Acute Kidney Injury
Identification, management, and prevention in the general public

Deborah H. Brooks MSN, ANP-BC, CNN, CNN-NP
brooksdh@musc.edu
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Objectives
At the completion of this activity, the learner should be able to:

• Define acute kidney injury (AKI)
• Recognize AKI and formulate a plan for diagnosis and management
• Discuss treatment options for AKI

Take home message
• AKI can be subtle
• AKI needs to be treated as soon as it’s suspected
• Creatinine is not stable in AKI so one number isn’t enough
• Treat hypertension
• Treat diabetes
• Work on lifestyle: diet, exercise, smoking
• Refer for nephrology consult as needed
Kidney disease definitions

- **AKI** – Acute kidney injury (acute renal failure ARF reserved for severe injury requiring RRT)
- **CKD** – Chronic kidney disease (permanent changes in kidney function. Diagnosed with less than 60% function OR chronic lab or imaging studies revealing disease)
- **ESRD** – End stage renal disease (end stage kidney disease). Insufficient kidney function to sustain life.
- **RRT** – Renal replacement therapy (KRT – kidney replacement therapy)
- **Transplantation** – Living or nonliving donation
Classification of CKD: this is not AKI

<table>
<thead>
<tr>
<th>Stage or GFR category</th>
<th>GFR ml/min</th>
<th>Severity</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (G1)</td>
<td>&gt;90</td>
<td>Normal</td>
<td>Screen &amp; treat risk</td>
</tr>
<tr>
<td>2 (G2)</td>
<td>60-89</td>
<td>Mild decrease*</td>
<td>Diagnose &amp; treat</td>
</tr>
<tr>
<td>3a (G3a)</td>
<td>45-59</td>
<td>Mild to moderate</td>
<td>Treat comorbidities</td>
</tr>
<tr>
<td>3b (G3b)</td>
<td>30-44</td>
<td>Moderate to severe</td>
<td>Consider referral to nephrology</td>
</tr>
<tr>
<td>4 (G4)</td>
<td>15-29</td>
<td>Severe decrease</td>
<td>Prepare for KRT or transplant</td>
</tr>
<tr>
<td>5 (G5)</td>
<td>&lt;15</td>
<td>Kidney failure</td>
<td>KRT, transplant, or death</td>
</tr>
</tbody>
</table>

GFR: ml/min/1.73 m²
KRT: kidney replacement therapy

*May be normal for age

NKF, 2009; KDIGO, 2012

Acute Kidney Injury (AKI)

- AKI is a major risk factor for developing chronic kidney disease (CKD)
- Acute tubular necrosis (ATN) accounts for ~3% of ESRD causes
- 2011 UN recognized kidney disease is a major health burden
- Healthy People 2020 initiatives includes kidney disease. Goal is 10% increase in patients with AKI who have medical f/u 6 months after diagnosis.
- Prevention and early recognition are key factors in CKD and AKI.

AKI in the US

- AKI new hospitalizations have declined from 2012 to 2013
- Probability of recurrent AKI hospitalization within 2 years is 48% for age ≥66 with AKI hospitalization (2011)
- If age ≥66, in hospital mortality if 9.5% with initial AKI (2013)
- Less than ½ of AKI hospitalizations age ≥66 are discharged home (2013)
- Trend data found higher AKI-D [requiring dialysis] in 6 hospital diagnoses (Hsu)
  - Septicemia
  - Hypertension
  - Respiratory failure
  - Coagulation/hemorrhagic disorders
  - Liver disease
  - Shock
- The increase of AKI-D was not seen in procedures & surgeries

2011 UN, 2013; Hsu et al, 2015

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2011 UN, 2013; Hsu et al, 2015
AKI in the US

- Currently the FDA does not recognize AKI as an end point for clinical trial registration (Grams et al, 2016)
- 30-40% decline in eGFR as surrogate endp’t for ESRD might help with prevention/treatment trials
- After discharge for AKI
  - < 20% of patients see a nephrologist within a year
  - < 5% see a nephrologist if no preexisting CKD or DM is present

Kidney trivia worth remembering

- Kidneys receive 25% of cardiac output every minute
- Kidney maintains autoregulation if SBP ~>65mm Hg
- Liver detoxes and kidneys eliminate
- AKI is common and potentially treatable. Time is of the essence.
- Patients with an episode of AKI have an increased mortality regardless of AKI type/length.
- About 30% of patients who recover from AKI are at risk for CKD, CV events or death.

