



Brief Update on Myxomatous Mitral Valve Disease (MMVD)

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Abbreviations: CHF- congestive heart failure, EPIC - Evaluation of Pimobendan In dogs with Cardiomegaly, LA - left atrium, LA:Ao - left atrium: aorta, LV - left ventricle, LVIDd - left ventricle internal diameter in diastole, VLAS - vertebral left atrial score, VHS - vertebral heart score

Introduction

Myxomatous mitral valve disease is the most common heart disease of dogs, accounting for about 75% of canine heart disease. Smaller breed dogs (<20kg) are predisposed, but larger dogs are also sometimes affected.

Clinical signs of left heart failure due to MMVD may include coughing, dyspnoea, tachypnoea, exercise intolerance, collapse, syncope, cardiac murmur, cardiac arrhythmia, irregular pulse, and pale or cyanotic mucous membranes. It is important to keep in mind the high prevalence of chronic tracheobronchial disease in the same population most at risk for MMVD. Thus do not presume that CHF is present if a typical left apical murmur is heard in a coughing dog without further investigation. Patients with respiratory sinus arrhythmia and also those with an in-clinic respiratory rate of <30 are very unlikely to have CHF.

Pathophysiology

The characteristic finding of MMVD is progressive degeneration of the mitral valve in particular (the tricuspid valve is also involved in about 30% of cases). The cause remains unknown, but it is clear that there is a hereditary component in certain breeds. Deformation of the valve apparatus is caused by changes in cellular components and extracellular matrix, which eventually interferes with normal function and allows regurgitation. In severe cases, the regurgitant fraction may be more than 75%. The valvular regurgitation increases cardiac workload because of volume overload and the left ventricle and left atrium undergo compensatory eccentric hypertrophy to maintain forward stroke volume. As the disease progresses other complications may develop such as arrhythmias, myocardial failure and rupture of chordae tendinae, which further compromises cardiac pumping function.

Classification

The American College of Veterinary Internal Medicine (ACVIM) staging system for MMVD is as follows:

<i>Stage A</i>	Dogs at high risk, no identifiable structural disorder
<i>Stage B1</i>	Structural heart disease present, no clinical signs, no radiological or echocardiographic evidence of cardiac remodelling or remodelling that is not severe enough to meet criteria that warrant initiating treatment
<i>Stage B2</i>	Structural heart disease present, no clinical signs, cardiac remodelling that meets criteria to initiate treatment
<i>Stage C</i>	MMVD severe enough to cause clinical signs of heart failure, responsive to standard treatment
<i>Stage D</i>	End-stage MMVD with signs of heart failure refractory to standard treatment

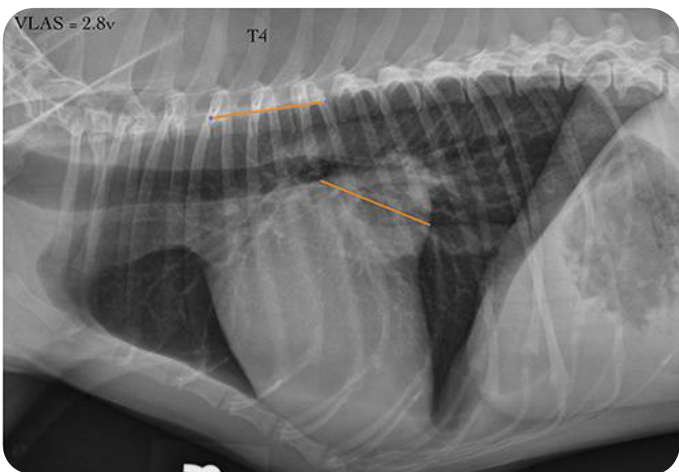
When presented with a patient with a heart murmur and no apparent clinical signs, it is important to try and establish if the patient is in Stage B1 or B2, because it is advisable that patients in Stage B2 should start treatment. Treating these patients with pimobendan can significantly delay the onset of heart failure as was demonstrated by the EPIC (Evaluation of Pimobendan in Dogs with Cardiomegaly) study.

