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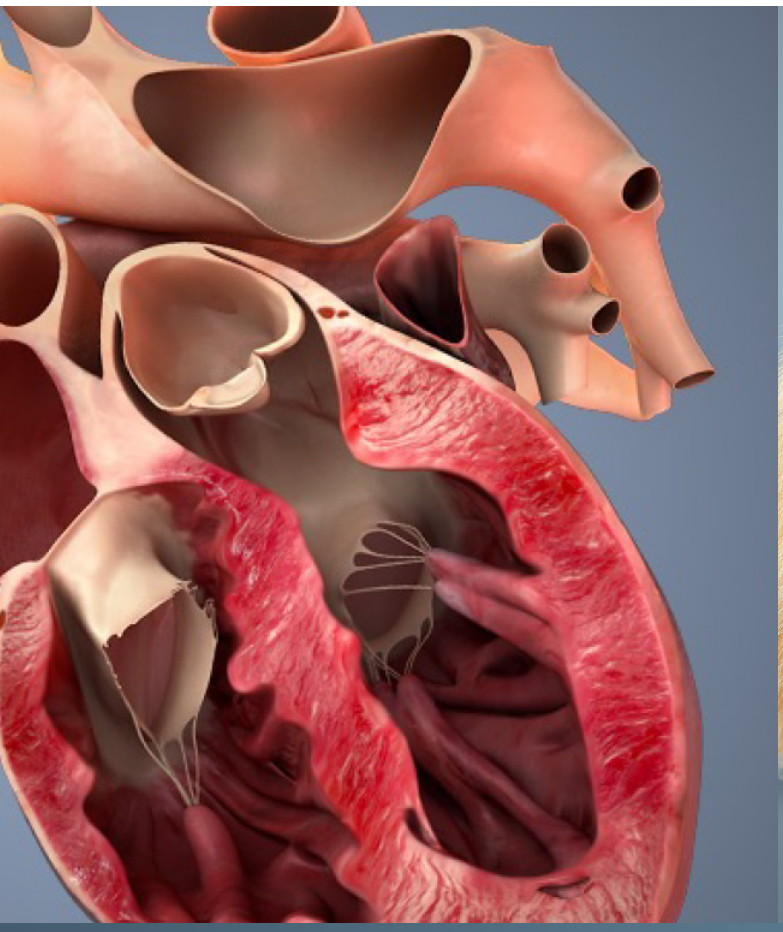
Clinical & Nutritional Management of Myxomatous Mitral Valve Disease in Dogs



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Diagnosis and Management of MMVD in dog

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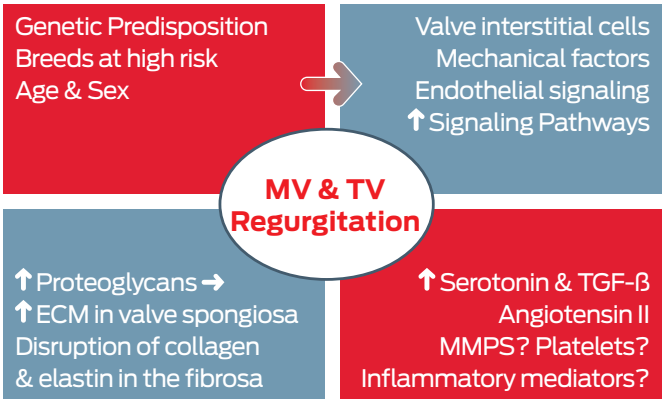
Introduction

The most important heart disease of the dog is chronic mitral regurgitation caused by myxomatous mitral valve disease (MMVD). The condition is variously called *degenerative valvular disease*, *valvular endocardiosis*, or simply *mitral regurgitation* (MR), although the last term does not specify the underlying disease. Concurrent involvement of the tricuspid valve with myxomatous degeneration is common and leads to valve prolapse and tricuspid regurgitation (TR). It is estimated that 70% of canine heart disease is caused by myxomatous valve disease. The clinical disorder is easily recognized with the stethoscope. Echocardiographic examination can confirm valvular lesions, valvular regurgitation, and cardiac remodeling.

Myxomatous valvular disease is characterized by nodular thickening of the mitral and tricuspid valve leaflets, an endocardium that is smooth and glistening, and by valve leaflets that can appear expansive and prolapse into the atrium. The histologic lesion is one of myxomatous change with disruption of the central mitral valve layers by acellular proteoglycans (glycosaminoglycans). Severity of the valvular disease has been graded at autopsy by Whitney, and this spectrum of disease is apparent when viewed by two-dimensional (2D) echocardiography. Ruptured chordae tendineae are common and associated with progressive MR as well as the acute onset of congestive heart failure (CHF).

