Acute Kidney Injury
Hospital Acquired AKI

- ATN
- TIN
- Obstruction
- Acute/chronic
- Prerenal
- Renovascular
- RPGN
Evaluation of AKI

Acute Renal Failure
Oliguric vs Nonoliguric

Prerenal
volume depletion
redistribution
cardiogenic

Renal
ischemic/nephrotoxic
glomerulonephritis	
tubulointerstitial nephritis

Postrenal
intrarenal
ureteral
bladder
# Urinalysis in AKI

<table>
<thead>
<tr>
<th>Renal Failure</th>
<th>Protein</th>
<th>Blood</th>
<th>Sediment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-renal</td>
<td>No</td>
<td>No</td>
<td>Bland/hyaline casts</td>
</tr>
<tr>
<td>ATN</td>
<td>+</td>
<td>+</td>
<td>Muddy brown granular casts</td>
</tr>
<tr>
<td>GN</td>
<td>++</td>
<td>++</td>
<td>RBC casts Dysmorphic RBC’s</td>
</tr>
<tr>
<td>TIN</td>
<td>+</td>
<td>+</td>
<td>Eosinophils, WBC’s WBC casts</td>
</tr>
<tr>
<td>Obstruction</td>
<td>Variable</td>
<td>Variable</td>
<td>RBC’s, WBC’s Crystals</td>
</tr>
</tbody>
</table>
Liquid Biopsy

- RBC cast
- WBC cast
- Granular cast
- Eosinophils
Urine Electrolytes

- From 1978
- Limited patient populations
- Numerous exclusion criteria
- Numerous exceptions to the rule
- No recent validation
- May have poor predictive value

<table>
<thead>
<tr>
<th>Urine Na⁺</th>
<th>Prerenal</th>
<th>Oliguric ATN</th>
<th>Nonoliguric ATN</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20 mM/L</td>
<td>18/30 (60%)</td>
<td>0/24 (0%)</td>
<td>2/13 (6%)</td>
</tr>
<tr>
<td>20-40 mM/L</td>
<td>12/30 (40%)</td>
<td>14/24 (59%)</td>
<td>11/31 (35%)</td>
</tr>
<tr>
<td>&gt;40 mM/L</td>
<td>0/30 (0%)</td>
<td>10/24 (41%)</td>
<td>18/31 (59%)</td>
</tr>
<tr>
<td>FeNa</td>
<td>&lt;1%</td>
<td>27/30 (90%)</td>
<td>1/24 (4%)</td>
</tr>
</tbody>
</table>

Ann Intern Med 1978; 89: 101
Renal Ultrasound Use in AKI

- 2218 ultrasounds
- 51% (1131) for AKI
  - AKI
  - Rule out obstruction/hydronephrosis
  - Oliguria
- 21% done when Cr normal
- 1.3% had obstruction
  - Men
  - Age over 65
  - History of:
    - Benign prostatic hypertrophy
    - Nephrolithiasis
    - Prior abdominal or pelvic malignancy
    - Chronic indwelling foley
- 71% of hydronephrosis was incidental
- Obstructive nephropathy
  - 27% without hydronephrosis
  - 73% with hydronephrosis

Renal Ultrasound Findings

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydronephrosis</td>
<td>42</td>
</tr>
<tr>
<td>Obstruction with ARF</td>
<td>12</td>
</tr>
<tr>
<td>Mild or unilateral, not cause of renal failure</td>
<td>30</td>
</tr>
<tr>
<td>Abscess</td>
<td>2</td>
</tr>
<tr>
<td>Renal Mass</td>
<td>9</td>
</tr>
<tr>
<td>Congenital Malformation</td>
<td>8</td>
</tr>
<tr>
<td>Congenital Absence of Kidney</td>
<td>2</td>
</tr>
<tr>
<td>Bilateral Staghorn Calculi</td>
<td>1</td>
</tr>
</tbody>
</table>

Clinical Pearls in AKI

- **Rhabdomyolysis**
  - Urine heme positive
  - No RBCs on micro

- **Myeloma**
  - Negative protein on dipstick
  - Proteinuria with collected urine

