Triple Therapy for ALL? Current recommendations in canine heart disease

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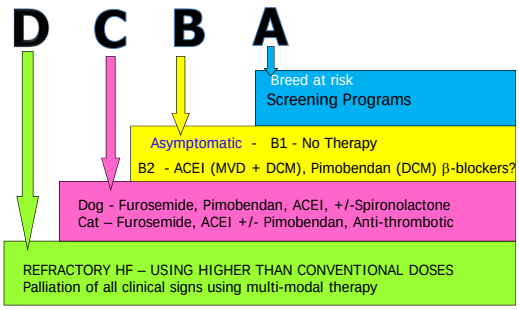
Discussion Agenda

- Goals of acute v. chronic HF management
- Treatment recommendations:
  - Pimobendan
    - Digoxin
  - Diuretics
    - Furosemide, Torsemide, Spironolactone,
  - Vasodilators
    - ACE-Inhibitors, Sildenafil, Amlodipine
- Summaries for dog HF treatment

Staged Diagnostic and Treatment Strategies Based on Heart Failure Classification



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Goals of Acute HF Rx:

- Restore comfort at rest:
  - Mechanical removal of life-threatening fluid accumulations
  - Oxygen supplementation
  - Reduce anxiety
  - Reduce the work of breathing

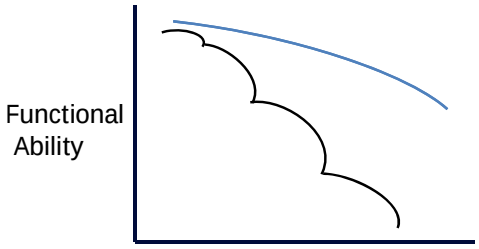
- Hemodynamic stabilization
  - Assess and optimize preload, afterload, heart rate & rhythm, and contractility
- Keep them eating

Goals of Chronic Rx

- Maintain acute hemodynamic gains.
- Improve quality of life
  - Exercise tolerance
  - Appetite / weight
- Improve survival
- Minimize hospitalizations
- Optimize owner & patient compliance
- Economic impact
- Moderately low salt intake

Educated client and scheduled HF rechecks will hopefully prolong life and avoid expensive ER admissions

Heart Failure Decompensations



First Heart Failure Recheck

- 3-7 days after initial HF episode
- Evaluate response to therapy
- Evaluate owner's emotional and financial commitment – LIFELONG MEDICATIONS
- PE, blood pressure, chest x-rays, renal and electrolyte blood work +/- ECG if arrhythmia ($200 - 250)
- Doses of drugs are adjusted, if needed
- Phone updates and periodic rechecks are discussed
- Diet and nutraceuticals are also discussed

All Cause Canine Heart Failure

Furosemide
ACE-inhibitor
Pimobendan

Low salt diet

Amlodipine
Sildenafil

Nutraceuticals

Nitroglycerin
Nitroprusside

Digoxin
Dobutamine

Hydrochlorthiazide

Atenolol
Carvedilol

Spironolactone

Diltiazem

Sotolol
Lidocaine

Sedation
Oxygen

Torsemide

Congestion at rest?

Low perfusion at rest?

NO YES

	NO	YES
NO	DRY and WARM	WET and WARM
YES	DRY and COLD	WET and COLD

SIGNS of LOW PERFUSION

Inotropes	Diuretics	Vasodilators
Contractility	Fluid Volume (preload)	Preload Afterload
Pimobendan Dobutamine	Furosemide	Nitroglycerin Nitroprusside (Withhold ACEI)

ACUTE (IN HOSPITAL) MANAGEMENT OF SEVERE HF

DOG

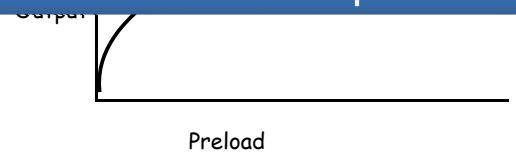
- **Furosemide:**
  2-4 mg/kg IM or IV bolus +/- CRI (Max 12 mg/kg/day)
- **Oxygen**
- **Sedation: Butorphanol 0.1- 0.2mg/kg IV or IM**
- **Pimobendan:**
  0.25 mg/kg PO BID – TID (when able to swallow)
- *Nitroglycerin: ¼-1" transdermal q 8-24 hr for 1-2 d or Nitroprusside 1 - 10 ug/kg/min IV (careful BP monitoring)*
- *Dobutamine: if cardiogenic shock (hypotensive, hypothermic, low output signs)*
- *Diltiazem/digoxin: if concurrent atrial fibrillation*

Furosemide (Lasix, Salix®)

- Onset of action and peak
  - IV 5 min and 30 min
  - PO < 1 hour and ~2 hours
- Dose: 1- 4 mg/kg q 24 hrs–TID (max12mg/kg/d)
- After initial bolus, we often use
  - CRI: 0.25 – 0.5 mg/kg/hr x 2 - 4 hr IV
- CHRONIC GOAL - Lowest effective dose
- Adverse Effects
  - Hypovolemia, hypokalemia, hyponatremia
  - Azotemia

