Update on the Management of degenerative valve disease and congestive heart failure

Meg Sleeper VMD
University of Florida Veterinary School
Gainesville, Florida

Outline
- Definitions and conceptual framework for managing canine heart disease and failure
- Basic physiology and cardiac drug review
- Staging degenerative valve disease for diagnostics and treatment
- Client education and follow up
- Case studies

Heart Disease
- The presence of a structural abnormality of the heart
- Depending on its nature and severity, heart disease may or may not cause heart failure

Heart Disease in Dogs
- CVHD: chronic valvular heart disease; HWD: heart worm disease; DCM, dilated cardiomyopathy

Heart Failure (HF)
- HF is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood
- HF results when the heart cannot pump enough blood to meet tissue needs at normal venous pressures

Heart Failure Cascade
- Renin Angiotensin Aldosterone System
- Hemodynamic stress
- Injury
- SNS/Cytokines
- Apoptosis/necrosis
- Remodeling
- Dysfunction
- FAILURE
ACC/AHA Classification of Heart Failure

- **At risk for heart failure**
  - STAGE A: No structural disease, but high risk for developing heart disease
  - STAGE B1: Asymptomatic disease, no cardiac remodeling
  - STAGE B2: Asymptomatic disease, cardiac remodeling

- **Heart failure**
  - STAGE C: Past or current signs/symptoms of HF
  - STAGE D: End stage HF, signs refractory to Rx

Canine Heart Failure

- STAGE A: High risk, no known injury, no clinical signs
- STAGE B1+B2: Structural injury, no clinical signs
- STAGE C: Structural injury, current or past clinical signs
- STAGE D: Structural injury, refractory signs

Sites for pharmacologic intervention

- **Preload**
- **Afterload**
- **Contractility**
- **Heart rate**

Cardiac output = preload \* contractility \* HR

Preload reducers

- **Diuretics**
  - Furosemide
  - Hydrochlorothiazide
  - Spironolactone
  - Venodilators
  - Nitroglycerine

Preload

The stretch of the left ventricle just before the onset of contraction (i.e. *end-diastolic volume*).

Diuretics

Three major groups of diuretics used for HF—

- Loop Diuretics (ascending loop of Henle)
- Thiazide Diuretics (early distal tubule)
- Potassium sparing / aldosterone antagonist diuretics (distal tubule and collecting duct)
**Furosemide: Indications & Pharmacologic Properties**

- **Mechanism** – decreases **PRELOAD**
  - **Initial therapy in acute pulmonary edema**
- **IV** vs. **oral**:
  - Diuresis begins 5-20 min after IV dose
  - IV dose peaks at 30 mins
  - IV duration is 2 hours
  - Oral onset 60 mins
  - Peak effects occur in 1-1.5 h following oral dose
  - Duration 4-6 hours

**Furosemide Dose range for cats and dogs**

- **Dogs**
  - Most common dose: 1-2 mg/kg q12-8 hours
  - Titrate dose to affect
  - Can give 8-10 mg/kg in 1-2 mg/kg doses hourly in acute cases
- **Cats**
  - 1 mg/kg q 12 hours
  - Titrate dose to affect
  - Can give 6-8 mg/kg in 1-2 mg/kg doses hourly in acute cases, but significant azotemia risk

If clinical signs are present with a total daily dose of >6 mg/kg furosemide, alternative preload reducers may be necessary: **Furosemide refractoriness**

---

**Afterload**

The load against which the ventricle contracts, i.e. the **resistance to the ejection of blood from the ventricle (myocardial wall stress)**.

Determined by:
- Peripheral resistance (blood pressure)
- Heart size (chamber size/wall thickness)

**Afterload reducers**

- **Arteriodilators**
  - ACE inhibitors
  - Pimobendan
  - Nitroprusside
  - Hydralazine

**ACE Inhibitors: Indications**

- All cause congestive heart failure
- No benefit in compensated valvular heart disease, regardless of left atrial size
- Unknown benefits in feline cardiomyopathies (DCM, HCM, UCM, etc)

**Myocardial Contractility**

Strength of the cardiac muscle contraction (systolic function). At the molecular level, contractility is a load-independent interaction between calcium ions and the contractile proteins.

