Acute Renal Failure

Mark D. Baldwin D.O.
F.A.C.O.I.
ACOI Board Review Course 2015
Definition of Acute Renal Failure/Acute Kidney Injury

• An abrupt increase in the BUN and Creatinine with corresponding problems in handling of fluids, Potassium, Phosphorus, and acid-base balance. This is usually a greater than 50% decline in the GFR.
Problems with the Definition

• Serum Creatinine does NOT reflect the degree of renal dysfunction or improvement
• Urine output or lack of may also not reflect the degree of dysfunction
• A better definition may be Acute Kidney Injury (AKI)
Types of Acute Kidney Injury

- Acute Renal Failure can be:
  - Oliguric <400 ml/da
  - or
  - Non-Oliguric >400 ml/da

  Non-Oliguric has a much better prognosis
Acute Renal Failure

--In the Pre-Dialysis Era, ARF had a 50-70% Mortality Rate.

--Today with Dialysis, ARF still has a 50-70% Mortality Rate

--Thus Patients die With ARF rather than Of ARF
Types of Acute Renal Failure

ARF

Pre-Renal  Post-Renal

Intrinsic Renal

Vascular  Glomerular  Interstitial  Tubular
Phases of Acute Renal Failure

• **Initiation Phase**-drop in BP, nephrotoxins, early sepsis—rise in BUN/Cr, decreasing urine output

• **Oliguric Phase**-usually less than 400 ml/da, may require dialysis

• **Recovery/Diuretic Phase**-increasing urine output, decreasing BUN/Cr, Potassium, Phosphorus, and Magnesium
Differentiation of AKI

Acute Tubular Necrosis 45%
Pre-Renal 21%
Acute on Chronic R.F. 13%
Obstruction 10%
Glomerulonephritis/vasculitis 4%
Acute Interstitial Nephritis 4%
Athroemboli 1%

Based on 748 cases from 13 tertiary care centers

Kidney Int 1996; 50(3):811
RIFLE Criteria

- Risk- 1.5 fold increase in Creatinine or 25% decline in GFR or decrease urine output of <0.5 ml/kg/hr for 6 hours
- Injury-Two fold increase in Creatinine or 50% decline in GFR or decrease urine output of < 0.5 ml/kg/min for 12 hours
- Failure-Three fold increase in Creatinine or 75% decline in GFR or decrease urine output of 0.5 ml/kg/min for 24 hours or Anuria for 12 hours
- Loss- Complete loss of renal function, requiring dialysis for > 4 weeks
- ESRD-Complete loss of renal function, requiring dialysis for >3 months

Bellomo, et al
Crit Care. 2004 Aug;8(4):R204-12
Acute Dialysis Qualitative Initiative (ADQI)
RIFLE and Risk of Death

- Risk (1.5 fold increase) 2.4 relative mortality risk
- Injury (2 fold increase) 4.14 relative risk
- Failure (3 fold increase) 6.37 relative risk

- From a review of 13 studies of Critical care patient with AKI vs. without AKI
AKI-KDIGO Guidelines 2012

1. Increase serum creatinine >0.3 mg/dl w/in 48 hours OR
2. Increase serum creatinine >1.5x baseline w/in 7 days OR
3. Decreased urine volume <0.5ml/kg/hr over a 6 hour period or greater

Approach to a Patient with AKI (2)

• History and Physical
• Review Intake/Output, Blood Pressures
• History of recent Cardiac Cath, Angiogram, Cardiac Surgery, Hypotensive episodes
• Urinalysis including microscopic exam
• Renal ultrasound-rule out obstruction
• Renogram-can show diminished flow to the kidneys
• ANA, ANCA, Anti-GBM, C3, C4, ASO, Hepatitis Serology
• Renal Biopsy
Approach to a patient w/ AKI

- Recent UTI type illness, nasal congestion, cough, hemoptysis
- Rash, arthralgias, abdominal pain
- New medication or herbal meds
- Vomiting, diarrhea
- “Bad habits”
Approach to a patient with AKI (3)

- A thorough evaluation of the patient’s volume status is essential
Post Renal Obstructive

