Acute Kidney Injury

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Disclosures
Investigator-initiated research grants from Merck, Otsuka, and Satellite Health Care
Expert witness testimony for GE Healthcare and Salix

Goals
• Introduction to new terminology, definition
• Incidence, mortality, costs of AKI
• Approach to the patient with AKI
• Specific clinical scenarios

Case
• 64 year old man with HTN, DM, osteoarthritis, BPH
• Presents to ED complaining of nausea, vomiting
• Meds: lisinopril 40 mg/d, metformin 1gm bid, ibuprofen 800 mg tid
• Exam: BP 100/60, HR 104, RR 16
  – Lungs clear; CV RRR nl s1 s2, no rub, no JVD
  – Abd soft
  – Ext no edema
• Labs
  134 100 84
  5.6 18 3.2

Acute Kidney Injury
or the syndrome formerly known as “Acute Renal Failure”

• “Acute”
  Happening within hours to days
• “Kidney”
  (more familiar than “Renal”)
• “Injury”
  Not always “failure.” Refers to organ damage…

Defining AKI

> 0.3 mg/dL increase
  0.5 mg/dL if < 1.9
  1.0 mg/dL if 2.0 – 4.9
  1.5 mg/dL if > 4.9

25% increase to at least 2.0 mg/dL within 48h
50% increase to at least 1.4 mg/dL.
50% increase to at least 2.0 mg/dL.
Defining AKI

- 50% increase within 48h
- > 30 different definitions in the nephrology literature

New consensus definition

- Increase in creatinine of ≥ 0.3 mg/dL in 48h OR
- 1.5x baseline in 7d OR
- Oliguria < 0.5ml/kg/h x 6h

AKI is deadly

- Even when mild

AKI is increasingly common

- 5 to 7% of admissions, up to 50% of ICU pts
- Between 1988 and 2002: Four-fold increase in AKI, six-fold increase in AKI-D (Waikar JASN 2006)
- Community-based estimate: 522 AKI, 30 AKI-D per 100,000

AKI is expensive

- 60% increase in cost with post-CABG AKI defined as 50% increase in SCr
- Additional $5000 when SCr increases by > 0.3
- $10 billion annually

Approach to the patient with AKI
Approach to the patient with AKI

- Pre-renal
- Intrinsic renal
- Post-renal

Pre-renal azotemia

- Serum creatinine increases due to renal hypoperfusion
- No structural injury to kidney
- Recovery with restoration of hemodynamics

Causes
- Hypovolemia
- Decreased cardiac output
- Decreased effective circ. volume
- Congestive heart failure, cirrhosis
- Impaired renal hemodynamics
  - NSAIDs, ACE, ARB

Pearl: all NSAIDs including Cox-2 inhibitors; both ACE and ARB's

Common causes of AKI

<table>
<thead>
<tr>
<th>Outpatient</th>
<th>Inpatient</th>
<th>International</th>
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<tbody>
<tr>
<td>Pre-renal</td>
<td>Medical ICU: ATN from sepsis, drugs</td>
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<tr>
<td>• ACE-I when vomiting</td>
<td>• Cardiac floor: contrast, cardiac surgery, cardio-renal</td>
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<tr>
<td>• ACE-I + NSAID</td>
<td>• SICU: rhabdomyolysis, sepsis, postop ATN</td>
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<tr>
<td>Obstruction</td>
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<td>Sub-Saharan Africa</td>
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<td>• BPH, stones</td>
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<td>• Malaria (1% of severe cases)</td>
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<td></td>
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<td>• Diarrhea</td>
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<td>Tropics</td>
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<td>• Leptospirosis</td>
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<td></td>
<td></td>
<td>Others</td>
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<tr>
<td></td>
<td></td>
<td>• Post-strep GN</td>
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<td></td>
<td></td>
<td>• Crush syndrome</td>
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First steps

- **Is this acute or chronic**
  - Baseline SCr (if available)
  - Chronic
    - Anemia (non-specific)
    - Small kidneys (< 8cm)
    - "Increased echogenicity"
- **How urgent is this?**
  - Hyperkalemia (K > 6.0, or rising fast)
  - Anuria
  - Severe hypoxemic respiratory failure
  - Intoxication: methanol, ethylene glycol, salicylates, lithium

64M with HTN, DM, OA, BPH. In ED with N/V. Meds: ACE, NSAID, metformin
Exam: BP 100/60, HR 104, RR 16; unrevealing exam
Labs: BUN 84, Creat 3.2, K 5.6, Bicarb 18

Physical examination

- Pre-renal
  - Orthostatic hypotension, tachycardia, decreased skin turgor, etc
  - Hepato-renal: stigmata of liver disease
  - Cardio-renal: signs of heart failure
- Post-renal
  - Palpable bladder. Pearl: normal urine output does not rule it out
- Intrinsic renal
  - ATN: nonspecific (volume overload if present)
  - Glomerulonephritis: (variable)
  - Vasculitis: palpable purpura
  - Atheroembolic disease: livedo reticularis, blue toes
  - Interstitial nephritis: rash, fever (eos)—only 10% of cases

Studies

- Chem 7, BUN, creatinine, Ca, Phos, uric acid, CPK
- CBC with diff
- Renal ultrasound or computed tomography
- Urinalysis
- Urine sediment
- Fractional excretion of Na – pears... BEWARE exceptions
  - Traditional teaching: ATN > 1 or 2%; pre-renal < 1%
  - Non-pre-renal with low FeNa: contrast, rhabdo, early sepsis, obstruction, acute glomerulonephritis
  - Pre-renal with high FeNa: diuretic use, pre-existing CKD

Case

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- Obtain baseline labs: creatinine 1.0 baseline
- Risk stratify: not emergent, but urgent
- Immediate considerations:
  - Pre-renal azotemia (NSAID, ACE-i)
  - Obstruction (history of BPH)
  - Stop the metformin (note gap acidosis)
- Volume challenge, d/c ACE-I and NSAIDs, further evaluation of obstruction and labs [U/A, urine sediment, FeNa]
- New appreciation of longer-term risks following an episode of AKI, even if complete recovery

Further Lab evaluation of intrinsic AKI

- Pre-renal thought to be unlikely
- Post-renal ruled out
- No good cause for ATN
  - No sepsis, surgery, nephrotoxin exposures, contrast, rhabdomyolysis, tumor lysis, ingestion, etc.