Frank-Starlings Law

Diuretics Never Improve Cardiac Output



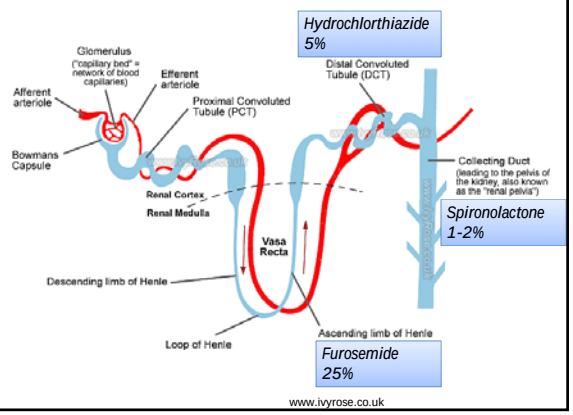
Torsemide


Effect of torsemide and furosemide on clinical, laboratory, radiographic and quality of life variables in dogs with heart failure secondary to mitral valve disease

Effects of oral administration of furosemide and torsemide in healthy dogs

Am J Vet Res 2007

- New loop diuretic – first or second line diuretic?
- Torsemide's superiority over furosemide is likely due:
  - antifibrotic effects on the myocardium
  - blunting of loop diuretic resistance effects that appear mediated by torsemide's antagonism of aldosterone
- Dose is 1/10th of the furosemide dose
  - 5, 10, 20 mg tablets and injectable
- Longer duration of action of oral torsemide (12 hr) vs. furosemide (6 hr)



Additional Diuretics

- Sequential Nephron Blockade
  - Furosemide, Torsemide: loop diuretics:
  - Thiazides, spironolactone: distal tubules
- Spironolactone/hydrochlorthiazide (Aldactazide®)
  - Will add in with end-stage refractory HF

Spironolactone (Aldactone®)

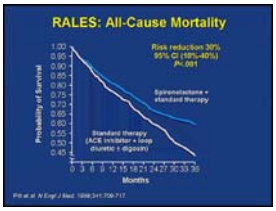
- Competitive antagonist of aldosterone
- Potassium sparing diuretic
- Weak diuretic, synergism with furosemide
- Slow onset of action, peak in 48 - 72 hours
- Dose: 2 mg/kg/day
- Adverse effect: Azotemia, hyperkalemia

Role of Aldosterone in HF

Aldosterone promotes:

Retention of Na
Loss of K and Mg
Sympathetic stimulation
Parasympathetic inhibition
Myocardial and vascular fibrosis
Baroreceptor dysfunction
Impairs arterial compliance

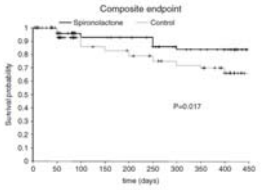
Aldosterone blockade:



J Vet Intern Med 2010;24:331–341

Efficacy of Spironolactone on Survival in Dogs with Naturally Occurring Mitral Regurgitation Caused by Myxomatous Mitral Valve Disease

F. Bernay, J.M. Bland, J. Häggström, L. Baduel, B. Combes, A. Lopez, and V. Kaltsatos



Results: Primary endpoint reached by 11/102 dogs (10.8%) in the spironolactone group (6 deaths, 5 worsening) versus 28/110 (25.5%) in control group (14 deaths, 8 euthanasia, 6 worsening). Risk of reaching the composite endpoint significantly decreased by 55% (hazard ratio [HR] = 0.45; 95% confidence limits [CL], 0.22–0.90; log rank test, $P = .017$). Risk of cardiac-related death or euthanasia significantly reduced by 69% (HR = 0.31; 95% CL, 0.13–0.76; $P = .0071$). Number of dogs not completing the study for cardiac and other miscellaneous reasons similar in spironolactone (67/102) and control groups (66/110).

Vetmedin® (pimobendan)

Dual Mode of Action ("Inodilation")

Direct heart muscle action

Calcium sensitizer

- Promotes efficient use of existing calcium
- Increases force of contraction
- Does not increase myocardial energy requirements

Balanced vasodilation

Selective peripheral phosphodiesterase III inhibitor

- Dilates both arterial and venous vessels
- Reduces preload and afterload
- Improves cardiac function

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Vetmedin®
Pharmacokinetics and Pharmacodynamics

- Rapid absorption
  - Mean peak plasma levels achieved 0.5-1.0 hour after administration of a single oral dose
- Pimobendan is oxidatively demethylated to an active metabolite (UD-CG 212)
- Elimination half-life
  - Pimobendan: 0.5 hours
  - UD-CG 212: 2.0 hours
- Prolonged pharmacodynamic effect (>8h)
- Routes of excretion
  - Feces: 95%
  - Kidneys: 5%

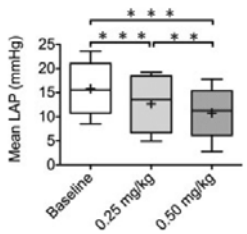
Vetmedin®
Labeling

- **Indications**
  - Management of the signs of mild, moderate, or severe (modified NYHA Class II, III, or IV) CHF in dogs due to Valvular Insufficiency (MVD) and Dilated Cardiomyopathy (DCM)
  - Use with concurrent therapy for congestive heart failure (eg, furosemide, etc) as appropriate on a case-by-case basis
- **Dose rate**
  - 0.23 mg/lb (0.5 mg/kg) per day, in two divided doses that are not necessarily equal
  - Chewable 1.25, 2.5, 5 and 10 mg scored tablets
  - Dose escalate for worsening HF –
    - Can increase dose and frequency

