Hospital Acquired Acute Kidney Injury

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NSUCOM / Broward General Medical Center
Definition of Acute Kidney Injury

<table>
<thead>
<tr>
<th>Table 1. RIFLE Classification of Acute Renal Failure (ARF)</th>
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</thead>
<tbody>
<tr>
<td><strong>Glomerular Filtration Rate</strong></td>
</tr>
<tr>
<td><strong>Risk</strong></td>
</tr>
<tr>
<td><strong>Injury</strong></td>
</tr>
<tr>
<td><strong>Failure</strong></td>
</tr>
<tr>
<td><strong>Loss</strong></td>
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<tr>
<td><strong>End stage</strong></td>
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</tbody>
</table>

ESRD = end stage renal disease; SCr = serum creatinine.
Epidemiology of Hospital AKI

- 2012 data, non-ICU incidence up to 20%
- ICU acquired AKI up to 60%
- Associated with increased mortality
- Increased length of stay by average of 4 days
- In 2005, increased estimated cost stay $7,500
- High prevalence in elderly
  - By age 70, 30-50% of cortical glomeruli lost

Age and Hospital Acquired AKI

Hospital Acquired AKI Complications

Outcomes AKI Medicare Age 66 +

Risk Factors for Hospital AKI

• Age related decrease in GFR
• Co-existing illness (HTN, DM, CVD, Infection)
• Hypotension / Hypovolemia
• Medication related nephrotoxicity
• Contrast induced nephropathy
• Peri-operative factors

The Aging Kidney

• Reduced renal mass (30-50% sclerosis)
• Advance arteriosclerosis of vessels
• Loss of urine concentrating and diluting ability
• Reduced capacity to retain H2O and salts
• Reduced muscle mass
• Advanced co-morbidities

Calculating Glomerular Filtration Rate

90 year old male:
Weight: 40 kg
Serum Cr= 1.3 mg/dl

GFR = 35 mL/min

21 year old male:
Weight: 110 kg
Serum Cr= 1.9 mg/dl

GFR = 71 mL/min
Understanding GFR Calculations

• Cockcroft-Gault Equation
  • Overestimates GFR

• Modification of Diet in Renal Disease (MDRD)
  • Underestimates GFR when > 60 mL per minute
  • May misidentify patients as having CKD.

• Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)
  • Best GFR estimation in reduced and normal kidney function

## Equation Variables for GFR Estimation

<table>
<thead>
<tr>
<th>Equation</th>
<th>Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Kidney Disease Epidemiology Collaboration</td>
<td>Age, sex, race, serum creatinine level</td>
</tr>
<tr>
<td>Cockcroft-Gault</td>
<td>Age, weight, sex, serum creatinine level</td>
</tr>
<tr>
<td>Modification of Diet in Renal Disease</td>
<td>Age; sex; race; and serum urea, nitrogen, albumin, and creatinine levels</td>
</tr>
</tbody>
</table>

Am Fam Physician. 2011;84(10):1138-1148
Etiology of Hospital AKI

Acute renal failure

Prerenal causes

Tubular necrosis

Ischemia (50% of cases)

Toxins (35% of cases)

Intrinsic causes

Interstitial nephritis (10% of cases)

Postrenal causes

Acute glomerulonephritis (5% of cases)

NEJM. 1996; 334:1448-1460
Pre-Renal AKI

• Hypotension
• Hypovolemia
  – Diuretics
• GI losses
• Decreased cardiac output
  – Cardiorenal syndrome
• Systemic arterial vasodilation
  – Sepsis
  – Cirrhosis and hepatorenal syndrome

NEJM. 1996; 334:1448-1460
Avoiding Iatrogenic Hypotension

• Appropriate adjustments in anti-hypertensive medication
  – Recognize when to hold ACE-I or ARB
  – Diuretics dose adjustment
  – Post operative state

• Relative hypotension
  – Abrupt drop in systolic pressure 15-20mmHg.