- **Pregnancy**
  - HELLP
  - HUS

- **Drugs**
  - ACE-I/ARB
  - NSAIDS

- **Altered sensorium**
  - HUS/TTP

- **Cholesterol emboli**
  - Rash/purpura
  - Eosinophilia

- **ANCA disease**
  - Systemic symptoms
  - Subacute illness
  - Pulmonary-renal

- **Obstruction**
  - Hyperkalemia
  - Bland sediment
  - Anuria
AKI Background

• Acute kidney injury is common
  o 5-7% of hospitalized patients
  o 35% of ICU patients

• It is associated with a high mortality rate

• It is an independent contributor to mortality

• It is difficult to define, predict and prevent

• No proven effective therapy

• The role of dialysis is still unsettled
Prevalence of AKI

MMWR 2008; 57:0309-312
### Incidence by Disease

<table>
<thead>
<tr>
<th>Condition</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>68.4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>52.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>47.4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>46.4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>45.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>33.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver disease</td>
<td>33.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rheumatic disease</td>
<td>21.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid cancer</td>
<td>21.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertensive disease in pregnancy</td>
<td>6.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td></td>
<td>63.9%</td>
<td></td>
</tr>
<tr>
<td>Critical care</td>
<td></td>
<td>60.3%</td>
<td></td>
</tr>
<tr>
<td>HSCT</td>
<td></td>
<td>55.9%</td>
<td></td>
</tr>
<tr>
<td>Cardiac surgery</td>
<td></td>
<td></td>
<td>52.2%</td>
</tr>
<tr>
<td>Vascular surgery</td>
<td></td>
<td></td>
<td>50.0%</td>
</tr>
<tr>
<td>Thoracic surgery</td>
<td></td>
<td></td>
<td>47.3%</td>
</tr>
<tr>
<td>Usage of contrast media</td>
<td></td>
<td></td>
<td>34.2%</td>
</tr>
<tr>
<td>Abdominal surgery</td>
<td></td>
<td></td>
<td>27.2%</td>
</tr>
<tr>
<td>Obstetric procedures</td>
<td></td>
<td></td>
<td>1.0%</td>
</tr>
</tbody>
</table>

Pitfalls of Creatinine

- Creatinine is filtered and secreted
- Rate of rise dependent on:
  - Age
  - Gender
  - Race
  - Muscle mass
  - Fluid balance
  - Sepsis
- Creatinine rise is a LATE consequence of renal failure
- Creatinine rise underestimate the degree of injury
Fluid Balance and AKI

- Retrospective review
- FACCT trial
- 1000 patients
- Liberal vs. conservative
- AKI:
  - 0.3 mg% or 50% Cr rise
  - 48 hours
  - vs. Cr > 2 mg% in study
- Reclassified by formula
  - Cr x [(TBW+F)/TBW]

Liu K, et al., Crit Care Med 2011; 39: 2665-2671
### Unmasking AKI


<table>
<thead>
<tr>
<th>Before Adjustment for Fluid Balance</th>
<th>After Adjustment for Fluid Balance</th>
<th>Group</th>
<th>Survivors, No. (%)</th>
<th>Nonsurvivors, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No And No</td>
<td>No</td>
<td>$A^a$</td>
<td>289 (88%)</td>
<td>39 (12%)</td>
</tr>
<tr>
<td>No And Yes</td>
<td>Yes</td>
<td>$B^b$</td>
<td>90 (69%)</td>
<td>41 (31%)</td>
</tr>
<tr>
<td>Yes And No</td>
<td>No</td>
<td>$C^c$</td>
<td>48 (89%)</td>
<td>6 (11%)</td>
</tr>
<tr>
<td>Yes And Yes</td>
<td>Yes</td>
<td>D</td>
<td>304 (62%)</td>
<td>183 (38%)</td>
</tr>
</tbody>
</table>
**Sepsis and Creatinine**

- Mouse study
- Sepsis
  - Cecal puncture/ligation
- AKI
  - Bilateral nephrectomy
- Sepsis and AKI
  - Both procedures
- Inflammatory cytokines increased in sepsis and sepsis plus AKI
- Creatinine rise in AKI blunted by presence of sepsis

AKI After Bypass

- 4118 patients
- Cardiac or thoracic aorta surgery
- Cox regression for correction of other risks
- Effect of Cr change at 48 hrs
- 30-day mortality:
  - 2.6% if Cr fell by 0.3 mg/dL
  - 6% if Cr increased up to 0.5 mg/dL
  - 33% if Cr increased more than 0.5 mg/dL