Renal Basics

- Kidneys are 1% of body weight and use 20-25% of the oxygen.
- 25% of the cardiac output is delivered to the kidneys each minute
- 1000 to 1200ml of blood go through each glomeruli of each nephron every minute (~2 water bottles; ~600ml in regular store brand water bottle)
- Equals 650 ml of plasma (blood cells cannot be filtered)
- 1/5 of this goes through the renal tubules. (130 ml of filtrate)
- The entire plasma volume is filtered 60X a day or 180 liters of water per day. (304.6 water bottles per day)
- Not all of the filtered material is excreted.
- Normal urine output = 0.5ml/kg body weight/hr
- 30 to 40 ml per hour for an adult
- 720 ml to 960 ml per day from 180 liters of water per day of filtered fluid
  - results in 1.21 to 1.62 water bottles of urine per day
AKI Definition

Broad clinical syndrome includes
- Acute kidney diseases e.g. interstitial nephritis, glomerulonephritis, vasculitis
- Nonspecific conditions e.g. ischemia, toxic injury
- Extrarenal causes e.g. obstruction, prerenal azotemia
- Can have more than one cause/condition

AKI Categories

- **Pre renal** – decreased perfusion (volume, drugs, stenosis)
- **Intra renal** – damage/injury to glomerulus, blood vessels, tubules, interstitium
- **Post renal** – obstruction in urine flow (stones, cysts, tumor etc)

Intrarenal

- Glomerular disease
- Acute tubular necrosis (ATN) – (most common injury) ischemia, toxic agents: drugs, poison, myoglobin, tumor products
- Acute interstitial necrosis (AIN) – drugs, herbs, autoimmune, myeloma, sarcoid
**Defining AKI - RIFLE**

Acute Dialysis Quality Initiative group (ADQI)
- Changes occur in 7 or less days
- No baseline may be available so an estimated GFR is used (not validated in AKI – just CKD)
- Creatinine is unstable thus unreliable marker

<table>
<thead>
<tr>
<th>RIFLE</th>
<th>creatinine</th>
<th>GFR</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk</td>
<td>1.5 times baseline</td>
<td>25% ↓ GFR</td>
<td>&lt;0.5mL/kg/hr X6hr</td>
</tr>
<tr>
<td>Injury</td>
<td>2 times baseline</td>
<td>50% ↓ GFR</td>
<td>&lt;0.5mL/kg/hr X12hr</td>
</tr>
<tr>
<td>Failure</td>
<td>3 times baseline</td>
<td>75% ↓ GFR</td>
<td>&lt;0.3mL/kg/hr X24hr OR anuria 12hrs</td>
</tr>
<tr>
<td>Loss</td>
<td>Need RRT &gt; 4wks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESRD</td>
<td>Need RRT &gt; 3 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Defining AKI - AKIN**

AKIN – Acute Kidney Injury Network (international group)
- Modified RIFLE criteria
- Diagnostic: abrupt change within 48 hours (even small changes are seen)
- Limitation: requires 2 creatinine values in 48hr

<table>
<thead>
<tr>
<th>Caveats before applying criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ creatinine &gt;0.3mg/dl from baseline</td>
</tr>
<tr>
<td>&gt;50% ↑ creatinine</td>
</tr>
<tr>
<td>Oliguria &lt;0.5mL/kg/hr &gt;6hrs</td>
</tr>
</tbody>
</table>

**Defining AKI - KDIGO**

KDIGO - Kidney Disease: Improving Global Outcomes
- Combines RIFLE and AKIN criteria

**Definition**
- ↑ creatinine >0.3mg/dl from baseline in 48 hours OR
- ↑ creatinine 1.5 times from baseline in past 7 days OR
- Oliguria <0.5mL/kg/hr >6hrs

**Staging (if serum and urine don’t match, pick the higher stage)**

<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 X baseline or &gt;0.3mg/dl increase</td>
<td>&lt;0.5mL/kg/h 6-12hr</td>
</tr>
<tr>
<td>2</td>
<td>2-2.9 X baseline</td>
<td>&lt;0.5mL/kg/hr &gt;12hr</td>
</tr>
<tr>
<td>3</td>
<td>3 X baseline OR ↑ creatinine if &gt;4mg/dl or RRT OR ↓ GFR &lt;35m/1min if &lt;18yrs OR anuria for &gt;12hr</td>
<td>&lt;0.3mL/kg/h &gt;24 hr OR anuria for &gt;12hr</td>
</tr>
</tbody>
</table>
Examples of AKI – subtle
(taken directly from KDIGO pg 28)

