The Bernie & Phil Chronicles...

Retirement

Day 4,377:
ANY SIGN OVER THERE, PHIL?

NONE THAT I CAN SEE, BERNIE
...HOW ABOUT YOU?

NAW...
BUT IT'S STILL EARLY
STILL NO GROUPIES.

Y'KNOW... I'M BEGINNING TO WONDER IF IT'S TRUE THAT MEN GET SEXIER WITH AGE.
Cardiorenal Syndrome
by Dr. Dale Erickson
Primary disorder of one of these two organs often results in secondary dysfunction or injury to the other
OH, SURE, IT'S THOSE STUPID BRAINS BRAGGING AGAIN... THEY TAKE CREDIT FOR EVERYTHING...

HAVE YOU EVER THOUGHT ABOUT WHY WE'RE DOING THIS? JUST TO KEEP THE HEART IN SHAPE!
REMEMBER, IF I GO, WE ALL GO!

WHAT DID I TELL YOU? ACTUALLY, I THINK THE ARTERIES HAVE HIM WORRIED...
Generally defined as a condition in which the kidney dysfunctions (pre-renal syndrome) because of a problem with cardiac function: The term has been borrowed from other organ systems, e.g. hepatorenal syndrome.

- The concept is by fixing the heart, kidney function will get back to normal.

- Not that simple: Current concept is more complex. CRS can be described a pathophysiological disorder where acute or chronic dysfunction of one organ may produce acute or chronic dysfunction of the other. 5 CRS subtypes.

Cardiorenal Syndrome

“The kidney presents in the highest degree the phenomenon of ‘sensibility’; the power of reacting to various stimuli in a direction which is appropriate for the survival of the organism; a power of adaptation which gives one the idea that its component parts must be endowed with intelligence.”


- Bottom line: Kidney is very smart organ.
- Problem with the bottom line: There is maladaptive price to be paid with increase in RAAS, catecholamines, vasopressin > high neurohormonal milieu, vasoconstrictor state.
CRS–5 subtypes

CRS type1 = acute cardiac failure > AKI,

(e.g. ischemic insult from MI, results in acute hypoperfusion, decreased O2 delivery, reduced GFR)
60 year old male with ACS

- Admitted to Presbyterian ICU in cardiogenic shock, coma, ventilator, NG tube feedings, pressors, pulmonary edema > AKI.
- After 3 weeks woke up, got off ventilator, recovered renal function, discharged home.
- Lived another year. A very important year.
Figure 1  CRS Type 1

Pathophysiological interactions between heart and kidney in type 1 cardiorenal syndrome (CRS) or “acute CRS” (abrupt worsening of cardiac function, e.g., acute cardiogenic shock or acute decompensation of chronic heart failure) leading to kidney injury. ACE = angiotensin-converting enzyme; ANP = atrial natriuretic peptide; BNP = B-type natriuretic peptide; CO = cardiac output; GFR = glomerular filtration rate; KIM = kidney injury molecule; N-GAL = neutrophil gelatinase-associated lipocalin; RAA = renin angiotensin aldosterone. Figure illustration by Rob Flewell.
CRS 5 subtypes cont.

- **CRS Type 2** = Chronic Heart Failure > Chronic Kidney Disease.

- Mechanisms: Long term hypoperfusion of kidneys (renal congestion) may play a role.

- **ESCAPE** study (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Effectiveness): Only link was with right atrial pressure and renal dysfunction, not linked to EF.

- Not clearly understood: Neurohormonal abnormalities with increase of vasoconstrictive mediators (epinephrine, angiotensin, endothelin).
Pathophysiological interactions between heart and kidney in type 2 cardiorenal syndrome (CRS) or “chronic CRS” (chronic abnormalities in cardiac function, e.g., chronic heart failure) causing progressive chronic kidney disease (CKD). Figure illustration by Rob Flewell. LVH = left ventricular hypertrophy; RAA = renin angiotensin aldosterone.
Case Profile

- 70 yo African-American male with complaints:
  - Sudden onset of extreme breathlessness, increasing peripheral edema. No Chest pain.
- **JVP 12 cm.** Chest: Crackles to scapula bilaterally
  - Heart: regular rhythm, **S3.** Liver edge down.
  - Extremities: 2 plus edema to mid calf.
  - Chest X-ray: Pulmonary vascular congestion.
Case Profile Assessment

- Congestive Heart Failure: decreased E.F.
- CKD Stage 4, worsening chronic renal failure.
- Cardiorenal syndrome, Type 2.
- Hypertension.
- Diabetes Type 2, not well controlled.

How to manage? Stay tuned.
CRS type 3 (Renocardiac syndrome), abrupt AKI causes acute heart dysfunction (heart failure, arrhythmias, pulmonary edema).

AKI has been identified in 9% of hospital pts when RIFLE (risk, injury, failure, loss and ESRD) definition is used.

Admission to Presbyterian 7–C with severe diarrheal illness, volume depletion > AKI.

Acute hemodialysis with VAS–cath.