J Vet Intern Med 2011

The Effect of Pimobendan on Left Atrial Pressure in Dogs with Mitral Valve Regurgitation

S. Suzuki, R. Fukushima, T. Ishikawa, L. Hamabe, D. Aytemiz, H. Huai-Che, S. Nakao, N. Machida, and R. Tanaka



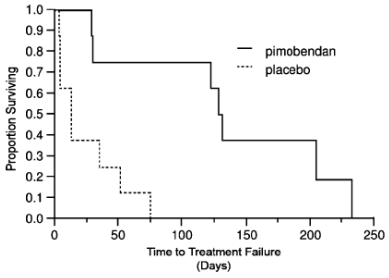
Questions about using Pimobendan?

- When to add in pimobendan in dogs with HF secondary to MVD or DCM?
- Does one still use digoxin together with pimobendan?
- Should one use pimobendan in dogs prior to the onset of HF?
- Can one or should one use pimobendan without an ACE inhibitor in a dog with HF?
- Are there other indications for pimobendan?
  - Cats with congestive heart failure?
  - Dogs with severe pulmonary hypertension (idiopathic or due to heartworm disease)?
  - Dogs with other causes of HF, e.g., PDA or endocarditis?
- What are the adverse effects?

J Vet Intern Med 2008;22:997–904

Effect of Pimobendan on Case Fatality Rate in Doberman Pinschers with Congestive Heart Failure Caused by Dilated Cardiomyopathy

M.R. O'Grady, S.L. Minors, M.L. O'Sullivan, and R. Horne



JVIM 2008

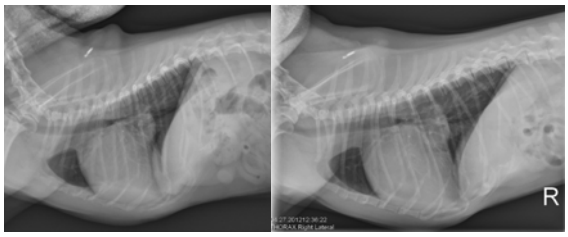
When to add in pimobendan in dogs with HF secondary to MVD?

- First onset of heart failure*
- Helpful in older dogs with concurrent renal insufficiency – allows lower furosemide dose and improves azotemia
- Will reduce the heart size in some dogs as seen by thoracic radiographs
  - Helpful for dogs with concurrent collapsing trachea and bronchi to reduce compression from left atrial enlargement

**Haggstrom, JVIM, 2008*

9 yo MC Chihuahua
5/6 systolic murmur PMI left apex

March 2011 April 2012



Occasional cough Frequent cough

Pimobendan: What are the adverse effects?

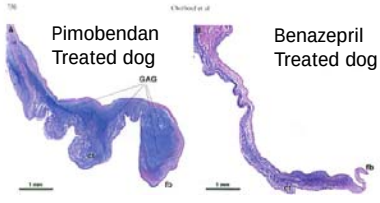
- Well tolerated drug
- Concerns about tachyarrhythmia
- May worsen MR if given too early
- NCSU Cardiology has used higher than recommended doses and frequencies with no adverse effects and improved clinical signs

Chetboul JVIM 2007

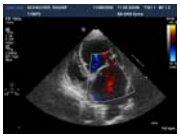
- Small prospective comparative study in dogs with asymptomatic MVD for 512 days (12 dogs)
- Benazepril (0.25 mg/kg q 24 hr) vs. Pimobendan (0.25 mg/kg q 12 hrs)
- Pimobendan treated dogs had improved LV systolic function parameters but had worsening of MR and histologically MV were more diseased.

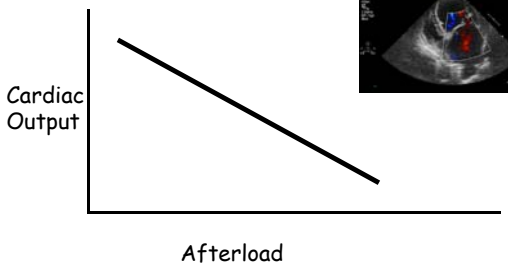
Chetboul JVIM 2007

Postmortem histopathologic evaluation of mitral valve



VASODILATORS IN HF
Afterload and Cardiac Performance





ACE inhibitors in Heart Failure
Enalapril, Benazepril

- ACE inhibitors also impart survival and quality of life benefits in canine HF
- With rare exception, all HF dogs on chronic management of HF should be on furosemide, ACE-I and Pimobendan
- Exceptions include:
  - Previous intolerance of ACE-I
  - Renal failure (creatinine > 3 mg/dl) and active HF
    - Might add in at low dose if if azotemia improves
  - Peracute management of HF with concern for azotemia and low GFR

AMLODIPINE
(Norvasc® and generic)

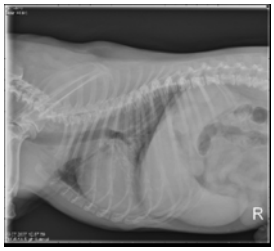
- Calcium channel blocker with primary effect of vasodilation (minimal cardiac effects)
- Indicated for treatment of systemic hypertension in both cats and dogs
- Also indicated for adjunctive treatment of advanced CHF in dogs
- Improves renal perfusion but may activate RAAS
- Adverse effects – hypotension, gingival hyperplasia
- Dose - 0.1- 0.2 mg/kg PO q 24 hrs (dog/cat) to BID

