Diagnosis and Management of Acute Kidney Injury

Ashita Tolwani, M.D., M.S.
Professor of Medicine
University of Alabama at Birmingham
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Disclosures

- Consultant for Baxter
- Patent on 0.5% citrate anticoagulant solution for CRRT
AKI Outline

- Epidemiology
- Definition
- Pathophysiology and differential diagnosis
- Overview of prevention and management

Epidemiology of AKI
Acute Kidney Injury: Why Do We Care?

- AKI is common (KDIGO definition)
- 21% of all hospital admissions
- 50% of ICU patients
- AKI is associated with increased risk of CKD, ESKD, CV disease, and death
- Dialysis-requiring AKI ICU patients have the worst outcomes
- 11% of ICU patients with AKI require dialysis and 10-30% survivors remain dialysis dependent at time of hospital discharge
- AKI can be prevented, treatable, and reversible
- Healthcare workers are not well informed about AKI and its consequences

Worldwide, 2,000,000 people will die this year of AKI!
How Does AKI Mortality Compare with Other Common ICU Conditions?

Mortality %

60-DAY ARDS  28-DAY SEPTIC SHOCK  90-DAY SEVERE AKI

Natural History of AKI

Cerda et al, CJASN 2008
Definition of AKI

- More than 30 different definitions exist with a variety of quoted incidence rates, risk factors, and morbidity and mortality rates.
- A staging system is needed to stratify patients so that both accurate identification and prognostication are possible.
Using RIFLE, Patients with AKI Have Poorer Outcomes

Analysis of 71,000 pts/13 studies to validate RIFLE Criteria

<table>
<thead>
<tr>
<th>Study or subcategory</th>
<th>Mortality risk vs non-AKI (RR)</th>
<th>Mortality injury vs non-AKI (RR)</th>
<th>Mortality failure vs non-AKI (RR)</th>
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<tbody>
<tr>
<td>Overall</td>
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<tr>
<td>ICU</td>
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<td>General ICU</td>
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<td>General ICU (without ICU criteria)</td>
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<td>Akesson</td>
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<td>02 General ICU (without ICU criteria)</td>
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<td>Dettermann</td>
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<tr>
<td>03 Cardiac surgery</td>
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<td>Kullman</td>
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<td>Lin</td>
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<td>04 Other ICU</td>
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<td>Coca</td>
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<td>Lopez (1995)</td>
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<tr>
<td>Lopez (papdts)</td>
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<tr>
<td>05 Not confined to ICU</td>
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<tr>
<td>Uchino</td>
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</tbody>
</table>

Mild AKI have poor outcomes

Mortality Risk in Hospitalized Patients

Chertow et al, JASN 16: 3365-3370, 2005
AKIN Criteria (Rifo V2.0)

- **R (I)**: Increased SCr x1.5 OR > 0.3 mg/dL
- **I (II)**: Increased SCr x2
- **F (III)**: Increased SCr x3 or SCr ≥4mg/dl (Acute rise of ≥0.5 mg/dl)

UO < .5ml/kg/h x 24 hr or Anuria x 12 hr

RRT Started

**High Sensitivity**

**High Specificity**

Criterion must be reached within 48hr

KDIGO AKI Guidelines: Definition of AKI

2.1.1: AKI is defined as any of the following (Not Graded):
- Increase in SCr by ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours; or
- Increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume <0.5 mL/kg/h for 6 hours.

