MANAGEMENT OF CHRONIC DEGENERATIVE MITRAL VALVE DISEASE IN DOGS

PAUL SMITH

CHRONIC degenerative mitral valve disease (CDMVD), also referred to as myxomatous mitral valve disease and endocardiosis, is the most common cardiac disease in dogs. The early stages are typified by a few small, discrete areas of opacity or nodules in the region of valvular apposition. Ultimately, the condition progresses to also involve the basal portion of the valve and chordae tendineae. The valvular changes result in progressively worsening mitral regurgitation and, in some cases, can lead to the development of heart failure. This article discusses current treatment strategies for canine CDMVD and reviews their rationale.

AETIOLOGY

The aetiology of CDMVD is unknown. It has been considered for some time to be a dystrophic process characterised by a genetically influenced degeneration of collagen. However, a more recently cited possibility is that the myxomatous degeneration is the result of a succession of repeated healing events, with abnormal valve structure or function playing an inciting role. Trauma may lead to alteration of endothelial cell function and thereby trigger subendothelial changes in the valve that ultimately lead to myxomatous degeneration. Some vasoactive substances (e.g., endothelin and nitric oxide) have also been speculated to play a role in the pathogenesis.

DIAGNOSIS

The presence of CDMVD is usually suspected from the signalment, history and clinical examination. A heart murmur is almost always identified. The intensity of the murmur is usually greatest at the left heart apex and in most small breed dogs corresponds to the severity of the disease. An exception to this is in cases of a ‘honking’ or musical murmur, where the severity of the disease may be mild despite an apparently high intensity murmur. A murmur may also be more difficult to appreciate in the presence of fulminant heart failure (HF) during which the heart rate is usually substantially elevated and the breathing sounds marked.

In those animals in which there is a high index of suspicion for CDMVD, thoracic radiography may be employed to provide further evidence of the disease. However, it cannot be used to conclusively differentiate CDMVD from other heart diseases. Thoracic radiography is therefore most useful where there are clinical
Heart testing in the Cavalier King Charles spaniel

CDMVD is a highly heritable disease that probably has a polygenic mode of inheritance. The prevalence is age- and breed-related, with the Cavalier King Charles spaniel (CKCS) being predisposed to earlier development of the disease than other breeds. Coupled to this, most CKCSs have a murmur attributable to CDMVD by the time they are 10 years of age. Under these circumstances a heart testing scheme based on age of onset, with selection of dogs with the latest onset of murmurs, would seem to be the best one could offer, the ultimate aim being to gradually push the onset of CDMVD in the CKCS to later ages and thereby reduce the prevalence of HF in this breed.

In 1990, the UK Cavalier King Charles Spaniel Club, in conjunction with Dr Peter Darke, a veterinary cardiologist, and Dr Bruce Catanach, a geneticist, set up a database and heart testing scheme for CKCSs. Heart testing can be performed by all veterinary surgeons and is by way of auscultation (see table below). Further information is available through the club’s website (www.thecavalierclub.co.uk) as well as from the Veterinary Cardiovascular Society website (www.bsava.com/vcs).

THE CAVALIER KING CHARLES SPANIEL CLUB HEART TESTING SCHEME RECOMMENDATIONS

<table>
<thead>
<tr>
<th>Breed</th>
<th>Stud dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>Should be a minimum of 2.5 years of age with a clear heart, and parents with clear heart certificates, issued at ≥5 years of age</td>
<td>Should preferably be at least 2.5 years of age with a clear heart, and parents with clear heart certificates, issued at ≥5 years of age</td>
</tr>
<tr>
<td>It is strongly advised that breeding stock under five years of age is limited to those with clear heart certificates. However, an older dog with a slight heart murmur should not be ignored</td>
<td></td>
</tr>
</tbody>
</table>

Medical treatment to prevent and/or reverse the valvular degeneration is presently unavailable. Overall treatment objectives are therefore to improve quality of life and increase survival.

PRE-CHF

Although CDMVD is common, especially in older small breed dogs, it is considered to be relatively benign and only a small percentage of dogs go on to develop HF. ACE inhibitor therapy was not shown to prevent volume overload hypertrophy in dogs with chronic MR (Dell’italia and others 1997). Furthermore, treatment with enalapril (an ACE inhibitor) in asymptomatic dogs with CDMVD neither delayed the onset of HF nor speeded it up (Kvart and others 2002). The available data therefore do not support the use of ACE inhibitors in dogs with CDMVD prior to the onset of HF.

