An update on treatment and prognostic indicators in canine myxomatous mitral valve disease

Mitral regurgitation caused by myxomatous mitral valve disease is the most common cause for congestive heart failure and cardiac-related mortality in dogs. Typically, it takes several years for the disease to progress from mild, clinically silent myxomatous mitral valve disease to severe disease with signs of congestive heart failure. A proportion of dogs will never progress into congestive heart failure before they die from other causes or old age. Some variables have been shown to be predictive of onset of congestive heart failure and they might be useful to identify dogs that need more frequent monitoring and eventually treatment. Results from several controlled clinical trials are available concerning medical treatment of dogs with myxomatous mitral valve disease with or without congestive heart failure. These trials provide estimates of treatment effects and also allow identification of other variables with prognostic value for the outcome after the onset of congestive heart failure. Use of prognostic variables together with qualitative and quantitative results from clinical drug trials may aid the clinician and owner to plan and decide on optimal management of the myxomatous mitral valve disease dog. The purpose of this article is to review the current knowledge of prognostic variables and therapy for this common condition in dogs.

J. Häggström, K. Höglund* and M. Borgarelli†

DOI: 10.1111/j.1748-5827.2009.00800.x
Accepted: 19th June 2009

Conflicts of Interest: MB has received funding for research from Boehringer Ingelheim, Merial and Intervet, which was not related to this work; JH has received funding for research from Boehringer Ingelheim and acts as scientific advisor for Ceva Santé Animal and Orion Pharma, KH declares no conflicts of interest.

Department of Clinical Sciences, Faculty of Veterinary Medicine and Animal Sciences, Swedish University of Agricultural Sciences, Box 7054, 750 07 Uppsala, Sweden
*Department of Anatomy, Physiology and Biochemistry, Faculty of Veterinary Medicine and Animal Sciences, Swedish University of Agricultural Sciences, Box 7011, 750 07 Uppsala, Sweden
†College of Veterinary Medicine, Kansas State University, 1800 Anderson Avenue, 66506 Manhattan Kansas, USA
Individuals. Furthermore, different types of CHF medication have been shown to influence the outcome in dogs with CHF caused by MMVD (Ertinger and others 1998, The BENCH Study Group 1999, Häggström and others 2008). Use of prognostic variables together with qualitative and quantitative results from clinical drug trials may aid the attending clinician and owner to plan and decide on optimal management of the dog with MMVD. The purpose of this article is to review the current knowledge of prognostic variables and therapy for this common condition in dogs.

**Indicators for Progression of MR and Development of CHF**

Once mild MR caused by MMVD has been diagnosed in a dog, the question of long-term prognosis arises. It is well known that some breeds, such as Cavalier King Charles spaniel (CKCS), develop MMVD at a younger age than other breeds (Thrusfield and others 1985, Häggström and others 1992, Beardow and Buchanan 1993, Egenvall and others 2006). Within breeds where the inheritance of MMVD has been studied, the age of onset has been shown to be inherited as a polygenic threshold trait (Swenson and others 1996, Olsen and others 1999) and males develop the disease at a younger age than females (Häggström and others 1992, Pedersen and others 1999, Serfass and others 2006). Presumably, most of the dogs in that study had rupture of minor chords because rupture of major chordae tendineae is generally considered to be associated with an acute increase of MR and a poor prognosis (Häggström and others 2005).