2.1.2: AKI is staged for severity according to the following criteria. *(Not Grade)*

- **Stage 1**: Increase in SCr by 1.5-1.9 times baseline; OR
  - Increase in sCR by ≥0.3 mg/dL (≥26.5 μmol/L); OR
  - Urine output <0.5 mL/kg/h for 6-12 hours
- **Stage 2**: Increase in SCr by 2.0-2.9 times baseline; OR
  - Urine output <0.5 mL/kg/h for ≥12 hours
- **Stage 3**: Increase in SCr by 3.0 times baseline; OR
  - Increase in SCr to 4.0 mg/dL (353.6 μmol/L); OR
  - Initiation of renal replacement therapy; OR
  - In patients <18 years, decrease in eGFR to 35 mL/min/1.73 m²; OR
  - Urine output <0.3 mL/kg/h for ≥24 hours; OR
  - Anuria for ≥12 hours

KDOQI Commentary AJKD 2013
Problems with Serum Creatinine

- Creatinine is influenced by age, muscle mass, gender, and ethnicity
- Creatinine does not reflect the presence or absence of structural injury and thus provides no guidance on AKI etiology or the likelihood of response to various targeted therapies
- The rise in serum creatinine is delayed by 2-3 days after the injury has occurred
- Fluid therapy may dilute serum creatinine and therefore delay diagnosis
- Inter-laboratory variation in measuring creatinine, and bilirubin and other compounds interfere with the colorimetric modified Jaffe assay hence affect serum creatinine levels

Serum Creatinine and GFR in AKI

- Nutrition
- Muscle mass
- Protein metabolism
- Infection
- Edema
- Volume of distribution
- Drugs
- Tubular excretion
- Renal excretion
- Nonlinear
- Filtration (GFR)

Star RA, Kidney Int, 1998
Relationship Between GFR and Creatinine

GFR (mL/min)

Serum Creatinine (mg/dL)

Days


Conceptual Model for AKI

Normal
Increased risk
Damage
↓ GFR
Kidney failure
Death

Ideal Biomarker
Creatinine
What Can an Ideal AKI Biomarker Teach Us?

- Predict and diagnose AKI early (before increase in serum creatinine)
- Identify the primary location of injury (proximal tubule, distal tubule, interstitium)
- Pinpoint the type (pre-renal, AKI, CKD), duration and severity of kidney injury
- Identify the etiology of AKI (ischemic, septic, toxic, combination)
- Predict clinical outcomes (dialysis, death, length of stay)
- Monitor response to intervention and treatment
- Expedite the drug development process (safety)

Prasad Devarajan: Biomarkers in Acute Kidney Injury: Search for a Serum Creatinine Surrogate

Potential Biomarkers for AKI

- **Proximal Tubule Injury**
  - Urine IL-18
  - Urine KIM-1
  - Urine L-FABP
  - Urine Cystatin C
  - α1-microglobulin
  - β2-microglobulin
  - Urine α-GST
  - Urine Neutin-1
  - Urine NAG

- **Glomerular Filtration**
  - Serum Creatinine
  - Blood urine Nitrogen
  - Serum Cystatin C
  - Plasma NGAL

- **Distal Tubule**
  - Urine NGAL
  - Urine π-GST

- **Glomerular Injury**
  - Urine albumin excretion

- **Loop of Henle Injury**
  - Urine uromodulin

Other Mechanisms / Sites of Injury not specific to the Nephron

- Hepcidin – Iron trafficking
- TIMP-2/IGFBP7 – G1 cell cycle arrest

Adapted from Koyner and Parikh-Brenner and Rector’s The Kidney

Courtesy of J. Koyner
Biomarkers after AKI
Early Detection

Urinary Biomarkers Associated with Tubular Damage

New Paradigm for the Spectrum of AKI

<table>
<thead>
<tr>
<th>NO AKI</th>
<th>STRUCTURAL (subclinical) AKI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creat (-)</td>
<td>Creat (-)</td>
</tr>
<tr>
<td>Biomarker (-)</td>
<td>Biomarker (+)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FUNCTIONAL AKI</th>
<th>INTRINSIC AKI (structural &amp; functional)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creat (+)</td>
<td>Creat (+)</td>
</tr>
<tr>
<td>Biomarker (-)</td>
<td>Biomarker (+)</td>
</tr>
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</table>
Pathophysiology and Differential Diagnosis of AKI

Classification of the Etiologies of AKI

AKI

Prerenal AKI
- Acute Tubular Necrosis

Intrinsic AKI
- Acute Interstitial Nephritis
- Acute GN

Post-renal AKI
- Acute Vascular Syndromes
- Intratubular Obstruction
Evaluation of Cause of AKI