In view of these findings, and given that the combination of a cough and a typical heart murmur does not necessarily constitute HF, it is particularly important that a distinction between respiratory and cardiac disease as a cause of the clinical signs is made before initiating a life-long course of HF therapy. Appropriate clinical signs, with the disappearance of a sinus arrhythmia, an elevated heart rate and radiographic evidence of interstitial/alveolar oedema usually with pulmonary venous congestion are required to confirm a diagnosis of CHF.

Agents that improve endothelial cell function (eg, endothelin-receptor blockers, carvedilol [a non-selective - and -adrenergic receptor blocker with antioxidant activity] and other antioxidant therapies) may in the future be shown to have some protective effects and could be employed prior to the onset of HF in order to delay its onset. Carvedilol may offer the additional benefit of preserving systolic function (ie, preventing the deterioration in contractility [myocardial failure] that accompanies chronic volume overload). This may be of particular importance if the transition from compensation to HF is directly attributable to the development of myocardial failure in CDMVD. Mast cell blockade has also been shown to attenuate the collagen loss and destructive remodelling associated with volume overload in dogs with MR. The potential role of these agents requires further evaluation.

ACUTE HF

Dogs with acute HF secondary to CDMVD usually have clinical signs associated with pulmonary congestion and oedema (ie, CHF), or poor peripheral perfusion and a reduced cardiac output (ie, forward HF). A diagnosis must be attained without causing undue stress to the animal as this can exacerbate the clinical signs. Treatment objectives in the immediate term are to alleviate life-threatening pulmonary oedema and improve forward flow. Management of concurrent arrhythmias, if present, signs, in which case it is used with other tests to differentiate cardiac from respiratory disease, and to determine whether congestive HF (CHF) is present.

Echocardiography is required to confirm the diagnosis by identifying the characteristic features of the disease. Assessment of left ventricular and left atrial size and wall motion are also of importance in determining the effects of mitral regurgitation (MR) on the heart. The severity of MR can be subjectively graded and the presence/absence of concurrent cardiac abnormalities can also be assessed. A distinction from mitral valve (MV) endocarditis cannot be made; however, dogs with bacterial endocarditis usually present with atypical clinical signs (eg, lameness, systemic illness, neurological signs) and may have abnormal haematology (eg, leucocytosis) and serum biochemical findings that are not usually seen with CDMVD.

Electrocardiography is unnecessary in the diagnosis of CDMVD, but is particularly useful in assessing heart rate and rhythm. Cardiac arrhythmias (eg, supraventricular and ventricular premature complexes and atrial fibrillation) are particularly common in animals with severe MR and a rhythm diagnosis may help to guide therapy. Abnormalities of complex size may provide additional evidence to support the presence of left atrial and/or left ventricular enlargement.

TREATMENT

Medical treatment to prevent and/or reverse the valvular degeneration is presently unavailable. Overall treatment objectives are therefore to improve quality of life and increase survival.

PRE-CHF

Although CDMVD is common, especially in older small breed dogs, it is considered to be relatively benign and only a small percentage of dogs go on to develop HF. ACE inhibitor therapy was not shown to prevent volume overload hypertrophy in dogs with chronic MR (Dell’italia and others 1997). Furthermore, treatment with enalapril (an ACE inhibitor) in asymptomatic dogs with CDMVD neither delayed the onset of HF nor speeded it up (Kvart and others 2002). The available data therefore do not support the use of ACE inhibitors in dogs with CDMVD prior to the onset of HF.

In view of these findings, and given that the combination of a cough and a typical heart murmur does not necessarily constitute HF, it is particularly important that a distinction between respiratory and cardiac disease as a cause of the clinical signs is made before initiating a life-long course of HF therapy. Appropriate clinical signs, with the disappearance of a sinus arrhythmia, an elevated heart rate and radiographic evidence of interstitial/alveolar oedema usually with pulmonary venous congestion are required to confirm a diagnosis of CHF.