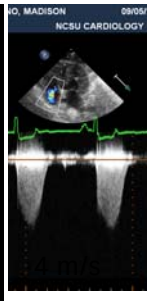
SILDENAFIL
(Viagra®, Revatio®)

- Phosphodiesterase V inhibitor that nitric oxide induced vasodilation
- Vascular bed selectivity
- Use in dogs with pulmonary hypertension with favorable outcomes (Bach JVIM 2006)
- Also useful as adjunctive tx in Stage D HF dogs with pulmonary hypertension secondary to MVD
- 1-2 mg/kg BID to TID
- Affordable generic 20 mg tab
  - Distributer - Cardinal Health, 614.757.5000)
  - Manufacturer - Apotex (800.706.5575)

13 yo FS Jack Russell Terrier
Syncope, murmur, dyspnea

- Enalapril 0.5 mg/kg BID
- Furosemide 1 mg/kg BID





PA systolic pressure ~ 4 V ^{2} x 4 Triscupid regurg velocity = 4^2 m/s x 4 = 64 mmHg TR gradient

13 yo MN Jack Russell Terrier
Syncope, murmur, dyspnea

Diagnosis: Advanced valvular heart disease
Severe Pulmonary Hypertension

- Enalapril 0.5 mg/kg BID
- Furosemide 1 mg/kg BID
- ADD PIMOBENDAN 0.25 mg/kg BID
- NO SYNCOPE for 3 months
  - Then added Sildenafil 1 mg/kg BID
- Dose escalated Pimobendan and Sildenafil

Fish oils for heart failure

- Omega 3 Fatty Acids (EPA + DHA)
- High dose 40-50 mg/kg/day
- Anti-arrhythmic effects
- Decrease interleukin 1 and cardiac cachexia
- Improves appetite

Boxer Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

- Prospective study
- 3 groups of boxers (10 each/group)
- > 1000 VPCs/day
  - Fish oils
    - 780 mg EPA and 497 mg DHA per day
  - Flax seed oil
  - Sunflower oil (placebo)
- FISH OIL group decreased ventricular arrhythmias by ~ 60 %

Smith J Vet Intern Med 2007

Classic syncope in boxer with Arrhythmogenic RV Cardiomyopathy

Arrhythmogenic Right Ventricular Cardiomyopathy of Boxers (ARVC)

Typical clinical signs:
1. Asymptomatic arrhythmia
2. Syncope - arrhythmia

Inherited genetic mutation.

Homozygous positive more likely to have DCM phenotype and die suddenly.
http://www.ncstatevets.org/genetics/

Usually no structural heart disease until later in disease.

Ambulatory ECG

Holter monitor

Event recorder

Implantable loop recorder

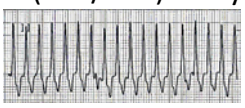
ALIVE COR – I-phone

ALIVE Cor – iphone app

Ventricular Tach (300/min) 8 yo Boxer in HF

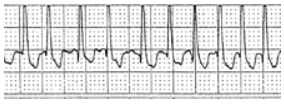
- Lidocaine acutely
- Then Sotolol (Mexilitine)
- Fish Oils

SVT (300/min) in 2 yo Labador in HF



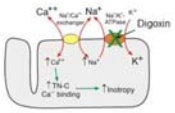
- Diltiazem acutely
- Then Diltiazem or Sotolol
- Radiofrequency Ablation?

Atrial Fib (220/min) in 5 yo Grt Dane in HF



- Digoxin
- Diltiazem

Digoxin: When to use?



- Weak positive inotrope, negative chronotrope, slows AV nodal conduction
- CHF dt DCM (together with pimo)
- SV arrhythmia (A. Fib, SVT) + CHF (together with diltiazem)

- WHEN NOT TO USE
  - Cats, Azotemia, Non-compliant owner

Diltiazem – Formulations

- **IV Diltiazem** – 0.1 mg/kg IV slow repeat up to -0.5 mg/kg allowing 20 min between doses
  - CRI depends on IV loading dose
    - BE CAREFUL – DON'T FLUSH CATHETER!!!!

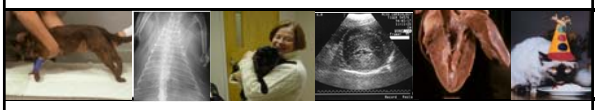
- **Oral Diltiazem**
  - Non Sustained release – 30 mg tablets
    - Dog dose - 0.5 – 1.5 mg/kg PO q 8 hr
    - Cat dose – 7.5 mg PO q 8 hr

  - Sustained release – Dilacor, Cardiazem CD
    - Dilacor : 60 mg tablets in capsule / 2 – 6 mg/kg BID (Dog)
    - Cardiazem CD: sprinkles in capsule / 10 mg/kg q 24 hr (Cat)

