Standards of care in the management of Mitral Valve Disease
Mitral Valvular Disease: importance

Large Window of Therapeutic Opportunity - Before Congestive Heart Failure

Canine Heart Disease
- Chronic Valvular Heart Disease: 68%
- Heart Worm Disease: 14%
- Dilated Cardiomyopathy: 9%
- Pericardial: 5%
- Congenital: 4%
Guidelines for the Diagnosis and Treatment of Canine Chronic Valvular Heart Disease
ACVIM Consensus Panel Report

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The Meaning of Consensus...

“Consensus” = unanimous (10 of 10) agreement on diagnostic, therapeutic, or dietary recommendations

“Majority recommendation” means that 6 or more of the 10 participants felt the treatment or diagnostic effort was appropriate at the stage of cardiac disease in question

This was based on:

- clinical trial evidence
- other published experimental
- anecdotal evidence
- clinical experience
- expert opinion

i.e. potential benefits clearly outweigh potential risks
ACVIM Cardiac Disease Classification

- **At Risk**
- **Murmur & No Enlargement**
- **Murmur & Enlargement**
- **Failure or History of Failure: Hospitalized**
- **Failure or History: At Home**
- **Refractory: Hospitalized**
- **Refractory: At Home**

**Classification:**
- **A**
- **B₁**
- **B₂**
- **Ca**
- **Cc**
- **Da**
- **Dc**
Treatment of Mitral Regurgitation
Stage A Therapy Recommendations: Consensus

- No drug therapy is recommended
- No dietary therapy is recommended
- Potential breeding stock should no longer be bred if MR is identified early (<6-8 years)
Stage B1 Therapy Recommendations: Consensus

- No drug or dietary therapy is recommended
- Re-evaluation is suggested (radiography or echo-Doppler) in approximately 12 months
- Some panelists recommend more frequent follow-up in large breed dogs
Stage B2 Therapy Recommendations: No Consensus

- **ACE inhibitors** *(panel majority)*
  - with significant left heart enlargement
  - dramatically increased left heart size on successive exams

Clinical trials addressing ACEI in asymptomatic Mitral Regurgitation have shown either no effect or a small positive effect in delaying the onset of heart failure

- **No treatment** *(panel minority - pending further clinical trials)*
SVEP Trial

One breed – Cavalier King Charles Spaniel
Early Mitral Regurgitation (~50% cardiomegaly)
Dosage: 0.37 mg/kg/d

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. Atkins C.E., Keene B.W. et al. JAVMA. 2007. 231(7): 1064. Fig.2.

Median survival
Enalapril = 895 days
Placebo = 778 days
Difference = 117 days
Percent = 15%
P = .06 (1-tailed analysis)

VETPROOF: CHF-Free Survival if > 60 days

E: 64%*
P: 45%

E: 21%*
P: 10%
A recent survey of 100 ACVIM-Boarded Cardiologists indicated that nearly 70% felt that chronic ACE-Inhibition was warranted in Mitral Regurgitation Stage B2.

Stage C Recommendations for Acute Therapy: Consensus

- **Furosemide IV or IM** (2 mg/kg)
  - followed by 2 mg/kg doses IV, IM or SC hourly until decrease of respiration rate /effort or total of 8 mg/kg over 4 hours.

- **Furosemide Constant Rate Infusion** at 1 mg/kg/hour following the initial bolus for life-threatening pulmonary edema
  - expectoration of froth associated with severe dyspnea;
  - radiographic “white-out lung”;
  - poor initial response to furosemide bolus with failure of respiratory effort and rate to improve over 2 hours
Stage C Recommendations for Acute Therapy: Consensus

- **Pimobendan** (0.25 – 0.3mg/kg orally every 12 hours.)
  - Use of Pimobendan in acute heart failure therapy is supported by hemodynamic and experimental evidence / anecdotal experience of the panel.
Stage C Recommendations for Acute Therapy: Consensus

- **O₂** via a humidity and temperature-controlled cage or incubator or via nasal canula.