It is of interest to identify variables that could predict time to onset of CHF in a dog diagnosed with MMVD and MR. The ideal prognostic variable would change linearly with time and allow a detailed estimation of when CHF could be expected. Unfortunately, such a variable has yet to be identified. At present, the variables that have been shown most effective to predict the onset of CHF do not change dramatically (accelerate) until CHF is imminent or present. These variables include: echocardiographic variables, such as left atrial size (left atrial (LA) to aortic root (AO) ratio (LA/AO)), left ventricular end-diastolic and end-systolic size [percentage increase in LVIDd and LVIDs from expected values based on body weight (LVIDd inc. and LVIDs inc.), end-diastolic and end-systolic volume indices (EDVI-1 and ESV-I)], transmitral flow pattern [peak velocity of early transmitral filling (E-peak velocity)], vertebral heart score (VHS) obtained from thoracic radiographs, blood concentrations of natriuretic peptides (NT-proANP and NT-proBNP), heart rate and heart rate variability (Fig 1) (Häggström and others 1999, Olsen and others 2003). The degree of leaflet thickening has also been shown to influence long-term prognosis (Pedersen and others 1999, Olsen and others 2003). Rupture of chordae tendineae has been reported to be a common feature of MMVD (Buchanan 1977, Beadow and Buchanan 1993). One study reported a comparatively favourable long-term prognosis in dogs with ruptured chordae tendineae (Serres and others 2007). The degree of leaflet thickening has also been shown to influence long-term prognosis (Pedersen and others 1999, Olsen and others 2003). Rupture of chordae tendineae has been reported to be a common feature of MMVD (Buchanan 1977, Beadow and Buchanan 1993). One study reported a comparatively favourable long-term prognosis in dogs with ruptured chordae tendineae (Serres and others 2007).

**FIG 1. Hazard ratios and 95% confidence intervals (CI) obtained from the Cox Proportional Hazard analysis of 558 dogs with MMVD (Borgarelli and others 2008). Ten out of the 14 clinical variables were significantly associated to the outcome, which was time from the first consultation to cardiac related death in the univariate analysis. However, only the left atrial to aortic root ratio (blue bar) remained significant in the final multivariate model, although the maximal diastolic transmitral E-wave velocity (blue bar) was close (P=0.054) to the chosen 5% level of significance (P<0.05). Modified from Borgarelli et al 2008 with permission from the publisher. Abbreviations: M, male; F, female; Y, yes; N, No; HR, heart rate; SAP systolic arterial blood pressure; LA/Ao, left atrial to aortic root ratio; MVP, mitral valve prolapse; EDVI-1, end-diastolic volume index; ESV-I, end-systolic volume index; E peak velocity, peak velocity of E wave

The purpose of this article is to review the current knowledge of prognostic variables and therapy for this common condition in dogs.
and Murphy 2006, DeFrancesco and others 2007, Borgarelli and others 2008, Boswood and others 2008, Moonarmart 2008, Tarrow and others 2009). The intensity of the heart murmur has also been shown to be prognostic in studies including dogs of only one breed (Häggström and others 1992, Pedersen and others 1999, Kvart and others 2002, Olsen and others 2003), but not in a study including many breeds (Borgarelli and others 2008). In fact, all the mentioned variables (including heart murmur intensity) are indirect estimations of MR severity and volume overload (Choong and others 1988, Buchanan and Bucheler 1995, Häggström and others 1996b, Häggström and others 2000, Doxey and Boswood 2004, Boswood and Murphy 2006, van Kimmenade and Januzzi 2009). Because of the influence of MR on all the above variables, it can be hypothesised that accurate estimation of the regurgitant volume and/or effective regurgitant orifice area would, as described in people (Enriquez-Sarano and others 2005), be a powerful method to predict the onset of CHF in dogs. In addition to the indirect measurements of MR listed above, the regurgitant volume and effective regurgitant orifice area are, today, most commonly estimated by colour Doppler echocardiography. The regurgitant volume and severity of MR can either be semi-quantified by relating the area of the regurgitant jet (ARJ) as a proportion of the LA area (LAA) (the ARJ/LAA method) (Pedersen and others 1999) or be indirectly measured using the proximal isovelocity surface area (PISA) method (Kittleson and Brown 2003). The latter technique also allows estimation of effective regurgitant orifice area by dividing the regurgitant flow rate by the velocity of the MR jet (Kittleson and Brown 2003). Although colour Doppler techniques are efficient in detecting MR and discriminating low-degree MR from moderate to severe, neither method has been shown to reflect MR volume accurately, and they are less efficient in separating moderate MR from severe (Kittleson and Brown 2003). This is a problem because in dogs developing CHF presumably MR increases from moderate to severe, which means that current Doppler-derived estimations of severity of MR are not variables of high diagnostic or prognostic value. Thus, colour echocardiography is useful to detect MR but is unlikely to provide information on severity of MR not already obtained from standard LA and left ventricular (LV) measurements. This might change in the future with the development of new echocardiographical modalities, such as three-dimensional echocardiography.