Enlargement of the left atrium (LA) and left ventricle (LV) and variable enlargement of the right heart chambers develop over time. Other complications of MMVD include: 1) pulmonary hypertension (PH), 2) left atrial splitting with cardiac tamponade (or an acquired atrial septal defect), and 3) atrial arrhythmias including premature atrial complexes and atrial fibrillation (AF). Fortunately, studies by Borgarelli and colleagues have shown that 6-year cardiac mortality in dogs diagnosed with preclinical disease is relatively low (about 10%). However, considering the millions of dogs affected by MMVD, these complications result in frequent clinical presentations.

Figure 1. Factors involved in MMVD

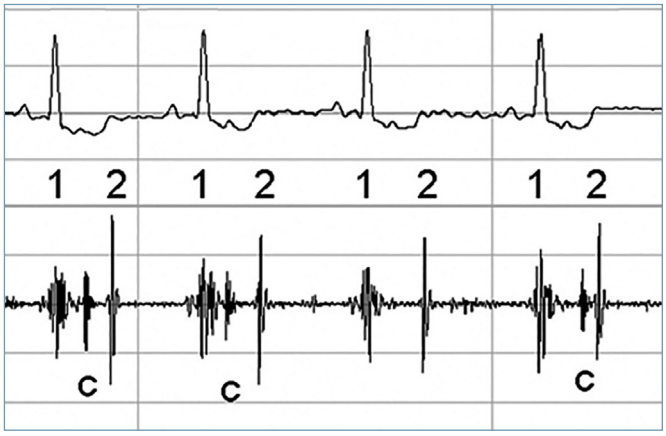


The proposed pathogenesis of MMVD has been summarized in the extensive reviews of Markby (2017) and Oyama (2020). As shown in *Figure 1*, increasing age and genetic predisposition are important. Transformation of the valve is promoted by serotoninergic, TGF-beta, and potentially angiotensin II pathways. Functional changes in valve interstitial cells are thought to underlie the myxomatous change. Endothelial cell signaling, metalloproteinase activity, and other factors could also be relevant. The result is an increased deposition of proteoglycans that expand the extracellular matrix of the valve spongiosa and disrupt the fibrosa layer, eventually leading to valvular incompetency. The process develops over many years. Typically, a four- to six-year interval occurs between the first detection of a focal, soft murmur and the onset of CHF. Chronic MMVD progresses to CHF in a substantial number of dogs. This syndrome is triggered by limited forward flow and increased venous pressures caused by MR. Left atrial compliance and the volume of MR determine clinical signs to a large degree. Global LV systolic and diastolic function are usually hyperdynamic in smaller dogs, even in the setting of CHF. Functional characteristics of heart failure include impaired exercise capacity, secondary pulmonary dysfunction (tachypnea, cough, respiratory distress), and metabolic disturbances related to congestion and impaired organ perfusion. Both quality and duration of life are limited by cardiac failure and there is keen interest in treating CHF and preventing the syndrome, if possible.

Diagnosis

Smaller breeds are at highest risk. It is especially common in the Cavalier King Charles spaniel, Dachshund, and Shih Tzu among dozens of affected breeds. Chronic MMVD in larger breeds causes less valve thickening but progressive LV systolic dysfunction is more likely to occur, such that the end-stage of disease can be confused with dilated cardiomyopathy. Clinical signs vary from none (typical), to cough from left bronchial compression, to coughing and respiratory distress due to life-threatening pulmonary edema. A subset of dogs, especially those with chronic pulmonary hypertension or AF, develop predominantly right-sided CHF. These signs include marked exertional limitations, collapse and syncope, jugular venous distension, and ascites. Premature atrial complexes are common, and AF is particularly deleterious; it often leads to decompensation. Primary bronchopulmonary comorbidities create diagnostic challenges. These include laryngeal dysfunction, tracheal collapse, chronic bronchitis, bronchomalacia, and pulmonary fibrosis.