<table>
<thead>
<tr>
<th>Form of AKI</th>
<th>BUN:Cr</th>
<th>$U_{Na}$ (mEq/L)</th>
<th>$FE_{Na}$</th>
<th>Urine Sediment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prerenal</td>
<td>&gt;20:1</td>
<td>&lt;10</td>
<td>&lt; 1%</td>
<td>Normal, hyaline casts</td>
</tr>
<tr>
<td>Post-renal</td>
<td>&gt;20:1</td>
<td>&gt;20</td>
<td>variable</td>
<td>Normal or RBC’s</td>
</tr>
<tr>
<td>Intrinsic</td>
<td>&lt;10:1</td>
<td>&gt;20</td>
<td>&gt; 2%</td>
<td>Muddy brown casts; tubular epithelial cells, granular casts</td>
</tr>
<tr>
<td>ATN</td>
<td>&lt;20:1</td>
<td>&gt;20</td>
<td>&gt;1%</td>
<td>WBC’s WBC casts, RBC’s, eosinophils</td>
</tr>
<tr>
<td>AIN</td>
<td>variable</td>
<td>&lt;20</td>
<td>&lt;1%</td>
<td>Dysmorphic RBC’s, RBC casts</td>
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<td>AGN</td>
<td>variable</td>
<td>&gt;20</td>
<td>variable</td>
<td>Normal or RBC’s</td>
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<tr>
<td>Vascular</td>
<td>variable</td>
<td>&gt;20</td>
<td>variable</td>
<td>Normal or RBC’s</td>
</tr>
</tbody>
</table>
**Fractional Excretion of Na⁺ (FENa)**

\[
\left( \frac{\text{Urine Na} \times \text{Serum Cr}}{\text{Serum Na} \times \text{Urine Cr}} \right) \times 100 < 1\% = \text{pre-renal} \\
\left( \frac{\text{Urine Na} \times \text{Serum Cr}}{\text{Serum Na} \times \text{Urine Cr}} \right) \times 100 > 2\% = \text{ATN}
\]

- Normal renal function <1%
- Most accurate with **oliguric** AKI

**Caveat:**
- < 1% without volume depletion
  - Contrast nephropathy
  - Acute GN
  - Rhabdomyolysis
- Possibly > 2% with prerenal state:
  - Diuretics, severe CKD

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**Steiner AJM 1984:77:699-702**

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**Fractional Excretion of Urea (FEurea)**

\[
\left( \frac{\text{Urine UN} \times \text{Serum Cr}}{\text{Serum UN} \times \text{Urine Cr}} \right) \times 100 < 35\% = \text{Pre-renal} \\
\left( \frac{\text{Urine UN} \times \text{Serum Cr}}{\text{Serum UN} \times \text{Urine Cr}} \right) \times 100 > 50\% = \text{ATN}
\]

- Better than FENa in patients on **diuretics**
- Rationale: Urea reabsorbed in proximal tubule + inner medulla, not affected by loop and thiazide diuretics
Pre-renal Urine Sediment

Hyaline Casts

Pre-renal AKI – Decreased Renal Blood Flow

<table>
<thead>
<tr>
<th>Cause</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume depletion</td>
<td>Renal losses; GI fluid losses; hemorrhage; burns</td>
</tr>
<tr>
<td>Decreased cardiac output</td>
<td>Heart failure; massive pulmonary embolus; acute coronary syndrome</td>
</tr>
<tr>
<td>Systemic vasodilation</td>
<td>Sepsis; cirrhosis; anaphylaxis; anesthesia</td>
</tr>
<tr>
<td>Intrarenal vasoconstriction</td>
<td>Drugs (NSAIDs, COX-2 inhibitors, amphotericin B, calcineurin inhibitors, contrast agents); hypercalcemia; hepatorenal syndrome</td>
</tr>
<tr>
<td>Efferent arteriolar vasodilation</td>
<td>Renin inhibitors; ACE inhibitors; ARBs</td>
</tr>
</tbody>
</table>