<table>
<thead>
<tr>
<th>Ex</th>
<th>Baseline Scr mg/dl</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 7</th>
<th>&gt;50% ?</th>
<th>&gt;0.3mg in &lt;48hr ?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1</td>
<td>1.3</td>
<td>1.2</td>
<td>1.5</td>
<td>2</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>B</td>
<td>1</td>
<td>1.1</td>
<td>1.2</td>
<td>0.4</td>
<td>0.7</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>C</td>
<td>0.5</td>
<td>0.6</td>
<td>0.7</td>
<td>0.4</td>
<td>0.7</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>D</td>
<td>1</td>
<td>1.1</td>
<td>1.2</td>
<td>1.3</td>
<td>0.4</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>E</td>
<td>1</td>
<td>1.3</td>
<td>1.5</td>
<td>1.8</td>
<td>2.2</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>F</td>
<td>?</td>
<td>3</td>
<td>2.6</td>
<td>2.2</td>
<td>1</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>G</td>
<td>?</td>
<td>3.1</td>
<td>3</td>
<td>2.9</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

Would have been missed if not labs were drawn.

AKI confounding events

• Different reporting labs – Scr has been standardized
• Drug interference – cephalosporin, trimethoprim, cimetidine (inhibition of tubular secretion so Scr increases but no change in eGFR)
• Dilution from large quantities of fluid resuscitation
• Massive blood transfusions may mimic donor’s Scr
• Rhabdomyolysis with increased Scr from muscle breakdown
• Muscle wasting e.g. advanced liver disease

Possible causes

• History is #1 important – what is different? Do they have CKD?
• Community acquired or hospital acquired AKI?
• Really important to treat the underlying disease if possible.
• Nephrotoxic drugs contribute to 20-30% of AKI.

<table>
<thead>
<tr>
<th>Community</th>
<th>Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>OTC meds, herbs, supplements,</td>
<td>Meds, procedures</td>
</tr>
<tr>
<td>recreational drugs</td>
<td></td>
</tr>
<tr>
<td>Past medical history with risk of</td>
<td></td>
</tr>
<tr>
<td>AKI, Travel exposure: disease,</td>
<td></td>
</tr>
<tr>
<td>animal, food</td>
<td></td>
</tr>
</tbody>
</table>
Diagnostic tests - standard

Laboratory
- BMP
- CBC with differential
- Urinalysis with sediment
  - Prerenal – Normal
  - Intrarenal – RBC casts, cellular debris
  - Post renal – normal unless infection present

Imaging
- Renal ultrasound – small size indicates CKD
  - Normal cm size: Left 11.2-10.5 (9.5); right 10.9-10 (9)
  - (70 years age – loss of parenchyma)

Urine casts

- Hyaline cast
- Granular cast
- Fatty cast
- Cellular cast
- Waxy cast

Urine Casts

- Hyaline cast
  - CKD, pyelonephritis
- Granular cast
  - Advanced CKD
- Leukocyte
  - Pyelo, GN, interstitial nephritis, inflammation
- Erythrocyte (red cell)
  - Glomerulonephritis, Contact sports

http://bdmeditech.blogspot.com

www.aafp.org/afp/2005/0315/p1153.html
Clinical utility of diagnostic tests for AKI management

- Urine tests – urinalysis, sediment, sodium, creatinine, urea, eosinophils, total protein, and protein electrophoresis (UPEP)
- Blood tests – anti-neutrophil cytoplasmic antibody (ANCA), anti-glomerular basement membrane (anti-GBM) antibody, cryoglobulins, complement component 3 (C3), complement component 4 (C4), free light chains, and protein electrophoresis (SPEP)
- Radiology tests – renal ultrasound and computerized tomography of the abdomen/pelvis (CTAP)
- Pathology test – renal biopsy

Combine with history and physical for best results

Case study – s/p acute illness

- 35yo female sees PCP for fatigue X2 weeks.
- URI 3 weeks ago otherwise good health.
- Exam is unremarkable.
- CBC and BMP are WNL. Serum creatinine 1.1mg/dl. 6months ago was 0.6mg/dl.
- Are you concerned? **YES** [Scr is double baseline.]
- Is there a diagnosis? **NOT YET** [is this an acute or chronic change?]
- What is the probable cause? **Meds, dehydration**
- What is the recommended treatment?
  - Stop any NSAIDS, ask about herbal products and stop them.
  - Have her hydrate with po fluid.
  - Repeat bmp labs including urinalysis and urine sodium and protein and creatinine.

Case study: AKI – why?