• May be acute, chronic or acute on chronic
• Functional renal recovery depends on duration of the obstruction
• Post obstructive diuresis will lead to ARF unless fluid and electrolyte balances are closely monitored maintained
• The nephrologist’s role is in contacting the interventional radiologist or urologist to remove the obstruction
Post Renal Obstructive
Pre-Renal Failure

- A decrease in either total circulatory volume or effective circulatory volume (i.e. CHF or Sepsis). This leads to activation of the Renin-Angiotensin-Aldosterone System and ADH. Thus enhanced Na and H2O reabsorption.
Causes of Pre-Renal Failure

- Dehydration
- Vomiting, Diarrhea, NG losses, fistulas
- Excessive sweating
- Sepsis
- Diuretic phase of ARF or Post-Obstructive Diuresis
- CHF
- ACE-I or ARBs
- “3rd Space” Losses
Fractional Excretion of Sodium \( FE_{Na} \)

- May be helpful in differentiating Acute Prerenal from Intrinsic or Postrenal Injury

- \( FE_{Na} = \frac{Pc r \times UNa}{PNa \times UCr} \times 100 \)

- Not accurate if measure after a patient has received diuretics or in acute on chronic kidney injury

- Normal value is 1%
## Urinary Indices

<table>
<thead>
<tr>
<th></th>
<th>Pre-Renal</th>
<th>Acute Tubular Necrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN/Cr</td>
<td>$&gt;15$-$20/1$</td>
<td>$&lt;10$-$15/1$</td>
</tr>
<tr>
<td>Spec Grav</td>
<td>$&gt;1.020$</td>
<td>$&lt;1.010$</td>
</tr>
<tr>
<td>U osm</td>
<td>$&gt;500$</td>
<td>$&lt;400$</td>
</tr>
<tr>
<td>U Na</td>
<td>$&lt;10$</td>
<td>$&gt;30$-$40$</td>
</tr>
<tr>
<td>FeNa</td>
<td>$&lt;1%$</td>
<td>$&gt;1%$</td>
</tr>
<tr>
<td>Sediment</td>
<td>Nothing or a few hyaline casts</td>
<td>Numerous Dirty brown casts</td>
</tr>
</tbody>
</table>
Intrinsic Renal Failure-Acute Tubular Necrosis

- Direct insult to the kidney
- May be a result of vascular, glomerular, interstitial, or tubular causes
- Final common pathway of untreated pre-renal or post renal failure
Pathophysiology of ATN

• Hypoxia of the tubular microvasculature leads to tubular necrosis and loss of reabsorption and secretory abilities of the tubules. Thus, Acute Tubular Necrosis.
Pathophysiology of ATN-2

- Afferent and Efferent Arteriolar Vasoconstriction
- Mesangial Contraction
- Release of Reactive Oxygen species, NO, ATII, PG’s, Catecholamines
- Tubular Necrosis due to tubular obstruction and back-leak
Pathophysiology of ATN-3

- Cellular Edema
- Increased free Ca++
- Release of compartmentalized enzymes
- Destruction in Cytoskeleton
- Reperfusion injury from reactive Oxygen species, WBC’s, Complements, and cellular debris
Pulmonary-Renal Syndromes

Patient’s frequently present with pulmonary hemorrhage, hematuria, and renal failure.

- Systemic Lupus
- Goodpasture’s Syndrome
- IgA Nephropathy (Berger’s Disease)
- ANCA Mediated-Wegner’s and Polyarteritis Nodosa
- Henoch-Schoenlein Purpura
- Post Streptococcal GN
Common Causes of Intrinsic Renal Failure

• Sepsis
• Drugs
• Rhabdomyolysis
• SLE, Wegners, Goodpatures
• Polyarteritis Nodosa
• IgA Berger’s, HSP
• Sustained Hypotension
• Post CABG, Angiogram (cross clamp and pump time)
• Post Streptococcal GN
• Allergic Interstitial Nephritis
• Hemolytic Uremic Syndromes
Management of Acute Kidney Injury (1)

- TREAT UNDERLYING CAUSE!!!!!!! i.e. Sepsis, volume depletion and drug toxicity
- “Renal dose Dopamine” not recommended
- Fenoldopam is not recommended
- Atrial natureitc peptide is not recommended
- Recombinant insulin growth factor-1 (rh)IGF-1 is not recommended
- N-acetylcysteine is not recommended for post surgical AKI

