troponin testing

Recent studies have documented that BNP testing can help guide treatment decisions. Both c-BNP and NT-proBNP tests are available, but there is more research to guide interpretation of NT-proBNP. Dogs with DMVD that have an NT-proBNP < 1500 pmol/L have a lower chance of developing CHF in the next 6 to 12 months (maybe 10-20% chance for CHF), while dogs with an NT-proBNP concentration > 1500 pmol/L might have a 70% or greater chance to develop CHF in the next 6 to 12 months. The presence of an NT-proBNP > 1500, plus a VHS > 11.5, plus a markedly enlarged left atrium on echocardiography helps to more specifically identify dogs at high risk for CHF, and these 3 tests can be seen as complimentary (for the dedicated owner who is not limited financially).

Dogs with DMVD and CHF usually have an NT-proBNP > 1800 pmol/L, and most dogs with active CHF have a value > 3000 pmol/L. Identification of a normal range NT-proBNP should result in reconsideration of a diagnosis of CHF – it might be CHF, but it is more likely that the dog has clinical signs due to something other than CHF.

Dogs with DMVD can have elevated cardiac troponin I concentration, and there is a chance that more significantly elevated values might be associated with a somewhat worse outcome. Cardiac troponin I is not predictably elevated in dogs with DMVD, so the routine measurement of this value has less clinical application (pending additional research).

Electrocardiography

ECG findings in dogs with DMVD can include evidence of left ventricular hypertrophy and left atrial enlargement (P mitrale). ST segment slurring is seen in some dogs with LVH, and ST depression may result from hypoxemia. Sinus rhythm or sinus tachycardia are typical, although many dogs have atrial premature depolarizations. Ventricular arrhythmias are uncommon in dogs with DMVD and when seen might trigger concerns for a worse prognosis, a concurrent disease, or recent myocardial insult (maybe get a cardiac troponin I concentration). Atrial fibrillation develops in some dogs, especially those with marked left atrial enlargement.

Echocardiography

Diffuse valvular thickening may be appreciated, particularly of the "anterior" mitral leaflet, in dogs with DMVD, and ruptured chordae tendineae may be seen as the valve tip prolapses into the LA during systole. As the quality of images from echo machines has gotten better and better, more and more dogs with DMVD are identified to have a least a small chordal rupture, even in the still compensated stages of the disease. Left atrial enlargement is often severe in dogs with CVD and CHF. Fractional shortening is normal to exuberant in dogs with CVD, until the latter stages of the disease. Mitral regurgitation can be clearly identified on color-flow Doppler. Tricuspid valve prolapse and regurgitation are also commonly seen. Pulmonary hypertension, evidenced by an increased tricuspid regurgitation velocity, often develops as CHF advances. The E wave from mitral inflow is often increased, as is the E:E' (or some prefer the E:IVRT). Dogs with CHF should have at least moderate left atrial enlargement, unless CHF is due to an acute ruptured chordae tendinae. Endocardial splitting can develop and may result in pericardial effusion and cardiac tamponade, or the split may go through the interatrial septum and result in a left-to-right ASD. Pleural effusion may develop in dogs with biventricular heart failure.

Treatment of dogs with DMVD

Treatment of DMVD can be divided into several stages of CHF or clinical scenarios. Below is an attempt to summarize these stages and clinical scenarios.

Stage A – The dog without a murmur that is at risk for DMVD

Except for dogs used for breeding, there is no need to identify these dogs. It is prudent to have these dogs eat a balanced diet and to maintain a normal body condition score. Certain screening protocols and breeding recommendations have been proposed for dogs actively used in a breeding population.

Stage B – The asymptomatic dog with a murmur due to DMVD

Dogs with a I/VI or a II/VI murmur usually require no additional testing.

Dogs with a III/VI or louder murmur might be candidate for pimobendan administration. Since pimobendan, in the EPIC trial, resulted in a significant delay until the onset of CHF (perhaps 15 months) and prolonged survival time, it seems appropriate to start dogs on pimobendan if the fulfill the 4 key criteria from the EPIC trial. These 4 criteria are 1) at least a III/VI murmur; 2) VHS > 10.5v; 3) LA/Ao > 1.6 on a short axis echocardiographic view; and 4) a normalized left ventricular end diastolic dimension (LVIDd) of > 1.7 via echocardiography. Thus, to determine whether pimobendan is clearly indicated in the asymptomatic dog with DMVD, one needs a physical exam, and thoracic radiographs, and an echocardiogram -- these are the criteria we typically use to determine eligibility for starting pimobendan. As some owners cannot afford echocardiography, some researchers have suggested that a VHS of > 11.5v might identify the population of dogs that would have fulfilled these criteria. Others have suggested that since an NT-proBNP > 1500 pmol/L identifies dogs at increased risk for developing CHF within a year, the presence of VHS > 11.5v or an NT-proBNP > 1500 pmol/L might be triggers for pimobendan administration.

The role for ACE inhibitors (e.g., enalapril, benazepril, lisinopril) or angiotensin receptor blockers in management of asymptomatic dogs with DMVD is more hotly debated, and perhaps the role is less clear-cut. In our clinics, we try to obtain blood pressure measures on dogs with DMVD and if a dog is persistently hypertension (above 160 mmHg) then we start an ACEi. We also might look for concurrent proteinuria, as this is another indication for giving an ACEi, and if proteinuria is documented in a dog with DMVD then we start the ACEi. Finally, for dogs already on pimobendan who have marked LA enlargement, where CHF seems imminent, we also will start an ACEi. If we elect to start an ACEi then we obtain baseline kidney values and electrolytes, we repeat these values in 10-14 days, and the recheck them q 6 months until the onset of CHF.