Thus radiography and echocardiography are recommended. However, echocardiography is the only way to conclusively diagnose MMVD. In the absence of echocardiography, the VLAS (Vertebral Left Atrial Score) may be useful: The VLAS is a measurement that evaluates left atrial size and provides a method of quantifying atrial dilation. A line is drawn from the centre of the most ventral aspect of the carina to the most caudal aspect of the LA where it intersects with the dorsal border of the caudal vena cava. Transpose the line to the cranial edge of the T4 vertebral body. VLAS values of ≥ 3 are likely consistent with a classification of stage B2. A baseline radiograph when the dog is asymptomatic is useful and also allows one to look for concurrent tracheal and/or bronchial disease. Blood pressure measurement is recommended.

Echocardiography is used to examine valve morphology and movement, evaluate cardiac chamber enlargement, assess the size and velocity of the regurgitant jet, evaluate for pulmonary hypertension, calculate the left atrium:aortic root ratio (LA:Ao) (a measure of the extent of left atrial dilation) and calculate fractional shortening.

Criteria to classify a patient into Stage B2 are: Murmur intensity 3/6 or more, LA:Ao ratio on right-sided short axis view in early diastole of ≥ 1.6 , normalised LVIDD ≥ 1.7 , breed adjusted VHS of > 10.5 . Echocardiographic evidence of LA or LV enlargement is the most reliable evidence.

If no echocardiography is available a general breed VHS of ≥ 11.5 (or comparable breed adjusted VHS, if available) as well as the VLAS should be used.



Treatment

Stage A

All small breed dogs and especially those with known breed predisposition such as Cavalier King Charles Spaniels, Dachshunds, Miniature Poodles, should have annual auscultation.

No drug or dietary treatment is recommended

Stage B1

No drug or dietary treatment is recommended. Evaluation every 6-12 months with echocardiography (or radiography if echocardiography unavailable)

Stage B2

Start Pimobendan at 0.25-0.3mg/kg q12h. Provide a diet with mild sodium restriction and adequate protein and calories. Pimobendan was shown to prolong the preclinical period by a median of 15 months and can decrease the heart size.

Some cardiologists also advise starting an angiotensin-converting enzyme (ACE) inhibitor such as enalapril or benazepril at this stage although clinical trials on the efficacy of ACE inhibitors in stage B have shown mixed results.

Stage C

Acute in hospital cases: Intravenous furosemide by continuous rate infusion (CRI) at 0.66-1mg/kg/hr or 2mg/kg iv every 1-2 hrs until respiratory rate improved (or total dose of 8mg/kg over 4 hrs reached). Oxygen supplementation. Butorphanol, buprenorphine or acepromazine are drugs to be considered to treat anxiety. Pimobendan (0.25-0.3mg/kg q12hrs). Consider Dobutamine and ACE inhibitors.

Chronic outpatient: Furosemide 2mg/kg q8-12hrs, Spironolactone in addition at 1-2mg/kg q12-24hrs. Pimobendan and ACE inhibitor. For intractable cough consider bronchodilators and cough suppressants.

Stage D

Patients that require furosemide at dosages ≥ 8 mg/kg over 24hrs to maintain comfort despite concurrent pimobendan, ACE inhibitor and spironolactone treatment have progressed to stage D.

Pimobendan may be increased off-label to 0.3-0.5mg/kg q8hrs. The potent loop diuretic torsemide can be used at 0.1-0.2mg/kg po q24hrs instead of furosemide. Sildenafil (1-2mg/kg po q8hrs) for patients with evidence of pulmonary hypertension.

Digoxin may be added when atrial fibrillation is present. Amlodipine or hydralazine may be added for additional afterload reduction.

Prognosis

The EPIC study indicated that the administration of pimobendan to patients in Stage B2 could delay the onset of heart failure by, on average, 15 months.

This is very significant because once heart failure is present, survival times are usually less than a year. Several studies have looked at survival times. In one study of 105 dogs being treated medically the mean survival time (MST) for dogs in Stage B2 was 649 days, 220 days for stage C and 55 days for stage D.

Surgery

As medical therapy only addresses the symptoms, surgery offers the hope of an actual cure. Mitral valve repair surgery is being done at a few centres in the world.

Currently, it is available in Japan, Singapore, France, the United Kingdom and more recently in the USA at the University of Florida (in conjunction with the Japanese team led by cardiologist Masami Uechi). Dr Uechi has performed around 700 surgeries and claims a success rate of around 90%. Despite the cost of surgery (around USD 45000), there is a waiting list.