	ACUTE (IN HOSPITAL) MANAGEMENT OF SEVERE HF
DOG	• **Furosemide: 2-4 mg/kg IM or IV bolus +/- CRI (Max 12 mg/kg/day)** • **Oxygen** • **Sedation: butorphanol 0.1- 0.2mg/kg IV or IM** • **Pimobendan: 0.25 mg/kg PO BID – TID (when able to swallow)** • *Nitroglycerin: ¼-1" transdermal q 8-24 hr for 1-2 d or Nitroprusside 1 - 10 ug/kg/min IV (careful BP monitoring)* • *Dobutamine: if cardiogenic shock (hypotensive, hypothermic, low output signs)* • *Diltiazem/digoxin: if concurrent atrial fibrillation*

	CHRONIC (OUT PATIENT) MANAGEMENT OF HF
DOG	• **Pimobendan: ↑contractility and ↓afterload (often ↑ dose and frequency over time)** • **ACE-I: 0.5 mg/kg PO q 12-24 hr ↓RAAS remodeling, ↓Na+ retention** • **Furosemide: Lowest effective dose ↓fluid retention/preload** • **Spironolactone: 2 mg/kg PO q 24 hr ↓myocardial fibrosis** • **Dietary Na+ restriction (< 100 mg sodium / 100 Kcal or < 0.25 %)** • **Fish oils: 40 mg/kg/day of Omega 3 FA** • *Sildenafil: 1 – 2 mg/kg PO q 8 – 12 hr if pulmonary hypertension* • *Amlodipine: 0.1-0.2 mg/kg PO q 12 – 24 hr for additional vasodilation* • *Diltiazem/digoxin: if A-fib* • *Periodic abdominocentesis for Right HF*

Updates in the management of feline heart failure



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Cat Heart Failure

- < 5% cats present for cough
- Inconsistent radiographic pulmonary edema pattern
- 40% may not have murmur on initial ER examination
- Hypothermia + bradycardia are not uncommon
- Antecedent event is common
  - Corticosteroids
  - Boarding
  - Vet visit
  - Procedure

Rush J Am Vet Med Assoc 2002

Corticosteroid-associated HF in cats

- 11% of 271 cats with CHF received steroid within 90 days
- 28.8 odds ratio of long acting steroid inj. with HF ($p < 0.005$)
- Survivors had better median survival than other cats (439 d)

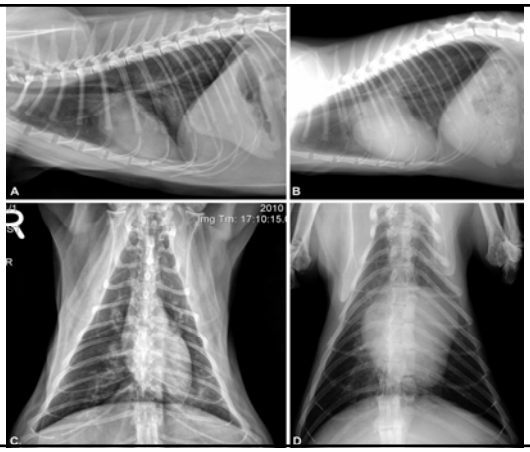
Smith ACVIM abst. 2002

Hemodynamic effects of methylprednisolone acetate administration in cats

Trasida Ployngam, DVM, MS; Anthony H. Tobias, BVSc, PhD; Stephanie A. Smith, DVM, MS; Sheila M. F. Torres, DVM, PhD; Sheri J. Ross, DVM

Am J Vet Res 2007

- Plasma volume ↑ by 13 % in 3 – 6 d. > 40 % in 3/12 cats
- Volume expansion as a result of an intra- to - extracellular fluid shift secondary to glucocorticoid mediated extracellular hyperglycemia.



RADIOGRAPHIC AND ECHOCARDIOGRAPHIC ASSESSMENT OF LEFT ATRIAL SIZE IN 100 CATS WITH ACUTE LEFT-SIDED CONGESTIVE HEART FAILURE

KARSTEN E. SCHOBER, ELLEN WETLI, WM TOD DROST

1. Radiographic LA enlargement can be absent even in the presence of LAE enlargement on ECHO
2. PV enlargement is a poor indicator of left-sided CHF in cats with PAs more often enlarged as compared to PV
3. Cardiomegaly is a consistent finding in cats with left-sided CHF making radiographic assessment of heart size diagnostically more important than evaluation of left atrial size in cats with respiratory distress.

J Vet Radiol US 2013

Focused ER Echocardiography

- 2D Helpful to distinguish HF from respiratory
  - Enlarged LA
  - Echo smoke – spontaneous echo
  - Pleural + pericardial effusion
  - Left ventricular hypertrophy
  - Right ventricular hypertrophy
  - Systolic function
  - Lung rockets

- Advanced echocardiographic techniques:
  - Pulmonary arterial pressure
  - Left ventricular filling pressures

Portable bedside ultrasound: the visual stethoscope of the 21st century

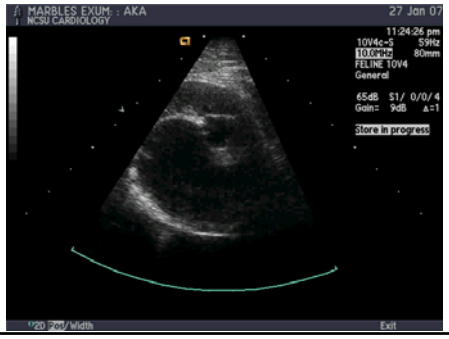
Lawrence M Gillman[1*] and Andrew W Kirkpatrick[2]

Abstract

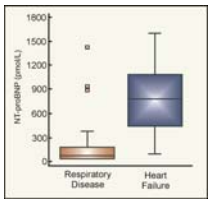
Over the past decade technological advances in the realm of ultrasound have allowed what was once a cumbersome and large machine to become essentially hand-held. This coupled with a greater understanding of lung sonography has revolutionized our bedside assessment of patients. Using ultrasound not as a diagnostic test, but instead as a component of the physical exam, may allow it to become the stethoscope of the 21st century.

