



Finding a Consensus on Canine CVHD

Canine chronic valvular heart disease (CVHD) is the most important nonparasitic cardiovascular disease in veterinary medicine, but controversy remains about the best treatment.

THE PLAYERS

Canine CVHD, also known as endocardiosis, myxomatous valve degeneration, and mitral regurgitation (MR), affects approximately 85% of dogs 13 years of age or older and accounts for 75% of heart disease in dogs.¹ For such a substantial disease, it may be surprising that there still is controversy and general lack of agreement about the appropriate medical management, both before and after the onset of heart failure.

To this end, the American College of Veterinary Internal Medicine's (ACVIM) Board of Regents recently selected a group of European and American board-certified cardiologists to present a formal consensus for the diagnosis and treatment of CVHD.¹ The 10 panel members represented diverse points of view on cardiac therapeutics.

The consensus statements and recommendations of the panel are not to be taken as "cutting edge" but rather as a sampling of the "collective wisdom" that occurs when reasonable people reach a compromise after reviewing published data and their own experiences.

THE PANEL

Bruce Keene, DVM, MSc, Diplomate ACVIM, Panel Chair
Clarke Atkins, DVM, Diplomate ACVIM (Internal Medicine & Cardiology)
John Bonagura, DVM, MS, Diplomate ACVIM
Stephen J. Ettinger, DVM, Diplomate ACVIM (Internal Medicine & Cardiology)
Philip R. Fox, DVM, MS, Diplomate ACVIM/ECVIM (Cardiology) & ACVECC
Virginia Luis-Fuentes, VetMB, PhD, CertVR, DVC, MRCVS, Diplomate ACVIM & ECVIM
Sonya G. Gordon, DVM, DVSc, Diplomate ACVIM (Cardiology)
Jens Häggström, DVM, PhD, Diplomate ECVIM (Cardiology)
Robert Hamlin, DVM, PhD, Diplomate ACVIM
Rebecca Stepien, DVM, Diplomate ACVIM

THE PROCESS

Based on available evidence, the ACVIM panel determined whether the potential benefits of a given treatment option clearly outweighed the risk for adverse events and if the financial impact on the patient and client would be justifiable.

CONTINUES

Consensus was defined as all 10 panel members agreeing to a particular recommendation, but we also revealed when a *majority* of the panelists agreed on a recommendation even if the criteria for consensus were not met.

HEALTH CARE SCHEME

Although a number of classification schemes that grade cardiac disease in dogs are already in place, we created a novel scheme modeled after one used by the American Heart Association and the American College of Cardiology. Our system avoids the inclusion of progressive exercise intolerance when grading disease severity and adds a category for dogs that show no clinical signs but are at risk for the disease (eg, cavalier King Charles spaniels, dachshunds, miniature and toy poodles).

In this article, I describe some of the more important consensus and majority findings from the panel, as well as offer some insights into how these findings can translate into everyday patient care based on my own practice.

Note: Not all consensus recommendations would be appropriate for each patient. For example, it is unlikely that a dog on pimobendan would also receive dobutamine.

STAGE

A

ACVIM classification

- Patient at risk
- No clinical signs

From the panel

- No drug or dietary therapy recommended at this stage
- Dogs used for breeding should be removed from the breeding program if MR is present

For my patients

For dogs with stage A CVHD, I make the dog's owner aware of the need for annual examinations, what may lie ahead if the disease progresses, and what an aggressive diagnostic and therapeutic approach might entail. I also discuss what can be done for a patient if the owner has financial constraints. I discuss diet and exercise and the role of dietary restrictions as heart failure ensues. I also give the owners a prognosis and inform them as to how various predictable and unpredictable circumstances might alter the general expectation.

STAGE

B₁

ACVIM classification

- Murmur present
- No cardiomegaly

From the panel

- Consensus: No drug or dietary therapy recommended at this stage for dogs with hemodynamically insignificant MR, defined here as radiographic or echocardiographic evidence of a normal or equivocally enlarged left atrium, left ventricle, or both, in addition to normal left ventricular systolic function, normal vertebral heart score on radiography, normal blood pressure, and normal laboratory results

For my patients

I suggest to owners that the dog may benefit in the long-term from a diet that is mildly to moderately restricted in sodium content, while the dog's appetite is presumably still good. I also suggest blood pressure control—most likely with the addition of amlodipine and an ACE inhibitor in the relatively unusual circumstance in which systemic hypertension accompanies CVHD. This is true at any stage of CVHD.