AKI and Mortality

- 19,982 adults
- Absolute and relative increases in serum Cr
- Multivariate analysis
- Mortality
- Length of stay
- Cost

Unadjusted
Age and gender adjusted
Multivariate adjusted

Defining AKI

RIFLE Criteria for AKI

Stage | Creatinine Criteria | Urine Output Criteria
--- | --- | ---
1 | Increase in serum creatinine of ≥0.3 mg/dL or increase of ≥150%-200% (1.5-fold to 2-fold) above baseline | < 0.5 mL/kg/h for >6 hours
2 | Increase in serum creatinine of ≥200%-300% (>2-fold to 3-fold) above baseline | < 0.5 mL/kg/h for >12 hours
3 | Increase in serum creatinine of >300% (>3-fold) above baseline, or a serum creatinine ≥4 mg/dL with an acute rise of ≥0.5 mg/dL | <0.3 ml/kg/h x 24 hours or anuria x 12 hours

Acute Kidney Injury Network “AKIN” Criteria for AKI

# RIFLE Performance

## Mortality risk vs non-AKI

<table>
<thead>
<tr>
<th>Study or subcategory</th>
<th>RR (random) 95% CI</th>
<th>Study or subcategory</th>
<th>RR (random) 95% CI</th>
<th>Study or subcategory</th>
<th>RR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 General ICU (Cr and UO criteria)</td>
<td></td>
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<tr>
<td>Abosaif</td>
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<tr>
<td>Ahlstrom</td>
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<td></td>
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<tr>
<td>Cruz</td>
<td></td>
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<td></td>
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<tr>
<td>Hoste</td>
<td></td>
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</tr>
<tr>
<td>02 General ICU (without UO criteria)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Lopes (HIV)</td>
<td></td>
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<tr>
<td>Lopes (sepsis)</td>
<td></td>
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<tr>
<td>Ostermann</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>03 Cardiosurgery</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Kuittunen</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Lin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>04 Other ICU</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Coca</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Lopes (bmt)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Lopes (burns)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>05 Not confined to ICU</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uchino</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

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*Kidney Int 2008; 73: 538-546*
## Staging of AKI

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum creatinine</th>
<th>Urine output</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5–1.9 times baseline OR $\geq 0.3 \text{mg/dl (} \geq 26.5 \mu\text{mol/l)}$ increase</td>
<td>$&lt;0.5 \text{ml/kg/h for 6–12 hours}$</td>
</tr>
<tr>
<td>2</td>
<td>2.0–2.9 times baseline</td>
<td>$&lt;0.5 \text{ml/kg/h for } \geq 12 \text{ hours}$</td>
</tr>
<tr>
<td>3</td>
<td>3.0 times baseline OR Increase in serum creatinine to $\geq 4.0 \text{mg/dl (} \geq 353.6 \mu\text{mol/l)}$ OR Initiation of renal replacement therapy OR, In patients $&lt;18$ years, decrease in eGFR to $&lt;35 \text{ml/min per 1.73 m}^2$</td>
<td>$&lt;0.3 \text{ml/kg/h for } \geq 24 \text{ hours}$ OR Anuria for $\geq 12 \text{ hours}$</td>
</tr>
</tbody>
</table>
ADQI 2013

Intact kidney

No AKI

Tubular damage
RIFLE/KDIGO negative
Biomarker negative (CRIAKI)

Function loss
RIFLE/KDIGO positive
Biomarker negative (CRIAKI)

Function loss and tubular damage
RIFLE/KDIGO positive
Biomarker positive (CRIAKI)

ADQI 2013

Function criteria and/or injury criteria

<table>
<thead>
<tr>
<th>RIFLE-R or AKIN-1</th>
<th>Biomarker positivity (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RIFLE-1 or AKIN-2</td>
<td>Biomarker positivity (+)</td>
</tr>
<tr>
<td>RIFLE-F or AKIN-3</td>
<td>Biomarker positivity (+++)</td>
</tr>
</tbody>
</table>