### THERAPY OF ASYMPTOMATIC MR

Ideally therapy in MMVD should reverse or halt the progression of the valvular degeneration. However, no therapy is currently known to have this effect. Human patients with MMVD usually undergo surgical repair or valve replacement before the MR causes CHF but surgery is rarely an option in dogs. Cardiac remodelling, such as eccentric hypertrophy, occurs during progression of MMVD in response to the increasing valve leakage and volume overload (Dell’Italia and others 1997). Medical therapy that counteracts the increasing MR and the remodelling process should theoretically have the potential to delay the onset of CHF. Drugs that have been suggested to counteract the increasing MR and cardiac remodelling, on the basis of experimental studies in dogs, include direct acting arterial vasodilators, such as amlodipine (Braunwald and others 1998) and antifibrotic agents, such as anti-aldosterone drugs (Suzuki and others 2002). Beta-blockers (Sabbah and others 1994, Nemoto and others 2002), angiotensin converting enzyme (ACE)-inhibitors (Sabbah and others 1994, Shimoyama and others 1995), beta-blockers (Sabbah and others 1994, Shimoyama and others 1995, Uehara and Takahashi 1998), and angiotensin II antagonists (Sabbah and others 1994, Shimoyama and others 1995, Uehara and Takahashi 1998) have been shown in acute experiments to increase forward stroke volume and decrease MR by allowing a more complete emptying of the left ventricle into the aorta (Kittleson and others 1983, Uehara and Takahashi 1998). Whether or not this is beneficial in asymptomatic MMVD remains to be proven. Moreover, recent research suggests that the hypertrophic response to MR is inadequate as a consequence of a comparably low afterload (Matsuo and others 1998, Borgarelli and others 2007), which is considered one of the most important triggers for hypertrophy (Matsuo and others 1998). This argues against a preventive effect of reducing the afterload in chronic MR by use of an arterial vasodilator.

### Beta-receptor blockers

Beta-receptor blockers have been shown to improve left ventricular function in a canine experimental model of chronic MR (Sabbah and others 1994, Nemoto and others 2002). There are presently no clinical data supporting prophylactic effect of beta-blockers in asymptomatic MR caused by MMVD. It should also be noted that this type of drug must be used with caution in dogs with progressed MR because of their negative inotropic and chronotropic effects.

### ACE inhibitors

ACE inhibitors are frequently prescribed to dogs with MMVD before the onset of heart failure. The rationale behind this treatment strategy is that the renin-angiotensin-aldosterone system (RAAS) plays a major role in regulating blood pressure, fluid and electrolyte balance (Macgregor and others 1980) and that angiotensin II is a major myocardial growth factor (Sabbah and others 1994, Shimoyama and others 1995). Clinical trials have shown that ACE inhibitor therapy has a preventive effect on cardiovascular events in people at risk of developing organic heart disease (The HOPE Investigators 2000). It was assumed that asymptomatic dogs with MR caused by MMVD would benefit from ACE inhibitor treatment. To date, two large placebo-controlled multicentre trials, the SVEP and the VetProof trials (Kvart and others 2002, Atkins and others 2007), have been conducted to study the effect of monotherapy of the ACE inhibitor enalapril on the progression of clinical signs in asymptomatic MMVD in dogs. Both controlled clinical trials failed to show an overall significant difference between placebo and treatment groups in time from onset of therapy to confirmed CHF, regardless of whether the dogs had evidence of cardiac remodelling or not.