ACE = angiotensin-converting enzyme, ACVIM = American College of Veterinary Internal Medicine, CVHD = chronic valvular heart disease, IMPROVE = invasive multicenter prospective veterinary evaluation of enalapril study, MR = mitral regurgitation, RAAS = renin-angiotensin-aldosterone system

STAGE B₂

ACVIM classification

- Murmur and cardiomegaly present

From the panel

- Consensus: None
- Majority: ACE inhibitor
- Majority: Highly palatable, mildly sodium-restricted diet
- Majority: Against use of beta-blocker, pending clinical trials

For my patients

My viewpoint is controversial,² as I prescribe an ACE inhibitor at this stage of the disease because of an abundance of supporting evidence.^{3,4} In an unpublished survey of 100 board-certified veterinary cardiologists, almost 60% prescribed ACE inhibitors in small breeds of dogs and nearly 70% prescribed the drugs in large breeds at this stage.⁵

For some of my more dedicated owners, I often prescribe up-titration of a beta-blocker and would consider adding spironolactone. I base the latter approach on recent research conducted at North Carolina State University College of Veterinary Medicine. This study indicates that “aldosterone escape” can occur when benazepril is used in healthy dogs that are undergoing furosemide-induced activation of the renin-angiotensin-aldosterone system (RAAS).⁶

LATE-BREAKING DATA

The consensus statement was prepared before the publication of a placebo-controlled, double-blind study that demonstrated the positive impact of spironolactone when added to standard therapy in dogs with heart failure.¹⁸ The panel may have reached consensus on the use of spironolactone in dogs with stage C disease if this information had been available during our deliberations.

STAGE C_a

ACVIM classification

- Acute heart failure requiring hospitalization

From the panel

- Consensus: Furosemide (PO, IM, IV, or CRI^{7,8})
- Consensus: Pimobendan
- Consensus: Oxygen via cage or nasal cannula
- Consensus: Mechanical removal of thoracic or abdominal fluid
- Consensus: Relieve dyspnea/discomfort via appropriate humidity, environmental temperature, and body positioning
- Consensus: Sedation with buprenorphine and/or acepromazine or morphine
- Consensus: Nitroprusside (a mixed vasodilator) and/or dobutamine (inotropic effect, afterload reduction, reduction of mitral orifice size) via CRI
- Majority: ACE inhibitor, based on human research evaluating IV enalaprilat (the active metabolite of enalapril)^{9,10} and the results of the IMPROVE trial¹¹

For my patients

I was in the minority in advocating the use of nitroglycerin in patients at this stage of the disease. I believe that additional off-loading therapy is beneficial and can be used in place of nitroprusside, which can be cumbersome (requires protection from light; CRI; shelf-life of 24 hours after reconstitution; blood pressure monitoring). Otherwise, my treatment approach is the same as that of the panel as a whole.

STAGE C_c

ACVIM classification

- Chronic heart failure requiring at-home care

From the panel:

- Consensus: “Triple therapy approach”—furosemide PO, ACE inhibitor,¹¹⁻¹⁶ and pimobendan¹⁷
- Consensus: Against beta-blocker in patients with signs of heart failure
- Majority: Highly palatable, mildly sodium-restricted diet
- Majority: Spironolactone (see **Late-Breaking Data**)
- Majority: Digoxin for cardiac inotropic support and to slow the ventricular response to atrial fibrillation in dogs so afflicted

For my patients

My personal approach to C_c patients is to use triple therapy as well as spironolactone. This would be accompanied by moderate sodium restriction in a well-balanced commercial canine diet.

CONTINUES

STAGE **D_a****ACVIM classification**

- Refractory heart failure requiring hospitalization

From the panel

- Consensus: Maximum recommended or tolerated doses of furosemide, pimobendan, and an ACE inhibitor, assuming already in therapeutic regimen
- Consensus: When indicated, antiarrhythmic should be used before a patient is considered refractory to standard therapy
- Consensus: Additional furosemide (IV, IM bolus, or CRI) until respiratory distress has decreased or for a maximum of 4 hours if renal function is adequate
- Consensus: Fluid removal from chest or abdomen as needed to aid in respiration/comfort
- Consensus: Relieve dyspnea/discomfort via appropriate humidity, environmental temperature, and body positioning (assumed from Stage C_a recommendations)
- Consensus: Sedation with buprenorphine and/or acepromazine or morphine (assumed from Stage C_a recommendations)
- Consensus: Mechanical ventilation and oxygen supplementation
- Consensus: Vigorous afterload reduction in dogs that can tolerate arterial vasodilation (nitroprusside, hydralazine, amlodipine)
- Consensus: Nitroprusside (a mixed vasodilator) and/or dobutamine (inotropic effect, afterload reduction, reduction of mitral orifice size) via CRI
- Majority: ACE inhibitor, based on human research evaluating IV enalaprilat (the active metabolite of enalapril)^{9,10} and the results of the IMPROVE trial¹¹ (Note: this applies to cases not receiving an ACE inhibitor when admitted to the hospital)

For my patients

My approach to Stage D_a patients includes the already prescribed ACE inhibitor and spironolactone. Oral furosemide would be replaced with furosemide CRI, and heart rate and rhythm would be controlled with drugs such as digoxin, lidocaine, and/or sotalol. Beta-blocker, if previously initiated, would be continued but would not be instituted at this phase.

