Acute Kidney Injury

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Technical Definition: AKI

The KDIGO guidelines define AKI as follows:

1. Increase in serum creatinine by ≥0.3 mg/dL within 48 hours
2. Increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the prior seven days
3. Urine volume <0.5 mL/kg/hour for six hours

The diagnostic criteria should only be applied after volume status has been optimized. Urinary tract obstruction needs to be excluded if urine volume is used as a sole criteria.

Staging System of AKI

<table>
<thead>
<tr>
<th>Stage</th>
<th>RIFLE CRITERIA</th>
<th>Urine Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Risk</td>
<td>Increase in serum creatinine to 1.5 to 1.9 times baseline, or increase in serum creatinine by ≥0.3 mg/dL.</td>
<td>Reduction in urine output to &lt;0.5 mL/kg/hour for 6 to 12 hours</td>
</tr>
<tr>
<td>2. Injury</td>
<td>Increase in serum creatinine to 2.0 to 2.9 times baseline</td>
<td>Reduction in urine output to &lt;0.5 mL/kg/hour for ≥12 hours</td>
</tr>
<tr>
<td>3. Failure</td>
<td>Increase in serum creatinine to 3.0 times baseline, or increase in serum creatinine to ≥4.0 mg/dL or the initiation of renal replacement therapy in patients &lt;18 years, decrease in estimated glomerular filtration rate (eGFR) to &lt;35 mL/min/1.73 m².</td>
<td>Reduction in urine output to &lt;0.3 mL/kg/hour for ≥24 hours, or anuria for ≥12 hours</td>
</tr>
</tbody>
</table>
Hospital discharge status of first hospitalization for Medicare patients aged 66+ with or without diagnosis of AKI during stay, 2014

Without diagnosis of AKI during stay

With diagnosis of AKI during stay

CAUSES OF AKI

Prerenal Causes

- Absolute ↓ in ECV
  - Volume depletion
  - Hemorrhage

- Relative ↓ in ECV
  - Heart Failure
  - Cirrhosis

- Impaired renal autoregulation with low ECV
  - NSAIDS
  - ACEI/ARBs

- Vasoconstriction /Oclusion
  - Hyperparathyroidism
  - Calcineurin inhibitors
  - Renal artery stenosis
LOW ECV: RENAL AUTOREGULATION

RENAL AUTOREGULATION IN LOW ECV AND NSAID USE

RENAL AUTOREGULATION IN LOW ECV AND ACEI/ARB USE
RENAL AUTOREGULATION IN LOW ECV, NSAID AND ACEI/ARB USE

Prerenal Azotemia

• Can complicate any clinical scenario with decreased effective circulating volume (true or relative).
• Generally, reversible with treating the underlying etiology.
• If unable to correct in a timely manner, can progress to ischemic ATN.
• Pre renal azotemic and ischemic ATN thought to cause up to 75% of AKI in the hospitalized setting.


Post-renal Failure

Upper Urinary Tract Obstruction:
Causes: Intrinsic obstruction of ureters from stones or extrinsic compression by retroperitoneal fibrosis or tumors.
Bilateral obstruction with superimposed infection is a medical emergency.

Lower Urinary Tract Obstruction:
Most common in-hospital cause of obstruction.
Pain meds are common culprits.
Enlarged prostate most common cause in general.
Post-renal Failure

- Diagnosis: H/o ↓ urine output (not always reliable)
  - Physical exam: suprapubic fullness
  - Ultrasound: hydronephrosis or enlarged bladder
  - Bladder scan to check for post-void residual
- Treatment: Relieve the obstruction
  - Need to monitor for post-obstructive diuresis
  - Urine output may be > 5-6 liters
  - Patients can develop hypernatremia if unable to drink water (intubated/sedated/elderly)

Intrinsic Renal Failure

- Glomerulonephritis
- Eclampsia
- Malignant HTN
- Acute Tubular Necrosis
- Acute Interstitial Nephritis
- Acute Pyelonephritis