Two case series on benazepril treatment have been published in which a beneficial...
effect of benazepril was claimed in asymptomatic dogs with MR (Kitagawa and others 1997, Pousselou and others 2008), but not in CKCS (Pousselou and others 2008). Because the pharmacokinetic characteristics of benazepril are similar to other ACE inhibitors currently approved for veterinary use (Hamlin and Nakayama 1998), it can be assumed that the treatment effects are similar. Unblinded conditions and lack of randomisation lead to an overwhelming risk for systematic errors in case series addressing treatment effects, most notably with retrospective case series. Therefore, the results from these case series are outranked by the results from the two placebo-controlled clinical trials of enalapril (Kittleson and others 2009).

Suggested reasons for the non-significant findings in the clinical trials include lack of activation of circulating RAAS activity in asymptomatic MMVD dogs (Häggström and others 1997), low concentration of angiotensin II receptors in the canine mitral valve (Mow and Pedersen 1999) or poor effect of ACE inhibitors on myocardial remodelling and progressive ventricular remodelling in MR (Häggström and others 1996a, Dell'Italia and others 1997). Indeed, more recent research has shown that myocardial remodelling caused by MR is a very complex process, which does involve angiotensin II, but is very difficult to counteract even if ACE and/or angiotensin II receptors are blocked (Perry and others 2002). Studies in young, healthy experimental dogs, in which MR had been induced by chordal sectioning, showed that MR causes a dissolution of myocardial interstitial collagen weave, which promotes myocyte slippage and cardiac dilatation (Dell'Italia and others 1997, Stewart and others 2003). However, naturally occurring MR secondary to MMVD affects primarily middle-aged to old dogs and progresses slowly. Therefore, experimental models may not reflect the natural progression of the disease.

**Spironolactone**

A proportion of dogs with MMVD have been reported to have intramyocardial arterial changes associated with areas of fibrosis, so called replacement fibrosis (Falk and others 2006). In experimental heart failure, spironolactone has been shown to counteract cardiac fibrosis (Yang and others 2008). Whether spironolactone can counteract intramyocardial arterial changes and replacement fibrosis in dogs with MMVD, and whether a reduction in myocardial fibrosis is associated with a better long-term prognosis remains to be proven.

**Furosemide**

The cornerstone for treatment of dogs with CHF caused by MMVD is furosemide. This diuretic agent contracts the extracellular fluid compartment resulting in reduced pulmonary venous and capillary pressures and accordingly alleviates clinical signs of pulmonary congestion and oedema (Boswood and Murphy 2006, Hori and others 2008). There is a general consensus among experts that furosemide is essential in the treatment of dogs with CHF, and the vast majority of the large controlled multi-centre trials have allowed furosemide treatment in the protocol. However, the efficacy of furosemide has not been established in controlled clinical trials in dogs. The comparison of furosemide with placebo would be considered unethical in dogs in heart failure secondary to MMVD and studies comparing furosemide with other diuretic agents have, to the author’s knowledge, not been undertaken.