---

14 15 16 17
Positive inotropes

- Pimobendan
- Dobutamine
- Digoxin

Pimobendan

- **Rapid absorption**
  - Mean peak plasma levels achieved 0.5-1.0 hour after administration of a single oral dose
- **Indication**
  - Management of the signs CHF in dogs due to degenerative valve disease or dilated cardiomyopathy in addition to other appropriate therapy
- **Dose rate**
  - 0.23 mg/lb (0.5 mg/kg) per day, in two divided doses that are not necessarily equal

Heart Rate: Limitations

- **Inverse force-frequency relationship**
- **Impaired Diastolic Filling due to elevated HR**

Negative chronotropes (supraventricular)

- Digoxin
- Beta blockers
  - Atenolol, metoprolol, sotalol
- Calcium channel blockers
  - Diltiazem

“Guidelines Should Come With an Expiration Date, Because They Are a Record of the Past.”

Warren Warwick, MD
Director, University of Minnesota
Cystic Fibrosis Center

Guidelines Should Come With an Expiration Date, Because They Are a Record of the Past.
ACVIM classification of CHF

2009 Guidelines—Specialty of Cardiology Consensus Panel of the ACVIM

<table>
<thead>
<tr>
<th>STAGE</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>High-risk dogs with no structural abnormality or murmur</td>
</tr>
<tr>
<td>B</td>
<td>Structural abnormality but no clinical signs of heart failure</td>
</tr>
<tr>
<td>C</td>
<td>Structural abnormality and current or previous clinical signs of heart failure</td>
</tr>
<tr>
<td>D</td>
<td>Clinical signs of heart failure refractory to standard treatment</td>
</tr>
</tbody>
</table>

Heart disease
Heart failure

Consensus recommendations for stage A (degenerative valve disease)
- No drug therapy recommended
- No dietary recommendations
- Potential breeding considerations

Diagnostic Recommendations

<table>
<thead>
<tr>
<th>STAGE</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Small breed dogs with murmurs</td>
</tr>
</tbody>
</table>

Essential Diagnostics: Baseline radiograph with VHS
- Baseline blood work
- Blood pressure

ACVIM classification of CHF

<table>
<thead>
<tr>
<th>STAGE</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Dogs with murmurs that have not yet developed clinical signs of CHF</td>
</tr>
</tbody>
</table>

STAGE B1
- No cardiac enlargement

STAGE B2
- Cardiac enlargement present

CANINE VERTEBRAL HEART SCORE

VHS = L + S
VHS = 6 + 4.5 = 10.5
Normal = 8.7–10.7

Baseline Bloodwork

Basic laboratory work includes a minimum of
- Hematocrit
- Total protein concentration
- Serum creatinine concentration and
- Urinalysis

Baseline parameters will
- Give you a reference point for hydration and renal function and
- Concurrent diseases and therapy may effect these values
  - Eq. Diuretics and specific gravity
Blood Pressure Monitoring Recommendations

Why Monitor?
- Rule out systemic hypertension
  - From concurrent renal disease
- Progression of disease
  - Increases afterload
  - Increases regurgitation
- Systemic hypertension is controllable

Benefits of echocardiography
- Atypical disease (unusual breed or murmur; heart enlargement pattern)
- Confirming whether dog meets EPIC criteria
- Presence of co-morbidities

Baseline ECG- No consensus
- Determine Heart Rate
- Rhythm – regular vs irregular
- Can suggest enlargement patterns
  - Thoracic radiographs are definitive tool for enlargement patterns

Consensus recommendations for stage B- Therapy (DVD)
- B1 (hemodynamically insignificant MR)
  - No drug or dietary recommendations
  - Re-evaluation with radiographs or echocardiography at least yearly
- B2 (hemodynamically significant MR)
  - According to the EPIC trial, starting pimobendan resulted in an average extension of 15 months to heart failure
  - Re-evaluation with physical examination +/- radiographs or echocardiography every 6 months

