

**Managing Asymptomatic Dogs with Heart Disease**

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Clinical staging of heart diseases can provide veterinarians and pet owners with a rationale and framework for screening programs (aimed at reducing the prevalence of disease through selective breeding as well as identifying affected individuals at an early stage of their disease to facilitate more effective treatment), facilitating clinical trials to evaluate treatments and educating clients about their pet's diagnosis and prognosis.

In 2009, a consensus panel convened by the American College of Veterinary Internal Medicine Specialty of Cardiology adopted a staging and classification system for CVD that provides objective staging criteria for canine patients with structural heart disease.<sup>1</sup>

This system recognizes 4 stages of heart disease and failure:

- **Stage A** patients are at high risk for developing heart disease but have no identifiable structural heart disease (e.g. normal Cavalier King Charles Spaniels, Doberman Pinschers, or Boxers).
- **Stage B** patients have structural heart disease (e.g. the typical murmur of mitral valve regurgitation is present), but have never shown symptoms. Because prognosis and treatment may differ depending on severity of structural disease, **Stage B** is subdivided into **Stages B1** and **B2**.
  - **Stage B1** refers to asymptomatic patients with no radiographic or echocardiographic evidence of cardiac remodeling.
  - **Stage B2** refers to asymptomatic patients who have hemodynamically significant valve regurgitation as evidenced by radiographic or echocardiographic findings of left-sided heart enlargement (or echocardiographic enlargement and systolic dysfunction in DCM). Asymptomatic Boxers with ARVC at Stage B2 have typical right ventricular ectopy evident on resting or Holter (24 hour) ECG.

- **Stage C** denotes patients with past or current clinical signs or symptoms of heart failure associated with structural heart disease
- **Stage D** refers to patients with end-stage disease whose clinical signs of heart failure are refractory to standard therapy with pimobendan, an ACEI, and standard doses of furosemide ( $\geq 6$  mg/kg/day) and spironolactone.

This seminar will only address asymptomatic heart disease patients in Stages A and B.

With the exception of surgically managed congenital heart diseases (e.g. patent ductus arteriosus), pericardial diseases, and infectious heart diseases (e.g. heartworm disease, bacterial endocarditis), the common heart diseases of dogs (chronic myxomatous valvular disease [CVD] and dilated cardiomyopathy [DCM]) are rarely curable.

### **Diagnostic Screening Strategies for Stage A**

A sensible screening strategy for CVD in predisposed breeds (e.g. Cavalier King Charles Spaniels, dachshunds, miniature poodles and others) is cheap and easy to implement, because development of the typical heart murmur generally announces its presence years before the onset of clinical symptoms. All dogs should undergo regular (yearly) evaluations for the presence of heart disease by their family veterinarian as part of their routine health care. Unless they are participating in an organized research study or registry, there is no evidence to support a clinical benefit of additional cardiac diagnostic testing (e.g. ECG, echocardiography, or NT-proBNP) for asymptomatic small breed patients with normal findings on physical examination.

Screening strategies for dogs with a known predisposition to either DCM or arrhythmogenic right ventricular cardiomyopathy (ARVC) are more complex and difficult to implement. These diseases are not reliably associated with the presence of physical diagnostic findings years before the onset of symptoms, and currently available screening tests

(echocardiography and Holter ECG monitoring) are relatively expensive, and their diagnostic accuracy is highly operator dependent. For animals (e.g. Boxers, Doberman Pinschers, some giant breed dogs) with known predisposition, recommended screening tests include both Holter ECG monitoring and echocardiographic evaluation; both tests should ideally be interpreted (if not performed) by a board certified cardiologist. There is no definitive information on the age at which screening should begin or the ideal frequency of screening exams for asymptomatic animals with normal physical examination findings, but a sensible recommendation might be to initiate yearly screening exams at age 2 for breeding animals and dogs owned by highly motivated, concerned clients with no financial restrictions.

**Management Strategies for Stage A:** No specific drug or dietary therapy is recommended for patients without evidence of heart disease.

#### **Diagnostic Strategies for Staging: B1 vs. B2**

Stage B patients all have structural heart disease, and all are free of clinical signs of heart failure. These patients are generally recognized during a screening examination of a Stage A patient (see above – they become Stage B as soon as their heart disease is recognized), or during a routine health examination.