BP dropping in the middle of the night,

Cardiac arrest > expired.

Post mortum: Pericarditis / tamponade.

Uremic pericarditis seen less frequently.

Rx.: Frequent dialysis, pericardial drainage, with instillation of dexamethasone.

Pericarditis seen more frequently in 3rd. World.
Pathophysiological interactions between heart and kidney in type 3 CRS or “acute renocardiac syndrome” (abrupt worsening of renal function, e.g., acute kidney failure or glomerulonephritis) causing acute cardiac disorder (e.g., heart failure, arrhythmia, pulmonary edema). MPO = myeloperoxidase; other abbreviations as in Figure 1. Figure illustration by Rob Flewell.
CRS Type 4 (Chronic Renocardiac syndrome)

- Characterized by primary CKD (e.g. chronic glomerular disease).
- >Decrease cardiac function, LVH, diastolic dysfunction.
- 5 stages of CKD, based on severity.
- Current estimates of CKD in US, 11%.
- >50% of deaths in CKD are CV deaths.
- CKD cardiac risk factor = to smoking.
- Anemia, Ca/Phos abnormalities, obesity, Sodium/H2O overload, Chronic inflammation, accelerated ASHD.
Figure 4  CRS Type 4

Pathophysiological interactions between heart and kidney in type 4 cardiorenal syndrome (CRS) or “chronic renocardiac syndrome” (chronic kidney disease [CKD]), e.g., chronic glomerular disease, contributing to decreased cardiac function, cardiac hypertrophy, or increased risk of adverse cardiovascular events. BMI = body mass index; EPO = erythropoietin; LDL = low-density lipoprotein. Figure illustration by Rob Fiewell.
Stage 1, GFR >90, with other manifestation (i.e, proteinuria)

Stage 2, GFR 60-89  What’s the point?> to slow progression.

Stage 3, GFR 30-59  Slow progression

Stage 4, GFR 15-29  Dialysis/transplant

Education. “Fistula first” emphasis.

Stage 5, GFR 0-14  When to start dialysis?
CRS 5 subtypes cont.

- **CRS type 5** (secondary CRS)
  - Characterized by presence of acute or chronic dysfunction due to systemic disorders (e.g. sepsis, diabetes, lupus, vasculitis, amyloidosis).

- **SEPSIS**: In acute setting sepsis represents most common and serious condition that can induce AKI and cause profound myocardial depression.

- **Mechanisms**: Unclear, but it is clear that several systemic diseases may affect both organs simultaneously. May involve TNF and other mediators > low CO > viscous cycle.
ESRD secondary to Lupus, on CAPD.
Admission to Presbyterian ICU. Dx: peritonitis, septicemia, and shock.
Rx: Central line, antibiotics, volume resuscitation, pressors, for hours Systolic BP 60–70. Needed dialysis.
Could not safely dialyze, hypotension. No CAVH.
After many hours, suddenly BP came up.
Successfully dialyzed, recovered.
Pathophysiological interactions between heart and kidney in type 5 cardiorenal syndrome (CRS) or “secondary CRS” (systemic condition, e.g., diabetes mellitus, sepsis, causing both cardiac and renal dysfunction). LPS = lipopolysaccharide (endotoxin); RVR = renal vascular resistance.

Figure illustration by Rob Fiewell.
BODY FLUID VOLUME REGULATION

Afferent limb

1. Total blood volume
2. Total plasma volume
3. Total Extracellular Fluid Volume
4. Cardiac output

Efferent limb

1. GFR
2. Vasopressin
3. RAAS, Aldosterone
4. Atrial natriuretic Peptide (de Wardener’s “third factor”)

Comment: ANP released by ventricle and atrial cells in response to volume expansion increases GFR and decreases Na reabsorption. Nesiritide Rx.
Decrease C.O. > Arterial Underfilling < Arterial Vasodilation

Increase
Peripheral Vascular Resistance

Renal Sodium and H2O Retention

Increase CO

Restoration of Arterial Circulation
# Body Fluid Distribution

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Amount</th>
<th>Volume 70kg man</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Body Fluid</td>
<td>60% Body weight</td>
<td>42.0 liters</td>
</tr>
<tr>
<td>Intracellular Fluid</td>
<td>40% Body weight</td>
<td>28.0 liters</td>
</tr>
<tr>
<td>Extracellular Fluid</td>
<td>20% Body weight</td>
<td>14.0 liters</td>
</tr>
<tr>
<td>Interstitial Fluid</td>
<td>2/3 of ECF</td>
<td>9.4 liters</td>
</tr>
<tr>
<td>Plasma Fluid</td>
<td>1/3 of ECF</td>
<td>4.6 liters</td>
</tr>
<tr>
<td>Venous Fluid</td>
<td>85% of Plasma</td>
<td>3.9 liters</td>
</tr>
<tr>
<td>Arterial Fluid</td>
<td>15% of Plasma</td>
<td>.7 liters</td>
</tr>
</tbody>
</table>
Cardiorenal Syndrome

“We shall never understand anything until we have found some contradictions.”