Client Education
- Educate the client about
  - Identify early warning signs
    - Coughing, changes in breathing pattern, sleep behavior
    - Demonstrate obtaining a respiratory rate and suggest they begin keeping a log of their findings at home.
  - Establish a baseline for normal and give them a cut off
  - Monitor weekly once a patient is B2
  - Omega 3 fatty acid supplementation

Consensus recommendations for stage C- Diagnosis (DVD)
- Thoracic radiography, echocardiography, basic laboratory testing
- Echocardiography once patient is stable
- No consensus about BNP testing
Consensus recommendations for stage C - Therapy (DVD)

- Acute CHF
  - Furosemide (1-4 mg/kg with dose depending on severity of clinical signs and response)
  - Pimobendan (0.25-0.3 mg/kg PO q12h)
  - Oxygen supplementation
  - Mechanical treatments (i.e. thoracocentesis, etc)
  - Optimal nursing care
  - Sedation if indicated (Butorphanol-0.2-0.25 mg/kg IM or IV)
  - Nitroprusside for poorly responding patients

- Chronic CHF (home based therapy)
  - Continue oral furosemide (1-3 mg/kg q 6-12 h; use the lowest effective dose)
  - Continue or start ACEI (enalapril 0.5 mg/kg q12h)
  - Continue pimobendan (0.25-0.3 mg/kg PO q12h)
  - Participation in a structured, home based extended care program
  - Aggressive management of anorexia or weight loss to avoid cardiac cachexia
  - Modest salt restriction
  - Monitor serum potassium

Consensus recommendations for stage D - Diagnosis (DVD)

- By definition stage D heart failure patients are refractory to treatments for stage C.
- Diagnostic steps are similar to those for stage C

Consensus recommendations for stage D - Therapy (in addition to those drugs started under stage C)

- Acute
  - In the absence of severe renal failure, increase furosemide dose as needed
  - Fluid removal
  - Oxygen supplementation; mechanical ventilation may be useful in some patients
  - More vigorous afterload reduction
    - Nitroprusside, hydralazine, amlodipine

- Chronic (home based therapy)
  - In the absence of severe renal failure, increase furosemide dose as needed
  - Spironolactone if not already started
  - Consider triple diuretic therapy
    - Furosemide, hydrochlorothiazide, spironolactone
  - Beta blockade should not be initiated unless clinical signs of CHF are controlled
  - More vigorous afterload reduction
    - Hydralazine, amlodipine
  - Same dietary recommendations as stage C

Consensus recommendations for stage D - Therapy (in addition to those drugs started under stage C)

- Acute
  - In the absence of severe renal failure, increase furosemide dose as needed
  - Fluid removal
  - Oxygen supplementation; mechanical ventilation may be useful in some patients
  - More vigorous afterload reduction
    - Nitroprusside, hydralazine, amlodipine

- Chronic (home based therapy)
  - In the absence of severe renal failure, increase furosemide dose as needed
  - Spironolactone if not already started
  - Consider triple diuretic therapy
    - Furosemide, hydrochlorothiazide, spironolactone
  - Beta blockade should not be initiated unless clinical signs of CHF are controlled
  - More vigorous afterload reduction
    - Hydralazine, amlodipine
  - Same dietary recommendations as stage C

George

- 9-year-old male
- Miniature Poodle
- 6 month history of a systolic left apical murmur
- 1 week history lethargy and exercise intolerance
- 12 hour history difficulty sleeping and breathing
George Radiographs

George Acute Therapy
- Preload reduction
- Increase contractility (positive inotropes)
- Afterload reduction (arterial dilators)

Furosemide, oxygen therapy, +/- pimobendan or dobutamine

George Chronic Therapy
- Furosemide
- ACEI (enalapril)
- Pimobendan
- Owner education: respiratory log, etc.
- Renal panel in 7-10 days
- Add in spironolactone at 6 month recheck (or sooner if recurrence of CHF)

George echocardiogram

George echocardiogram

George echocardiogram
Additional drugs in the arsenal

- Preload reducers
  - Hydrochlorothiazide
  - Spironolactone
- Afterload reducers
  - Amlodipine
- Heart rate control
  - Digoxin
  - Dilatiazem
  - Beta blockers - atenolol

Questions?