Figure 2. Canine: MV click

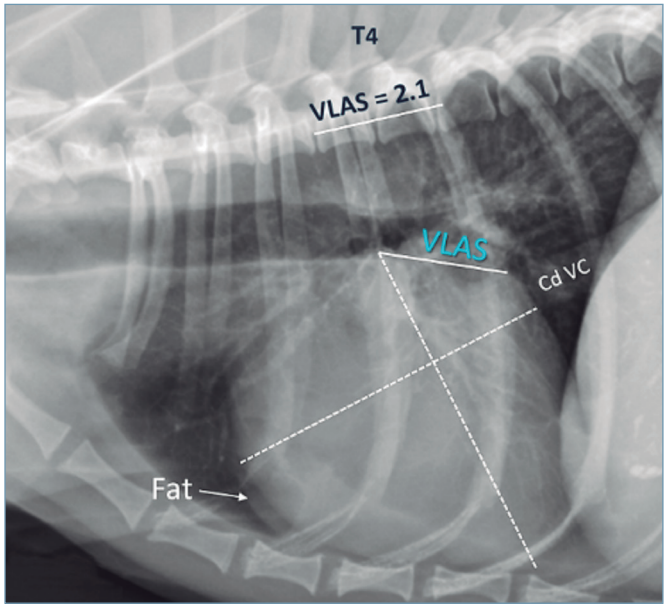


Auscultation reveals the first detectable physical examination findings in the form of a systolic murmur or systolic click(s). Single or multiple clicks are thought to indicate prolapse of the valve leaflets (*Figure 2*); these can be loudest over the right side due to tricuspid valve prolapse. Mitral clicks can vary in their timing and are often misinterpreted as (diastolic) gallop sounds. In contrast to an S3 gallop, isolated clicks are systolic, higher pitched, and unassociated with CHF. The systolic murmur of MR is the hallmark feature of MMVD. It is loudest where it radiates down to the left apex or immediately dorsal over the mitral area. The murmur can be soft, localized and decrescendo with mild MR, but eventually the murmur increases in intensity throughout systole and radiates widely. There is a general correlation to murmur intensity and the severity of disease, but this association is most consistent for grades 1/6 and 2/6 (localized) murmurs. Loud holosystolic murmurs of MR, even those with precordial thrills (grades 5/6 and 6/6), occur in both dogs with CHF as well as those without any symptoms. Hypotension from severe CHF or a ruptured LA can result in a marked decrease in murmur intensity. Conversely, high systemic blood pressure increases the intensity. Tricuspid regurgitation is suggested by a prominent murmur over the right thorax, especially when accompanied by a precordial thrill or a murmur of different character. When the murmur of TR is louder than that of MR, either PH or a laterally directed regurgitant jet is likely.

Dogs with MMVD should have noninvasive blood pressure measurements performed. This is indicated to screen for systemic hypertension secondary to chronic kidney disease or hyperadrenocorticism. In some situations, early antihypertensive therapy with an angiotensin converting enzyme (ACE) inhibitor, telmisartan, or amlodipine might be needed to lower blood pressure. This is also relevant to dogs with CHF.

Radiographic findings of MMVD are characterized by progressively increasing size of the LA and LV. Gradual cardiomegaly might occur over four or five years before CHF supervenes. Increased chamber volumes also correlate to elevated concentrations of the natriuretic peptides, which are released from the stretched LV and LA. Thoracic radiographs are indicated to stage MMVD, identify comorbidities responsible for any respiratory signs, and verify the presence of CHF. It is practical to track vertebral heart sum (VHS) and vertebral left atrial sum (VLAS), *Figure 3*, over yearly examinations. Studies

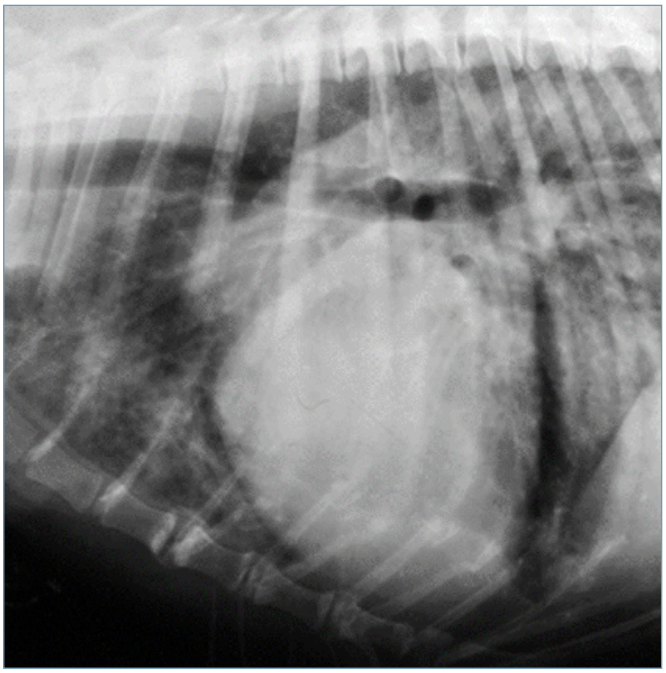
Figure 3. Measuring cardiac size



by Lord and colleagues have shown that sudden increases in VHS (for example about 0.1 vertebral body/month), are a strong predictor of impending CHF. This VHS "velocity" is a reasonable substitute for dogs who cannot undergo serial echocardiographic examinations; it also can help decide when to begin treatment (see below).