Acute Tubular Necrosis

- Ischemic
- Toxic
ACUTE TUBULAR NECROSIS

RENAL

TUBULI
GLomeruli
INTERSTITIUM
BLOOD VESSEL
COLLECTING SYS

ISCHEMIC

PROLONGED PRERENAL STATE

EXOGENOUS

ENDOGENOUS

SOMETHING GIVEN TO THE PATIENT

ANTIBIOTICS
CANCER DRUGS
IODINATED CONTRAST MEDIUM
MANNITOL
**CONTRAST INDUCED NEPHROPATHY**

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Clinical Features</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced Age</td>
<td>Increase in serum creatinine 48-72 hours after contrast exposure</td>
<td>Prevention is the key.</td>
</tr>
<tr>
<td>Underlying CKD</td>
<td>Initially non-oliguric</td>
<td>IV fluids pre and post contrast exposure</td>
</tr>
<tr>
<td>Type II DM</td>
<td>Generally non-oliguric</td>
<td>Stop diuretics and ACE/ARB where appropriate</td>
</tr>
<tr>
<td>Volume depletion</td>
<td>Initially pre-renal urine indices with high urine specific gravity ultimately leads to ATN</td>
<td>Supportive medical management and in some cases, may need dialysis support.</td>
</tr>
<tr>
<td>Anemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contrast load</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concomitant use of nephrotoxic agents</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence reported: 0.6 to 2.3% but higher if risk factors present</td>
<td></td>
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</tbody>
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**ACUTE TUBULAR NECROSIS**

- Acute Tubular Necrosis
- ISCHEMIC
- PROLONDED PERRENAL STATE
- ENDOGENOUS
- SOME THING THE BODY PRODUCES IN EXCESS
- MYOGLOBIN - RHABDO
- LIGHT CHAINS - MYELOMA
- HEMOGLOBIN - HEMOLYSIS

Tumor Lysis Syndrome: Lysis of tumor cells post chemotherapy exposure. The higher the tumor burden, the greater the risk.

**PATHOGENESIS OF ATN**

Muddy brown casts
**ATN – CLINICAL COURSE**

- **INITIATION PHASE:** (hours to days)
  Evolving tubular injury
  Potentially reversible if diagnosed early
- **MAINTENANCE PHASE:** (typically 1-2 weeks)
  May be prolonged to 1-3 months in some cases
  Established renal injury
  Generally oliguric during this phase
  Muddy brown urine with casts noted in sediment
- **RECOVERY PHASE:**
  Repair and regeneration of tubules.
  Polyuric phase and if patient is intubated/no access to free water, at risk for hypernatremia, replace 1/2-1/3 of UOP with hypotonic fluid.
  At risk for CKD despite recovery.

**ACUTE GLOMERULONEPHRITIS**

- Unexplained renal failure
- Can be hypertensive
- Subnephrotic range proteinuria, >3.5 gm/day
- Active urine sediment with +ve blood, protein, WBC, dysmorphic RBC and RBC casts.
- Kidney biopsy for definitive diagnosis
- Post Strep GN
- Lupus Nephritis
- ANCA Vasculitis
- Anti GBM
- Ig A/HSP

**ACUTE GLOMERULONEPHRITIS**

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- Can be hypertensive
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- Active urine sediment with +ve blood, protein, WBC, dysmorphic RBC and RBC casts.
- Kidney biopsy for definitive diagnosis
ACUTE INTERSTITIAL NEPHRITIS

Etiology:
1. Medications – PPIs, Bactrim, Quinolones
2. Infections
3. Autoimmune

- Classic triad of fever, rash, and eosinophilia seen in < 10% of cases.
- Urine eosinophils neither sensitive nor specific.
- Sterile pyuria
- Definitive diagnosis by kidney biopsy

1. Generally reversible once the offending agent is stopped.
2. Treating underlying infection or autoimmune disease.

VASCULAR CAUSES

1. TTP/HUS
   - Thrombotic Thrombocytopenic Purpura
   - Hemolytic Uremic Syndrome
   - Malignant HTN: BP > 180/120 with end organ damage
   - Scleroderma: Autoimmune disease causing thickened skin and kidney problems
   - Preeclampsia: new onset HTN after 20 weeks, proteinuria can be present. Can cause AKI.