Creatinine criteria

- Stage 1: ≥1.5 times baseline OR 0.3 mg/dl increase
- Stage 2: ≥2 times baseline
- Stage 3: ≥3 times baseline OR increase to ≥4.0 mg/dl

Urine output criteria

- <0.5 mg/kg/h for ≥6 h
- <0.5 ml/kg/h for ≥12 h
- <0.3 ml/kg/h for ≥24 h OR anuria for ≥12 h

NAG, β2M, α1M, RBP, Cystatin C, KIM-1, NGAL, CYR-61, IL-1β, OPN, FABP, NHE3
NGAL and Subclinical AKI

# Early Renal Consults in AKI

## Nephrology Recommendations and Therapeutic Implementation

<table>
<thead>
<tr>
<th></th>
<th>EARLI Group</th>
<th>Control Group</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic recommendations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine studies(^a)</td>
<td>79.1</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Other laboratory tests</td>
<td>28.6</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Other(^b)</td>
<td>14.3</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Therapeutic recommendations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Holding ACEi/ARB therapy</td>
<td>48.4</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>IV fluids</td>
<td>45.1</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Adjusting diuretic dosages</td>
<td>35.2</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Adjusting other medications(^c)</td>
<td>19.8</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Other(^d)</td>
<td>7.7</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Preventative recommendations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacovigilance related</td>
<td>17.6</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Contrast precautions</td>
<td>8.8</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Therapeutic implementation within 24 h of AKI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Holding ACEis/ARBs</td>
<td>32.0(^e)</td>
<td>10.0(^e)</td>
<td>0.01</td>
</tr>
<tr>
<td>Adjusting diuretic dosages</td>
<td>25.5(^f)</td>
<td>7.1(^f)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

## Primary and Secondary Outcomes of Patients in the EARLI and Control Groups

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>EARLI</th>
<th>Control</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary outcome(^a)</td>
<td>3 (3.3)</td>
<td>11 (12.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>Peak SCr (mg/dL)</td>
<td>(1.8 \pm 0.1)</td>
<td>(2.1 \pm 0.2)</td>
<td>0.01</td>
</tr>
<tr>
<td>Dialysis</td>
<td>1 (1.1)</td>
<td>1 (1.2)</td>
<td>—</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>4 (4.4)</td>
<td>7 (8.2)</td>
<td>0.4</td>
</tr>
<tr>
<td>Cardiovascular events</td>
<td>1 (1.1)</td>
<td>1 (1.2)</td>
<td>—</td>
</tr>
</tbody>
</table>

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\( \) \(^a\) = P < 0.05; \(^b\) = \( n = 1 \); \(^c\) = \( n = 2 \); \(^d\) = \( n = 8 \); \(^e\) = \( n = 17 \); \(^f\) = \( n = 10 \)

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**Am J Kidney Dis 2011; 57: 228-234**

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![Graph showing proportion per group (%)](image)
AKI and Inflammation

Diagram showing the interaction between viruses, bacteria, fungi, toxic, ischemia, and trauma leading to cell necrosis or apoptosis. The activation process involves PAMPs and DAMPs with inflammasomes, leading to cytokine production and immune cell activation.

- DC (Dendritic Cells): Maturation, AG-presentation, Migration, ROS, IL-1β, TNF, IL-6, Chemokines, IFN-α/β, IL-12
- MØ (Macrophages): ROS, IL-1β, TNF, IL-6, Chemokines
- MC (Macrophages): TNF, IL-6, Chemokines, IFN-α
- EC (Endothelial Cells): TNF, IL-6, Chemokines, Adhesion molecules, Permeability
- Podocytes: Permeability, TNF, IL-6, Chemokines
- Tubular cells: TNF, IL-6, Chemokines
Cytokine Release in Renal Injury
IL-6 and AKI Induced ALI

IL-6 and AKI Induced ALI

Distant Effects of AKI

**Brain**
- KC & G-CSF
- GFAP & microglia
- Vascular permeability

**Heart**
- TNF-α, IL-1
- Neutrophil trafficking
- Apoptosis
- Fractional shortening

**Lung**
- Vascular permeability
- Dysregulated channels
- Cytokines/chemokines
- Transcriptomic changes
- Leukocyte trafficking
- Altered response to ventilator-associated injury