**Pimobendan and levosimendan**

Pimobendan and levosimendan act by increasing the affinity of myocardial myofilaments for calcium and by suppressing phosphodiesterase III activity, resulting in increased myocardial force of contraction and vasodilatation (Pagel and others 1996). Accordingly, these substances are sometimes referred to as inodilators. Levosimendan is currently under development for veterinary use with only data from experimental studies in dogs available to date (Pagel and others 1996). Current published documentation of the clinical efficacy and safety of pimobendan in blinded prospective trials in dogs with MMVD includes one single centre trial (Smith and others 2005) and two multi-centre trials (Lombard and others 2006, Häggström and others 2008). These trials showed that pimobendan was well tolerated and no proarrhythmic effects were reported. The study by Smith and others (2005) showed that the likelihood of an adverse heart failure outcome in dogs receiving pimobendan was 25 per cent of that for the ACE inhibitor ramipril.
However, the small sample size of this study unintentionally led to differences at baseline for some of the variables, which potentially could have influenced the results. The VetSCOPE study (Lombard and others 2006) showed a better clinical status and improved survival over a 56-day period for dogs receiving pimobendan compared with those not receiving pimobendan. The most recent study, the QUEST trial (Häggström and others 2008), offers the most compelling evidence of beneficial actions of pimobendan. The most recent study, the QUEST trial (Häggström and others 2008), offers the most compelling evidence of beneficial actions of pimobendan. The most recent study, the QUEST trial (Häggström and others 2008), offers the most compelling evidence of beneficial actions of pimobendan. The most recent study, the QUEST trial (Häggström and others 2008), offers the most compelling evidence of beneficial actions of pimobendan.

**ACE inhibitors**

The effects of different ACE inhibitors in dogs with MMVD-induced CHF is the most thoroughly studied area in veterinary cardiovascular medicine. At present, results from four prospective placebo-controlled clinical trials (The COVE Study Group 1995, The IMPROVE Study Group 1995, Ettlinger and others 1998, The BENCH Study Group 1999), and more than five open label or comparative trials (Häggström and others 1996a, Sent and others 2000a,b, Amberger and others 2004, Moesgaard and others 2005), have been published. These studies report that ACE inhibitors are well tolerated in dogs with MMVD and CHF, and that, in combination with diuretics, they improve clinical signs (The BENCH Study Group) and prolong survival compared with dogs not receiving an ACE inhibitor (Ettlinger and others 1998, The BENCH Study Group 1999). The reason for this may be that ACE inhibitors combined with diuretics, such as furosemide, act by suppressing high RAAS activity caused by severe CHF and by counteracting the stimulation of RAAS occurring in diuretic therapy. (Häggström and others 1996a, Häggström and others 1997). Thus, ACE inhibitors may decrease the tendency for fluid retention and counteract peripheral vasoconstriction and other negative effects on the heart. In man, the administered dose of ACE inhibitor is frequently lower than those used in the landmark trials, and it has been suggested that this lower dose leads to a worse outcome when compared with a higher dose (Schwartz and others 2003, Thomas and Geltman 2006). The doses of ACE inhibitors administered to dogs enrolled in all the clinical trials of ACE inhibitors (including the QUEST trial) have been within the recommended dose range for dogs. In fact, it appears that the effect of ACE-inhibitors is comparable at different doses within the recommended dose range in dogs (Toutain and others 2000). There is currently no evidence in dogs to support the suggestion that additional benefits would be obtained by administering doses higher than the recommended dose range.

**Spironolactone**

The RALES study showed that a sub-diuretic dose of the aldosterone antagonist spironolactone improved survival in people with CHF (Pitt and others 1999). Spironolactone has since been developed for veterinary use and was recently approved in Europe for use (in addition to other CHF therapy) in dogs with CHF attributable to MMVD. The approval was based on a set of clinical trials, indicating improved quality of life and prolonged survival in dogs with CHF caused by MMVD receiving spironolactone. Publication of these trials is pending. Spironolactone alone is not a potent diuretic. Its diuretic effect is, in similarity to that of ACE-inhibitors, dependent on aldosterone activity (Tan and others 2004). Aldosterone concentrations increase in some dogs receiving an ACE-inhibitor and furosemide. This phenomenon is dependent on dose of furosemide and has been attributed to the fact that ACE-inhibitors do not completely block ACE activity (Häggström and others 1996a). Other enzymes, such as chymase, can catalyse the reaction in which angiotensin