Management of Acute Kidney Injury (2)

• In absence of hemodynamic shock, isotonic crystalloid is preferred over albumin or starches for volume expansion
• Closely follow hemodynamic and oxygenation parameters in at risk patients
• Keep blood glucose in the 110-149 mg/dl range
• Do not use diuretics to prevent AKI
• Use loop diuretics in AKI ONLY to treat volume overload

Management of Acute Kidney Injury (3)

- Utilize the enteral route for nutrition if at all possible
- Do not restrict protein in AKI as a way to avoid AKI or renal replacement therapy (RRT)
- If necessary give aminoglycosides as a single dose, closely following levels prior to subsequent dosages

Figure 2

AKI Stage

<table>
<thead>
<tr>
<th>High Risk</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinue all nephrotoxic agents when possible</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ensure volume status and perfusion pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider functional hemodynamic monitoring</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitoring Serum creatinine and urine output</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoid hyperglycemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider alternatives to radiocontrast procedures</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Non-invasive diagnostic workup

Consider invasive diagnostic workup

Check for changes in drug dosing

Consider Renal Replacement Therapy

Consider ICU admission

Avoid subclavian catheters if possible
Drug Induced ARF

- Can be due to Direct toxicity to the tubules i.e. Aminoglycosides
- Can be due to Acute Interstitial Nephritis i.e. TMP/STX, Methicillin
- Can be due to Multiple causes i.e. Contrast
- Can be due to vasoconstriction of the renal arterioles i.e. NSAIDs or Cyclosporine
Common Drugs in ARF

- Contrast Media
- NSAIDs-The MOST Common Drug
- Aminoglycosides
- Penicillins
- Sulfas
- Cephalosporins
- Cyclosporine
- Foscarnet
Common Drugs in ARF (cont)

• Vancomycin
• COX-2 inhibitors
• ACE-I or ARBs in patients w/ RAS
• Intravenous immunoglobulin
• Mannitol
• Hetastarch
• SPICE K-2
Contrast Induced Nephropathy (CIN)

- High risk patients for acute kidney injury following contrast infusion
- CKD S Cr>1.5 mg/dl
- Diabetes mellitus
- Acute kidney injury (current)
- Hypotension/ sepsis
- Age >70 years old
- Myeloma
- Organ transplantation
- HIV

- Cardiovascular disease
- Cirrhosis
- Nephrotic syndrome
- Dehydration
- Recent or repeated contrast studies
- Intra-arterial>intravenous injection
- High osmolar contrast
- Volume of contrast

CIN Prophylaxis

- IV hydration w/ NS, \( \frac{1}{2} \) NS or 3 x 50 ml ampules of Sodium Bicarbonate in 850 ml Sterile Water given at a rate of 1ml/kg/hr for 6-12 hours before and after procedure.
- The higher the creatinine to longer the hydration
- Hold Metformin at least 48 hours before procedure
CIN Prophylaxis (2)

• N-acetylcysteine (NAC) mixed reviews as to efficacy in treating CIN, but CANNOT substitute adequate hydration

• Non-ionic contrast

• Minimizing volume of contrast

• 48 hours between studies

MRI with Gadolinium

- Risk of Nephrogenic Systemic Fibrosis in patients w/ CKD or AKI
- Use w/ caution in any patient w/ a GFR 30-44 ml/min/1.75 m²
- Hydration is of no value
- Avoid in GFR<30 or AKI
- Consider other imaging methods

ACR Committee on Drugs and Contrast Media. *ACR manual*. America College of Radiology; 2013. p. 81–9, 9
Rhabdomyolysis

- Although well recognized in trauma, it is often over looked in non traumatic causes.
- Myoglobin is not directly toxic in euvolumic patients
Causes of Non-Traumatic Rhabdomyolysis

- Impaired level of consciousness
- Seizures
- Stroke
- Drug Overdose
- Decreased PO4
- Decreased K
Causes of Non-Traumatic Rhabdomyolysis

