Cardio-Renal Syndrome: What the heart knows

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What the heart knows today the head will understand tomorrow.

— James Stephens —
Vignette

• 55 year old man with HFrEF (LVEF 35%) and CKD (Cr 1.4 mg/dl) admitted with 30 lbs of weight gain and typical HF symptoms.

• Home meds: Sacubitril/valsartan low dose, Carvedilol mid-dose, Furosemide 40 mg BID

• Exam: BP 130/80, HR 80, JVP 15 cm, Pitting edema

• Labs: proBNP 8500, Cr 1.4 mg/dl

• Initial management: IV lasix 40 mg BID, Continued home medication

• Hospital day 2: Stable vitals, No weight change, Cr 1.7 mg/dl
Worsening Renal Function

- Definition: Cr increase ≥ 0.3 mg/dl (5 days)
- Common endpoint in clinical trials
- Cr/CysC changes **poorly correlated** with tubular injury markers
- Not clear either is a surrogate for future mortality

Ahmad et al. Circulation. 2018
Questions

• Should the diuretics be changed?
• Should the Entresto be held?
• What are the goals of diuresis?
## Cardiorenal Syndrome Classifications

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Nomenclature</th>
<th>Description</th>
<th>Clinical Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1 CRS</td>
<td>Acute CRS</td>
<td>HF resulting in AKI</td>
<td>ACS resulting in cardiogenic shock and AKI, AHF resulting in AKI</td>
</tr>
<tr>
<td>Type 2 CRS</td>
<td>Chronic CRS</td>
<td>Chronic HF resulting in CKD</td>
<td>Chronic HF</td>
</tr>
<tr>
<td>Type 3 CRS</td>
<td>Acute renocardiac syndrome</td>
<td>AKI resulting in AHF</td>
<td>HF in the setting of AKI from volume overload, inflammatory surge, and metabolic disturbances in uremia</td>
</tr>
<tr>
<td>Type 4 CRS</td>
<td>Chronic renocardiac syndrome</td>
<td>CKD resulting in chronic HF</td>
<td>LVH and HF from CKD-associated cardiomyopathy</td>
</tr>
<tr>
<td>Type 5 CRS</td>
<td>Secondary CRS</td>
<td>Systemic process resulting in HF and kidney failure</td>
<td>Amyloidosis, sepsis, cirrhosis</td>
</tr>
</tbody>
</table>

ACS indicates acute coronary syndrome; AHF, acute heart failure; AKI, acute kidney injury; CKD, chronic kidney disease; CRS, cardiorenal syndrome; HF, heart failure; and LVH, left ventricular hypertrophy.

Approximately 40% of AHF patients have CRS 1 phenotype
Acute HF Therapies
Hemodynamics of Heart Failure

SYSTOLIC FAILURE

DIASTOLIC FAILURE

Stroke Volume (ml)

Left Ventricular End-Diastolic Pressure (mmHg)

A = operating point for non-failing heart
B = operating point for failing heart
C = effects of a diuretic or venodilator
D = effects of mixed vasodilator or inotropic drug
Overlap between AHF and WRF

**Acute Heart Failure**
- Elevated CVP
- Diminished CO
- Pulmonary congestion
- Third spacing of fluid
- SNS and RAAS activation
- Hypotension +/-

**Worsening Renal Function**
- Elevated renal venous pressures
- Elevated intra-abdominal pressure
- Reduced renal arterial blood flow
- RAAS activation
- Nephrotoxic medications
Venous pressure is key


Less about cardiac output

• ESCAPE
• CRF not ARF associated with worse outcomes
• Renal dysfunction not associated with CI, was associated with RAP
Try to be RIGHT in your assessments

• Assessment of right heart filling pressures
  • JVP
    • Central Venous Catheter / Pulmonary Artery Catheter
• Right Ventricular failure
• Tricuspid valve regurgitation
• Liver congestion
• Elevated intra-abdominal pressure
How Much and How Fast?
Rate of Diuresis

• Goal diuresis is 3-5 L/day

• Conventional Strategy
  • Give 2 x home loop diuretic dose IV
  • If 24 hour output inadequate, double loop diuretic dose

• Spot Urine Strategy
  • Check UNa @ 2 hr, UOP @ 6 hr: Goal > 50-70 mEq/L and 100-150 ml/hr
  • If inadequate double loop diuretic dose
Mechanisms of Diuretic Resistance

- Rangaswami et al. Circulation. 2019;139:e840–e878
Chronic HF Therapies during Acute HF
Chronic Kidney Disease and HF-GDMT

<table>
<thead>
<tr>
<th>Treatment</th>
<th>CKD 1 and 2</th>
<th>CKD 3</th>
<th>CKD 4 and 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRT</td>
<td>Strong</td>
<td>Strong</td>
<td>Absent</td>
</tr>
<tr>
<td>ICD</td>
<td>Strong</td>
<td>Strong</td>
<td>Weak</td>
</tr>
<tr>
<td>H-ISDN</td>
<td>Weak</td>
<td>Weak</td>
<td>Absent</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Weak</td>
<td>Weak</td>
<td>Weak</td>
</tr>
<tr>
<td>Ivabradine</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Absent</td>
</tr>
<tr>
<td>β-blocker</td>
<td>Strong</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>MRA</td>
<td>Strong</td>
<td>Strong</td>
<td>Absent</td>
</tr>
<tr>
<td>ARNi</td>
<td>Strong</td>
<td>Strong</td>
<td>Absent</td>
</tr>
<tr>
<td>ACE inhibitor/ARB</td>
<td>Strong</td>
<td>Strong</td>
<td>Weak</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
</tbody>
</table>

SGLT2i
Reduce Mortality in Heart Failure

**Chronic Heart Failure**
- ACEi
- ARB
- ARNi
- Beta blocker
- MRA
- IDN/HZN (African American)
- SGLT2i

**Acute Heart Failure**
- ????????????
Discontinuation of GDMT in AHF

• RAASi: Temporary 30% reduced GFR ≠ renal injury
• Discontinuation
  • Worse post-discharge HF outcomes
  • Impaired diuresis
• Alternative vasodilators largely unproven
• Newer GDMT improved renal outcomes?
  • SGLT2i
  • Sacubitril/Valsartan
Take Home Points

• Cardiorenal syndrome is a general term – determine primary problem
• Decongestion better for cardiac AND renal function
• Consider mechanisms of diuretic resistance
  • Reach threshold
  • Consider hemodynamics
  • Judicious use of thiazides
• Modest increase in creatinine is not a crisis
• Chronic medical therapies for HF - strong evidence, try not to stop
• Acute decongestive therapies - weak evidence
Cuchulain stirred, Stared on the horses of the sea, and heard The cars of battle and his own name cried; And fought with the invulnerable tide.

— William Butler Yeats —
What we need

• RCT of continued/discontinued ACE/ARB in CKD - STOPACEi
• RCT of continued/discontinued ACE/ARB in Acute HF - ?
• Better clinical markers of tubular injury
• Acute heart failure trials with SGLT2i - Enrolling