Acute Tubular Necrosis (ATN)

- Prolonged renal ischemia
  - Sepsis
  - Progression of pre-renal disease
  - Surgery
- Direct drug nephrotoxicity
- Three clinical phases of ATN:
  - Initiation (oliguric phase)
  - Maintenance
  - Recovery (polyuric phase)

Patient Risk Factors Drug Nephrotoxicity

- Age > 65
- Female
- CKD
- Decreased total body water and weight
- Failure to recognize compromised GFR
  - Overdosing antibiotics
- Hypoalbuminemia
  - Increases free drug level

Mechanism of Drug Induced ATN

• Persistent low intraglomerular perfusion
  – ACE-I or NSAID in setting of acute illness

• Tubular cell toxicity (dose dependent)
  – Aminoglycoside / Vancomycin
  – Cisplatin / Carboplatin
  – Tenofovir
  – Amphotericin B

• Renal Vasoconstriction
  – Contrast nephropathy

Am J Kid Dis. 2010; 2:399-409
Altered Glomerular Hemodynamics

- **NSAID**
  - Constriction
  - Afferent

- **ACE-I / ARB**
  - Dilatation
  - Efferent

Fresenius Website http://www.fmc-renalpharma.com
Drug Induced Interstitial Nephritis

• AKI develops 3-5 days, but can be >10 days.
• Clinical presentation:
  – Rash — 15 %
  – Fever — 27 %
  – Eosinophilia — 23 %
  – Triad of rash, fever, and eosinophilia — only 10 %
• Treatment
  – Stop inciting meds
  – Consider Prednisone (Grade 1 C evidence)

# Interstitial Nephritis

<table>
<thead>
<tr>
<th>Medication class</th>
<th>Specific examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td>Cephalosporins*, ciprofloxacin⁶ (Cipro), ethambutol (Myambutol), isoniazid (INH), macrolides, penicillins*, rifampin* (Rifadin), sulfonamides*, tetracycline, vancomycin⁷ (Vancocin)</td>
</tr>
<tr>
<td>NSAIDs*</td>
<td>Almost all agents²</td>
</tr>
<tr>
<td>Diuretics*</td>
<td>Furosemide (Lasix), thiazides, triamterene (Dyrenium)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Acyclovir (Zovirax), allopurinol* (Zyloprim), amlodipine⁸ (Norvasc), azathioprine (Imuran), captopril (Capoten), carbamazepine (Tegretol), clofibrate (Atromid-S), cocaine, creatine⁹, diltiazem¹⁰ (Cardizem), famotidine (Pepcid), indinavir¹¹ (Crixivan), mesalazine¹² (Asacol), omeprazole¹³ (Prilosec), phenteramine¹⁴ (Zantryl), phenytoin (Dilantin), pranlukast (Ultair)¹⁵, propylthiouracil¹⁶ (Propacil), quinine (Quinamm), ranitidine (Zantac)</td>
</tr>
</tbody>
</table>
Other Kidney Disease from Medication

• **Crystal Deposition Disease**
  – Indinavir, acyclovir
  – Tumor lysis syndrome / Uric acid

• **Drug-induced thrombotic microangiopathy**
  – Cyclosporin / Tacrolimus
  – Plavix

• **Rhabdomyolysis**
  – Cocaine
  – Statin Rx
Contrast Induced Nephropathy (CIN)

- Prevalence
  - 1-2% in patients w/ normal GFR
  - 25% in patients with CKD
- Third most common cause of hospital AKI
- Usually non-oliguric ATN
- AKI seen 1-2 days after iodinated contrast
  - CT scan or Angiogram study
- Resolution AKI approximately 3-7 days

Patient Risk Factors of CIN

- Hypotension / volume depletion
- Diabetes
- Decompensated CHF
- Age > 75
- Contrast-media volume and osmolality
- Pre-existing CKD
- Concurrent nephrotoxic medication

Kidney Intern 2012; S(2): 69-88
Contrast Nephropathy and ATN

Vasoconstriction
- Ca²⁺ influx
- Endothelin release
- Selective vasoconstriction corticomedullary junction
- Impaired vasodilation
- Duration up to 4 hours

Vasodilation
- Medullary hypoxia
  - \( \text{PaO}_2 \) 15–20 mm Hg

Vasoconstriction
- Impaired vasodilation
  - \( \downarrow \text{NO production} \)

Direct tubular toxicity

Oxidative stress
- \( \text{OH}^- \text{O}_2^- \)
- free radicals
## Prophylactic Strategies for Prevention of Contrast-induced Nephropathy Based on Estimated Glomerular Filtration Rate