A prolonged pre-renal state can lead to ATN
Pathogenesis of Pre-renal AKI

Volume Depletion  →  Renal Vasoconstriction  →  Decreased GFR

Angiotensin II
Adrenergic nerves
Vasopressin

Liver Failure  →  Sepsis

Nitric oxide  →  Prostaglandins

Impaired Autoregulation Can Lead to “Normotensive AKI”

Pre-renal Azotemia: Medications

Angiotensin-converting enzyme inhibitors

Nonsteroidal anti-inflammatory drugs

Intrarenal Mechanisms for Autoregulation of the GFR

Abdominal Compartment Syndrome

- Intra-abdominal hypertension:
  - Intra-abdominal pressure $\geq 12$ mm Hg; or
  - Abdominal perfusion pressure $< 60$ mm Hg

- Abdominal compartment syndrome
  - Intra-abdominal pressure $\geq 20$ mm Hg; and
  - One or more new organ failures

Systemic Effects of Increased Abdominal Pressure

- Cardiac
  - $\downarrow$ venous return
  - $\downarrow$ cardiac output
  - $\uparrow$ CVP, PCWP & SVR

- Pulmonary
  - $\uparrow$ intrathoracic & airway pressures
  - $\downarrow$ PaO2
  - $\uparrow$ PaCO2

- GI
  - $\downarrow$ splanchnic perfusion

- CNS
  - $\uparrow$ intracranial pressure,
  - $\downarrow$ perfusion pressure

- Renal
  - $\downarrow$ renal perfusion
  - $\downarrow$ GFR
  - $\downarrow$ urinary output
Clinical Settings for ACS

- Trauma patients following massive volume resuscitation
- Massive ascites
- Post liver transplant
- Mechanical limitations to the abdominal wall
  - Tight surgical closure
  - Burn injuries
- Bowel obstruction
- Pancreatitis

Abdominal Compartment Syndrome

- Diagnosis
  - Measurement of intra-abdominal pressure
    - Clamp drainage tube of Foley catheter
    - Instill 25 mL sterile water into the bladder via the aspiration port
    - Measure pressure using a manometer or transducer attached to the aspiration port.
    - The manometer or transducer should be zeroed at the level of the mid-axillary line at the iliac crest

- Treatment
  - Abdominal decompression
Treatment of Pre-renal AKI

- Correction of volume depletion
- Discontinuation/dose adjustment of medications
  - NSAIDs
  - RAAS blockers
  - CNIs
- Evaluation for causes of “effective” volume depletion
  - Heart failure
  - Cirrhosis
  - Nephrotic syndrome
  - Sepsis
- Treat hypercalcemia
- Recognize and treat abdominal compartment syndrome

Intrinsic Renal Disease

Glomerulonephritis
- Postinfectious GN
- Endocarditis-associated GN
- Systemic vasculitis
- Membranoproliferative GN
- Rapidly progressive GN
- IgA nephropathy

Small blood vessels
- Malignant hypertension
- HUS/TTP
- (Pre)Eclampsia
- DIC
- Scleroderma
- Vasculitis
- Cholesterol emboli

Interstitial nephritis
- drugs
  - penicillins
  - sulphonamides
  - rifampin
  - NSAID’s
  - phenytoin
  - allopurinol
- infections
- systemic disease
  - SLE
  - sarcoid
  - sjogrens
- malignancy
- idiopathic

Acute tubular necrosis
Acute Tubular Necrosis

**Causes**

**Ischemic:** causes of prolonged prerenal AKI

**Drug-induced:** aminoglycosides; vancomycin; polymyxins; lithium; amphotericin B; pentamidine; cisplatin; foscartern; tenofovir; cidofovir; carboplatin; ifosfamide; zoledronate; contrast agents; sucrose; immunoglobins; mannitol; hydroxyethyl starch; dextran; NSAIDs; synthetic cannabinoids; amphetamines