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C3, C4: depressed complements in diffuse GN (post-strep, lupus, cryo)
(also: atheroemboli, TTP/HUS, eos, hemolysis)
ANCA, antiGBM: time is nephrons.
ANA: lupus
LDH, haptoglobin: hemolysis, thrombotic microangiopathy
BIOPS

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BIOPS
Patterns of creatinine elevation

- Return to baseline after 48-72 hrs of fluid replacement: **pre-renal azotemia**
- Rapid (> 2mg/dL per day) rise: **rhabdomyolysis** [anecdotal]
- Rise within 24h, peak within 3-5d, return to baseline ~1 wk: **contrast nephropathy** (note typically non-oliguric)
- **Aminoglycosides**: rise after 5d therapy (can be after discontinuation), return towards baseline over 2-3 weeks (note, nonoliguric)

Newly recognized cause of AKI?

**Acute Kidney Injury During Warfarin Therapy Associated With Obstructive Tubular Red Blood Cell Casts: A Report of 9 Cases**

- Case series of 9 patients biopsied with high INR and AKI
  - Hypothesized association: glomerular hematuria leads to tubular obstruction with RBCs, leading to AKI
  - CKD patients may be susceptible to AKI if excessively anticoagulated

Complications of AKI

- Volume overload
- Hyperkalemia
- Metabolic acidosis
  - GAP: retained anions (phosphate, urate, hippurate, sulfate)
  - NON-GAP: impaired distal H+ excretion
- Hypocalcemia, hyperphosphatemia
- Bleeding from uremic platelets
- Pericarditis
- Long term: increased risk of CKD, ESRD

Preventing AKI

- Avoidance of nephrotoxins
- Adequate intravascular volume
- N-acetylcysteine: slim evidence for contrast nephropathy, but no harm
- Furosemide: observational studies suggest harm, RCT suggests no benefit
  - Clinical experience: widespread use
- Bicarbonate IVF: some evidence in contrast nephropathy

Treating AKI

- Pre-renal: improve hemodynamics
- Post-renal: relieve obstruction
- Intrinsic renal:
  - Acute tubular necrosis: **no proven therapies**
    - Specifically, no evidence for dopamine
  - Acute interstitial nephritis: withdrawal of suspected drug, ? Steroids
  - Acute glomerulonephritis: (depends on type)
  - Scleroderma renal crisis: ACE-inhibitors

Renal replacement for AKI

- “Indications”
  - A
  - E
  - I
  - O
  - U
Renal replacement for AKI

- "Indications"
  - Acidosis
  - Electrolytes (K⁺)
  - Ingestions (NOT digoxin)
  - Overload (fluid)
  - Uremia (pericarditis, encephalopathy)

Take home

- AKI is common, often deadly
- Pre-renal  Post-renal  Intrinsic renal
- Indications for dialysis
  - A  E  I  O  U
- Patterns of creatinine elevation
  - Pre-renal, contrast, rhabdo, aminoglycosides
- Beware the common exceptions to FeNa

Case 1
1. A 66-year-old previously healthy man is admitted to the hospital for crushing substernal chest pain. Vital signs on admission were: blood pressure 126/78, pulse 102 beats per minute, respiratory rate 20 per minute. Electrocardiogram reveals ST-segment elevation in leads II, III, and avf. He is treated with aspirin, unfractionated heparin, metoprolol, nitroglycerin, and captopril, and then taken to the cardiac catheterization laboratory where he undergoes successful percutaneous coronary intervention of an acutely occluded right circumflex artery. During the procedure the blood pressure remained above 120/70, and he remained hemodynamically stable thereafter. The serum creatinine concentration was 0.7 mg/dL on admission and rose to 1.4 mg/dL on hospital day 3, when captopril was discontinued. The serum creatinine rose to 7.8 mg/dL by hospital day 9, when hemodialysis was initiated. Skin examination was notable for livedo reticularis.

The renal vessels most likely involved in the pathophysiology of his acute kidney injury are the:
- **A) afferent arterioles**
- B) efferent arterioles
- C) interlobular veins
- D) interlobar veins
- E) interlobar arteries

Case 2
2. A 75 year old man is admitted to the hospital for severe diarrhea for the past four days. The past medical history is notable for hypertension and osteoarthritis. His medications included lisinopril 40 mg daily, ibuprofen 800 mg three times daily, and metoprolol 50 mg daily. The physical examination is notable for BP 100/60, pulse 120 beats per minute, and decreased skin turgor. Labs show serum creatinine of 4.6 mg/dL, potassium 5.8 meq/L, and fractional excretion of sodium of 0.4%.

In addition to pre-renal azotemia, the following causes of acute kidney injury can be associated with a fractional excretion of sodium below 1%:
- **D) All of the above (A, B, and C)**
- A) rapidly progressive glomerulonephritis
- B) rhabdomyolysis
- C) contrast nephropathy
- D) none of the above

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References