Artificial mechanical valves have not been successful due to the formation of clots and thus instead of a valve replacement, a valve repair is performed. This consists of replacing any ruptured or stretched chords with artificial chords made from Gore-Tex. Gore-Tex is a patented type of waterproof fabric made with a variant of polytetrafluoroethylene (PTFE) known as expanded PTFE (ePTFE).

It is commonly used as a waterproof, breathable fabric in the clothing industry. The porosity of Gore-Tex permits the body's own tissue to grow through the material. Gore-Tex is used in a wide variety of medical applications, including sutures, vascular grafts, heart patches, and synthetic knee ligaments. A draw-string type of suture is also placed around the valve annulus to draw it back down to a smaller size. These two steps combined improve the contact between the valve edges, meaning less leakage occurs across the mitral valve. As it is a repair, the valve will not return to normal and a small amount of leakage will remain in most cases, but at a much lower level than previously.

There are studies underway to seek ways of non-invasive valve replacement or repair with catheter-based interventions, but the small size of many of the dogs that develop MMVD limits what can be done non-invasively to treat the disease.

Other future treatments may involve stem cell therapy (currently being studied at Cornell University).

Unfortunately, a cure or treatment that is affordable and can extend life for many years is probably still far in the future.

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MULTIPLE-CHOICE QUESTIONS

QUESTION 1

Which of the following statements are false?

- MMVD accounts for around 75% of canine heart disease
- A coughing dog with a heart murmur can be presumed to have CHF
- Dogs with respiratory sinus arrhythmia are unlikely to have CHF
- There is a high prevalence of chronic airway disease in older small-breed dogs
- None of the above

QUESTION 2

Which of the following statements are false?

- MMVD affects the tricuspid valve in about 50% of cases
- The cause of MMVD is unknown
- The left atrium and left ventricle undergo compensatory hypertrophy
- Complications of MMVD can include arrhythmias and myocardial failure
- None of the above

QUESTION 3

Which of the following statements regarding the classification of MMVD is false?

- Stage D: End-stage CHF
- Stage C: Dogs that have CHF and responding to standard treatment
- Stage B1: Cardiac remodelling that meets the criteria to initiate treatment
- Stage B2: Cardiac remodelling that meets the criteria to initiate treatment
- None of the above

QUESTION 4

Which statement is true?

- It is not important to distinguish between Stage B1 and B2
- Echocardiography is recommended for every dog with a murmur
- VLAS is a measurement of left ventricular size
- VLAS values of ≥ 2 are likely consistent with a classification of stage B2
- None of the above

QUESTION 5

Which of the following criteria are used to classify a patient into Stage B2:

- Murmur intensity 3/6 or more
- LA:Ao ratio of ≥ 1.6
- normalised LVIDD ≥ 1.7
- Breed adjusted VHS of > 10.5
- All of the above

QUESTION 6

Which of the following statements regarding treatment is false?

- Dogs in Stage A should have annual auscultation
- Dogs in stage B1 should start on pimobendan
- Stage C: Treat with pimobendan, furosemide, spironolactone, ACE inhibitor
- Dogs in stage B2 should start on pimobendan
- Consider a bronchodilator for intractable coughing

QUESTION 7

Regarding the treatment of patients in Stage D, which statement is true?

- Torsemide can be used instead of furosemide
- Pimobendan dose can be increased to every 8 hrs
- Sildenafil for patients with evidence of pulmonary hypertension
- Amlodipine or hydralazine may be added for additional afterload reduction
- All of the above

QUESTION 8

Regarding surgery for MMVD, which statement is true?

- Involves open heart surgery to replace the valve
- Involves catheter-mediated valve replacement
- Involves replacing ruptured or stretched chords
- Is available in South Africa
- None of the above

QUESTION 9

Regarding Gore-Tex, which statement is false

- It is a waterproof fabric used in the clothing industry
- It is not used in human medical applications
- It is porous allowing body tissue to grow through it
- It is used in MMVD surgery
- None of the above

QUESTION 10

Regarding the VLAS measurement, which statement is true?

- Aims at quantifying left atrial size
- Aims at quantifying left ventricular size
- A line is drawn from the centre of the most ventral aspect of the carina
- A line is drawn from the centre of the most dorsal aspect of the carina
- A and C



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