Agents that improve endothelial cell function (eg, endothelin-receptor blockers, carvedilol [a non-selective - and -adrenergic receptor blocker with antioxidant activity] and other antioxidant therapies) may in the future be shown to have some protective effects and could be employed prior to the onset of HF in order to delay its onset. Carvedilol may offer the additional benefit of preserving systolic function (ie, preventing the deterioration in contractility [myocardial failure] that accompanies chronic volume overload). This may be of particular importance if the transition from compensation to HF is directly attributable to the development of myocardial failure in CDMVD. Mast cell blockade has also been shown to attenuate the collagen loss and destructive remodelling associated with volume overload in dogs with MR. The potential role of these agents requires further evaluation.

ACUTE HF

Dogs with acute HF secondary to CDMVD usually have clinical signs associated with pulmonary congestion and oedema (ie, CHF), or poor peripheral perfusion and a reduced cardiac output (ie, forward HF). A diagnosis must be attained without causing undue stress to the animal as this can exacerbate the clinical signs. Treatment objectives in the immediate term are to alleviate life-threatening pulmonary oedema and improve forward flow. Management of concurrent arrhythmias, if present,
is beyond the scope of this review, but the improved tissue oxygenation that accompanies successful treatment of HF is often sufficient.

Maintaining a small left ventricle through preload reduction and enhancement of contractility has been shown to decrease regurgitant volume by reducing the effective regurgitant orifice area. Afterload reduction, mediated through arteriodilators, may also contribute to this beneficial effect; however, extreme caution must be observed in the acute setting as many animals will be hypotensive. Treatment objectives are therefore achieved through preload and afterload reduction, and enhancement of systolic performance.

The nature and aggressiveness of therapy is tailored to the individual. In all dogs with acute HF, minimisation of stress and activity (ie, cage rest) is important during the initial treatment stages. Animals should be given free access to water, and drinking and urination should be monitored. Oxygen supplementation by way of a mask (1 to 10 litres/minute), flow-by delivery (2 to 5 litres/minute), nasal catheter (50 to 100 ml/kg/minute) or oxygen cage should also be employed, where possible; however, care should be taken to avoid excessive stress or hyperthermia.

**Diuretics (frusemide)**

Diuretics act on the kidney to increase urinary sodium excretion (natriuresis) and increase urine flow. The associated reduction in blood volume results in decreased intraventricular filling pressures (reduced preload) and pulmonary capillary pressures, leading to decreased fluid accumulation in the pulmonary interstitium in left-sided CHF. Each class of diuretic acts at a different site within the nephron.

Frusemide is a loop diuretic. It needs to be excreted by the proximal tubule to reach its site of action and is therefore dependent on renal blood flow. Loop diuretics are the most potent diuretics and, unlike other classes of these drugs, there is an increasing diuretic response with increasing doses (high ceiling diuretic). Frusemide is the single most important agent used for the treatment of acute CHF. In acute HF, especially when administered intravenously, relief of dyspnoea may occur even before diuresis through venodilation and preload reduction. The dose needed is variable and depends on several factors including the severity of CHF. The minimum effective dose should be administered at all times, and unless there is massive pulmonary oedema it is unusual for 10 mg/kg/24 hours to be exceeded during the initial stabilisation phase. Once the dyspnoea and tachypnoea have abated, the dose and frequency of dosing should be reduced immediately to avoid problems associated with dehydration, electrolyte depletion and acid-base abnormalities.

**Pimobendan**

Pimobendan (Vetmedin; Boehringer Ingelheim) is a benzimidazole derivative with combined inotropic (enhanced contractility) and peripheral vasodilating properties. Pimobendan also has direct lusitropic (enhanced relaxation) effects. In contrast to the drug’s positive inotropic action, the positive lusitropic effect has been shown to be more pronounced in failing rather than normal hearts. The beneficial haemodynamic effects of pimobendan in HF may therefore be mediated largely through improvement of ventricular diastolic function (improved relaxation). Pimobendan may be particularly useful in acute HF as it has a high oral bioavailability (approximately 70 per cent) and relatively rapid onset of action after oral administration.