Dogs with CVD may develop a left apical holosystolic heart murmur typical of mitral valve insufficiency that remains hemodynamically insignificant for years, causing no cardiac enlargement (Stage B1). Asymptomatic dogs of typical breed and age (i.e. small or toy breed dogs, excluding American Cocker Spaniels, over 7 years of age or Cavalier King Charles Spaniels over 5 years of age.) with a new murmur and no other physical signs of significant disease should be offered a basic diagnostic work-up to assess the hemodynamic significance of their CVD. Thoracic radiography is recommended in all of these patients to assess the

hemodynamic significance of their disease, and to obtain baseline thoracic radiographs at a time when the patient is asymptomatic for CVD. Blood pressure measurement is recommended for all patients. In small or toy breed dogs with typical murmurs, echocardiography is recommended to answer specific questions regarding either cardiac chamber enlargement or the cause of the murmur if those questions have not been answered adequately by auscultation and thoracic radiography.

Echocardiography is indicated in dogs with murmurs that are not easily explained. Young dogs, American Cocker Spaniels and larger dogs should undergo echocardiographic examination because the murmur of mitral regurgitation is more likely to be caused by something other than CVD (e.g. congenital heart disease, DCM). Basic laboratory work (a minimum of PCV/TP; serum creatinine, and urinalysis) is indicated in all patients.

Because their prognosis differs substantially, asymptomatic patients with murmurs of mitral valve insufficiency are further sub-categorized into 2 groups based on the results of the above evaluation:

- **Stage B1:** Asymptomatic dogs with CVD are Stage B1 if their mitral regurgitation is essentially hemodynamically insignificant. In asymptomatic animals, the overall hemodynamic significance of mitral regurgitation is probably best assessed by evaluating the left atrial size. Stage B1 dogs are radiographically and echocardiographically normal, or may have at most an equivocally enlarged left atrium or left ventricle with normal (not hyperdynamic) left ventricular systolic functional indices on echocardiography. They have a normal radiographic vertebral heart score, are normotensive, and have normal laboratory results.

- **Stage B2:** Asymptomatic dogs with CVD are Stage B2 if they have significant left atrial enlargement, with or without an enlarged left ventricle. Dogs diagnosed with DCM or ARVC are considered to be Stage B2 because they have evidence of cardiac remodeling (or arrhythmia, which is presumably a manifestation of underlying structural heart disease). These dogs also need to have their systemic blood pressure and basic laboratory parameters evaluated.

Stage B2 dogs with DCM may have soft (low intensity) heart murmurs or gallop sounds, but their diagnosis must be established echocardiographically by observing a dilated, hypocontractile left ventricle, with or without ventricular ectopy or other rhythm disturbance. Dogs with ARVC have typical right ventricular ectopy on a resting or Holter ECG (generally more than 1,000 VPCs / 24 hours), with or without echocardiographically identifiable structural cardiac changes.

### **Management Strategies for Stage B1**

No therapy (pharmacologic or dietary) is recommended for Stage B1 CVD. In small dogs, yearly reevaluation is suggested (either radiography or echocardiography, with blood pressure measurements and basic laboratory work). In dogs that are atypical for a primary diagnosis of CVD (e.g. larger breeds), more frequent reevaluation may be warranted.

### **Management Strategies for Stage B2**

Medical and dietary management of stage B2 heart disease is controversial, regardless of the underlying nature of the disease (e.g. CVD, DCM, or ARVC). In CVD for example, no consensus could be reached among the ACVIM panel regarding therapy at this stage.

The results of clinical trials addressing the efficacy of angiotensin converting enzyme inhibitors (ACEI) for the treatment of dogs in Stage B2 have generally been disappointing to varying degrees, showing either no effect (SVEP) or a small positive effect in secondary trial

endpoints to delay the onset of congestive heart failure (VETPROOF).<sup>2,3</sup> The reasons for the lackluster performance of ACEI for this purpose remain unclear, but consideration of all of the data, including significant differences in patient populations, trial methodologies and drug dosages, suggests that part of the problem may be dose related (i.e. higher dosages of ACEI may be more effective for this purposes than once daily, lower dosages). For patients with severe left atrial enlargement on initial examination, or substantial left atrial size increases on interval examinations, the author prescribes an ACEI (e.g. enalapril, 0.5mg/kg BID). This course of action was also recommended by a majority of the ACVIM panel members, and the strength of this recommendation increases for large breed dogs with CVD. In DCM, there is some clinical evidence to support the use of ACEI to delay the onset of heart failure, and most cardiologists (including the author) routinely prescribe ACEI for stage B2 DCM.<sup>4</sup>

A large, randomized, placebo-controlled clinical trial to test the efficacy of a beta adrenergic blocker (bisoprolol) to delay the onset of heart failure in dogs with stage B2 CVD was recently halted because of lack of efficacy (currently unpublished data). The author still recommends the addition of a beta blocker to delay the onset of heart failure in stage B2 DCM or ARVC.