**Pigment:** rhabdomyolysis; intravascular hemolysis

**Sepsis**

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Pathogenesis of Ischemic AKI

**Ischemia**

- Microvascular Injury
- Vasoconstriction
- Leukocyte Adhesion
- ↑ Permeability
- Microvascular Congestion

**Inflammation**

- DAMPS
- Immune Cells
- Cytokines

**DAMPs**

- Innate Immunity

**Acute Tubular Injury**

- Apoptosis
- Necrosis

**Tubular Obstruction**

- Backleak

**Continued Ischemia**

- Decreased GFR

Adapted from Bonventre and Weinberg JASN 14:2199-2210, 2003
**Histology: Normal Kidney/Tubules**

- “Back-to-Back” tubules
- “Plump” Epithelial Cells
- Intact Brush Border
- Minimal Intra-tubular material

**Acute Tubular Necrosis**

- Interstitial edema
- Flattened Epithelial Cells
- Loss of Brush Border
- Colloidal intra-tubular casts
Acute Tubular Necrosis Urine Sediment

Muddy Brown Granular Casts and Renal Tubular Epithelial Cells

Contrast Media-Nephrotoxicity

Increase in serum creatinine occurs within 24 to 48 hours following contrast exposure

Contrast Media

- PGE₂
- ANP
- Ado
- Endothelin
- Vasopressin
- Osmotic Load

- Systemic Hypoxemia
- Blood viscosity

- Blood flow
- Oxygen Delivery
- Oxygen Consumption

Direct Cellular Toxicity

Renal Medullary Hypoxia

Rudnick et. al. Seminars in Nephrology 17:15-26, 1997
Risk Factors for Contrast-Associated AKI

- **Patient Related**
  - Preexisting renal insufficiency
  - Diabetes mellitus
  - Intravascular volume depletion
  - Reduced cardiac output
  - Concomitant nephrotoxins

- **Procedure related**
  - Increased dose of radiocontrast
  - Multiple procedures within 72 hours
  - Intra-arterial administration
  - Type of radiocontrast

Strategies for Prevention of Contrast-Associated AKI

- **Effective**
  - Low- or Iso-osmolal contrast agents
  - Intravenous isotonic fluids
  - Avoidance of concomitant nephrotoxins

- **Ineffective or harmful**
  - Furosemide
  - Mannitol
  - Dopamine
  - Fenoldopam
  - Prophylactic RRT

- **Uncertain**
  - Intravenous sodium bicarbonate
  - N-acetylcysteine
  - Theophylline
  - ANP
  - Statins
  - Iron chelators
  - RIPC
Acute Interstitial Nephritis

- **Clinical Suspicion**
  - Fever, Rash
  - Culprit Drug or Disease Process
- **Blood Tests**
  - Increased serum creatinine (AKI)
  - Leukocytosis, eosinophilia, anemia, elevated ESR, transaminitis
- **Urine Studies**
  - Dipstick/low grade proteinuria
  - Pyuria, hematuria, WBC casts
  - Eosinophiluria
- **Imaging Tests**
  - Renal US/CT Scan
  - Gallium Scan
  - FDG-PET Scan
- **Kidney Biopsy**
  - Gold Standard

The triad of Fever, Rash and Eosinophilia: <5-10%

**Causes**

**Drug-induced:** cephalosporins; penicillin; methicillin; fluoroquinolones; sulfonamides; rifampin; NSAIDs; COX-2 inhibitors; proton pump inhibitors; 5-aminosalicylates; indinavir; abacavir; allopurinol; phenytoin; triamterene; furosemide; thiazide diuretics; phenytoin; carbamazepine; Chinese herb nephropathy