**Liver**
- Leukocyte influx
- Oxidation products
- Antioxidants (GSH)
- Altered liver enzymes

**Bone marrow**
- Anemia
- Coagulation disorders
- Immune dysfunction

**Gastrointestinal tract**
- Channel-inducing factor
- Potassium excretion
Prevention and Therapy

• Hard to predict who will get AKI
• It’s a numbers game in prevention trials
  o Post contrast
  o CAB surgery
• Positive results in treating AKI in animals
• No positive results in humans
  o Too late (reliance on Cr changes)
  o Different models
  o Different animals
• Lasix is not a treatment for AKI
  o Volume overload
  o Learn how to dose it properly
• Low dose dopamine
  o Not “renal dose”
  o Atrial fibrillation
Prophylaxis for RCAN

Forced Diuresis and RCAN

- Study period 1996-2000
- Low recruitment
  - Tepel study (NAC)
  - Solomon study (lasix)
- Waited to 2008
- 92 patients
  - Cr > 1.6 mg/dl
  - Coronary angiography
  - Hydration vs. hydration with mannitol plus lasix
    - ½ NS 500 ml bolus
    - 125 ml/hr x 4hrs +/- 25 g mannitol and 100 mg lasix
- 25% or 0.5 mg/dl increase at 48-hours

Bicarbonate and RCN

- **3 large trials (1145 pts)**
  - AKI 10.7% vs. 12.5%
  - RR 0.85 (95% CI: 0.6-1.2)
  - No heterogeneity

- **12 small trials (1145 pts)**
  - RR 0.50 (95% CI: 0.3-0.9)
  - Significant heterogeneity
  - Lower methodological quality

NAC and Contrast AKI

- 19 randomized controlled trials
- 4 prospective non-randomized studies
  - 5 showed significant benefits
  - 13 showed non-significant benefits
  - 10 concluded NAC was not beneficial
- 11 meta-analyses
  - 7 concluded NAC beneficial
  - 4 concluded data inconclusive
- No standards
  - Dose, definitions, route and timing of administration, contrast type or route of administration, underlying disease state, and “standard of care”
- No better in 2014

Arch Intern Med 2006; 166: 161-166
Acetylcysteine for CIN Trial

- Randomized controlled trial
- 2308 at risk patients
  - Age > 70
  - Cr > 1.5 mg/dl
  - Diabetes
  - Heart failure
  - Hypotension
- 600 mg NAC bid on 2 days
- Bicarbonate or saline
- Primary end point-25% Cr increase
  - 12.7% vs. 12.7%

ACT Investigators, Circulation 2011; 124: 1250-59
Prophylaxis Guidelines

• Should know eGFR or creatinine prior to procedure
• Should screen for other risk factors
  o Hypertension
  o Diabetes mellitus
  o Proteinuria
  o CHF
  o NSAID use
  o Age ≥ 75
• Consider Nephrology consult for high risk patients
  o eGFR ≤ 30 ml/min
  o eGFR ≤ 60 ml/min with 2 or more risk factors
• Hold AM dose of diuretic if medically permissible
• Use a standardized fluid protocol
  o Isotonic saline or isotonic bicarbonate
• Oral NAC is optional
Animal Studies

- Lasix
- ANP
- IGF-1
- Low-dose dopamine
- Fenoldopam
- Thyroxine
- Growth Hormone
- EGF
- HGF
ANP and AKI in the ICU

- 504 ICU patients
- Mean CrCl 10 mL/min
- Mean SCr 4.5 mg/dL
- No effect on:
  - Dialysis need
  - Mortality
  - Urine output
- More hypotension
- TOO LATE?

New Engl J Med 1997;336:828
IGF-1 and AKI

- 72 ICU patients
- Mean GFR 7 mL/min
- Mean SCr 6 mg/dL
- No effect on:
  - GFR
  - Dialysis need
  - Mortality
- TOO LATE?

