Chronic Kidney Disease: The Silent Killer?

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No Disclosures

What is Chronic Kidney Disease?

Chronic Kidney Disease (CKD)
- Functional or structural kidney damage
  - eGFR < 60 mL / min /1.73 m² x 3 months
- United States: > 20 m affected (7%)
  - 47% of individuals > 70 yrs
- End-stage renal disease (RRT): > 500 k
- Risk factors: diabetes; hypertension (90%)
  - Risk of dying of CV disease in older patients with CKD is greater than risk of needing RRT!

Modification of Diet in Renal Disease (MDRD)
http://www.nkdep.nih.gov

eGFR = 186 x (Scr)⁻¹.¹₅₄ x (Age)⁻₀.₂₀₃
 x 0.₇₄₂ (if female); x 1.₂₁₂ (if African-American)

For example: 64 yr-old woman,
baseline Scr 1.9 mg/dL
eGFR = 186 x (1.9)⁻¹.¹₅₄ x (64)⁻₀.₂₀₃ x (0.₇₄₂)
eGFR = 26.6 mL / min /1.₇₃m²

How severe is her CKD?

National Kidney Foundation (NKF)
Kidney Disease Outcomes QI Classification

<table>
<thead>
<tr>
<th>CKD Stage</th>
<th>eGFR (mL/min/1.73M²)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt; 90</td>
<td>Kidney damage with NL GFR</td>
</tr>
<tr>
<td>2</td>
<td>60 - 89</td>
<td>Mibly decreased GFR</td>
</tr>
<tr>
<td>3a</td>
<td>45 - 59</td>
<td>Moderately decreased GFR</td>
</tr>
<tr>
<td>3b</td>
<td>30 - 44</td>
<td>Moderately severe decrease</td>
</tr>
<tr>
<td>4</td>
<td>15 - 29</td>
<td>Severely decreased GFR</td>
</tr>
<tr>
<td>5</td>
<td>&lt; 15 (or RRT)</td>
<td>End-stage kidney disease</td>
</tr>
</tbody>
</table>

1.12 m adults without dialysis or transplantation

Risk of CKD
CV Events
Hospitalization
Death

CKD CRASH 2-16 - January 24, 2016
Renal Risk in CABG Surgery

Yeo KK et al. Am J Cardiol 2008; 101:1269-74

Limitations of eGFR

Sladen RN. Anesth Analg 2011; 112:1277-9
- It is an estimated, not actual GFR!
- Provides reliable assessment of eGFR between 20 - 60 mL / min / 1.73 m² only
- GFR > 60 mL / min / 1.73 m² is referred to as “normal”
- Largely dependent on SCR
  - affected by depleted muscle mass
  - cannot track acute changes in GFR!

How Should We Modify Our Perioperative Management?

Top Ten Caveats

1. Anticipate cardiovascular disease

Cardiovascular Disease in CKD

- Causes 40% of all deaths in CKD
  - LVH, diffuse calcinosis, fibrosis, CAD
  - vitamin D deficiency contributes (Ca++)
  - high incidence of arrhythmias (worsen CKD)
  - increased thromboembolism, bleeding
- Silent ischemia (autonomic neuropathy)
- Risk of sudden cardiac death (20-40%)
  - increases with severity of CKD
  - reversed by renal transplant, but not by HD

Protein-Bound Uremic Toxins (PBUT)

Cardiorenal Syndrome (Organ Crosstalk)


Indoxyl sulfate, p-cresol, homocysteine, ADMA
- Highly protein bound, poorly dialyzed
- Toxic to kidneys and heart
- Induce oxidative stress, endothelial dysfunction
- Vascular smooth muscle cell proliferation
- Fibrogenic, pro-hypertrophic (LVH)
- Promote atherosclerosis, adverse CV events

Indoxyl Sulfate Metabolism


- Indoxyl sulfate (from tryptophan in diet) accumulates in CKD
- Cardiotoxic
- AST-120 (Kremezin), an oral charcoal, absorbs indole in ileum
- Improves cardiac and renal function in animal CKD
Diastolic Dysfunction in CKD
Farshid A et al. BMC Nephrol 2013; 14; 280.
- Common in CKD especially with HTN
  - LVH, diffuse calcinosis, fibrosis, CAD
  - increases with grade of CKD (85% stage 4-5)
- LV ejection fraction > 50%
  - impaired diastolic relaxation
  - evaluated by transthoracic echocardiogram
  - requires higher filling pressure, slower HR
- Increased risk of cardiac mortality

Sudden Cardiac Death (SCD)
Franczyk-Skora B et al. BMC Nephrol 2012; 13; 162.
- SV, V arrhythmias - 80-90% of patients on HD
  - cardiac fibrosis, sympathetic hyperactivity
- Exacerbated during HD and hours afterwards
  - 50% of all deaths in HD patients
- Prolonged QT - iron overload and deposition
  - Torsades de pointes, VF, asystole
  - electrolyte shifts - hypokalemia, hypomagnesemia
  - catecholamine bursts (hypovolemia, HD)
  - drugs: antidepressants, droperidol, ciprofloxacin