---

**FIG 2.** Kaplan-Meier plot from the QUEST trial (Häggström and others 2008) showing the percentage of patients remaining in the study as a function of time. The study involved 124 dogs treated with pimobendan (plus conventional therapy) and 128 dogs treated with benazepril (plus conventional therapy). The pimobendan dogs had a significantly longer time period in the study compared to the benazepril treated (pimobendan 267 days, interquartile range (IQR) 122-523 days vs. benazepril 340 days, IQR 67-311 days; P=0.0099). With permission from the publisher.
Il is formed (Stewart and others 2003). Furthermore, an antifibrotic effect of the aldosterone blocker spironolactone has been shown in experimental studies (Suzuki and others 2002). It remains to be proven that aldosterone antagonists have an antifibrotic effect in geriatric dogs and whether this effect confers a beneficial prognosis in this population of dogs.

**Beta-receptor blockers**

Finally, there is another set of drugs used in dogs with CHF caused by MMVD. Beta-receptor blockers have been shown to improve survival in people with CHF (Packer and others 2001), but this has never been shown in dogs with CHF caused by MMVD. Currently, there is only one case series published (Marcondes-Santos and others 2007). In fact, many experts advise against the use of beta-blockers in acute CHF because they may drastically exacerbate the condition by the nature of their negative inotropic and chronotropic effects (Kittleson 2000, Häggström and others 2005). The current expert recommendation is that, if beta-blocker therapy is to be instituted, the dog should be stabilised on other CHF therapy, and the dose should be gradually increased under careful monitoring (Kittleson 2000, Häggström and others 2005).

**Digoxin**

Digoxin is still one of the most commonly prescribed cardiac drugs for dogs (Kittleson 2000), although scientific evidence of efficacy in dogs with naturally occurring heart disease is scarce (Uehara and Takahashi 1998). The reasons why experts and practitioners use it are old habits, antiarrhythmic effects and its neuromodulatory effects (it resensitises the baroreceptors to prevailing blood pressure that may decrease sympathetic tone and has a vagomimetic effect). Digoxin, as opposed to beta-blockers, has the benefit of being a negative chronotrope without negative inotropic effect (Eichhorn and Gheorghiade 2002), and this may be useful to control heart rate in some dogs with CHF. The positive inotropic effect of digoxin has been shown in numerous experimental settings (Eichhorn and Gheorghiade 2002), but is difficult to establish in clinical settings. Studies in people with CHF have indicated that digoxin improves quality of life and decreases hospitalisation, but digoxin has never been shown to improve survival in people nor in dogs with CHF (Packer and others 1993, The Digitalis Investigation Group 1997). It is unlikely that a large clinical trial of digoxin in dogs will be performed because a very large study population would be required to detect an effect, which, if present, is likely to be small.

**Arterial vasodilators**

The arterial vasodilating agents hydralazine and amlodipine have, as mentioned above, the potential to decrease the MR. There are currently only a few published studies addressing treatment effects of these drugs in dogs (Kittleson and others 1983, Häggström and others 1996a) and many experts use them as a salvage agent in dogs with severe MR. Whether or not this is the optimal use of arterial vasodilating agents is currently not known.

**Thiazide diuretics**

Hydrochlorothiazide is a diuretic agent that has been used to manage dogs with CHF caused by MMVD. Similar to spironolactone, it is a weak diuretic on its own. It is therefore used together with other diuretics such as furosemide and spironolactone to block the nephron more effectively (Kittleson 2000). The information for this type of therapy in dogs is currently restricted to a few case reports and experimental studies performed in the 1960s and 1970s (Buchanan and others 1968, Kasumoto and others 1973).