What to do?

- Patient is congested, breathless.
- Would you admit? Why? Admission is a sign of badness of CHF.
- What care plan to initiate? Diuretics to achieve decongestion and euvolemia.
- Diuretics: IV or PO? Why?
  - IV diuretics: continuous infusion furosemide 20-40 mg bolus > 5 mg/hour
- What else? Ace inhibitor! Why? Evidenced based 20% reduction in mortality with ACE/ARB in CHF.
Case Questions?

What else can be done to help this patient?

- Aldosterone blockade.

- Spironolactone, (the only diuretic to have shown to improve survival in Heart Failure in NYHA class III-IV pts.) further blocks aldosterone, not completely suppressed by ACE inhibition.

- Aldosterone increases Na uptake / CV fibrosis.

- RALES trial>30% risk reduction of mortality.

- Risk is hyperkalemia, only 2% in this study.

- Convert to PO loop diuretics, i.e. furosemide, for volume management.
Kidneys and Heart Produce Chemicals that Mediate pathophysiological changes in vascular tone, salt and water balance, cellular hypertrophy, and fibrosis.

- Kidneys produce renin in the JG apparatus, which activates the Renin-Angiotensin-Aldosterone System (RAAS).
- Heart synthesizes components of Natriuretic Peptide System (NPS).
RAAS and NPS act as counter regulators in renal and cardiovascular homeostasis, producing opposing effects throughout evolution of disease.

These Systems also act indirectly through their influence on neuro-hormones such as the sympathetic amines, vasopressin, and endothelin-1.
Pathophysiology of Cardiorenal S.

- In CKD and Heart Failure, the RAAS produces increase in Angiotensin 2 (Ang II) which affects vascular tone and renal function, ultimately leads to vasoconstriction and volume expansion.

- Ang II also produces differential contractions of afferent and efferent glomerular arterioles and mesangial cells, thus increase GFR, causing sodium and H2O reabsorption directly in PCT and indirectly in collecting duct via release of aldosterone.
Pathophysiology of Cardiorenal S.

- **RAAS** modulates its own activity by stimulating counteregulatory factors, i.e., natriuretic peptides.

- **Ang II** and Aldosterone contribute to chronic cardiorenal damage by promoting glomerular hypertrophy and fibrosis as well inducing myocardial hypertrophy and fibrosis (cardiac remodeling).

- In Diabetics, **Ang II** acts synergistically with hyperglycemia to promote hyperfiltration and proteinuria=diabetic nephropathy.
Heart Failure Rx. Goals

- **Decongestion.** Help the patient to feel better.
- Achieve **euvolemia**-diuretics.
- Patient **Education**, sodium restriction, potassium?
- Assessment of ventricular function. **Echocardiogram.**
- Initiate **ACE inhibitor/ARB.**
- **Smoking cessation.**
- Beta blockade, evidence is for **cavedilol, metoprolol** (long acting topral, lopressor)
- **Aldosterone antagonist** Rx.
- **Coumadin** in pts. with A. Fib., when appropriate.
Heart Failure Treatment

Which strategies most effective in decreasing mortality?

- ACE/ARB drugs.
- Beta-Blockade drugs, carvedilol, metoprolol (evidenced based), revolutionary.
- Other strategies are important, but ACE and Beta-Blockade the most important.

PERFORMANCE MEASURES

Association between performance measures and clinical outcome.

*Indicators of survival in Heart Failure:*

1. Repeat hospitalizations.
2. **CKD**, huge impact on survival.
3. Advanced age.

DATA from 4 million Medicare discharges from 1992-1997, 30 day mortality 10-12%
Performance Measures

Mortality no better in 2007. *WHY?*

“Less to do with what we know and more to do with *what we do* with what we know.”

*What do we know?*

- **ADHERE** Study: 200,000 cases of decompensated heart failure (2006).
  - Only 51% on an ACE at discharge.
  - Only 57% on a Beta-Blockade, even worse if pt. also had CKD.
Risk Reduction of Death

- **Digoxin and diuretics**: 2 year risk of death, 35% (Only indication for dig is rate control of A. F.)

- **Add ACE/ARB**: 2 year risk improved to 27%, being sensitive to renal parameters

- **Add aldosterone antagonist**: 2 year risk 19%

- **Add Beta-Blocade**: 2 year risk 12%

- **Add appropriate device** Rx. 2 year risk<5%

- **What about CKD patients w/ Heart Failure>** Risk reduction similar, can use ACE with CKD stage
  - 3-4, monitoring potassium carefully
CASE PROFILE:

70 yo man has improved chance of survival with multidisciplinary approach.

- Nurses, P.A.s, N.P.s, dieticians, social workers, pharmacists, primary care physicians, specialist physicians (cardiologists and nephrologists), exercise physiologists, all working together as a TEAM

- Heart Failure Clinic

- Health Plex – Cardiac Rehab.

- New Heart- Cardiac Rehab.
The End