PYELONEPHRITIS

   - new urine/blood cultures with WBC casts in urine
   - Perinephric stranding on imaging
   - Treatment with fluids and ABX.
ESTABLISHING DIAGNOSIS

• Detective work:
  • History of inciting events – any nausea/vomiting/diarrhea/decreased oral intake, heavy exercise, fevers or rash, over the counter/herbal medication use, recent change in prescribed medications, recent hospitalizations, any contrast studies done in the recent past
  • Thorough chart review for in-hospital AKI
  • Is/Os (often times UOP is not documented accurately and hence cannot take it at face value unless catheter in place), trends in BP/HR and weights, intra-op notes if available, medication/contrast exposure
  • Physical exam in assessing volume status – JVD/crackles/edema/skin tenting but tough to assess volume status especially in cirrhotic patients whose total body volume is up but could be intravascularly dry.
  • Looking at the urine and urine sediment
  • Kidney biopsy for definitive diagnosis in Glomerulonephritis/Interstitial Nephritis/unexplained renal failure

PITFALLS OF CREATININE IN AKI

• AKI is not a steady state and hence cannot calculate estimated GFR using any of the available formulae
• Serum creatinine lags behind the actual injury
• Serum Creatinine levels depend on:
  - Clearance rate (changing in AKI)
  - Rate of production (changing in AKI)
  - Volume of distribution (changing in AKI)
• Creatinine produced predominantly by the muscles and hence, muscular people can have high serum creatinine and emaciated people with very low serum creatinine, not corresponding with the actual GFR.
• Drugs that block tubular secretion of creatinine can elevate serum creatinine without actual decrease in GFR – Ex: high dose bactrim, probenecid, high dose cimetidine

WHY WAS CREATININE THE CHOSEN ONE TO MEASURE RENAL FUNCTION?
WHY WAS CREATININE THE CHOSEN ONE TO MEASURE RENAL FUNCTION?

Up to 10% of urine creatinine results from tubular secretion

24 hour urine creatinine is an overestimate of true GFR

PLEASE DO NOT IGNORE THE UA

<table>
<thead>
<tr>
<th>Component Results</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Color</td>
<td>Yellow</td>
</tr>
<tr>
<td>Clarity</td>
<td>Clear</td>
</tr>
<tr>
<td>pH</td>
<td>7.5</td>
</tr>
<tr>
<td>SPEC QUALITY</td>
<td>1 Nit</td>
</tr>
<tr>
<td>Protein</td>
<td>Trace</td>
</tr>
<tr>
<td>Blood</td>
<td>Neg</td>
</tr>
<tr>
<td>Glucose</td>
<td>Neg</td>
</tr>
<tr>
<td>Ketones</td>
<td>Neg</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>Neg</td>
</tr>
<tr>
<td>UROEPIDOSTEN</td>
<td>Neg</td>
</tr>
<tr>
<td>MBSI</td>
<td>Neg</td>
</tr>
<tr>
<td>LEUKocytes</td>
<td>Neg</td>
</tr>
<tr>
<td>RBC (MICROSкоп)</td>
<td>Microscopic (1+ form)</td>
</tr>
<tr>
<td>Erythrocytes</td>
<td>None</td>
</tr>
<tr>
<td>SQUAMOUS EPITHELIAL</td>
<td>None</td>
</tr>
</tbody>
</table>
DIFFERENTIATING PRE-RENAL VS. ATN