Key radiographic findings of left sided heart failure include dilation of the LA and LV; pulmonary venous congestion or distension; and pulmonary infiltrates compatible with cardiogenic edema. These are typically bilateral interstitial and alveolar infiltrates located around the bronchial hilum. However, fulminant edema can be widespread (*Figure 4*). Sometimes pulmonary infiltrates demonstrate a right-sided preponderance. Pleural effusions – usually small – can be evident, and are most likely to be moderate to large only in end-stage CHF complicated by AF. Pulmonary edema in the urgent care setting can be appreciated by visualizing multi-centric, nonattenuating reverberations (B-lines) during a point-of-care ultrasound examination. This finding, in conjunction with clinical signs of MMVD and pulmonary edema, are sufficient to initiate diuretic therapy for CHF. Findings should be confirmed by radiography once the patient is stable. Radiographic signs of cardiogenic pulmonary edema should improve within 24 to 48 hours of diuretic therapy. Improvement is often accompanied by reduction in overall heart size, indicating reduced venous pressures and cardiac filling.

Figure 4. Congestive heart failure



Echocardiography is used to confirm the diagnosis and objectively stage dogs with MMVD. The typical 2D imaging features of thickened and prolapsing mitral valve leaflets with LV and LA dilation and Doppler evidence of MR support the diagnosis. Ruptured chordae tendineae might be visualized and cause flail leaflets. The characteristic color Doppler jet of MR is eccentric, and multiple jets are often evident. Spectral Doppler studies can further demonstrate the regurgitant jet and can provide insight into left atrial and systemic arterial pressures. In general, mitral filling waves less than 1 m/s are unlikely to be associated with active CHF. Velocities exceeding 1.3 m/s indicate a higher risk. Assessment of systolic function is challenging in primary MR, due to altered loading conditions. Nearly every small breed dog with CHF maintains a hyperdynamic LV chamber. Estimating volumes and systolic function from M-mode studies in this setting are discouraged, as they are overinflated. The key point is that the patient can be experiencing life-threatening pulmonary edema despite having a normal to increased ejection fraction on a point-of-care ultrasound exam. Diastolic function is also difficult to assess because LV preload and systolic function are increased. Abnormalities on the right side usually show tricuspid valve prolapse or thickening, TR, and variable amounts of chamber enlargement. Often there is dilation of the pulmonary trunk, branch pulmonary arteries, or other findings suggestive of pulmonary hypertension such as a high velocity TR jet. In left-sided CHF, the pulmonary veins are dilated relative to arteries.

Clinical laboratory tests and biomarkers are obtained to gauge the risk of cardiac enlargement, CHF, and comorbidities. Elevated blood troponin (cTnI) indicates heart muscle injury. Although increases in cTNI are usually mild, they can carry prognostic information. High circulating B-type or brain natriuretic peptide (BNP) or the nitrogen terminal of its prohormone (NT-pBNP) suggests structural heart disease and volume overload, with or without overt CHF. There are emerging data regarding the use of this biomarker for predicting Stage B2 in dogs with moderate to loud murmurs, especially when combined with results of thoracic radiography or echocardiography or other clinical laboratory tests. Progressively increasing NT-pBNP, or values exceeding 1,500 to 1,600 pmol/L, highlight a higher risk for CHF. Reductions in concentrations might indicate a more favorable prognosis once therapy has started. However, natriuretic test results should not be assessed in isolation, nor should any therapy be initiated based solely on a high value.

Routine serum biochemistries, especially renal function tests and electrolytes, should be obtained in CHF patients.

These can be abnormal owing to pre-existing disease or following therapy for CHF that contracts the plasma volume (diuretics) or alters intra-renal hemodynamics (ACE-inhibitors). Mild to moderate azotemia is a common trade-off during therapy of advanced CHF. These are acceptable provided appetite is still good and signs of uremia are not evident. Nevertheless, rising serum urea nitrogen (and creatinine) should prompt reconsideration of drugs and dosages that affect renal function. Anemia, infection, and hyperthyroidism (from excess or inappropriate supplementation) increase demands for cardiac output and should be ruled out in decompensating cardiac patients. A heartworm antigen test should be obtained from dogs living in or arriving from geographic regions endemic for dirofilariasis.