Keywords: Point of care ultrasound, Physical exam, Pleural rub

Enlarged Left Atrium



NTproBNP in dyspneic cats



This box and whisker plot shows the results of a 12 center study evaluating the value of NTproBNP in correctly identifying the cause of dyspnea (breathlessness) in 139 cats. 85 cats had heart failure, 54 had respiratory disease.

On ROC analysis with a cutoff value *>265* pmol/L

Sensitivity: 91%
Specificity: 85 %
for correctly identifying the cause of the breathlessness.

Fox PR, et al. Comparison of NTproBNP concentration in cats with acute dyspnea from cardiac or respiratory disease J Vet Cardiol 2009.

SNAP® Feline proBNP Test

The SNAP® Feline proBNP Test is a simple, affordable test that gives you information about heart health during the patient visit. The test provides a chemistry analyte that indicates the stretch and stress on the myocardium.

- Measurement of the most stable cardiac biomarker, NTproBNP
- Proven accuracy, with results in 10 minutes
- Affordable assessment tool for all patients with cardiac risk factors

- 99.5% agreement with the Cardiopet proBNP Test when concentrations of NTproBNP were <100 pmol/L.
- 95.0% agreement with the Cardiopet proBNP Test when concentrations of NTproBNP were ≥270 pmol/L.

Interpreting Results

ACCF/AHA Guidelines for the Diagnosis and Management of Heart Failure in Adults

- "Concentrations of BNP or NT-proBNP should be measured in patients being evaluated for dyspnea in which the contribution of HF is not known. Final diagnosis requires interpreting these results in the context of all available clinical data and ought not to be considered a stand alone test." *(Level of Evidence: A)*

American Heart Association.

Circulation. 2009

Chronic Feline Heart Failure

Furosemide

ACE-Inhibitors
Enalapril
Benazepril

Pimobendan

Anti-thrombotics
Clopidogrel
Aspirin
Dalteparin (LMWH)

Spironolactone

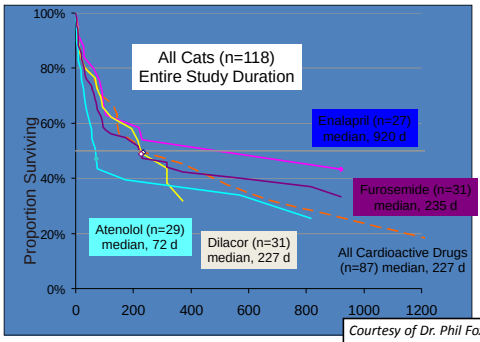
Diltiazem

Atenolol

Nutraceuticals

Sildenafil
Amlodipine

Kaplan-Meier Survival Curve Showing Time to Failure or Death for Treatment Group



Courtesy of Dr. Phil Fox
ACVIM 2003

	ACUTE (IN HOSPITAL) MANAGEMENT OF SEVERE HEART FAILURE
CAT	• **Furosemide:** **1-4 mg/kg IM or IV bolus +/- CRI (Max 12 mg/kg/day)** • **Oxygen** • **Sedation:** **Butorphanol 0.1-0.2mg/kg IM (Minimize Stress!!!)** • **Thoracocentesis: if pleural effusion** • **Pimobendan: Especially if refractory, LV systolic dysfunction or azotemia- 0.25 mg/kg PO BID (when able to swallow)** • *Nitroglycerin: ¼" transdermal q 8 – 24 hr for 1-2 d or Nitroprusside: 0.5-5 ug/kg/min IV (careful BP monitoring)* • *Puff: inhaled albuterol (2 puffs) or SQ terbutalline for peribronchiolar edema or refractory respiratory distress* • *Dobutamine: 1-5 ug/kg/min IV (ECG monitoring)*

Vetmedin® (pimobendan)

Dual Mode of Action ("Inodilation")

Direct heart muscle action

Calcium sensitizer

- Promotes efficient use of existing calcium
- Increases force of contraction
- Does not increase myocardial energy requirements

Balanced vasodilation

Selective peripheral phosphodiesterase III inhibitor

- Dilates both arterial and venous vessels
- Reduces preload and afterload
- Improves cardiac function

15

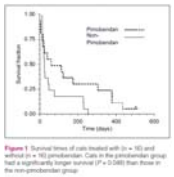
What about Pimobendan in cats with HF?