- 74 yo female PMH DM, HTN, dyslipidemia
- Presents with fatigue, not feeling well, less urine output

<table>
<thead>
<tr>
<th>Serum labs</th>
<th>Baseline</th>
<th>Hospitalized</th>
<th>Recovered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>1.7</td>
<td>8.5</td>
<td>1.6</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.7</td>
<td>5.8</td>
<td>3.1</td>
</tr>
<tr>
<td>CO2</td>
<td>23</td>
<td>10</td>
<td>21</td>
</tr>
<tr>
<td>eGFR</td>
<td>36</td>
<td>5</td>
<td>21</td>
</tr>
</tbody>
</table>

Urine sodium is **60**

Fractional excretion of sodium (FENa) 4%
Urine sodium: fractional excretion of sodium (FENa)

- Prerenal or ATN?
- Is Na being conserved or eliminated?
- <1% usually prerenal: Na reabsorbed in response to low glomerular flow
- 1-2% can be either pre or intrarenal
- >2% usually ATN: sodium wasting due to tubular damage (early) OR later ATN, well hydrated, fewer nephrons & >FENa is appropriate response
- Urine sodium is 60 - >20 is intrarenal
- Fractional excretion of sodium 4% - >1% intrarenal

\[
\text{FENa} = \left( \frac{\text{UNa} \times \text{SCr}}{\text{SNa} \times \text{UCr}} \right) \times 100
\]

\[
\begin{array}{|c|c|c|c|}
\hline
\text{UNa} & \text{SNa} & \text{UCr} & \text{SCr} \\
60 & 137 & 93 & 8.5 \\
\hline
\end{array}
\]

- [UNa X SCr/SNa X UCr] X 100 = 4%

Caveats for urine sodium

- In unstable patient one Scr is not sufficient to establish true GFR; e.g. septic shock Scr 1 but now oliguric; is 1 accurate?
- FENa more reliable than urine sodium. UNa varies with urine volume. FENa measures sodium handling by the glomerulus.
- FENa <1% more reliable in advanced AKI
- Prerenal and FENa >1%
  - Underlying CKD delays initial Na conservation response in prerenal event or sudden decrease in dietary sodium or active diuretic therapy
- Intrarenal AKI and FENa <1%
  - Postischemic ATN with some well preserved nephrons
  - ATN in addition to chronic prerenal disease e.g. heart failure
  - Nonoliguric ATN w/ persistent ischemia but less severe disease
  - Acute GN or vasculitis – look at urine sediment e.g. RBC, protein
  - Acute interstitial nephritis (nonoliguric & not severe) – look for urine WBC/casts, offending drug, eosinophilia

Back to the case study: AKI?

- Additional history: Naproxen daily for “several years” and several times a day recently for pain.
- Admitted for dehydration, metabolic acidosis, and hyperkalemia
- AKI with ATN 2nd to naproxen
- ANA, C3, C4, ANCA all negative
- Therapy: IVF with bicarbonate, strict I&O (short term catheter warranted), PO kayexelate, renal ultrasound n’l 10.2/10.4, discontinue NSAIDs
- Course: Scr decreased to 4.2 day 4; 2.6 day 6
- Long term: control b/p, DM, weight control, avoid NSAIDs

NSAIDs inhibit prostaglandins (they dilate afferent arteriole). Suppression can cause kidney ischemia from ↓ renal blood flow.
Case study - contrast dye

- 52 yo female with baseline Scr 1.3-1.4 (eGFR 44ml/min).
- Renal ultrasound reveals multiple renal cysts with one 9.5 X 8 X 8cm.
- MRI not possible due to surgical clips
- Contrast CT recommended
- What preparation is needed?

Preventing contrast induced (CI)-AKI

- Assess for risks – preexisting kidney dysfunction (CKD or AKI)
- eGFR < 60 ml/min per 1.73m² (<45 may be acceptable)
- Use urine protein dipstick if no Scr available; if it’s negative and no history of disease can estimate that Scr will be <2
- Unstable diabetes
- CHF
- Older age
- Volume depletion
- Use of nephrotoxic agents

Avoiding contrast induced nephropathy - CIN

- What is the baseline kidney function?
  - <30ml/min/1.73m² avoid contrast
  - 30-45ml/min/1.73m² hydrate before
  - >45ml/min/1.73m² use contrast in lowest dose possible
- What risks does the patient have?
- Are there alternative studies?
  - Outpatient
    - If eGFR <30ml/min per 1.73m² recommend creatinine within 7 days of having study to establish a baseline.
    - Everyone hydrate with 500-1000ml fluid 24 hr prior to study
  - ED/Inpatient
    - Obtain creatinine before scheduling contrast study.
    - 3ml/kg/hr X 1hr pre and post or 1ml/kg/hr X 6hr pre/post – monitor output, vs, lungs etc.
back to our case study....