Further off-loading therapy would include nitroprusside or the combination of nitroglycerin and amlodipine, depending on severity of signs. Inotropic support might include pimobendan (with a dose increase if previously prescribed) and/or dobutamine CRI. Sedation, mechanical fluid removal, ventilation, and oxygen therapy would be used as needed and described above.

It is important to emphasize that each case is different and the therapeutic requirements vary. No cookbook formula can be provided other than the use of “triple therapy” here. It is also important to understand that while most patients in D_a stage will be on cardiac therapy, some will not.

STAGE **D_c****ACVIM classification**

- Refractory heart failure requiring at-home care

From the panel

- Consensus: Continue triple therapy as adjusted in stage D_a
- Consensus: Increase dose of furosemide as needed to ease pulmonary edema or body cavity effusions
- Consensus: Monitor renal function Q₁₂ to 24 H after dose increase to gauge renal dysfunction
- Consensus: Spironolactone, if not previously initiated
- Consensus: Against beta-blockade unless signs of heart failure can be controlled
- Consensus: Highly palatable, mildly sodium-restricted diet

For my patients

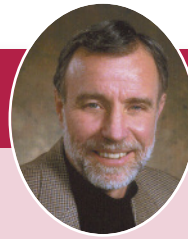
My approach to the refractory patient that has returned home would include maximum dose of an ACE inhibitor, continuation of spironolactone, and higher doses of furosemide and/or additional diuretics, such as hydrochlorothiazide or torsemide.

Pimobendan would be continued and the dose increased as needed to maintain a state free of clinical signs. An antiarrhythmic agent would be prescribed when needed, as mentioned above, and sodium restriction may be intensified.

Beta-blocker would be used only if initiated prior to decompensation. I would use thoracentesis and abdominocentesis as needed, and I would add sildenafil to the regimen if pulmonary hypertension is present.

Nutraceuticals, such as fish oil, may be added to help avoid or reverse cardiac cachexia.

How Clarke Atkins Does It



Stage A CVHD (At risk)

- No treatment
- Remove from breeding stock
- Advise client about disease progress & what to expect

Stage B₁ CVHD (Murmur and no enlargement)

- Diet: Mild sodium restriction
- Blood pressure: Possible hypertension control (eg, ACE inhibitor, usually with amlodipine)

Stage B₂ CVHD (Murmur & enlargement)

- ACE inhibitor
- Beta-blocker
- Possibly MRB (spironolactone)

Stage C_a CVHD (Failure or history of failure: hospitalized)

- Nitroglycerine therapy
- Diuretic (furosemide)
- ACE inhibitor
- Pimobendan
- Oxygen
- Dobutamine
- Thoracentesis or abdominocentesis
- Sedation
- Relief of dyspnea

Stage C_c CVHD (Failure or history of failure: at home)

- ACE inhibitor
- Diuretic (furosemide)
- MRB (spironolactone)
- Pimobendan
- Moderate sodium restriction

Stage D_a CVHD (Refractory: hospitalized)

- Diuretic (furosemide CRI) as needed
- ACE inhibitor (continue or institute)
- MRB (spironolactone)
- Inotropic support (pimobendan or dobutamine CRI)
- Antiarrhythmic agent as indicated (digoxin, diltiazem, lidocaine, sotalol)
- Relieve dyspnea
- Sedation
- Nitroprusside or nitroglycerin & amlodipine
- Oxygen
- Ventilation
- Beta-blocker continued (but not initiated)
- Thoracentesis or abdominocentesis

Stage D_c CVHD (Refractory: at home)

- Diuretic & MRB (furosemide [higher doses] & spironolactone and/or additional hydrochlorothiazide or torsemide)
- ACE inhibitor (perhaps increased dose)
- Pimobendan, typically at an increased dosage
- Antiarrhythmic as previously described
- Monitor renal function
- Spironolactone
- Greater dietary sodium restriction
- Beta-blocker continued (but not initiated)
- Sildenafil with pulmonary hypertension
- Nutraceuticals for cachexia
- Thoracentesis or abdominocentesis

CANINE CVHD—IDEALLY A SURGICAL DISEASE

Ideally, severe canine CVHD is a surgical disease, but valve repair or replacement efforts have not been met with adequate success. Recent case studies have shown that surgical mitral valve repair has resulted in high perioperative mortality¹⁹ and surgical valve replacement has resulted in postoperative thrombus formation,²⁰ but there have been some individual successes. However, the cost, small number of participating hospitals, and limited success have rendered surgical correction of canine CVHD impractical, leaving it as a medically managed disease in veterinary medicine for the foreseeable future.

ACE = angiotensin-converting enzyme, CVHD = chronic valvular heart disease, IMPROVE = invasive multicenter prospective veterinary evaluation of enalapril study, MRB = mineralocorticoid receptor blocker