There is now solid, published evidence to support the use of pimobendan in Doberman Pinschers with stage B2 DCM, and a large, randomized, placebo-controlled trial to test the efficacy of pimobendan for stage B2 CVD is currently in progress.

Dietary treatment (maintaining adequate protein and caloric intake in the context of modest sodium restriction, such as most high quality “senior” diets) is usually recommended for Stage B2 heart disease from any cause, and supplementation with EPA fish oils is also recommended for dogs with DCM or ARVC. Other nutraceuticals (e.g. L-carnitine, taurine,

other compounds) may also be recommended on a case by case basis, usually in the management of stage B2 DCM or ARVC.

## **Summary**

For the management of stage B2 CVD in small dogs, starting an ACEI appears to be sensible only when the left atrium becomes significantly enlarged; this recommendation is strengthened for large dogs with CVD. Recommendations on the use of pimobendan in this setting awaits completion and publication of the ongoing EPIC trial. For large breed dogs with CVD characterized by significant left atrial and ventricular enlargement with monitoring interval changes indicating diminished LV systolic function, the use of both pimobendan and gentle titration onto a beta blocker in addition to an ACEI are recommended by the author.

For the management of stage B2 DCM in Doberman Pinschers, the author currently recommends an ACEI combined with pimobendan and gradual up-titration of a beta blocker. In stage B2 ARVC, therapy beyond beta blockade (e.g. atenolol or metoprolol) is dependent on Holter results and the presence or absence of ventricular enlargement and dysfunction. An ACEI or specific ventricular antiarrhythmic drugs are used as needed based on serial monitoring. Up to date drug dosages and other relevant information for all of the drugs discussed in this paper can be found on NC State's website: [CardiologyCareNetwork.org](http://CardiologyCareNetwork.org).



## References

1. Atkins C, Bonagura J, Ettinger S, Fox P, Gordon S, Haggstrom J, Hamlin R, Keene B, Luis-Fuentes V, Stepien R: Guidelines for the diagnosis and treatment of canine chronic valvular heart disease. *J Vet Intern Med.* 2009 Nov-Dec; 23(6):1142-50.
2. Kvarn C, Häggström J, Pedersen HD, Hansson K, Eriksson A, Järvinen AK, Tidholm A, Bsenko K, Ahlgren E, Ilves M, Ablad B, Falk T, Bjerkfås E, Gundler S, Lord P, Wegeland G, Adolfsson E, Corfitzen J: Efficacy of enalapril for prevention of congestive heart failure in dogs with myxomatous valve disease and asymptomatic mitral regurgitation. *J Vet Intern Med.* 2002 Jan-Feb; 16(1):80-8.
3. Atkins CE, Keene BW, Brown WA, Coats JR, Crawford MA, DeFrancesco TC, Edwards NJ, Fox PR, Lehmkuhl LB, Luethy MW, Meurs KM, Petrie JP, Pipers FS, Rosenthal SL, Sidley JA, Straus JH: Results of the veterinary enalapril trial to prove reduction in onset of heart failure in dogs chronically treated with enalapril alone for compensated, naturally occurring mitral valve insufficiency. *J Am Vet Med Assoc.* 2007 Oct 1; 231(7):1061-9.
4. O'Grady MR, O'Sullivan ML, Minors SL, Horne R: Efficacy of benazepril hydrochloride to delay the progression of occult dilated cardiomyopathy in Doberman Pinschers. *J Vet Intern Med.* 2009 Sep-Oct;23(5):977-83
5. Summerfield NJ, Boswood A, O'Grady MR et al: Efficacy of Pimobendan in the Prevention of Congestive Heart Failure or Sudden Death in Doberman Pinschers with Preclinical Dilated Cardiomyopathy (The PROTECT Study). *J Vet Intern Med.* 2012 Oct 18. doi: 10.1111/j.1939-1676