avoiding CIN

- 52 yo female with baseline Scr 1.3-1.4 (eGFR 44ml/min).
- Renal ultrasound reveals multiple renal cysts with one 9.5 X 8 X 8cm.
- MRI not possible due to surgical clips
- Contrast CT recommended
- What preparation is needed?
  - Oral hydration 24 hours before – 1000ml
  - Hold NSAIDS
  - Hold ACE/ARB/renin inhibitor meds (not validated)
  - Evaluate fluid status – may need to hold diuretic
  - Hydrate after study
  - Repeat bmp in 2 days

Colloid or isotonic saline?
Correcting hemodynamic instability

- Albumin appears to be renoprotective but not more effective than isotonic saline. Saline may require more fluid.
- High molecular substitution starch (HES) used for albumin substitute may impair coagulation (↓VIII, von Willenbrand factor). Hypertonic HES may be have higher AKI rate.
- Goal is to achieve MAP >65mm Hg and urine output ≥0.5ml/kg/hr

Removal of solutes and fluid

- Diffusion – movement of solutes from higher to lower concentration.
- Convection – movement of solutes by force of water across the membrane.
- Adsorption – removal of solutes by binding to a membrane surface.
- Ultrafiltration (UF) – movement of water through a membrane under pressure.
Therapies for AKI: Dialysis

- **Hemodialysis (IHD)**—Intermittent therapy usually for 3-4 hours
  - Advantages are quicker removal of solutes especially potassium
  - More rapid balance of acid/base disturbances
  - More rapid fluid removal
  - Uses diffusion and convection for clearances
  - Dialysate includes Na, K, glucose, magnesium, Ca, bicarbonate
- **SLOW Efficient Daily Dialysis (SLEDD)**
  - Can done over longer time so is slower with less rapid fluid shifts
  - Clearance is by diffusion
  - Uses high flux dialyzers with higher clearances
  - Less hypotension

Alcohol and drugs

Kidney disease can be worsened with combinations and with additional diseases e.g. HIV, hepatitis C. AKI can become CKD.

- **Ethanol**—electrolyte d/o hypomagnesemia, hypokalemia, and dehydration
- **Heroin**—glomerular disease although may be related to other substances in the drug
- **Cocaine**—AKI from malignant hypertension and accelerated atherosclerotic changes. Look for serum eosinophils.
- **Methamphetamine**—AKI from accelerated hypertension
- **Ecstasy & stimulants** e.g. bath salts—AKI (ATN) 2nd to rhabdomyolysis (from seizures, repetitive muscle activity or toxic effect of drug), drug induced vasculitis, hyponatremia (death).

Treatments—hydration and antihypertensives e.g. ACE or ARB

Drug overdose and poisoning

Extracorporeal therapy added if supportive care is not sufficient to prevent tissue damage or death. Not used if endogenous metabolism and excretion is faster than exogenous care, e.g. cocaine.

- **Peritoneal dialysis** is not very effective but is helpful if HD can not be established e.g. small children
- **Hemodialysis** is effective for rapid removal of water soluble substances especially with low molecular weight e.g. salicylates, ethanol, ethylene glycol, lithium. Not effective with lipid soluble drugs e.g. amitriptyline (eliminates only the vascular available portion) or protein bound drug (can remove “free” unsaturated drug).
- **Hemoperfusion** uses cartridge with adsorbent particles e.g. activated charcoal or resins. Good for highly protein bound drugs (competes w plasma protein for the drug) or lipid soluble drugs. Filters are very expensive. Hemodialysis with a high flux (highly permeable) membrane may be available choice.
**Acute therapy: CRRT**  
Continuous Renal Replacement Therapy

- **Uses**
  - Acute kidney injury
  - Septic, hypotension, fluid overload, ARDS, brain hemorrhage, cerebral edema
  - Central catheter for access
- **Types**
  - SCUF
  - CVVH
  - CVVHD
  - CVVHDF

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**SCUF – Slow Continuous UltraFiltration**

- 8-12 hours
- Used for volume overload, HF, hypotension, sepsis
- No uremia present
- No replacement fluid, no dialysate
- Can be combined with other therapy without additional access e.g. ECMO

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**CVVH – Continuous Veno Venous Hemofiltration**

