A Rock and a Hard Place: Cardiorenal Syndrome in Clinical Canine Veterinary Patients

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Agenda

• Introduction: worsening renal function in CHF
• What do we know about this problem in dogs?
• 2 clinical cases, with limitations
Cardiorenal Syndrome

• Broadly: a clinical syndrome in which dysfunctional hearts and dysfunctional kidneys can “initiate and perpetuate disease in the other organ through common
  – hemodynamic
  – neurohormonal
  – immunologic/biochemical feedback pathways.”*

*Bock & Gottlieb, Circulation 2010
Progressive Cardiac Dysfunction

- ↑ Sympathetic Nervous System Activity
- ↑ Renin-Angiotensin-Aldosterone System Activity
- ↑ Afterload
- ↑ Contractility
- ↑ Volume
- Anemia

↓ Cardiac Output

↓ Renal Blood Flow/↓ GFR

↑ Renal Efferent Pressure

Oxidative Stress

Apoptosis, Fibrosis

Progressive Renal Dysfunction

*Modified from Bock and Gottlieb, Circulation 2010
# Cardiorenal Syndrome

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1: Acute CRS</td>
<td>Rapid worsening of cardiac function leads to acute kidney injury</td>
</tr>
<tr>
<td><strong>Type 2: Chronic CRS</strong></td>
<td>Chronic abnormalities in cardiac function lead to progressive chronic kidney disease</td>
</tr>
<tr>
<td>Type 3: Acute renocardiac syndrome</td>
<td>Acute, primary worsening of kidney function leads to acute cardiac dysfunction</td>
</tr>
<tr>
<td>Type 4: Chronic renocardiac syndrome</td>
<td>Primary chronic kidney disease contributes to decreased cardiac function, left ventricular hypertrophy, diastolic dysfunction and increase risk of cardiovascular events</td>
</tr>
<tr>
<td>Type 5: Secondary CRS</td>
<td>Acute or chronic systemic disorders (e.g. diabetes mellitus) cause combined cardiac and renal dysfunction</td>
</tr>
</tbody>
</table>
Clinical Significance of CRS

- ~27% of patients hospitalized with HF developed worsening renal function

Forman et al, JACC 2004
Clinical Importance of CRS

• Worsening azotemia during hospitalization is a poor prognostic sign

• ↑ Cr by 26 umol/L with final Cr ≥ 132.6 umol/L predicts in-hospital mortality*
  – Se: 73%
  – Sp: 72%

Weinfeld et al, Am Heart J 1999

*K Gottlieb et al, J Card Fail 2002
### Risk Factors for Worsening Renal Function

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admit Hct&lt;45%</td>
<td>0.39</td>
<td>0.17-0.90</td>
<td>.03</td>
</tr>
<tr>
<td>Loop diuretic dose day prior admit</td>
<td>1.04</td>
<td>1.004-1.076</td>
<td>.03</td>
</tr>
<tr>
<td>Admit Cr =132.6-221 umol/L (1.25-2.5 mg/dL*)</td>
<td>1.58</td>
<td>0.93-2.67</td>
<td>.09</td>
</tr>
<tr>
<td>History of HF</td>
<td>1.66</td>
<td>1.02-2.72</td>
<td>.04</td>
</tr>
<tr>
<td>History of DM</td>
<td>1.74</td>
<td>1.11-2.73</td>
<td>.02</td>
</tr>
<tr>
<td>Admit SBP&gt;160 mmHg</td>
<td>2.21</td>
<td>1.37-3.55</td>
<td>.001</td>
</tr>
<tr>
<td>CCB day prior to admit</td>
<td>2.28</td>
<td>1.22-4.26</td>
<td>.01</td>
</tr>
<tr>
<td>Admit Cr &gt;221 umol/L (2.5 mg/dl)</td>
<td>4.08</td>
<td>1.97-8.46</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*WRF: increase in Cr >0.3 mg/dl (>26.5 umol/L)*

data modified from Butler et al, Am Heart J 2004
# Treatment of HF Worsens Renal Function*