Staging

The four major clinical stages of myxomatous mitral valve disease, as outlined by the consensus panel of the ACVIM, are summarized in *Table 1*. Management of dogs in various stages is discussed later. The greatest challenge is identification of dogs who have sufficient cardiac remodeling to warrant treatment to delay CHF (Stage B2).

Table 1

ACVIM Stages of Myxomatous Mitral Valve Disease	
Stage A	Dogs at risk for developing myxomatous valvular disease
Stage B	A dog with objective evidence of MMVD (murmur of MR) without signs of heart failure
B1	Heart size is either normal or cardiomegaly is insufficient to begin therapy
B2	Sufficient remodeling (cardiomegaly) has occurred to begin treatment based on evidence from a clinical trial
Stage C	A dog is currently in congestive failure or previously experienced CHF (and is receiving medical therapy)
Stage D	A dog with CHF that is refractory to "standard" drug therapy & standard dosages
	Specific criteria for Stage D are less agreed (see text)
	Dogs in Stages C and D might be treated at home or in hospital

These criteria are largely guided by the results of the EPIC clinical trial by Boswood et al., 2016 (*Table 2*). A dog is classified as Stage B2 when the following criteria are met:

Table 2

EPIC Study Criteria for Stage B2 of Myxomatous Mitral Valve Disease
Small breed (<20 kg), older dogs (6 years of age or greater)
Grade 3/6 murmur or louder murmur of mitral regurgitation (radiating murmur)*
Normalized LV end-diastolic dimension (LVEDDN) ≥1.7. This is calculated from the M-mode (or 2D) echocardiogram as: LVEDDN = LVEDD (cm)/ bodyweight(kg)$^{0.294}$
LA/Ao (short-axis method) ≥1.6 indicating left atrial dilation
Vertebral heart scale/sum/score (VHS) >10.5**

* Ideally mitral regurgitation is confirmed using Doppler echocardiography

** The VHS criterion of >10.5 is normal for many dogs (see text)

As an example of calculating the LVEDDN: for a 9 kg dog, with a 2.9 cm LV diastolic diameter, LVEDDN = $2.9/9^{0.294}$ = 1.52. This dog would not fulfill criteria for Stage B2 and not be treated. Many people assume that finding LA dilation is an indication for treatment, but there is no evidence for that assumption. Additionally, both acquisition and measurement variabilities inherent to the short-axis LA/Ao are higher than for the minor LV dimension (LVEDD).

The VHS criterion of > 10.5 VB also is insufficient to warrant staring therapy, as many healthy dogs, including Cavalier King Charles spaniels, fall within this range. Dogs with a VHS >11.5 to 12 VB are more likely to fulfill EPIC criteria for Stage B2, but even these higher VHS cutoffs are normal for some breeds. In the author's opinion, serial radiographs measuring VHS and VLAS are very useful (Figure 3) when echocardiography cannot be done. A VHS velocity ≥0.1 VB/month over 6 months or more, in combination with a VLAS ≥3.0, justifies classifying a dog in Stage B2. As most dogs are never examined by echocardiography, this is a practical alternative.

Medical Therapy for Myxomatous Valve Disease

There is no treatment for **Stages A and B1**. The potential value of **therapy for Stage B2** has been evaluated in four clinical trials: SVEP, VETPROOF, EPIC, and DELAY (see references). The major findings are that pimobendan is effective in delaying the onset of CHF in dogs with Stage B2 MMVD; whereas, the value of renin-angiotensin-aldosterone system (RAAS) inhibition has either been unproven or demonstrated only modest trends towards delaying CHF and remodeling. In the author's opinion a pivotal study with aggressive RAAS inhibition combined with pimobendan has not yet been completed for Stage B2.

The benefits of pimobendan in Stage B2 MMVD were shown in the EPIC study where the median time to the primary (composite) endpoint was 1228 days in dogs treated with pimobendan (dosed at 0.2 to 0.3 mg/kg PO q12h) compared to 766 days (95% CI: 667-875) in the placebo group (P = .0038). In bottom line terms, the initiation of pimobendan therapy in dogs fulfilling the EPIC criteria "delayed the onset of CHF by nearly 15 months, on average". Overall survival benefit was not as dramatic (about 5 months), although survival in the pimobendan group was longer (median survival time 1059 days; 95% CI: 952-NA compared to the placebo median survival time of 902 days; 95% CI: 747-1,061 days). Additionally, reverse remodeling with pimobendan can occur at this stage of disease; this is characterized by reduction in LV size.