- Not labeled for use in cats
- Hypertrophic Cardiomyopathy is listed as a contra-indication however….
- Use has evolved from severe end stage HF secondary to presumed remodeled HCM to most hospitalized HF cat
- Allows decrease furosemide dose in azotemia and decreased intervals of thoracocentesis
- SAME DOSE as DOG (0.5 mg/kg/day)

Original Article

Effect of pimobendan on the clinical outcome and survival of cats with non-taurine responsive dilated cardiomyopathy

Lydia E Hambrook and Peter F Bennett



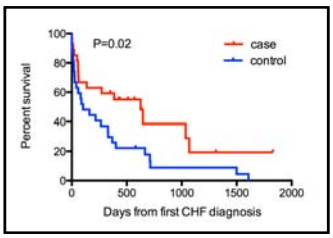
- Retrospective
- 16 cats each group:
- MST with Pimobendan = 49 d
- MST without Pimobendan = 12 d

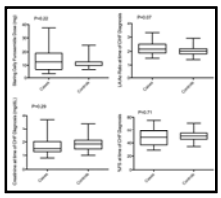
NCSU Pimobendan Retrospective in Feline HF due to HCM or HOCM

- 2003 – 2013 NCSU
- Cats treated pimobendan
  - Within 48hrs of HF diagnosis
  - FS of 30% or greater
  - Received at least 2 doses of pimobendan prior to death
  - Maintained the use of pimobendan from the time of inclusion to study end or death.
- Cats without Pimobendan
  - matching gender
  - age-matched +/- <24 months,
  - weight matched +/- <1 kg,
  - matching manifestation of CHF (pulmonary edema, pleural, pericardial, abdominal effusions).

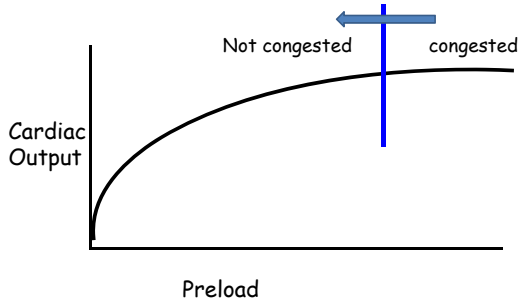
Drug	Cases (n=27)	Controls (n=27)
Pimobendan	27	0
Furosemide	27	27
Enalapril	21	24
Benazepril	2	0
Atenolol	3	9

626 days – Pimobendan
103 days – No Pimobendan





Frank-Starlings Law



Furosemide (Lasix, Salix®)

- Onset of action and peak
  - IV 5 min and 30 min
  - PO < 1 hour and ~2 hours
- Dose: 1- 4 mg/kg q 24 hrs–TID (max12mg/kg/d)
- After initial bolus, we often use
  - CRI: 0.25 – 0.5 mg/kg/hr x 2 - 4 hr IV
- CHRONIC GOAL - Lowest effective dose
- Adverse Effects
  - Hypovolemia, hypokalemia, hyponatremia
  - Azotemia

J Vet Intern Med 2008;22:335–341

Effect of Spironolactone on Diastolic Function and Left Ventricular Mass in Maine Coon Cats with Familial Hypertrophic Cardiomyopathy

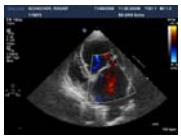
K.A. MacDonald, M.D. Kittleson, and P.H. Kass

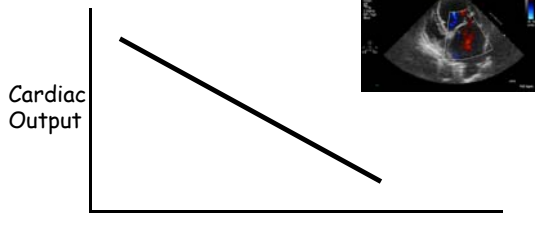
- 26 Maine Coon Cats w/ asymptomatic HCM
- Spironolactone (2 mg/kg q 12 hr) v. placebo x 4 mo
- No difference in LV mass, LA size, tissue doppler or mitral valve velocity profiles.
- 4 of 13 cats developed severe ulcerative dermatitis necessitating discontinuation of the drug.

Spironolactone in Feline HF

- Used in refractory HF (pl. eff, ascites) in addition to triple tx
- Concern with azotemia and ↑ K^+
- 1 – 2 mg/kg once daily
- Smallest tablet = 25 mg

VASODILATORS IN HF
Afterload and Cardiac Performance





ACE inhibitors in Feline HF
Enalapril vs. Benazepril

- Benazepril
  - Longer duration of action in cat = once daily dosing
  - Route of excretion is 85% via the biliary system (50% in dogs) = safer with renal impairment
  - Smallest tablet = 5 mg


SILDENAFIL
(Viagra®, Revatio®)

- Phosphodiesterase V inhibitor that nitric oxide induced vasodilation
- Vascular bed selectivity
- Used pulmonary hypertension in dogs
- ***Anecdotal benefit in cats with severe refractory pleural effusion (in addition to triple tx)***
- 1-2 mg/kg BID to TID
- Affordable generic 20 mg tab
  - Distributer - Cardinal Health, 614.757.5000)
  - Manufacturer - Apotex (800.706.5575)

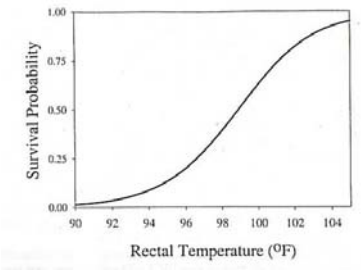
AMLODIPINE
(Norvasc® and generic)

- Calcium channel blocker with primary effect of vasodilation (minimal cardiac effects)
- Indicated for treatment of systemic hypertension in both cats and dogs
- Improves renal perfusion but may activate RAAS
- Adverse effects – hypotension, gingival hyperplasia
- Dose - 0.1- 0.2 mg/kg PO q 24 hrs (dog/cat) to BID

What's New in Thromboembolism?