**Glyceryl trinitrate**

Glyceryl trinitrate (Percutol; Dominion Pharma) is a nitrate used in acute CHF as a venodilator to reduce preload (see top table on page 380). The transdermal administration of glyceryl trinitrate ointment is designed to provide continuous controlled release of nitroglycerin. The ointment is usually applied to the inner pinna. Gloves should be worn when handling the ointment and a warning sign should be placed on the kennel sheet/
TREATMENT REGIMENS TYPICALLY USED BY THE AUTHOR IN THE MANAGEMENT OF ACUTE HF SECONDARY TO CANINE CDMVD

### Mild HF
- **Clinical findings**: Mild pulmonary oedema (interstitial lung pattern in the hilar region) with mild dyspnoea
- **Treatment regimen(s)**: If very mild, it may be possible to initiate chronic therapy (ie, all po – see table on page 381) with cage rest otherwise.

### Moderate to severe HF
- **Clinical findings**: Moderate to severe pulmonary oedema (alveolar lung pattern predominantly in the hilar region) with moderate to severe hyperpnoea
- **Treatment regimen(s)**: Frusemide (2 to 4 mg/kg every one to two hours iv initially [typically one to two doses], then every six to eight hours) plus nitroglycerin (6–25 mm/5 kg every six to eight hours topically) plus pimobendan (0.1 to 0.3 mg/kg every 12 hours po) with cage rest prior to initiating chronic therapy.

### Fulminant HF
- **Clinical findings**: Massive pulmonary oedema with palor/cyanosis, life-threatening hyperpnoea and extreme anxiety. Usually too dyspnoeic to receive medication po (ie, likely to inhale the medication).
- **Treatment regimen(s)**: With/without sedation (morphine 1 to 2 mg/kg iv to effect) and ventilatory support and Frusemide (4 to 8 mg/kg every one to two hours iv initially [typically two to three doses]) with/without nitroprusside (2.5 to 8 μg/kg/minute or until the mean systolic blood pressure is ≤70 mmHg). If the above sedation is not employed, then cage rest with/without oxygen supplementation is advised.

**Note**: Always use caution with chronic HF, the minimum effective dose should be used with caution where diuretics and ACE inhibitors are being administered concurrently to treat HF, as it can lead to increased sodium reabsorption, decreased aldosterone levels, and hypokalaemia.

### Nitroprusside
Nitroprusside is a donor of nitric oxide that dilates both arterioles (reduces afterload) and veins (reduces preload) through the formation of cyclic guanosine monophosphate in vascular tissue. It is rapidly metabolised after intravenous administration and is given as a constant rate infusion (see table above). The infusion rate needs careful titration against blood pressure to avoid potentially fatal hypotension. Consequently, its use should be restricted to centres with appropriate intensive care facilities and staff. Potential side effects include cyanide or thiocyanate toxicity and hypotension.

### ACE inhibitors
Despite extensive research, the mechanism of action of angiotensin converting enzyme (ACE) inhibitors and the role of non-ACE pathways in the formation of angiotensin II (AII) remain incompletely understood. ACE inhibitors work in part by lessening the adverse effects of AII (see table below). While this class of drug continues to be favoured in the treatment of chronic HF, it has no role in the acute setting. This is because most of the potentially beneficial effects of ACE inhibitors in dogs with CDMVD are slow in onset.

### CHRONIC HF
Dogs with chronic HF secondary to CDMVD usually have clinical signs associated with pulmonary congestion and oedema (ie, CHF). Syncope and/or signs of forward failure may also be present. Possible causes of syncope in this setting include inadequate forward flow during exercise-induced vasodilation, arrhythmias or pulmonary hypertension. Treatment objectives are to improve quality of life and increase longevity.

As with acute HF, treatment objectives are achieved through preload and afterload reduction, and enhancement of contractile performance (see table on page 381). Although it is widely believed that a reduction in afterload through the use of arterial vasodilators may increase aortic flow and decrease MR, this concept has been challenged by several recent publications (see diagrams on page 381). The potential for improving left ventricular performance in chronic MR may therefore be independent of changes in regurgitant volume.

### Frusemide
The administration of frusemide results in increased renin secretion so it is widely thought that all dogs receiving this drug should also be treated with an ACE inhibitor. Frusemide administration also results in the urinary loss of sodium, chloride, potassium and calcium. For equinatriuretic doses, frusemide results in less potassium loss than thiazides. For both classes of diuretic, the urinary loss of sodium, chloride, potassium and calcium.