<table>
<thead>
<tr>
<th>Estimated Glomerular Filtration Rate</th>
<th>Risk of Contrast-induced Nephropathy</th>
<th>Prophylactic Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60 mL/min</td>
<td>Very low risk</td>
<td>Adequate intravenous hydration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6-12 hours before exposure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4-12 hours after exposure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Use of low- or iso-osmolar contrast media</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hold medications that could adversely affect renal function</td>
</tr>
<tr>
<td>45-59 mL/min</td>
<td>Low risk</td>
<td>Adequate intravenous hydration</td>
</tr>
<tr>
<td>&lt;45 mL/min</td>
<td>Moderate risk</td>
<td>Use of low- or iso-osmolar contrast media</td>
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<tr>
<td></td>
<td></td>
<td>Hold medications that could adversely affect renal function</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider acetylcysteine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>600-1200 mg twice daily 12-24 hours before exposure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>600-1200 mg twice daily 24 hours postexposure</td>
</tr>
<tr>
<td>Unstable renal function, acute illness, acute renal failure</td>
<td>High risk</td>
<td>Adequate intravenous hydration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Use of low- or iso-osmolar contrast media</td>
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<tr>
<td></td>
<td></td>
<td>Obtain a serum creatinine 24-72 hours postexposure</td>
</tr>
</tbody>
</table>
Contrast Nephropathy Prevention

• Avoid NSAID and volume depletion
• Use of lower osmolar contrast agents
  – 290 mosmol/kg compared to 1500 mosmol/kg
• N-Acetylcysteine (Mucomyst)
  – Thiol compound with antioxidant + vasodilatory properties.
  – Conflicting data
  – Usually well tolerated

KDIGO Guideline Kidney Intern 2012; S(2): 69-88
Prevention of Contrast Nephropathy

• Normal Saline (0.9% NaCl)
  – 1mL/kg per hour, begun 6-12 hours prior + after contrast.

  – Outpatient setting:
    • Bolus 3 mL/kg over 1 hour prior
    • Then 1 to 1.5 mL/kg/hr for 4 to 6 hours after the procedure.

KDIGO Guideline Kidney Intern 2012; S(2): 69-88
Prevention of CIN: Bicarbonate

• Theory:
  – Alkalization may protect against free radical injury.

• Sodium Bicarbonate Infusion (150meq in D5W)
  – bolus of 3 mL/kg of isotonic bicarbonate 1 hour prior
  – Continue at a rate of 1 mL/kg per hour for 6 hours after the procedure.

KDIGO Guideline Kidney Intern 2012; S(2): 69-88
MRI and Gadolinium Renal Toxicity

• Free Gd3+ is toxic in un-chelated form.
  – 97% eliminated by kidney
  – CKD increases un-chelated Gd3+ tissue exposure

• Nephrogenic systemic fibrosis (NSF) skin disorder.

• Recent study show potential AKI nephrotoxicity in CKD.
Nephrogenic Systemic Fibrosis

• Primarily chronic ESRD.
• Disease onset is usually 2-4 weeks.
• Symmetric, thick, firm fibrotic plaques.
• Ankles, lower legs, feet, and hands.
• No proven therapy for NSF
• Immediate hemodialysis after exposure
• **Avoid** in ESRD, AKI or GFR <30.

Nephrogenic Systemic Fibrosis
Cholesterol Crystal Emboli

• 70% due to vascular catheterization or surgery
• Subacute AKI 1-2 weeks after procedure
• Different AKI than CIN
• Clinical:
  – Blue toe or livedo reticulares
  – Urine benign
  – Eosinophilia and hypocomplementemia

Cholesterol Crystal Emboli
Acute Glomerulonephritis

The spectrum of glomerular diseases

SLE

IgA nephropathy

Minimal change nephropathy

FSGS

Membranous nephropathy

Diabetic nephropathy

Amyloidosis

MCGN

Post-streptococcal glomerulonephritis

Small vessel vasculitis

Anti-GBM disease

Haematuria

Proteinuria

Nephrotic

Mechanism

- Injury to podocytes
- Changed architecture:
  - Scarring
  - Deposition of matrix or other elements

Nephritic

Mechanism

- Inflammation
- Reactive cell proliferation
- Breaks in GBM
- Crescent formation

http://www.edrep.org/pages/resources/glomerulonephritis.php
Obstructive Uropathy

• Nephrolithiasis
• BPH and bladder outlet syndrome
• Neurogenic bladder
  – Diabetes
  – Stroke
  – Trauma patients
• Urological Cancer
Medication Induced Urinary Retention

- Antiparkinson medication
- Anticholinergic medications
- Antipsychotics and anti-depressant
- Sympathomimetics (Sudafed)
- Antihistamines
- Narcotics / Morphine

• Appreciate significance of GFR esp. elderly.
• Early recognition of AKI and changes in GFR warrant changes in medication dosage.
• Avoid relative hypotension in hospital setting.
• Know when to adjust HTN meds and diuretics.
• IV contrast nephropathy prophylaxis + risk
• Avoid MRI Gd+3 in ESRD or Advanced CKD.
• Recognize obstructive uropathy risks.