- **Abdominal paracentesis or thoracocentesis** to relieve effusions judged sufficient to impair ventilation or cause distress.
Stage C Recommendations for Acute Therapy: Consensus

- Optimal nursing care
  - appropriate environmental temperature / humidity
  - elevate the head on pillows
  - place sedated patients in sternal posture.

- Sedation / anxiolysis for dyspnea-associated anxiety
  - Narcotics +/- an anxiolytic agent
    - butorphanol 0.2 to 0.25 mg/kg IM or IV
    - buprenorphine (0.0075 – 0.01 mg/kg) and acepromazine (0.01 – 0.03 mg/kg IV or IM or SC)
    - other narcotics (morphine and hydrocodone)
Stage C Recommendations for Acute Therapy: Consensus

- **ACE inhibitors** (panel majority)
  - e.g. enalapril 0.5mg/kg orally q12 hours

Evidence supporting efficacy and safety of ACEI in acute therapy when combined with furosemide & pimobendan is less clear than chronic stage C.

BUT clear evidence that acute administration of enalapril & furosemide in acute heart failure → significant improvement in pulmonary capillary wedge pressure compared to administration of furosemide alone.
Acute and Short-Term Hemodynamic, Echocardiography, and Clinical Effects of Enalapril Maleate in Dogs With Naturally Acquired Heart Failure: Results of the Invasive Multicenter PROspective Veterinary Evaluation of Enalapril Study: The IMPROVE Study Group. Sisson D.D. JVIM. 1995. 9 : 239. Fig.1
Furosemide PO 2mg/kg q12 hours or as needed to maintain patient comfort

- Chronic furosemide doses ≥ 6mg/kg q12 hours needed to maintain patient comfort in the face of appropriate adjunct therapy indicates progression to Stage D.

ACEI is continued or started e.g. enalapril, 0.5mg/kg PO q12 hours or equivalent dose of another approved ACE-inhibitor.

- Measure serum creatinine and electrolytes 3 – 7 days after beginning an ACEI.

Pimobendan 0.25 – 0.3mg/kg PO q12 hours.

Disease – Chronic CHF or History

Stage C Recommendations for Chronic Therapy: Consensus

Triple Therapy
Placebo-controlled, double-blind studies of ACE-I in CHF

The harmful effects of chronic RAAS activation and benefits of ACE-Inhibition have been shown in multiple clinical trials in dogs with both CVD & DCM.
Effect of Pimobendan or Benazepril Hydrochloride on survival times in dogs with Congestive Heart Failure caused by naturally occurring Myxomatous Mitral Valve Disease: The QUEST Study. Häggström J., Boswood A. et al. 2008. 22:1129. Fig.1.
Stage C Recommendations for Chronic Therapy: No Consensus

- **Spironolactone** 0.25 – 2.0 mg/kg PO q12 – 24h *(panel majority)*
  - For aldosterone antagonism, NOT diuretic effect
  - Spironolactone (2 mg/kg/day) is approved therapy in Europe.

However recent publication *(JVIM 2010)* indicates efficacy in Mitral Regurgitation

A preclinical pharmacokinetic and pharmacodynamic approach to determine a dose of spironolactone for treatment of congestive heart failure in dog. Guyonnet J., Elliott J. et al. 2010. 33(3): 265. Fig.3.
Spironolactone Preclinical Studies

N = 221 dogs - Average ISACHC Score = II (90%) - III
Double-blind, placebo-controlled
2 mg/kg once daily

ACVIM Consensus & Majority Recommendations

- Educate
- Spironolactone
- ACE-I
- Furos
d- Pimo

**Asymptomatic**
- ACE-I
- Spironolactone
- Furos
- Pimo
- Oxygen
- Sedation
-NP / Dobutamine
centesis

**Heart Failure**
- Furos
- Pimo
- ACE-I
- Oxygen
- Sedation
- Afterload

**Refractory Failure**
- Furos
- Pimo
- ACE-I
- Oxygen
- Sedation
- Afterload

*NPossibly via continuous rate infusion

**Sodium Restriction**
- Mild
- Moderate (senior diet)
- Moderate-Severe

**Majority Recommendation**

**Consensus Recommendation**