- Hyperthermia/Hypothermia
- ETOH
- HMG-Co Reductase inhibitors
- McArdle’s Syndrome
- Tetnaus
- Gas Gangrene
- Decreased Mg
- Decreased Na
Diagnosis of Rhabdomyolysis

- **KEY**: Large Blood on U.A. and few RBCs
- Elevated CPK
- Creatinine>>BUN
- Elevated-Lactate, LDH, PO4, Uric Acid, K
- Decreased Ca
Treatment of Rhabdomyolysis

- Alkaline diuresis D5W or D5 ½ NS with 1 amp NaHCO3 and 20 gm mannitol 6-12 l/da infusion. But must treat early and vigorously. Although the role of alkaline diuresis is not firmly established, it is still cautiously recommended.
- May require dialysis
Athroembolic-Cholesterol Embolic Renal Failure

- Can be Spontaneous in patients with severe athrosclerosis. Commonly seen following angiography, CABG, or Aortic Surgery.
- Due to showering of microemboli and probable local allergic reaction in the glomerulus.
Clinical Feature of Athroembolic Renal Failure

- Blue Toes
- Rash to anterior lower legs
- Livido reticularis
- Peripheral Eosinophilia
- Increased Sed Rate
- Urine Eosinophils
Hemolytic –Uremic Syndrome (TTP-HUS)

• Acute Renal Failure associated with microangiopathic hemolytic anemia and thrombocytopenia

• Etiology:
  - E. Coli 0157:H7 and 0104:H4-Shiga-like toxin, verocytotoxin
  - Shigella
  - Strep pneumonia
  - Inherited HUS
HUS

• Etiology (cont)
  - Drugs: Mitomycin
    - Cyclosporin
    - Oral contraceptives
  - Pregnancy related
  - Transplant related
  - Cancer related
Clinical Features of HUS

Diarrhea (especially in infectious HUS)
• Increased BUN/Creat, LDH
• Decreased Hb/Hct, Decreased Platelet
• Decreased Haptoglobin
• Increased Reticulocyte count
• Fragmented RBCs- Schistocyres, Helmet cells
• CNS Involvement-poor prognosis
• ? Role of ADAMTS-S13 activity, may predict relapse risk
Treatment of HUS

- Plasma Exchange
- Dialysis
- Steroids
- In refractory case may consider Eculizumab, Rituximab (esp CNS), N-acetyl cysteine

Henoch-Schoenlein Purpura

- IgA mediated multisystem condition
- Peak years in children and ~6\textsuperscript{th} decade
- Palpable purpura
- Polyarthalgias
- Abdominal pain, intussusception much more common in children vs adults
- Respiratory involvement w/ hemoptysis can be seen
HSP (2)

- Renal involvement more common in adults vs children
- Hematuria, nephrotic syndrome, AKI
- Renal involvement portends a poor prognosis as to full recovery from HSP
- Renal biopsy: +IgA on immunofluorescence (diagnostic) also may show crescents and ATN
HSP (3)

- May follow a bacterial or viral infection
- Skin biopsy shows leukocytoclastic vasculitis and IgA deposition
- Renal Biopsy: +IgA deposition on immunoflourescence
Mesangioproliferative GN
IgA
Treatment of Renal HSP

- Limited clinical trials in adults
- Adequate fluid status
- NSAIDs for non-renal HSP
- Cyclosporine and Plasma exchange may benefit
- Immunoglobulin
- Steroids:
  - May reduce duration of abdominal pain and risk of intussusception, decrease risk associated with GI procedures, rate of recurrence and renal involvement

Indications for Dialysis

1. Volume overload, refractory to diuretics
2. Symptomatic Uremia
3. Electrolyte Abnormalities - i.e. Hyperkalemia
4. Severe Acid-Based Abnormalities
5. Toxin Removal
Renal Replacement Therapy in Acute Kidney Injury

• In critically ill patient, Continuous Renal Replacement Therapy (CRRT) is preferred over intermittent RRT, especially those with hemodynamic instability, acute brain injury or other causes of increased intracranial pressure

• Avoid subclavian catheters, if at all possible

Toxins Removed by Dialysis

- Aspirin
- Lithium
- Theophyllin-to some degree
- Digoxin-to some degree
- Ethylene Glycol
- Methanol
- Isopropyl Alcohol