Some would recommend dietary sodium restriction, and at least having the owner paying attention to treats fed to the dog. Maintenance of a normal BCS is recommended at this stage, as well as feeding a complete and balanced diet. Rechecks are performed every 6 to 12 months for examination +/- thoracic radiographs +/- echocardiography +/- NT-proBNP +/- blood pressure measurement.

Stage C – The dog with DMVD and CHF

The management of CHF will be covered in greater detail in the following lecture, but a few summary points are presented here. The ACVIM consensus statement recommends that a certain number of diagnostic tests be done to confirm a diagnosis of CHF, and those tests (plus the ones we usually perform) include thoracic radiographs, echocardiography, an ECG (especially if arrhythmia), a CBC and serum biochemistry profile, a blood pressure, and an NT-proBNP.

Drug therapy at the onset of CHF usually includes furosemide (or torsemide), and ACE inhibitor such as enalapril, benazepril or lisinopril, and pimobendan. Many clinicians will also add in spironolactone, and the upcoming ACVIM consensus statement may include a recommendation to use all 4 of these drugs once CHF is diagnosed. Once dogs become refractory to this combination of medications then additional manipulations include optimizing doses of current medications, going to higher (off label) doses of pimobendan, adding in sildenafil if pulmonary hypertension is moderate to severe, adding in more diuretics (e.g., torsemide, injectable furosemide, hydrochlorothiazide), adding in hydralazine, or other medications.

Dietary sodium moderation is usually recommended at this stage, with attention paid to all dietary sources of sodium – severe sodium restriction might not be needed. We usually also recommend either a diet that is high in omega-3 fatty acids or fish oil supplementation.

1) For the dedicated owner, identification of what grade of cardiac murmur should lead to recommendation for thoracic radiographs and echocardiography?
    a. Murmur greater than or equal to I/VI
    b. Murmur greater than or equal to II/VI
    c. Murmur greater than or equal to III/VI
    d. Murmur greater than or equal to IV/VI
    e. Murmur greater than or equal to V/VI
2) An NT-proBNP concentration > 1500 pmol/L might trigger:
    a. Concerns for development of CHF in the next 6 to 12 months
    b. Suspicion that the dog might be a candidate to start pimobendan
    c. A recommendation to perform an echocardiogram
    d. All of the above
3) In a dog with cough and a cardiac murmur, and NT-proBNP concentration of < 900 pmol/L should lead to:
    a. Initiation of diuretics, and ACE inhibitor and pimobendan
    b. Initiation of sildenafil
    c. Consideration that respiratory disease might be the cause of the cough, instead of CHF
4) In a dog with a chronic cough and cardiomegaly plus pulmonary infiltrates who also has sinus arrhythmia, a loud S2, no murmur, and evidence of right heart enlargement on echocardiography, the most likely diagnosis is:
    a. Cor pulmonale (right heart enlargement due to chronic lung disease)
    b. DMVD and CHF
    c. Dilated cardiomyopathy and CHF
    d. PDA and CHF
5) In an asymptomatic dog with documented DMVD and a IV/VI systolic murmur, which 3 other factors would most appropriately trigger a decision to start pimobendan?
    a. VHS > 10.5, LA/Ao on echo > 1.6, and normalized LVIDd on echo > 1.7
    b. The presence of atrial premature depolarizations, a systolic blood pressure of 150 mmHg, and the presence of hepatomegaly
    c. A serum alkaline phosphatase > 1000 U/L, evidence of left heart enlargement on the ECG, and a cardiac troponin I concentration > 0.04 ng/ml
6) In a dog with DMVD and Stage C heart disease, initiation of at least 3 medications is recommended. Which of the following lists medications recommended at this stage?
    a. Sildenafil, benazepril, and hydrochlorothiazide
    b. Amiodarone, pimobendan and spironolactone
    c. Pimobendan, enalapril and furosemide
    d. Torsemide, amlodipine, and spironolactone
7) Dietary sodium moderation should take into account which of the following?
    a. The main diet of the dog
    b. Treats given
    c. Foods used to administer pills
    d. All of the above
8) In advanced CHF, the use of sildenafil is recommended when:
    a. Anemia has developed due to chronic disease
    b. Moderate to severe pulmonary hypertension is documented based on tricuspid regurgitation velocity
    c. The dog is also documented to have Cushing's disease (hyperadrenocorticism)
9) Omega-3 fatty acid (fish oil) supplementation has been proposed to have several benefits. Which of the following are the most commonly cited benefits?
    a. Reduction in cardiac arrhythmia and blunting of muscle loss/cardiac cachexia
    b. Immunomodulation resulting in improved prevention of secondary bacterial pneumonia
    c. Plasma membrane stabilization such that less fluid leaks out of damaged pulmonary capillaries.
10) In a dog with asymptomatic DMVD and moderate to marked cardiomegaly, which of the following statements is most correct?
    a. Benazepril use has been shown to delay the onset of CHF by an average of almost 15 months
    b. Pimobendan use has been shown to delay the onset of CHF and improve overall survival
    c. Spironolactone use has been documented to block norepinephrine receptors and cease further cardiac enlargement