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PRECLINICAL MMVD

a disease not visible to the
dog owner



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Degenerative Mitral Valve Disease (Dmvd, Also Known As Myxomatous Mitral Valve Disease, Mmvd) Is The Most Common Acquired Cardiac Disease In Dogs.

A study in England (Great Britain) suggested that around 3.5% of dogs presented to a primary veterinarian showed this disease (Mattin et al. 2015). DMVD is a condition of middle-aged to older dogs (9.5 ± 3.2 years), and of small breeds (median body weight: 10.9 kg) such as the Cavalier King Charles spaniel (CKCS), Whippet, Poodle, Yorkshire terrier, Shi-tzu, Chihuahua, miniature Schnauzer, Dachshund and other breeds. A polygenetic mode of inheritance has been demonstrated in CKCS (Swenson et al. 1996) and Dachshunds (Olsen et al. 1999). Dogs of larger breeds like border Collie (Mattin et al. 2015) or German shepherd dog (Borgarelli et al. 2004) can also be affected. An important difference between small and large dog breeds is the occurrence of arrhythmias (in particular atrial fibrillation), which are much more common in large breeds (Borgarelli et al. 2004).

Furthermore, there is a gender predisposition for male dogs to DMVD (Olsen et al. 1999). This disease is usually slow and progressive in nature (Serfass et al. 2006). Therefore, most patients are diagnosed when the typical heart murmur is observed. This murmur develops due to the turbulent jet caused by the incomplete closure of the mitral valve and is generally an incidental finding that is nevertheless in most cases clearly identifiable. The volume of the murmur has been shown to be correlated with the intensity of the disease (Ljungvall et al. 2009).

According to the most recent research, a clear need to take action is required, even in asymptomatic patients. Therefore, it is important to examine all dogs regularly by auscultation (when presented for check-ups, vaccinations, anthelmintic treatment or castration, etc), and to subsequently perform further diagnostics if a murmur is found to be present. The cause of the disease is a myxomatous degeneration of the valve tissue. This leads to irregular thickening of the valve, resulting in insufficient closure and regurgitation of blood from the left ventricle to the left atrium (Fox 2012). This process is progressive, and characterized by a long preclinical phase that can be prolonged by medication. In this preclinical phase, the dog is asymptomatic and has a normal quality of life. If signs such as exercise intolerance, cough or shortness of breath appear, the clinical phase of the disease has started and quality of life is impaired. The clinical phase of the disease can be seen as the tip of the iceberg in terms of the overall cardiac condition.

Therefore, the primary goal of disease treatment should be to prolong the asymptomatic phase. Disease progression is characterized by different stages. Since the stage of disease is crucial for deciding on treatment, it is mandatory to use a standardized and practical classification. The ACVIM-consensus statement fulfills these criteria (Atkins et al. 2009).

In **Stage A**, dogs have an increased risk of developing DMVD, but don't have any signs of structural heart disease. **Stage B** describes asymptomatic patients with structural cardiac disease. They are subdivided into **B1** (without volume overload) and **B2**. Stage B1 includes all patients without demonstrable radiographic or echocardiographic cardiac sequelae (left atrial or left ventricular dilation). In **B2** (with volume overload), the patients display hemodynamically significant regurgitation (cardiomegaly, seen in radiographs or echocardiography as dilation of the atrium and/or ventricle). Therefore, stage B2 consists of patients that have cardiac enlargement, but are still without any clinical signs. It should also be noted that these patients are usually elderly, and when first signs such as unwillingness to walk and cough appear, these symptoms are frequently attributed by the owner to the age of the patient.

Dogs in **stage C** show clinical signs at the time of evaluation, or previously had clinical symptoms attributable to structural heart disease and are under drug therapy. This stage includes patients with past or current clinical signs of congestive heart failure related to mitral valve regurgitation.