- Acute kidney injury
- 24 hr at 25ml/kg/hr
- Uses replacement fluid either pre (clotting risk) or post (solute lab accuracy) pump.
- Convection removes solutes.
- Ultrafiltration removes fluid.
CVVHD – Continuous Veno Venous Hemodialysis

- Uses dialysis & ultrafiltration (UF)
- Dialysate added to filter for countercurrent to increase diffusion of solutes (co-current flow with high urea and small ped to avoid disequilibrium)
- No replacement fluid
- Effluent bag has UF & dialysate

CVVHDF – Continuous Veno Venous Hemofiltration

- Dialysis & convection
- Dialysate is countercurrent
- Replacement fluid added, either pre (clogging risk) or post (solute clearance) pump.
- Diffusion removes small molecules
- Convection removes middle size e.g. cytokines

Nursing considerations: CRRT

- Risk of hypothermia – keep patient warm
- Monitor for infection – use aseptic technique
- Assess for bleeding – need close anticoagulation monitoring especially if on other therapy e.g. warfarin etc
  - Saline flushes
  - Heparin (avoid in HIT [heparin induced thrombocytopenia] due to decreased platelets and severe clotting)
  - Citrate pre dialyzer; calcium replacement post dialyzer
- Less risk of cerebral edema and altered mental status
- At risk for emboli – from procedure and disease process
- Medication doses need adjustment
- Immobility risk – ROM, pulmonary hygiene, position changes
Therapies for AKI: TP

- Therapeutic Apheresis (TP) – used to separate blood components
  - Plasmapheresis – plasma from whole blood w/ infused cells, fluid, and/or plasma
    - Hemolytic uremic syndrome (HUS) – platelets removed
    - Antiglomerular basement membrane (GBM) disease – if already on dialysis, function unlikely to return. Used for pulmonary hemorrhage
    - Antineutrophil cytoplasm antibody (ANCA) associated vasculitis e.g. small vessel vasculitis with pauci-immune rapidly progressive glomerulonephritis (RPGN); remove antibodies
    - Multiple myeloma – light chain cast nephropathy (removes paraproteins); may be combined with chemotherapy. HD also an option.
    - Antiglomerular basement membrane (GBM) disease – if already on dialysis, function unlikely to return. Used for pulmonary hemorrhage
    - Antineutrophil cytoplasm antibody (ANCA) associated vasculitis e.g. small vessel vasculitis with pauci-immune rapidly progressive glomerulonephritis (RPGN); remove antibodies
    - IgA nephropathy & Henoch-Schönlein purpura (HSP) – similar to ANCA vasculitis, may combine with immunosuppressive therapy
    - Cryoglobulinemia - remove large immune complexes e.g. Hep C
    - Pre or post transplant to remove antibodies – e.g. FSGS

TP considerations

- Plasmapheresis – plasma from whole blood w/ infused cells, fluid, and/or plasma
- Thrombocytapheresis – platelets removed for thrombocytopathy
- Leukapheresis – WBC removal e.g. leukemia or stem cell collection
- Erythrocytapheresis – RBC removal and replacement e.g. sickle cell; removal e.g. polycythemia vera
- Need an accurate diagnosis to determine type of TP, fluid replacement, access option
- Treatment based on volume rather than time
- Complications – volume changes, hypocalcemia from citrate binding, hemolysis
- Designate can order procedure and monitoring

Case study

- 52 yo male
- HTN, DM
- Baseline creatinine 1.3-1.5 for 7 years
- Tired – no illnesses, no bleeding
- electrolytes and urinalysis
- Medications
Increased creatinine

RBCs in urine

AKI?

- Look at meds: lasix, aldactone, benazepril, amlodipine. Is he dehydrated? Is it glomerular (FSGS)? Is it a drug interaction?
- IV contrast exposure? NO
- NSAID usage? NO

PLAN:
- Hold ACE, aldactone, lasix
- Bolus 1L fluid in ED
- Admitted and IV NS at 150/hr
- If no improvement in creatinine will likely need renal biopsy. Hold any heparin in case biopsy warranted.
Renal ultrasound

• No renal artery stenosis
• No hydronephrosis
• 10cm and 11cm kidneys - normal
• Echogenicity indicating medical renal disease

Labs improve: d/c home

<table>
<thead>
<tr>
<th>Date</th>
<th>Creatinine (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/25/15</td>
<td>5.26</td>
</tr>
<tr>
<td>11/26/15</td>
<td>5.7</td>
</tr>
<tr>
<td>11/26/15</td>
<td>5.6</td>
</tr>
<tr>
<td>11/26/15</td>
<td>4.8</td>
</tr>
<tr>
<td>11/27/15</td>
<td>4.3</td>
</tr>
</tbody>
</table>

• DC plan is scheduled t/u with renal
BUT he is home a few days and ........
• Presents to ED with new onset SOB and hemoptysis
• Creatinine is 6
• Admitted
• Labs indicate Positive antineutrophil cytoplasmic antibody [+ANCA]
Myeloperoxidase antibody [MPO]

Is this a TP candidate?