Thor

- 4-year-old male Great Dane
- Lethargy, exercise intolerance x 1 wk
- Difficulty sleeping and breathing x 12 hours
- No cough reported
- Rapid, irregular heart sounds w/ pulse deficits
- Tachypnea/dyspnea

Thor Radiographs

Electrocardiogram

Thor echocardiogram
Thor

Acute Therapy

- Thoracocentesis for removal of fluid
- Preload reduction
- Heart rate/rhythm management
- Increase contractility (positive inotropes)
- Afterload reduction (arterial dilators)
- Thor’s immediate plan: thoracocentesis

Electrocardiogram post tap

HR-120 bpm

Thor

Chronic Therapy

- Furosemide
- ACEI (enalapril)
- Pimobendan
- +/- Digoxin and/or diltiazem
- Owner education: respiratory log; etc.

At home management of heart failure patients: tips and tricks for clinicians and clients

Meg Sleeper VMD, DACVIM (cardiology)
Gainesville, FL

Once patient is in stage C of disease

- Once in stage C begin triad of heart failure medications
  - Pimobendan
  - Furosemide
  - ACE inhibitor
  - +/- spironolactone
- Titrate furosemide to the lowest possible dose that controls clinical signs (importance of respiratory log); generally not less than 1 mg/kg twice daily
- Furosemide forms: 12.5, 20, 40, 50, 80 mg tablets; 10 mg/mL elixir
- “Lasts 6 hours”
- Importance of monitoring renal function
  - Renal panels (SG is no longer useful)
  - Appetite changes

Dealing with furosemide refractoriness

- Use injectable (SQ) furosemide
- Triple diuretic therapy (add hydrochlorothiazide and spironolactone or aldactazide) CAUTIOUSLY
  - Hydrochlorothiazide: 2-4 mg/kg S-BID
  - Spironolactone: 1-2 mg/kg S-BID
  - Torsemide
- Importance of renal function monitoring
**Torsemide**
- Loop diuretic with longer duration of action and decreased susceptibility to resistance than furosemide
- Aldosterone antagonistic effects
- Dose: 1/10 daily furosemide divided into 2 doses per day

**Compounding medications**
- Transdermal cardiac medications generally cannot be measured systemically and are not recommended
- Combining multiple medications into one liquid medication or tablet
  - Possible loss of efficacy
  - Ease of administration
  - Less confusing for owners

**Resting respiratory log book**
- RR has been shown to be one of the most effective ways to identify early heart failure in human cardiac patients
- When utilized correctly, they:
  - Reduce hospitalizations
    - Decrease owner financial and emotional fatigue
  - Reduce episodes of fulminant heart failure
    - Cardiac cell death accelerates with the hypoxia associated with overt heart failure. The number of heart failure episodes has been linked to more rapid progression of heart disease in humans.

**Dealing with coughing**
- Cough is very uncommonly associated with heart disease in cats
- In dogs with valve disease, coughing is more likely to be associated with tracheitis than congestive heart failure, particularly if RR is normal
  - Benefit of owners maintaining a respiratory log
  - Options for severe tracheitis cases:
    - Hydrocodone
    - Butorphanol
    - Diphenoxylate/Lomotil
    - Maropitant/Cerenia
    - Prednisolone (cautiously)
    - Fluticasone

**Systemic blood pressure monitoring**

*Why Monitor?*
- Systemic hypertension is often silent and older dogs are at risk of developing it
- Because it results in increased afterload, it increases the cardiac workload and may speed the progression of heart disease
- Systemic hypertension is controllable
- Further diagnostics warranted to identify cause if present (renal disease)

*Tips for Measuring Blood Pressure*
- Patient positioning is essential
  - Lateral recumbency vs. sternal recumbency
  - Use the up leg
  - Base of tail
- Choose an appropriate cuff size
- Average of three measurements

Note: Each time you take a BP be consistent in patient positioning and cuff size. Record each piece of information when you record the BP.
Monitoring heart rate

- Atrial fibrillation, feline cardiomyopathy
- The optimal heart rate goal for dogs with atrial fibrillation and severe heart disease is poorly defined
  - Some authors have suggested < 140 bpm while others target 90-110 bpm
- Monitoring the heart rate at home is critical to good heart rate control (many dogs with atrial fibrillation require both diltiazem and digoxin for good heart rate control)
- Methods to monitor heart rate at home
  - 24 hour Holter monitor
  - Auscultation
  - Heart rate monitor
  - AliveCor
  - Voyce