<table>
<thead>
<tr>
<th>LAB VALUE</th>
<th>PRE-RENAL</th>
<th>INTRINSIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine Specific Gravity</td>
<td>&gt; 1.030</td>
<td>&lt; 1.010</td>
</tr>
<tr>
<td>Urine Osmolality (mosm/kg)</td>
<td>&gt; 560</td>
<td>&lt; 150</td>
</tr>
<tr>
<td>Urine Na (mEq/L)</td>
<td>&lt; 20</td>
<td>&gt; 40</td>
</tr>
<tr>
<td>Fractional excretion of sodium, FeNa (%)</td>
<td>&lt; 1</td>
<td>&gt; 1</td>
</tr>
<tr>
<td>Fractional excretion of urea, FeUrea (%)</td>
<td>&lt; 35</td>
<td>&gt; 35</td>
</tr>
<tr>
<td>U/P Creatinine ratio</td>
<td>&gt; 40</td>
<td>&lt; 20</td>
</tr>
<tr>
<td>Serum BUN/Cr ratio</td>
<td>&gt; 20:1</td>
<td>&lt; 10:1</td>
</tr>
</tbody>
</table>

What do they reflect?
- Intact tubular function
- Impaired tubular function

SERUM BUN/CR RATIO

<table>
<thead>
<tr>
<th>High BUN</th>
<th>Low BUN or Creatinine</th>
<th>High Creatinine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prenal state</td>
<td>Low protein diet</td>
<td>High muscle mass</td>
</tr>
<tr>
<td>High dose steroids</td>
<td>Cachectic patients</td>
<td>Using creatine supplements</td>
</tr>
<tr>
<td>Hypercatabolic states — high fevers, burns</td>
<td>Cirrhosis — high bilirubin</td>
<td>Rhabdomyolysis</td>
</tr>
<tr>
<td>High protein diet — look for protein load in ICU patients on tube feeds</td>
<td>Interference with creatinine measurement</td>
<td>Diet rich in animal protein</td>
</tr>
<tr>
<td>Gl bleed</td>
<td>Drug blocking tubular secretion</td>
<td>Drugs blocking tubular secretion</td>
</tr>
<tr>
<td></td>
<td>Interference with creatinine measurement — nephrotoxic, ketosis</td>
<td></td>
</tr>
</tbody>
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MANAGEMENT OF AKI

- Treatment of underlying etiology
  1. Volume repletion in volume depletion
  2. Treatment of heart failure
  3. Treatment of underlying infections
  4. Stopping offending medications
  5. Relieving obstruction.
- Track daily weights, BP and Inputs/outputs.
- Maintain mean arterial pressure (MAP > 60 mmHg).
- Dose medications to renal function — can be tricky.
- Avoid contrast studies and use least nephrotoxic medications when possible (should be the case in general).
- Management of electrolyte disturbances — hyperkalemia, metabolic acidosis, hyperphosphatemia.
HEMODIALYSIS IN AKI

• Exact timing – controversial and varying results in literature.
  - Early dialysis: exposing the patient to risks of dialysis when there is a
    chance for renal function to recover.
  - Too late: may affect overall morbidity/mortality
  - Dialysis is an invasive procedure: requires line placement and
    complications associated with line placement (many sick ICU patients
    have bleeding diathesis), increased risk of hypotensive episodes and
    arrhythmias during dialysis.

• General indications for dialysis: AEIOU still stand true to date.
  - Acidosis
  - metabolic acidosis refractory to medical management
  - Electrolytes
  - hyperkalemia refractory to treatment or rapidly rising levels in potassium
  - Intoxications with dialyzable drug, including
    - salicylates, lithium, isopropanol, methanol, and ethylene glycol (SLIME)
  - Overload
    - volume overload that does not respond to diuresis
    - especially with increased oxygen requirements
  - Uremia
    - elevated BUN with signs of uremia, such as uremic bleeding, encephalopathy,
      and pericarditis.

PROGNOSIS OF AKI

• Depends on severity of underlying illness.
• Most patients recover but "complete" recovery is not always the case
  even if serum creatinine reaches baseline.
• At risk for CKD with repeated AKI episodes.
• Mortality of > 50% in patients with AKI and multi-organ dysfunction.
• Often times, patients die with renal failure than from renal failure due
  to widely available renal replacement therapy options.
Questions?