Whether an ACE-inhibitor or spironolactone should be added in Stage B2, depends in part on one's perspective about the results of trials incorporating RAAS inhibition, and practically the availability of cost-effective generic inhibitors of RAAS. The author recommends if prescribed that higher ends of the dose range be used. For example, aim for dosages of 0.5 mg/kg PO q12h for enalapril (or an equivalent "pril") and 2 mg/kg PO q24h for spironolactone to optimize the potential for benefit. Adverse effects of these are low in dogs unaffected by CHF.

Therapy of dogs in stages C and D is more straightforward. With surgical repair of the valve impractical for all but a handful of dogs, medical therapies are used. Patients in acute CHF should receive intravenous furosemide, oral or intravenous pimobendan, sedation (butorphanol) and oxygen if required. Abdominocentesis is used to relieve pressure on the diaphragm and abdominal organs (including the kidneys) if there is a large volume ascites. In selected cases, direct-acting vasodilators that include sodium nitroprusside, nitroglycerin (IV or ointment), amlodipine and hydralazine (oral or IV) can be helpful to treat fulminating pulmonary edema.

Chronic medical therapy of Stage C MMVD is summarized in the following *Table 3*. This medical therapy should be augmented with appropriate dietary measures that minimize sodium intake while insuring consumption of sufficient calories and of high quality protein.

Table 3

Medical Therapy of Myxomatous Mitral Valve Disease	
Furosemide (Torsemide)	Loop Diuretic (torsemide for Stage D)
Pimobendan	Inodilator (positive inotrope + vasodilator)
Enalapril | Benazepril | Quinapril	Angiotensin converting enzyme inhibitors
Spironolactone	Mineralocorticoid receptor blocker
Other vasodilators (see text)	Acute CHF; Systemic or Pulmonary Hypertension; Stage D (refractory CHF)
Antiarrhythmic drugs	If needed for atrial fibrillation or ventricular ectopy

Conceptually one can consider long-term therapy as involving drugs with strong hemodynamic effects – loop diuretics and pimobendan – and drugs with effects of more chronic benefit in terms of inhibiting adverse effects of RAAS, namely ACE-inhibitors and spironolactone. There are clinical trials supporting the use of each of these agents for chronic CHF, although in the author's opinion, there is no study that combines all four drug types optimally. Generally, clinical trials of CHF in MMVD have focused on comparing one drug (or a drug combination) to either a placebo or a drug of another class. Although the VALVE study did not show a benefit of ACE-inhibitor therapy in dogs with Stages C and D heart failure, there are some challenges interpreting the trial results related to the dosages of furosemide and the administration of the ACE-inhibitor. The ACVIM consensus panel (of which the author is a member) recommended using each of the aforementioned drug classes in combination. Bottom line: it would be fair to say there are acknowledged differences of opinion among cardiologists regarding the value of RAAS inhibition in CHF caused by MMVD.

Dogs in **Stage D heart failure** are refractory to "standard" treatments. Although the precise definition of stage D is debated, most dogs will be receiving "quad therapy" (*Table 3*) and at least 6 to 8 mg/kg furosemide daily. For these dogs, administration of higher and more frequent (extralabel) dosages of pimobendan are considered (such as 0.3 to 0.5 mg/kg PO q8h). In terms of diuretic therapy, substitution of torsemide for furosemide is recommended (starting at 0.8 to 1 mg/kg of torsemide for each 10 mg of furosemide). For example, a dog receiving 20 mg of furosemide three times daily might receive in its place 2.5 mg of torsemide twice daily with follow-up serum biochemistries measured in 5 to 7 days. Eventually impaired renal function limits the dosage of loop diuretics, and in some cases, reduction of the ACE-inhibitor doses or replacing a "pril" with amlodipine might be needed.

Other treatments can be considered in end-stage CHF. Dogs with systemic hypertension or those with a sufficient blood pressure to tolerate arterial vasodilation might benefit from afterload reduction with amlodipine (using low initial dosages of 0.05 to 0.1 mg/kg/day PO). In cases with severe, symptomatic PH the addition of sildenafil (1-3 mg/kg PO q8h) or another PDE-V inhibitor, can improve exercise status and potentially help to control any ascites. It is recommended PDE-V inhibitors be withheld until effective treatment for left-heart failure has occurred and sufficient time has elapsed (at least two weeks) for reflex pulmonary arterial vasoconstriction to resolve. This is particularly important in dogs with severe LA dilation. If AF has developed, diltiazem and digoxin (if acceptable renal function) are added for rate control.