24 hour Holter monitor

- Gold standard for heart rate assessment
- Allows evaluation of exercising and sleeping heart rate
- Expense of repeated Holters

Auscultation

- Simple and inexpensive
- Auscultatory estimates of heart rate (particularly in A Fib) may be significantly inaccurate
- Snap shot heart rate assessment
  - Impossible to measure exercising heart rate or accurately assess the presence of pauses in heart rhythm

Heart rate monitor

- Designed for measuring heart rates in horses (hand held device counts HR for 6 sec; upper limit of 200 bpm)
- Within 10% of ECG calculated HR in most of 18 dogs (body wts 5-50 kg) including 6 with A Fib
- Easiest and most accurate in large dogs
- Snapshot heart rate assessment
- Can be purchased through Polar or various equestrian tack shops

Polar HRM results

- Device can be used with iphone
- Heart rate and rhythm monitoring
- Data can be saved as a pdf and forwarded
- Snap shot heart rate and rhythm assessment

Alivecor
Voyce Health Monitor

- Monitor worn as a collar that tracks various parameters
  - Resting heart rate
  - Resting respiratory rate
  - Activity intensity
  - Calories burned
  - Distance travelled
  - Quality of rest

Dietary considerations

- Avoid cachexia and obesity
- Monitor potassium and magnesium serum levels
  - Supplementation with potassium and/or magnesium on case by case basis
  - Particularly in patients with cardiac arrhythmias
- Omega-3 Fatty Acid
  - 180 mg eicosapentaenoic acid/120 mg docasahexaenoic acid; 1 per 10 pounds BW

Minimize routine re-checks

- Requires appropriate use of respiratory log
- Benefits
  - Decrease owner financial fatigue
  - Decrease risk of decompensation in a fragile patient
  - In reality, with the vast majority of dogs and cats, we are treating congestive heart failure rather than the underlying heart disease

Use of thoracic radiographs

- Cost effective method for staging disease
- Vertebral heart size (VHS) is an objective method to serially evaluate heart size changes
- Good screening method for identifying cause of dyspnea in cats
- In the months prior to the development of congestive heart failure, the VHS increases more rapidly in dogs
- Effective for dogs and cats with minimal inter-observer variability in multiple studies
- Breed variability

<table>
<thead>
<tr>
<th>Breed/Breed</th>
<th>R or L</th>
<th>VHS SD</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Various Breeds</td>
<td>L</td>
<td>9.5 ± 0.8</td>
<td>63</td>
</tr>
<tr>
<td>Various Breeds</td>
<td>R</td>
<td>9.8 ± 0.6</td>
<td>63</td>
</tr>
<tr>
<td>Various Breeds</td>
<td>-</td>
<td>9.7 ± 0.5</td>
<td>100</td>
</tr>
<tr>
<td>Yorkshire Terrier</td>
<td>R</td>
<td>9.7 ± 0.5</td>
<td>22</td>
</tr>
<tr>
<td>German Shepherd</td>
<td>R</td>
<td>9.7 ± 0.8</td>
<td>20</td>
</tr>
<tr>
<td>Turkish Shepherd</td>
<td>R</td>
<td>9.7 ± 0.67</td>
<td>120</td>
</tr>
<tr>
<td>Rottweiler</td>
<td>R</td>
<td>9.8 ± 0.1</td>
<td>38</td>
</tr>
<tr>
<td>Cavalier King Charles Spaniel</td>
<td>R</td>
<td>9.8 ± 0.5</td>
<td>JWB</td>
</tr>
</tbody>
</table>
Assessment of Cardiac Size

This VHS = 5.2 + 4.4 = 9.6

This VHS = 7.2 + 6.4 = 13.6

Assessment of Cardiac Size

Long Axis Line 5.2
Short Axis Line 4.4

Normal VHS = 10.5 – 11.0

This VHS = 7.2 + 6.4 = 13.6

Questions?