**Infection:** pyelonephritis; viral nephritides; leptospirosis; Legionella; Mycobacterium tuberculosis

**Autoimmune:** Sjögren syndrome; sarcoidosis; SLE; TINU syndrome; IgG4-related disease

**Malignancy:** lymphoma; leukemia; multiple myeloma
Acute Interstitial Nephritis

Acute Interstitial Nephritis Urine Sediment

White Blood Cell Cast
### Acute Interstitial Nephritis: Eosinophiluria

<table>
<thead>
<tr>
<th></th>
<th>Drug Induced-AIN</th>
<th>All Etiologies of AIN</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>All cases (n=548)</td>
<td>Pyuria (n=452)</td>
</tr>
<tr>
<td></td>
<td>&gt;1%</td>
<td>&gt;5%</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>35.6</td>
<td>23.3</td>
</tr>
<tr>
<td>Specificity</td>
<td>68.2</td>
<td>91.2</td>
</tr>
<tr>
<td>PPV</td>
<td>14.7</td>
<td>28.8</td>
</tr>
<tr>
<td>NPV</td>
<td>87.3</td>
<td>88.6</td>
</tr>
<tr>
<td>Positive LR</td>
<td>1.1</td>
<td>2.6</td>
</tr>
<tr>
<td>Negative LR</td>
<td>0.9</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Insensitive test with specificity and positive LR only potentially acceptable using **Urine Eos >5%** cutoff in setting of high pretest probability.

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### Acute Interstitial Nephritis - Summary

- Most commonly drug induced
- Complete “classic” triad is rarely present
- Common urinary findings include
  - Pyuria
  - WBC casts
- Eosinophiluria neither sensitive nor specific
- Primary treatment is discontinuation of offending agent/treatment of underlying etiology
- Role of glucocorticoids remain uncertain

*Muriithi AK, et al. CJASN 2013; 8: 1857-1862*
Acute Glomerulonephritis

- Nephritic presentation
  - Proteinuria (may be in nephrotic range (> 3.5 g/day))
  - Hematuria (dysmorphic RBCs)
  - RBC casts

- Diagnosis usually requires renal biopsy
  - Infection-related glomerulonephritis
  - Cryoglobulinemia
  - RPGN

Acute Glomerulonephritis: Dysmorphic RBCs and RBC Casts
# Acute Vascular Syndromes

## Causes

<table>
<thead>
<tr>
<th>Macrovascular</th>
<th>renāl artery occlusion; renāl vein thrombosis; polyarteritis nodosa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microvascular</td>
<td>TMA; HUS; TTP; APLS; HELLP; scleroderma renal crisis; hypertensive emergency; drugs (clopidogrel, cyclosporine, tacrolimus, anti-angiogenesis drugs, interferon, m-TOR inhibitors); drug-induced TMA (caused by quinine, cancer therapies [gemcitabine, mitomycin, bevacizumab, bortezomib, sunitinib], calcineurin inhibitors [cyclosporine, tacrolimus], drugs of abuse [cocaine, ecstasy, intravenous extended-release oxymorphone])</td>
</tr>
</tbody>
</table>

## Atheroembolic disease

**Atheroembolic Disease**
Atheroembolic Disease

- Risk factors
  - Atherosclerosis
    - CAD
    - AAA
    - PVD
  - Hypertension
  - Hypercholesterolemia
  - Diabetes Mellitus

- Precipitating factors
  - Arterial catheterization
  - Arteriography
  - Vascular surgery
  - Anticoagulation
  - Thrombolytic therapy

Atheroembolic Disease: Non-Renal Manifestations

- General
  - Fever
  - Myalgias
  - Weight loss
- Cutaneous
  - Livedo reticularis
  - Digital ischemia
- Neurologic
  - TIA/CVA
  - Altered mental status
  - Peripheral neuropathy
  - Spinal cord infarct

- Gastrointestinal
  - Anorexia
  - Nausea and vomiting
  - Nonspecific abdominal pain
  - GI bleeding
  - Ileus
  - Bowel ischemia/infarction
  - Pancreatitis
  - Hepatitis

- Musculoskeletal
  - Myositis

- Eyes
  - Amaurosis fugax
  - Retinal cholesterol emboli
Atheroembolic Disease: Renal Manifestations