• CXR reveals opacities – infection vs hemorrhage
• Diagnoses – autoimmune disease (ANCA associated vasculitis – microscopic polyangiitis)
• Differential includes other ANCA vasculitis e.g. GPA (granulomatosis w polyangiitis – Wegner’s), Goodpasture’s; infections (TB); inflammatory diseases such as Sarcoidosis (positive family history)
• Pulmonary consult: acute alveolar hemorrhage related to his rheumatologic process – treat for infection until diagnosed
• Rheumatology: microscopic polyangiitis; steroids & immunosuppression
• Nephrology: biopsy, supportive dialysis, apheresis
Biopsy

2 diagnostic findings:
Focal necrotizing glomerulonephritis, few crescents and mild chronic interstitial changes. [new]
Moderate diabetic glomerulopathy changes. [established]

Normal glomerulus

Crescentic GN hemoptysis and hematuria
Treatment plan

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/7/16</td>
<td>Plasmapheresis X 6 treatments</td>
</tr>
<tr>
<td>12/9/16</td>
<td></td>
</tr>
<tr>
<td>12/11/16</td>
<td></td>
</tr>
<tr>
<td>12/13/16</td>
<td></td>
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<tr>
<td>12/15/16</td>
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<td>12/17/16</td>
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<tr>
<td>12/25/16</td>
<td></td>
</tr>
<tr>
<td>12/27/16</td>
<td></td>
</tr>
</tbody>
</table>

Hemodialysis X 2
Starts rituximab 12/17 X 4 weeks
Starts prednisone taper

Novel urinary biomarkers

Diagnoses of AKI remains problematic for peds and adults
May detect, diagnose, and monitor AKI
May predict CKD progression in peds and adults

- **NGAL** - neutrophil gelatinase-associated lipocalin – indicates acute inflammatory changes and decreases with time
- **KIM-1** – kidney injury molecule-1 – stays elevated and indicates chronic fibrotic changes
- **L-FABP** – liver type fatty acid-binding protein – appears to be elevated after AKI; significance not completely known
- **IL-18** – interleukin 18 – inflammatory marker after AKI

Cooper et al., 2016
Fluid overload & mortality in CKD

Current Research
- Fluid overload may be an independent risk for all cause mortality & CV morbidity in CKD 4/5
- Fluid overload was >7% extracellular fluid (measured by body composition monitor)
- Group had lower eGFR, more HTN, DM, Cerebral VD
- Used more diuretics, CCB, BB
- Factors to consider: sodium intake, meds

Heart Kidney connection

Current Research
Heart disease is the major cause of death in CKD
- Elevated cardiac markers (troponins & NT-proBNP) even without evidence of HF were associated with rapid decline in kidney function.
- Provide opportunity to identify subclinical CVD & intervene to control CKD
- Use of cardiac markers may guide therapy to prevent cardiac disease and protect kidneys

Statin and AKI

Current Research
- Meta analysis (14 RCT, 1689 pt) indicates short term (<7 day) high dose atorvastatin (40-80 v 10-20mg) before CAG and PCI procedures with contrast media may prevent acute kidney injury especially in eGFR>60ml/min
- Need more and longer f/u studies for other clinical outcomes.
Avoid Nephrotoxic Substances

- NSAIDs (COX-2 inhibitors, ibuprofen) are potentially nephrotoxic
- Acetaminophen (Tylenol) better choice
- Avoid other nephrotoxic substances e.g. intravenous dye, aminoglycosides, amphotericin B, cyclosporin, tacrolimus, lithium
- ACE inhibitors/ARBs need monitoring
  Adjust doses or use drugs for short time frame.