Home monitoring of dogs with MMVD should begin in stage B2 and focus on "symptoms" of heart failure and quality of life indicators. These include comfortable sleeping, a good appetite, and the ability to perform at least mild exercise. The dog's general attitude and the absence of persistent clinical signs such as coughing or collapsing are other therapeutic goals. Resting or sleeping respiratory rate per minute (normally <25/minute for most dogs) is a practical way for the client to monitor their dog for emergence of pulmonary edema and prevent unplanned (stressful and costly) veterinary visits. Chronic pulmonary congestion increases lung stiffness and leads to tachypnea. Significant upward trends (5 to 10 breaths per minute) or values exceeding 35 breaths per minute are usually indicators that a dog should be reevaluated, at a minimum, with a telephone call and review of current therapy. Of course, medication compliance is always a concern and should be a focus of every client discussion.

Conclusion

Myxomatous valvular heart disease is a common disorder of the dog and responsible for the majority of cases of canine CHF. This degenerative disease is recognized in dogs of susceptible age and breed mainly through auscultation of the typical murmur of MR. The diagnosis of MMVD can be confirmed with echocardiography and further staged with radiography and circulating biomarkers. Owing to the long time course of MMVD, therapy should not be instituted prematurely but instead be based on staging through cardiac imaging. Using the ACVIM stages of MMVD, appropriate diagnostics, pharmacotherapy, dietary management, monitoring, and life-style modifications can be directed to delay the onset of CHF as well as treat this syndrome should it develop. In terms of medical management, pimobendan can substantially delay the onset of CHF in stage B2, and treatment with loop diuretics, pimobendan, and RAAS inhibition can provide good control of CHF for some time. There are unanswered questions about the optimal combination of drugs and their timing in the management of this disease. In the future wider availability of mitral valve surgery and catheter delivered devices can be anticipated.

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Nutritional Management in Canine Heart Disease

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Myxomatous mitral valve disease (MMVD) is the most common naturally occurring heart disease in dogs, and progresses to advanced heart disease in approximately 30% of affected dogs.[1] The American College of Veterinary Internal Medicine (ACVIM) guidelines for diagnosing and managing heart disease in dogs also propose dietary changes based on stage of disease. According to this system, the nutrients of concern for dogs with heart failure include sodium, long-chain omega-3 polyunsaturated fatty acids (n-3 PUFA), and adequate protein and calories.[2] These guidelines fail to consider all the nutrients that may be important to cardiac health. This paper and presentation discuss a broader view of nutrition for heart health, starting with demonstrating how nutrition can aid dogs even with subclinical valvular heart disease.

Nutrients for MMVD heart disease

Transcriptomic and metabolomics data show that MMVD is associated with deranged energy metabolism, increased oxidative stress and inflammation.[3] A cardiac protection blend (CPB) of nutrients was formulated to address these changes, in order to slow or prevent the progression of MMVD. The CPB includes medium-chain triglycerides (MCTs) containing C8 and C10 medium-chain fatty acids (MCFAs) as an alternative energy source, omega-3 fatty acids from fish oil, carnitine precursors and taurine, magnesium, and antioxidants.

The healthy heart relies predominantly on oxidation of long-chain fatty acids to produce up to 90% of its ATP, but fatty acid oxidation is disrupted in heart disease.[3,4] MCFAs and ketone bodies from medium-chain triglycerides can provide an alternate energy source. Compared to longer chain fatty acids, MCFAs are more rapidly available, increase the oxidative capacity of muscle mitochondria, decrease production of reactive oxygen species (ROS), and are relatively anti-inflammatory.[5,6]

The long-chain omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), help to reduce inflammatory mediators known to be associated with heart failure, such as TNFα, IL-1β and -6 and others, as well as reducing oxidative stress.[7,8] EPA also leads to increased production of the anti-inflammatory mediators resolvins and protectins. Other benefits associated with EPA and DHA are reduced cardiac arrhythmias, reduced cardiac remodeling and dysfunction, and reduced blood pressure.[7,9] In addition to direct cardiovascular benefits, the anti-inflammatory effects of EPA and DHA might help reduce the risk for cachexia, which is a common complication of advanced heart disease in dogs.[7]