- Renal infarction
- Acute kidney injury
- Subacute kidney injury
- Exacerbation of hypertension
- Proteinuria (may be nephrotic)
- Hematuria

Atheroembolic Disease: Laboratory Features

- Serum chemistries
  - ↑ BUN and creatinine
  - ↑ Amylase
  - ↑ CPK
  - ↑ LFTs
- Hematology
  - Leukocytosis
  - Eosinophilia
  - Anemia
  - Thrombocytopenia
- Serologic
  - ↑ ESR
  - ↓ Serum complement
- Urine
  - Eosinophiluria
  - Proteinuria
  - Hematuria
  - Pyuria
Atheroembolic Disease: Treatment

- Avoid anticoagulation
- Avoid vascular interventions
- ACE inhibitors / angiotensin receptor blockers
- Statin therapy
- Nutrition support
- Dialysis for management of volume status and uremia
- Role of steroid therapy is uncertain

Intrinsic Renal Disease: Intratubular Obstruction

- Common factors:
  - Include high excretion in urine
  - Low solubility in acidic urine
  - Exacerbated by hypovolemia

- Common crystals
  - Uric acid (tumor lysis syndrome)
  - Acyclovir
  - Sulfa
  - Methotrexate
  - Ethylene glycol (calcium oxalate deposition)

- Intratubular protein deposition
  - Multiple myeloma (Bence-Jones protein deposition)
Tumor Lysis Syndrome

- Rapid lysis of malignant cells leads to hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia, and AKI

- Management of patients at risk or presenting with TLS
  - Aggressive volume expansion to achieve a urine output of at least 80 to 100 mL/m²/h
  - Allopurinol to prevent formation of new uric acid (recommended as prophylaxis for patients at low/intermediate risk for TLS)
  - Rasburicase for patients at high risk of TLS or with TLS (contraindicated in patients with G6PD deficiency)
  - Urinary alkalinization is no longer recommended due to an increase in calcium phosphate crystal deposition
  - Management of hyperkalemia and hyperphosphatemia
  - RRT in refractory cases
# Prevention and Management of AKI

## Interventions in AKI

<table>
<thead>
<tr>
<th>Drug</th>
<th>Biological rationale</th>
<th>Animal experiments</th>
<th>Uncontrolled human data</th>
<th>Small RCT</th>
<th>Large RCT</th>
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<tbody>
<tr>
<td>Loop diuretics</td>
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<tr>
<td>Low-dose dopamine</td>
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<td>Favorable</td>
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<tr>
<td>Ca antagonist</td>
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<td>Theophylline</td>
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<tr>
<td>Prostaglandins</td>
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<td>Natriuretic peptide</td>
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<td></td>
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</tr>
<tr>
<td>α-receptor antagonist</td>
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<tr>
<td>Endothelin antagonist</td>
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</tbody>
</table>

The only FDA approved treatment of AKI is dialysis.
Prevention of ATN

- Recognition of underlying risk factors
  - Diabetes
  - CKD
  - Age
  - Cardiac/liver dysfunction

- Early recognition is key
  - Changes in creatinine are a late manifestation of renal injury
  - A “normal” normal serum creatinine may reflect significant renal insufficiency, particularly in the elderly

- Maintenance of renal perfusion
- Avoidance of nephrotoxins

Figure 2. Stage-based management of acute kidney injury (AKI). Shading of boxes indicates priority of action—solid shading (with white lettering) indicates actions that are equally appropriate at all stages whereas graded shading (with black lettering) indicates increasing priority as intensity increases. Abbreviation: ICU, intensive care unit. Reproduced with permission of KDIGO from the KDIGO Clinical Practice Guideline for Acute Kidney Injury.3
AKI Summary

- AKI is defined by a standardized creatinine-based definition
- AKI is common
- AKI is associated with mortality in a stage-dependent fashion
- Methods for earlier diagnosis of AKI and its progression may result in improved outcomes by facilitating targeted and timely treatment of AKI
- There is no treatment of ATN and prevention of precipitating factors is paramount