Prognosis and rectal temperature in cats with aortic thromboembolism



Smith J Vet Intern Med 2003

Initial Treatment Considerations

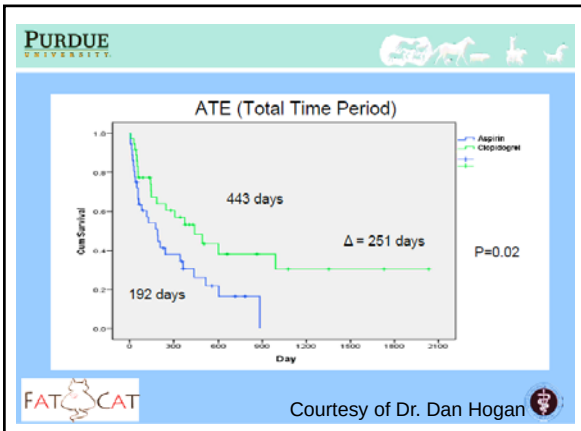
Analagesia/Sedation
Fentanyl
Buprenorphine
Other opiate

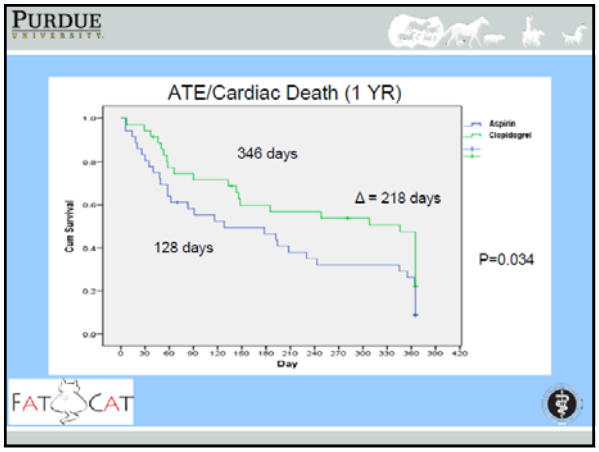
Tx Heart Disease
Furosemide
Pimobendan
Other?

Anticoagulant Therapy
UF Heparin
Clopidogrel
Aspirin
Low Molecular Weight Heparin
Warfarin
Thrombolytics

Clodipogrel (Plavix®)

- Inhibitor of ADP-induced platelet aggregation
  - direct inhibition of ADP binding to its receptor
  - subsequent inhibition of ADP-mediated activation of the GP IIb/IIIa complex
- Good feline in-vitro and in-vivo PK and PD data
- Dose 1 – 2 mg/kg/d (¼ of 75 mg tablet)
- FATCAT clinical trial: aspirin vs. Plavix® in post ATE
- Generic now available





How would we treat?

- PAIN
  - Fentanyl 2 mcg/kg bolus, then CRI
    - Buprenorphine 0.005 – 0.01 mg/kg IV,SQ
    - Other opioid
- ANTICOAGULANT – in hospital
  - Clopidogrel 75 mg PO first dose
    - Clopidogrel 18.75 mg (1/4 of 75 mg tab) PO q 24 hr
  - UF Heparin 100 u/kg IV then
    - UF Heparin 200 u/kg SQ TID or UF Heparin 600 u/kg/day IV
- ANTICOAGULANT – to go home
  - Clopidogrel 18.75 mg PO q 24 hr
  - If recurrent or severe add Dalteparin 100 u/kg SQ q 12 – 24 hr
- MANAGE HEART DISEASE/CHF
- SUPPORTIVE CARE

	ACUTE (IN HOSPITAL) MANAGEMENT OF SEVERE HEART FAILURE
CAT	• **Furosemide: 1-4 mg/kg IM or IV bolus +/- CRI (Max 12 mg/kg/day)** • **Oxygen** • **Sedation: butorphanol 0.1-0.2mg/kg IM (Minimize Stress!!!)** • **Thoracocentesis: if pleural effusion** • **Pimobendan: (when able to swallow)** • *Nitroglycerin: ¼" transdermal q 8 – 24 hr for 1-2 d or Nitroprusside: 0.5-5 ug/kg/min IV (careful BP monitoring)* • ***Puff: inhaled albuterol (2 puffs)** or SQ terbutalline for peribronchiolar edema or refractory respiratory distress*

	CHRONIC (OUT PATIENT) MANAGEMENT OF HF
CAT	• **Furosemide: lowest effective dose** • **Benazepril: 0.25 - 0.5 mg/kg PO q 24 hr** • **Pimobendan: 0.25 mg/kg PO q 12 hr** • **Clopidogrel: 1/4 of 75 mg tablet** • **Dietary Na+ restriction (e.g., G/d diet)** • *Diltiazem: if SVT or Afib and need rate control* • *Atenolol: continue or lower dose* • *Sildenafil* • *Spironolactone* • *Periodic thoracocentesis*