### POTENTIAL ADVERSE EFFECTS OF ANGIOTENSIN II

<table>
<thead>
<tr>
<th><strong>Heart</strong></th>
<th><strong>Coronary arteries</strong></th>
<th><strong>Peripheral vasculature</strong></th>
<th><strong>Sympathetic nervous system</strong></th>
<th><strong>Kidneys</strong></th>
<th><strong>Adrenal glands</strong></th>
<th><strong>Other</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial hypertrophy</td>
<td>Endothelial dysfunction with decreased release of nitric oxide</td>
<td>Vasoconstriction</td>
<td>Central adrenergic activation</td>
<td>Increased intraglomerular pressure</td>
<td>Increased formation of aldosterone</td>
<td>Polydipsia</td>
</tr>
<tr>
<td>Intestinal fibrosis</td>
<td>Coronary constriction via release of norepinephrine</td>
<td></td>
<td></td>
<td>Altered glomerular capillary permeability</td>
<td></td>
<td>Increased endothelin release</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Increased protein leakage</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Glomerular growth and fibrosis</td>
<td></td>
<td>Apoptosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Increased sodium reabsorption</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Decreased local formation of bradykinin (bradykinin promotes vasodilation and may lessen endothelial damage)</td>
</tr>
</tbody>
</table>
A loss of diuretic potency (diuretic resistance) occurs initially through activation of the renin-angiotensin-aldosterone system and in the long term via increased reabsorption of sodium associated with hypertrophy of the distal nephron segments. In severe and refractory CHF, it may therefore be necessary to employ the use of a diuretic acting at a more distal site within the nephron (eg, thiazide diuretic and/or spironolactone).

**ACE inhibitors**

In a long-term study designed to compare the efficacy and tolerability of benazepril with a placebo in 162 dogs with HF caused by dilated cardiomyopathy or CDMVD, a statistically significant benefit of benazepril was recorded for both survival and worsening endpoints in dogs with CDMVD (BENCH Study Group 1999). Although these results show that ACE inhibitors are efficacious in dogs with CDMVD and HF, the clinical response is not profound. In human patients with MR, long-term vasodilator therapy provides most benefit in those with the largest hearts, the poorest systolic function and the most disabling symptoms. This may also be the case in dogs with CDMVD. The author usually adds an ACE inhibitor to the treatment regimen after the HF has been alleviated (usually 24 hours after first presentation in the case of acute HF).

**Pimobendan**

Some cytokines may be involved in potentially important maladaptive mechanisms in cases of advanced HF. By differentially modulating cytokine production, pimobendan may additionally be beneficial in dogs with chronic HF for reasons unrelated to its vasodilatory, inotropic and lusitropic properties.

---

**TREATMENT REGIMENS TYPICALLY USED BY THE AUTHOR IN THE MANAGEMENT OF CHRONIC HF SECONDARY TO CANINE CDMVD**

<table>
<thead>
<tr>
<th>Mild HF</th>
<th>Moderate HF</th>
<th>Severe HF</th>
<th>Refractory HF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical findings</strong></td>
<td>Stable on standard therapy (low dose diuretics)</td>
<td>Stable on standard therapy (moderate dose diuretics). May still have a cough plus some exercise intolerance</td>
<td>Stable on standard therapy (high dose diuretics). Probably still has a cough plus exercise intolerance</td>
</tr>
<tr>
<td><strong>Treatment regimen(s)</strong></td>
<td>Frusenide (1 to 2 mg/kg every 12 to 24 hours po) plus an ACE inhibitor plus eicosapentaenoic acid and docosahexaenoic acid with/without spironolactone (2 mg/kg every 12 hours po) with/without digoxin</td>
<td>Frusenide (1 to 2 mg/kg every eight to 12 hours po) plus an ACE inhibitor plus eicosapentaenoic acid (40 mg/kg every 24 hours po) and docosahexaenoic acid (25 mg/kg every 24 hours po) plus spironolactone (2 mg/kg every 12 hours po) with/without digoxin</td>
<td>Frusenide (2 to 4 mg/kg every eight to 12 hours po) plus an ACE inhibitor plus eicosapentaenoic acid (40 mg/kg every 24 hours po) and docosahexaenoic acid (25 mg/kg every 24 hours po) plus spironolactone (2 to 4 mg/kg every 12 hours po) with/without digoxin with/without potassium gluconate (0.2 to 0.5 mmol/kg every eight hours po)</td>
</tr>
<tr>
<td><strong>Control patient</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Rationale for the use of a positive inotrope in canine CDMVD**

The favorably altered loading conditions in animals with MR help to preserve contractility during the course of the disease; however, volume overload and an elevation in heart rate may result in diminished contractility in the chronic state. Assessment of intrinsic myocardial contractility in MR cannot be reliably determined using conventional echocardiography as this is not completely independent of alterations in load. In addition, two-dimensional imaging does not adequately assess all planes of motion of the myocardium during contraction. The prevalence of impaired systolic function in dogs with CDMVD is therefore probably underestimated.