Kidney Int 1999;55:2423
ANZICS Study

- 324 patients
- Low-dose dopamine
- Increase SCr > 0.8 or oliguria > 4-hours
- Mean SCr 2.1 mg/dL
- No effect on:
  - Peak Cr
  - Urine output
  - Dialysis
  - Mortality

![Table]

Lancet 2000; 356: 2139
Approach to AKI

- Don't panic
- Oliguria doesn't kill you
- Look back: something happened much earlier
- Thorough review of the medical record
- Hypotension is not a requirement for "ischemic ATN"
- Don't let edema fool you
- Don't let a CVP fool you
- Understand fluid balance and types of fluids
  - Tube feeds don't require diuresis
  - Water can't give you pulmonary edema (or any edema at all)
- Judicious use of labs
  - Everyone needs a urinalysis
  - Not everyone needs an ultrasound
  - Urinary eosinophils and electrolytes are of very limited value (i.e. not useful at all)
- Adjust medications appropriately
- Creatinine is a biomarker so follow it accordingly
  - i.e. more than every 24 hours!
- Call us!
Dialysis

- It’s not a treatment for AKI
  - It merely controls or prevents certain complications of AKI

- You need to know when you **have to** do it
  - Life-threatening electrolyte and acid/base disorders
  - Refractory volume overload
  - Uremia

- It isn’t some “end-point” to be avoided
  - “I let the patient down because he ended up on dialysis.”- poppycock!!
  - Embrace the concept of renal support rather than renal rescue

- Unresolved questions:
  - When do you start?
  - What kind do you start?
  - How much do you do?
  - Is it useful for conditions other than renal failure?
    - Sepsis
    - Fulminant hepatic failure
CRRT vs. Intermittent HD

Crit Care Med 2008; 36:610-617
VA/NIH Cooperative Study

1164 patients
29 sites (20 VA, 9 NIH)
3 years

1:1 Randomization

Intensive Management Strategy (582 patients)
- IHD 6x/week @ Kt/V of >1.2/session

Conventional Management Strategy (582 patients)
- IHD 3x/week @ Kt/V of >1.2/session

Stable hemodynamics (SOFA 0-2)
- IHD 6x/week @ Kt/V of >1.2/session
- Continuous @ 35 mL/kg/hr, or
- SLED/EDD 6x/week

Unstable hemodynamics (SOFA 3-4)
- Continuous @ 20 mL/kg/hr, or
- SLED/EDD 3x/week

Powered to detect (90%) an absolute mortality reduction of 10% at 60 days assuming a mortality rate of 55% in controls and a drop out rate of 10%

60-Day All Cause Mortality

Odds Ratio: 1.09
95% CI: 0.86-1.40
P=0.47

### By Subgroups

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>No. of Patients</th>
<th>Intensive Therapy</th>
<th>Less-Intensive Therapy</th>
<th>Odds Ratio for Death at 60 Days (95% CI)</th>
<th>P Value for Interaction</th>
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<tbody>
<tr>
<td>Overall</td>
<td>1124</td>
<td>53.6</td>
<td>51.5</td>
<td>1.09 (0.86–1.40)</td>
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<td>SOFA cardiovascular score</td>
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<td>0–2</td>
<td>509</td>
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<td>37.8</td>
<td>1.33 (0.93–1.91)</td>
<td>0.93 (0.66–1.29)</td>
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<td>3–4</td>
<td>615</td>
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<td>Oliguria</td>
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<td>Female</td>
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<td>49.8</td>
<td>0.94 (0.63–1.41)</td>
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<tr>
<td>Yes</td>
<td>708</td>
<td>57.0</td>
<td>52.6</td>
<td>1.19 (0.88–1.62)</td>
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</tr>
</tbody>
</table>

Take Our Ball and Go Home?

- Selective Cytopheretic Device- immunomodulation
  - Downregulation of activated neutrophils
  - Septic AKI
- Mesenchymal stem cell infusion- regeneration
  - Post CAB surgery AKI
  - Post renal transplant delayed graft function
- BMP -7 mimetic peptide- anti-apoptotic
  - Post CAB surgery AKI
  - Post cisplatin AKI
- Recombinant alkaline phosphatase- anti-inflammatory
  - Septic AKI
Final Points

- AKI is common
- You die from AKI not with AKI
- AKI causes a systemic inflammatory response
- Serum creatinine is a poor biomarker for AKI
- Classic renal diagnostic tests are of limited value
  - Except for an urinalysis (“liquid biopsy”)
- There are limited options for prevention of AKI
  - Radiocontrast and CAB surgery
- No effective therapies are currently available
- Many questions remain regarding the exact role of dialysis