<table>
<thead>
<tr>
<th>Medication Given w/in 24 hrs of WRF (n=382)</th>
<th>WRF Cases (#, %)</th>
<th>Controls (#, %)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI</td>
<td>68 (36%)</td>
<td>67 (35%)</td>
<td>.92</td>
</tr>
<tr>
<td>ARB</td>
<td>8 (4%)</td>
<td>4 (2%)</td>
<td>.24</td>
</tr>
<tr>
<td>CCB of any type</td>
<td>47 (25%)</td>
<td>20 (10%)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Vasodilators</td>
<td>87 (46%)</td>
<td>67 (35%)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>134 (70%)</td>
<td>125 (65%)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Digoxin</td>
<td>47 (25%)</td>
<td>41 (21%)</td>
<td>.47</td>
</tr>
</tbody>
</table>

*data modified from Butler et al, Am Heart J 2004
What About Dogs?
CVHD, chronic valvular heart disease; HWD: heart worm disease; DCM, dilated cardiomyopathy.
Prevalence of Azotemia in Canine CVD

Chico

11 year old MN Yorkshire Terrier
First Presentation

• Complaint:
  – coughing episodes with excitement/exercise
  – 2 collapse episodes related to cough
  – history of collapsing trachea

• PE:
  – HR 120 bpm, regular rhythm, no pulse deficits
  – 4/6 systolic murmur L apex
  – 3/6 systolic murmur R apex
  – Normal pulse strength
First Presentation

- **Radiographs**
  - VHS 11.5
  - Severe LA/LV enlargement
  - Mainstem bronchial compression
  - Partial TC at thoracic inlet

- **Lab**
  - BUN: 4.28 mmol/L
  - Cr: 61.88 umol/L
  - USG: 1.025
Echocardiographic Diagnosis

• Degenerative mitral valve disease with anterior leaflet prolapse and moderate to severe mitral insufficiency - compensated (Class B2)
Creatinine umol/L

Creatinine Over Time (umol/L)

Begin ACEI

CHF: begin furosemide, pimo, spirono

1: 7/23/09
4: 4/21/10
5: 8/18/10
10: 1/12/11
Chico

- Creatinine remained the same until CHF
- CHF/addition of medications (incl. furosemide) led to significant increase (~44 umol/L; WRF= increase > 26 umol/L)
- Did not exceed laboratory normals at any time

- Necropsy:
  - Interstitial nephritis, lymphoplasmacytic, multifocal, subacute, mild.
  - Glomerulopathy: multifocal, chronic, mild.
  - “Renal changes are interpreted as incidental age-related changes.”
Toby: 11 year old MN Min Schnauzer

• Original diagnoses
  – MR/TR due to chronic degenerative valve disease
  – Systemic hypertension
  – Suspect hyperadrenocorticism

• First renal assessment (at dx of HT):
  – Cr: 79.56 umol/L
  – BUN: 10.71 mmol/L
Toby

- Creatinine values varied with changes with meds
  - Alterations in non-ACEI vasodilators
  - Increases in CHF therapy (i.e. furosemide)
- Azotemia responsive to fluids/temporary discontinuation of meds
Necropsy

- Chronic degenerative valve disease
- Pulmonary vascular changes consistent with PH
- Kidneys:
  a. Membranoproliferative glomerulonephropathy diffuse, chronic, severe
  b. Interstitial nephritis, lymphoplasmacytic, moderate, multifocal
- Disseminated mesothelioma (carcinomatosis)
Summary

• Concurrent valvular disease and renal dysfunction occurs in canine patients

• Many factors likely interact in individual patients
  – increasing aggressiveness of CHF therapy (i.e. furosemide)
  – non-ACEI vasodilators

• Can we interfere with this process?
  – present recommendations begin ACEI/spirono at time of CHF
  – would earlier therapy be protective?