Torsades de Pointes
“Twisting of the Points”
Yap YG, Cam AJ. Heart 2003; 89: 1363-72
- Prolonged QT
- Low K, Mg
- Catecholamines
- Drugs
  - haloperidol
  - droperidol

SCD: Prophylaxis
Whitman IR et al. JASN 2012 23; 1929-39
- Beta blockade
- Statins
- RAAS blockade
- AICD

Do A Cardiac Workup!
- Careful history (DM, HTN, CAD, arrhythmias)
- Look for anemia (EPO, iron, folate, GIB)
- ECG (QT, conduction problems, arrhythmias)
- TTE (LVH, diastolic dysfunction, CHF)
- Perioperative beta blockade
- Cardioprotective anesthetic, emergence

Autonomic Neuropathy in CKD
Accompanies peripheral neuropathy
- Delayed gastric emptying (aspiration risk)
- Silent myocardial ischemia
- Orthostatic hypotension

Metabolic Acidosis in CKD
- Early: hyperchloremic acidosis
  - tubular HCO₃ waste
- Late: anion gap acidosis
  - sulfate, phosphate accumulation
- Acute on chronic acidosis
  - hypercarbia, shock, diarrhea, stress
Acid-Base Management
• Check preoperative HCO₃ and Cl
  - hyperchloremic vs. anion gap acidosis
• Support ventilatory compensation
  - increase minute ventilation in OR
  - consider postoperative ventilation
• Recognize relationship to potassium

Potassium Balance
\[
\Delta \text{pH} = 0.1 \Rightarrow \Delta K^+ = 0.5 \text{ mEq/L}
\]

Hyperkalemia Protocol
- Calcium chloride: 1-2 g central IV
- NaHCO₃: 50 - 100 mEq
- Hyperventilate: 0.1 pH = 0.5 K⁺
- Insulin + glucose: 5u + 25g (50 mL 50%)
- Kayexalate enema: 0.5 g/kg
- Emergency dialysis: If K⁺ > 6.0 mEq/L

Acute Hyperkalemia in CKD
• Acute acidosis
• Catabolic stress
• Major trauma, surgery, sepsis
• Drugs
  - NSAIDs, ACE inhibitors
  - K⁺ sparing diuretics
  - β-blockers
  - Cyclosporin A, tacrolimus

Depleted Fluid Reserve
Hypovolemia ↔ Hypovolemia
• Anuria
  - excess Na⁺: edema, HTN
  - excess H₂O: hyponatremia
• Nonoliguric, polyuric
  - unable to concentrate urine

Principles of Fluid Management
• Correct fluid deficits
• Restrict maintenance fluid
• Monitor appropriately
• Be careful post-operatively!
  - withdrawal of positive pressure
  - reversal of sympathetic block

Perioperative Acidosis
35 yr old diabetic, cadaveric renal transplant

<table>
<thead>
<tr>
<th></th>
<th>PaCO₂</th>
<th>pH</th>
<th>HCO₃</th>
<th>K⁺</th>
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<tbody>
<tr>
<td>Preop</td>
<td>32</td>
<td>7.32</td>
<td>17</td>
<td>5</td>
</tr>
<tr>
<td>OR</td>
<td>40</td>
<td>7.25</td>
<td>18</td>
<td>5.3</td>
</tr>
<tr>
<td>PACU</td>
<td>44</td>
<td>7.21</td>
<td>19</td>
<td>5.6</td>
</tr>
<tr>
<td>PACU</td>
<td>48</td>
<td>7.18</td>
<td>19</td>
<td>5.9</td>
</tr>
</tbody>
</table>

4. Anticipate Acute Fluid Overload and Pulmonary Edema
5. Anticipate Anemia and Bleeding
Hematologic Impact of CKD
- Chronic anemia
  - erythropoietin deficiency
  - chronic blood loss (HD, GIB)
  - iron, folate deficiency
- Uremic thrombocytopathy
  - platelet dysfunction (normal count)
  - care with regional, axial anesthesia

Erythropoietin and CKD
- CKD-induced cardiac dysfunction
  - pro-inflammatory cytokines
  - anti-erythrocytic circulating factors
- Erythropoietin therapy
  - anti-inflammatory, anti-oxidative
  - decreased LVH, fibrosis, BNP
  - excess: CVA, MI, thrombosis, ESRD, death

Uremic Thrombocytopathy
- Acquired von Willebrand's Disease
  - vWF
  - VIII
  - platelets
  - Urea
  - endothelium

Desmopressin (DDAVP)
- 8-deamino D-arginine vasopressin
  - Derivative of arginine vasopressin (AVP)
  - vasodilator, long-acting
  - 0.3 µg/kg IV over 15-20 min (hypotension)
  - Improves platelet function for 1-12 hr
  - Releases vWF-VIII from endothelium
    - tachyphylaxis with repeat doses
    - not effective with ongoing pressor therapy