Stage D consists of patients with end-stage disease that do not respond to standard medical treatment. Dogs in stage C and D can be further divided into acute (hospital-based) and chronic (home monitored) patients.

ASYMPTOMATIC		SYMPTOMATIC	
Class A	patients at risk	Class C	heart failure (past or present signs)
Class B	1 heart murmur without cardiomegaly 2 heart murmur with cardiomegaly	Class D	heart failure resistant to therapy

Heart enlargement in mitral valve disease can be assessed using radiography (Vertebral Heart Score = VHS – normal range: 8.5 to 10.5). This method has a good interobserver compliance (Hansson et al. 2005), but many breed-specific reference ranges exist. Nevertheless, it has been shown that a high VHS-value in a dog with a cough is suggestive of a cardiac-related cough (Guglielmini et al. 2009), and that it can be used for the assessment of cardiac enlargement in mitral valve regurgitation (Lamb et al. 2001). Furthermore, the left heart chambers rapidly increase in size only in the last year before the onset of congestive heart failure (Lord et al. 2010). An increase of more than 0.08 VHS-units/month has to be considered as a risk factor (Lord et al. 2010). This means that radiographs should be taken on a biannual or annual basis, since an increase of 1 unit in one year is suggestive of decompensation. Therefore, interpretation of the current VHS should always be compared to preliminary results (Reynolds et al. 2012).

In fact, an appropriate tentative diagnosis can be made based on signalment and auscultation, but the differentiation between mitral endocardiosis and dilated cardiomyopathy can be challenging especially in large-breed dogs. An appropriate investigation by a veterinary cardiologist is always useful, even in the sole presence of a heart murmur without any clinical signs.

This is primarily because it has been shown that early treatment in both dilated cardiomyopathy and mitral valve regurgitation can prolong the time to development of congestive heart failure (O'Grady et al. 2009; Summerfield et al. 2012; Boswood et al. 2016). The exact diagnosis of underlying heart disease can be made based on well-established echocardiography. The dimensions of the left ventricle can be measured and compared by using a weight-independent index (Cornell et al. 2004). Furthermore, the valve morphology can be assessed echocardiographically, which may be helpful in assessment of disease stage.

For therapy of mitral valve endocardiosis, it is important to recognize those patients that might benefit from early treatment. To implement this, correct identification of the patient's ACVIM classification stage is important. For patients in stage B2 (i.e. asymptomatic dogs with cardiac enlargement) a clear positive effect of Pimobendan was demonstrated in the EPIC study (Evaluating Pimobendan in Preclinical Cardiomegaly; Boswood et al. 2016).

Pimobendan is a calcium-sensitizer (Lee et al. 1989; Takahashi, Endoh 2001) and phosphodiesterase-III inhibitor (Fujimoto, Matsuda 1990) with positive inotropic (Pouleur et al. 1988; Pouleur et al. 1989) and vasodilative action (Fujimoto 1994; Tsuda et al. 1992).

Prerequisites for the use of pimobendan in clinically asymptomatic patients are left atrial dilation (LA/Ao ≥ 1.6), left ventricular dilation (LVDD-I ≥ 1.7) and cardiac enlargement on radiographic examination (VHS > 10.5). A patient must meet all criteria, and cardiac enlargement detected in a radiographic examination should be followed by an echocardiographic examination to enable a decision on the use of Pimobendan treatment to be made.

Summary:

Degenerative mitral valve disease is the most common heart disease in dogs. An early diagnosis is crucial, as therapy in the asymptomatic stage significantly prolongs the time to development of clinical signs.

Therefore, older dogs of predisposed breeds, and preferably all dogs, should be screened for the presence of a heart murmur. This can be conducted on annual or even biannual check-up visits by the referring veterinarian. In the presence of a cardiac murmur, thoracic radiographs should be taken to determine cardiac size. If the VHS is greater than 10.5, echocardiography is crucial for deciding on the use of pimobendan treatment.

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