**PROGNOSTIC INDICATORS AFTER THE ONSET OF CHF**

Some clinical variables have been shown to have prognostic value after the onset of CHF in dogs with MMVD. The type of adjunct therapy influences survival. Hence, increased survival has been reported in dogs treated with pimobendan, as well as the ACE inhibitors enalapril and benazepril (Ettinger and others 1998, The BENCH Study Group 1999, Häggström and others 2008). Furthermore, the expected survival time decreases with increasing maintenance dose of furosemide, decreasing exercise tolerance, increasing cardiac size and severity of MR [VHS

![FIG 3. Hazard ratios and 95% confidence intervals obtained from the final multivariate Cox Proportional Hazard model of 252 dogs with MMVD and CHF in the QUEST Trial (Häggström and others 2008). Of the initial 33 included clinical baseline variables, only 7 remained significant in the final model. Factors associated with a reduced risk (Hazard Ratio <1) of reaching the endpoint of cardiac death, euthanasia or treatment failure included pimobendan treatment, the breed CKCS, and increased serum creatinine concentrations. Variables associated with an increased risk (hazard ratio>1) of reaching the same endpoint included higher increased daily furosemide dose, worse exercise tolerance score, higher VHS score, higher LVIdi (%), and LA/Ao ratio. With permission from the publisher. Abbreviations: LVIdi inc (%), percentage increase in left ventricular end-systolic diameter from expected values based on body weight; LA/Ao, left atrial to aortic root ratio; CKCS, Cavalier King Charles spaniel.](image-url)
score, left atrial size (LA/AO), decreasing serum creatinine concentration (possibly indicating cardiac cachexia) and decreasing systolic function (increased end-systolic dimension) (Fig 3) (Borgarello and others 2008, Häggström and others 2008). There are indications that breed could affect the outcome after onset of CHF. The CKCS breed has been associated with a better prognosis when compared with a group consisting of other breeds (Fig 3) (Häggström and others 2008). However, these results are not conclusive because it is possible that the difference found in this comparison was caused by an exceptionally poor outcome in one or more of the breeds included in the group compared with CKCS. Furthermore, the statistical analysis can only indicate that there was a factor associated with the CKCS breed that conferred a favourable outcome. This factor may be actual disease progression, but it may also be owner attitudes towards their pet, the drug or the medication. Finally, the development of a complication, such as atrial fibrillation, rupture of a major chordae tendineae, pulmonary hypertension and myocardial infarction, has been suggested confer a worse clinical outcome (Häggström and others 2005), but clinical evidence is lacking.

CONCLUSIONS

- Myxomatous mitral valve disease is a chronic disease with progression over years from mild MR without clinical signs of disease to severe MR with signs of CHF. Because the disease affects middle-aged to old dogs, not all dogs will progress into CHF before they succumb to other co-morbid conditions or old age.
- Risk factors associated with rapid progression at low-degree MMVD include age, severity of valvular changes and degree of MR.
- Risk factors for predicting the onset of CHF include different ultrasound and radiographical measurements that directly or indirectly reflect severity of MR (LA/AO, VHS and others), heart rate and heart rate variability, and blood concentrations of natriuretic peptides.
- No therapy or management has yet convincingly been demonstrated to halt or slow the progression of MMVD from mild disease without clinical signs to severe with clinical signs of CHF.
- Dogs with MMVD and signs of CHF are treated with a diuretic and other adjunct therapy. Evidence of efficacy (quality of life and survival) from controlled clinical trials is available for ACE inhibitors and pimobendan. Results from trials addressing the effects of spironolactone and levoevipan are pending.
- Prognostic variables after the onset of CHF include different echocardiographic and radiographic variables indicative of cardiac size and severity of MR, maintenance dose of furosemide, type of adjunct therapy, exercise tolerance, severity of cardiac cachexia and severity of systolic dysfunction.
- Presence of a complication to MMVD, such as atrial fibrillation, clinical signs of cardiac hypertension, rupture of major chordae tendineae and myocardial infarction, is expected to influence the prognosis, but their impact on outcome have not yet been estimated.

References


Haegstrom, J., Boswood, A., Gaskin, D., Jones, D., Smith, S., Swift, S., Bissessur, M., Gagdin, B., Reiden, J.


Journal of the American Veterinary Medical Association 229, 905-914.


Treatment and prognostic indicators in MMVD