Magnesium (Mg) serves as a co-factor in hundreds of enzymes, has a role in glucose and energy metabolism, protein production, ATP synthesis and utilization, and is important for cardiovascular function.[10-12] In humans, there is a significant association between low Mg and cardiovascular diseases or heart failure.[12,13] Mitral valve prolapse is strongly associated with Mg deficiency in humans, as well as in Cavalier King Charles Spaniel dogs,[14,15] although a causal role has not been confirmed. Magnesium also helps reduce inflammation and oxidative stress.[10,16] Inflammation plays an important role in the pathogenesis of heart failure, and inflammatory cytokines are elevated in the blood of dogs with MMVD.[17]

Taurine is a beta-amino acid that can be produced within the body from methionine and/or cysteine. In dogs, endogenous production is normally adequate to maintain health, however, some exceptions to this have been reported.[18,19] A deficiency of taurine can cause dilated cardiomyopathy (DCM) in both cats and dogs.[18-20] Taurine deficiency reduces the functionality of the mitochondrial respiratory chain, leading to decreased ATP production.[21]

Carnitine is an amino acid derivative that is produced endogenously from the amino acids lysine and methionine, or provided in the diet. Carnitine serves a key role in fat metabolism by transporting long-chain fatty acids across the inner mitochondrial membrane where they are used to produce ATP. Between 17% and 60% of dogs with DCM have a myocardial carnitine deficiency, many despite having normal plasma carnitine.[18] This suggests that dogs with DCM may experience problems getting carnitine into the heart muscle. Carnitine precursors support increasing

serum carnitine, which may increase myocardial uptake, and do not contribute to TMAO (trimethylamine N-oxide) production.

Heart disease is associated with increased production of reactive oxygen species and oxidative stress. Dietary supplementation with antioxidants, such as vitamin E, are important to decrease oxidative stress.

Dietary study in dogs with MMVD

A diet containing the CPB nutrients, or a control (CON) diet, were fed to 19 dogs with Stage B1 or B2 MMVD.[4,22] Within the 6-month study, the CON dogs showed an average 10% increase in left atrial diameter and LA/Ao, both key markers for worsening MMVD, while the CPB dogs showed an average decrease of 3% ($P < 0.05$). Mitral regurgitation (MR) worsened for 2 CON dogs (25%). In the CPB dogs, just one dog (10%) showed worsening MR while 30% improved over baseline ($p < 0.05$). Consistent with this, more than 33% of CON dogs showed progression of MMVD from stage B1 to B2 by 6 months, but none of the CPB dogs had progressed ($p < 0.01$).[4] Serum untargeted metabolomic analysis from this study identified 102 metabolites with significant changes. Most of the differences were related to fatty acids and to improved markers of energetics, reduced oxidative stress and inflammation.[22]

This study showed that the CPB blend of nutrients was able to beneficially impact the heart and slow early changes caused by MMVD in these dogs. These benefits included improved cardiac function, improved energetics, and reduced oxidative stress and inflammation in MMVD dogs.[4, 22]

Other nutrients of potential importance in heart failure

Sodium restriction is recommended for patients with dogs with stage B2 MMVD and with congestive heart failure.[2] Sodium is regulated predominantly via the RAAS (Renin-Angiotensin-Aldosterone System) which causes sodium to be retained by the kidneys, and water along with it. Low sodium diets may reduce the amount of water retained by the body, but low sodium intake causes the body to activate the RAAS. In addition to the impact on sodium and water balance, aldosterone promotes inflammation and oxidative stress. Excessive restriction of sodium is actually detrimental in heart failure, causing an increase in mortality in human patients and upregulation of RAAS in dogs and cats.[23] Further, pharmaceutical care in CHF, such as ACE-inhibitors or diuretics, combined with low sodium intake can result in other electrolyte abnormalities, such as hyperkalemia.[24] Current evidence suggests that 40 – 70mg/100Kcal ME should be safe while providing moderate sodium restriction.[24, 25]

Protein and energy intake are important in dogs with advanced heart disease to help reduce risks for cachexia.[26] Intake should be monitored, as dogs with advanced heart disease may have reduced appetites.

Summary

Dogs with heart disease or heart failure, like all dogs, need complete and balanced nutrition. Therapeutic diets must meet the nutritional needs of the patient, while also addressing the key nutrients appropriate to health management. For dogs with heart disease, the key nutrients extend far beyond sodium. Nutrients that aid mitochondrial function, support energy metabolism, address oxidative stress and inflammation, and promote normal sinus rhythm and maintain myocardial function are all important for heart health. A cardiac protection blend of nutrients (medium-chain triglyerides, omega-3 fatty acids, magnesium, taurine, carnitine precursors and antioxidants) helps to reduce changes associated with MMVD in dogs, and should provide cardiac support for dogs with more advanced heart disease.

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