Cryoprecipitate
- Patients exposed to amines
  - NE, EPI, AVP
- Recent administration of DDAVP
- Contains VWF, Factor VIII
  - also fibrinogen, Factor XIII

Vitamin D Deficiency and CKD
- Vitamin D3 - cholecalciferol
  - 25-OH D < 30 ng/mL
  - Decreased intake of dairy products
    - phosphate restriction
  - Decreased sunlight exposure
  - Vitamin D loss with proteinuria
  - Vitamin D loss in dialysate

6. Anticipate
renal osteodystrophy

Vitamin D Deficiency and CKD
- Vitamin D1 - cholecalciferol
  - 25-OH D less active
  - 1,25-OH$_2$ D more active
  - I-alpha hydroxylase (kidney)
  - anti-inflammatory innate immunity
  - healthy bones & joints
Renal Bone Disease
- Vitamin D deficiency (20-80% of ESRD)
- Hypocalcemia (impaired GI absorption)
- Increased parathyroid hormone (PTH)
  - mobilization of calcium from bones
  - metastatic calcification, osteodystrophy
  - brittle bones and joints
  - cardiac fibrosis (increased risk of CVD)
- Careful positioning and pressure protection!

7. Anticipate the Impact of Dialysis
Renal replacement therapy (RRT)

Renal Replacement Therapy (RRT)
Diffusion
Convection
Dialysis
Ultrafiltration

Dialysis (diffusion)
- Diffusion along Concentration Gradient

Dialysis (diffusion)
- Diffusion along Concentration Gradient

Convection (ultrafiltration)
- Hydrostatic Pressure

Convection (ultrafiltration)
- Solvent Drag
- Volume Shift

Renal Replacement Therapy (RRT)
- Diffusion
- Convection
- Osmotic Shift
- Volume Shift

Renal Replacement Therapy (RRT)
- Intermittent Hemodialysis (IHD)
- Continuous RRT (CRRT)
- Peritoneal Dialysis (PD)
**What Dialysis Does Well**

Controls manifestations of acute uremia
- Pulmonary edema
- Hyperkalemia, acidosis
- Acute uremia:
  - encephalopathy
  - enteropathy
  - serositis
  - thromboctopathy

**What Dialysis Does Poorly**

Controls manifestations of chronic uremia
- Cardiovascular complications (SCD)
- Anemia
- Renal osteodystrophy
- Peripheral neuropathy
- Impaired resistance to sepsis
- Poor wound healing

**Timing of Preoperative Dialysis**

- Ideal: afternoon, the day before surgery!
- Adverse effects of dialysis:
  - AV shunt (low SVR)
  - hypovolemia, hypotension, SCD
  - electrolyte imbalance (K, Mg, Pi)
  - myocardial ischemia, arrhythmias
  - dysequilibrium syndrome
  - residual anticoagulation

**Renal Drug Disposition**

- Few drugs are totally renal dependent
  - aminoglycosides, digoxin
- Many drugs are partially renal dependent (decrease maintenance doses)
  - metformin, cimetidine, penicillin, milrinone
  - pantoconium, vecuronium, rocuronium
  - atropine, glycopyrrolate, neostigmine
- Some drugs have active metabolites
  - morphine, meperidine, vecuronium

**Rocuronium**

Robertson EN et al. Eur J Anaesthesiol 2005; 22: 4-10

- Elimination is independent of renal function
- Pharmacodynamic data are conflicting
  - no difference, prolonged action, variable
- Immediately inactivated by sugammadex
  - complex is excreted by kidneys

**Morphine**

- 80% antianalgesic
- 10% analgesic (40 x potency)

**Drugs Cleared in the Blood**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism</th>
</tr>
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<tbody>
<tr>
<td>succinylcholine</td>
<td>PChE</td>
</tr>
<tr>
<td>esmolol</td>
<td>RBC esterase</td>
</tr>
<tr>
<td>cisatracurium</td>
<td>Hoffman</td>
</tr>
<tr>
<td>remifentanil</td>
<td>esterase</td>
</tr>
<tr>
<td>clevidipine</td>
<td>esterase</td>
</tr>
</tbody>
</table>

**9. Anticipate**

nausea, vomiting, aspiration and perioperative GI bleeding
Gastrointestinal Disease and CKD

Thomas R et al. Ren Fail 2012, Oct 18 (ePub)

- Delayed gastric emptying (aspiration risk)
  - autonomic neuropathy
- GI Bleeding (increased risk and mortality):
  - peptic ulcer disease (25%)
  - erosive esophagitis, gastritis, duodenitis
  - ischemic colitis (IHD)
  - thrombocytopenia (normal count)
- Risk increases with stage of CKD

Postop Complications

- Acute kidney injury (AKI on CKD)
- Myocardial ischemia, arrhythmias
- Postoperative pneumonia
- Inability to tolerate hemodialysis
- Poor wound healing and wound infection
- Prolonged ICU length of stay

The Bottom Line

CKD is a multisystem disease - and can be a silent killer!

Be careful out there!

Good Luck!!