### ADVERSE EFFECTS OF ALDOSTERONE

<table>
<thead>
<tr>
<th>Heart and vessels</th>
<th>Myocardial and vascular fibrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular damage</td>
<td></td>
</tr>
<tr>
<td>Impaired arterial compliance</td>
<td></td>
</tr>
<tr>
<td>Autonomic nervous system</td>
<td>Sympathetic nervous system activation (prevents uptake of norepinephrine by the myocardium)</td>
</tr>
<tr>
<td>Parasympathetic nervous system inhibition</td>
<td></td>
</tr>
<tr>
<td>Baroreceptor dysfunction</td>
<td></td>
</tr>
</tbody>
</table>

The results of a recent study support the use of pimobendan in dogs with HF caused by CDMVD (Smith and others 2005).

**Spironolactone**

Aldosterone formation does not stay fully blocked during ACE inhibitor therapy (aldosterone escape). Therefore, although spironolactone tends to be reserved for dogs with hypokalaemia or severe CHF that has become refractory to frusemide, by blocking the adverse effects of aldosterone (see table above) its administration in early CHF may have additional cardioprotective effects unrelated to its diuretic action. The optimal stage at which spironolactone should be introduced to the treatment regimen is unclear.

**Thiazide diuretics**

Thiazide diuretics (eg, hydrochlorothiazide) are mild to moderately potent diuretic agents, having approximately one-third of the potency of frusemide. Hydrochlorothiazide has a duration of action of 12 hours and is most commonly used in combination with amiloride (Moduretic/Moduret; Bristol-Myers Squibb). Amiloride is a potassium-sparing diuretic that acts at a portion of the nephron that is independent of aldosterone. The author tends to reserve this combination diuretic for dogs with refractory CHF, in which it is usually given once daily at an initial dose of 2 mg/kg. Care must be employed when introducing this combination as it can result in dehydration, electrolyte depletion and acid-base abnormalities. The frusemide dose may have to be reduced as the combination diuretic is initiated, and the dog’s demeanour and serum biochemistry and electrolytes should be evaluated during the first 24 to 48 hours and intermittently thereafter.

**Digoxin**

The author tends to prescribe digoxin to dogs with atrial fibrillation to slow the ventricular response rate. Other properties that may be of benefit in dogs with CDMVD include a modest positive inotropic effect, alteration of baroreceptor sensitivity (increased vagal tone and decreased sympathetic tone), diuresis and decreased renin release.

The starting dose is based on body surface area (0.22 mg/m² every 12 hours orally); however, this must be reduced for some animals (see below). Therapeutic serum concentrations are usually achieved in two to five days. Digoxin has a relatively low therapeutic index and serum concentrations above the therapeutic range may have serious consequences (eg, depression, anorexia, vomiting and/or cardiac arrhythmias). It is therefore important to administer the correct starting dose and monitor the animal carefully during the initial stabilization period. If signs of toxicity are observed, the dose may have to be decreased. The starting dose should be based on lean bodyweight (deduct estimated weight of ascitic fluid, if present) and reduced in those dogs that are particularly thin, or where there is hypoalbuminemia or renal insufficiency. Serum digoxin concentration six to eight hours after tablet administration should be determined five to seven days after starting treatment, or sooner if necessary. This should be within the therapeutic range (0.8 to 2.4 mg/ml). Beneficial autonomic effects and altered baroreceptor sensitivity may occur at the lower end of this therapeutic range. Consequently, toxicity may be avoided by aiming for a serum digoxin concentration at this lower end.