Medications - RAAS

<table>
<thead>
<tr>
<th>RAAS</th>
<th>Action</th>
<th>Result</th>
<th>Benefit</th>
<th>Monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEi</td>
<td>Block conversion of angiotensin I to</td>
<td>Relaxed blood vessels including afferent</td>
<td>Less proteinuria; ↓ rate of kidney decline</td>
<td>Angioedema, ↑ creatinine &amp;</td>
</tr>
<tr>
<td></td>
<td>angiotensin II in lungs</td>
<td>arteriole</td>
<td></td>
<td>potassium, teratogenic</td>
</tr>
<tr>
<td>ARB</td>
<td>Block angiotensin II AT1 receptors in kidney</td>
<td>Blocks aldosterone from adrenal glands</td>
<td>Less proteinuria; ↓ rate of kidney decline</td>
<td>↑ creatinine &amp; potassium,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>teratogenic</td>
</tr>
<tr>
<td>Renin</td>
<td>Release of renin from juxtaglomerular cells</td>
<td>-conversion of angiotensin -ogen (liver) to</td>
<td></td>
<td>↑ creatinine &amp; potassium;</td>
</tr>
<tr>
<td>inhibitor</td>
<td></td>
<td>angiotensin I</td>
<td></td>
<td>don’t combine w/ ACE/ARB;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>teratogenic</td>
</tr>
<tr>
<td>Aldosterone (potassium sparing)</td>
<td>Exchange Na for K; blocks reabsorption of Na &amp; H₂O</td>
<td>↓plasma aldosterone levels</td>
<td>Diuresis; augment ACE/ARB</td>
<td>↑ potassium, gynecomastia</td>
</tr>
</tbody>
</table>

Medications - Diuretics

<table>
<thead>
<tr>
<th>Diuretics</th>
<th>Action</th>
<th>Result</th>
<th>Benefit</th>
<th>Monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazide e.g. HCTZ, chlorthalidone</td>
<td>Inhibits DCT Na/Cl resorption</td>
<td>Diuresis</td>
<td>Augments RAAS</td>
<td>↑ uric acid; ↑ glucose; ↑ potassium</td>
</tr>
<tr>
<td>Loop e.g. furosemide</td>
<td>Inhibits Na/Cl resorption in entire glomerular loop</td>
<td>Diuresis, lower b/p</td>
<td>use if eGFR &lt;40ml/min; augments RAAS</td>
<td>↓ potassium, ↑ creatinine, Electrolyte imbalances</td>
</tr>
<tr>
<td>Potassium sparing e.g. spironolactone, eplerenone</td>
<td>Blocks mineralocorticoid receptors in DCT to prevent Na resorption</td>
<td>↓ Na/water resorption</td>
<td>Can use with other diuretics</td>
<td>↑ potassium, ↑ creatinine; use w/ caution w/ RAAS</td>
</tr>
</tbody>
</table>

JNC VII, JAMA, 2003; Kalatzisis & Bakris, 2011
## Medications – Blockers (Antagonists)

<table>
<thead>
<tr>
<th>Blockers</th>
<th>Action</th>
<th>Results</th>
<th>Benefits</th>
<th>Monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium – non-Dihydropyridine e.g. diltiazem, verapamil</td>
<td>Inhibits Ca⁺⁺ ion entry into arterial vascular smooth muscle and myocardium</td>
<td>↓ PVR, dilate</td>
<td>Less proteinuria, arrhythmia control</td>
<td>Heart block 2nd or 3rd</td>
</tr>
<tr>
<td>Calcium – dihydropyridine e.g. amlodipine, nifedipine</td>
<td>Inhibits Ca⁺⁺ ion entry into vascular smooth muscle &amp; myocardium</td>
<td>SBP control w/ ↓ systemic vascular resistance</td>
<td>↓ large vessel stiffness especially helpful in elderly</td>
<td>Don’t use as monotherapy w/ proteinuria; peripheral edema common</td>
</tr>
</tbody>
</table>

## Medications – Other antihypertensives

<table>
<thead>
<tr>
<th>Class</th>
<th>Action</th>
<th>Results</th>
<th>Benefits</th>
<th>Monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central alpha adrenergic agonists e.g. clonidine, guanfacine, methyldopa</td>
<td>Counter block sympathetic activity</td>
<td>↓ b/p &amp; pulse</td>
<td>Add on to RAAS or vasodilator; some proteinuria decrease</td>
<td>Don’t use w/ non-di Ca blocker – bradycardia or heart block</td>
</tr>
<tr>
<td>Vasoconstrictor e.g. minoxidil, hydralazine</td>
<td>Dilate peripheral vessels – arterial and venous</td>
<td>Bp lowering but tachycardia</td>
<td>Add on b/p med; use w/ BB</td>
<td>Fluid retention, pericardial effusion, hair growth, lupus syndrome</td>
</tr>
</tbody>
</table>
References


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