**Cough suppressants**

Mechanical irritation imparted to airways by an enlarged left atrium can induce a cough in the absence of pulmonary oedema. This may be worse in dogs with concurrent ‘tracheal collapse’. In this setting, where the cough is considered sufficiently significant to warrant further therapy, it is important not to increase diuretic doses. Instead, a cough suppressant (eg, codeine phosphate 0.5 to 2.0 mg/kg every 12 hours orally or butorphanol tartrate [Torbutrol; Fort Dodge] at 0.5 to 1.0 mg/kg every eight to 12 hours) may be employed to improve the clinical signs.

**Potassium supplementation**

Potassium depletion has been reported to result in arrhythmias, muscle weakness and decreased myocardial contractility. It may also potentiate the adverse effects of some cardiac medications (eg, digoxin). Potassium depletion is an inevitable side effect of frusemide administration and hence the serum potassium concentration should be routinely monitored. The administration of an ACE inhibitor with or without spironolactone may be employed to increase the serum potassium concentration. Potassium supplementation may also be necessary in some cases (see table on page 381); however, this is considered to be less effective than ACE inhibition and the use of low dose potassium-retaining diuretics.

**Nutritional modulation of cytokine production**

Cardiac cachexia is the muscle wasting commonly seen in animals with CHF. The weight loss occurs primarily as a result of the loss of lean body mass. It is thought to be a multifactorial process caused by the combined effects of anorexia, increased energy requirements and...
Mitral valve surgery

The treatment of choice in most human patients with mitral valve prolapse and severe MR is mitral valve surgery. An exception to this is in cases of severely reduced ventricular function as the surgical outcome is poor in these patients. Compared with valve replacement, successful valve repair results in superior haemodynamics and ventricular function, avoidance of a prosthetic valve and the need for long-term anticoagulation, and less distortion of ventricular shape. Consequently, in humans, valve repair rather than valve replacement is performed whenever possible.

If the myxomatous degeneration in canine CDMVD is the result of a succession of repeated healing events, with abnormal valve structure or function playing an inciting role, restoration of normal valve function with valve repair might arrest or slow further myxomatous degeneration. In a recent study, MV repair was associated with a resolution of CHF for a median period of one year (range four months to three years) in nine of 12 dogs that survived surgery (Griffiths and others 2004). Of these, two dogs had congenital mitral valve disease and seven had CDMVD. In a subsequent study published by the same group, mitral valve replacement with a mechanical prosthesis was performed in eight dogs with HF, seven of which had CDMVD and one had dilated cardiomyopathy (Orton and others 2005). The CHF resolved in all the surviving dogs with CDMVD and frusemide was no longer required after surgery. Median survival after surgery was 4.5 months (range 0.75 months to 5.25 years). These authors were of the opinion that dogs with severe MR tolerate MV replacement surprisingly well and, in contrast to humans, even relatively late in the course of CHF. Valve prosthesis thrombosis was the likely cause of death in all but one dog that survived MV replacement. This data shows that the immediate outcome was better in dogs undergoing mitral valve replacement than those undergoing mitral valve repair. The use of glutaraldehyde-fixed pericardial valve prostheses may overcome the problem of valve prosthesis thrombosis while avoiding the need to administer long-term anticoagulant therapy, and may be the optimal approach.

Despite early indications that mitral valve surgery might be a promising treatment modality in cases of canine CDMVD, due to the complexity of mitral valve surgery and limited experience in veterinary medicine, this is not likely to become a widely available alternative to medical treatment.

Metabolic alterations. An elevation in circulating inflammatory cytokines in CHF may also play a role. Omega-3 polyunsaturated fatty acid (ie, eicosapentaenoic acid and docosahexaenoic acid) supplementation may be employed to reduce inflammatory cytokine production. Fish oils contain high concentrations of omega-3 polyunsaturated fatty acids and may be added to food.

SUMMARY

Although the therapeutic strategy employed to manage HF is tailored to the individual animal, a relatively standard combination of drugs (ie, furosemide, ACE inhibitor and pimobendan) is employed after decompensation to HF in most cases. There is, however, some confusion about what stage some of these drugs should be initiated. Furthermore, there is a paucity of dependable data regarding some agents and strategies used to manage CHF. As the disease progresses the therapeutic strategy may change, with intensification to be anticipated with advancing disease. Acute exacerbations of decompensated CHF may also occur with chronic disease. Ultimately euthanasia may be necessary, in which case this should not be considered a failure if all other avenues have been explored or are considered unlikely to be effective.

References


Further reading