Acute Kidney Injury

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Case

- 55 yo male with a h/o diabetes and HTN presents to the ER with sudden onset of shortness of breath, CT angiogram performed which is + for PE. Patient admitted to ICU.

- Creatinine on arrival is 0.9 mg/dL, hospital day #1 is 1.1 mg/dL and on hospital day #2 creat is 1.4 mg/dL.

- Does this patient have AKI?
AKI - Definition

- The Acute Dialysis Quality Initiative (ADQI) was created by intensivists and nephrologists to develop consensus and evidence based guidelines for the treatment and prevention of acute renal failure.

- Recognizing the need for a uniform definition for ARF, the ADQI group proposed a consensus graded definition, called the RIFLE criteria.

- A modification of the RIFLE criteria was subsequently proposed by the Acute Kidney Injury Network, which included the ADQI group as well as representatives from other nephrology and intensive care societies.
AKI-RIFLE Criteria

- **RIFLE CRITERIA** — three graded levels of injury (Risk, Injury, and Failure) and two outcome measures (Loss and End-stage renal disease).
  
  - **Risk** — 1.5-fold increase in the serum creatinine or GFR decrease by 25 percent or urine output <0.5 mL/kg per hour for six hours
  
  - **Injury** — Twofold increase in the serum creatinine or GFR decrease by 50 percent or urine output <0.5 mL/kg per hour for 12 hours
  
  - **Failure** — Threefold increase in the serum creatinine or GFR decrease by 75 percent or urine output of <0.5 mL/kg per hour for 24 hours, or anuria for 12 hours
  
  - **Loss** — Complete loss of kidney function (eg, need for renal replacement therapy) for more than four weeks
  
  - **ESRD** — Complete loss of kidney function (eg, need for renal replacement therapy) for more than three months
AKI-RIFLE Criteria

- Shortcomings of the RIFLE criteria:

- The "risk," "injury," and "failure" strata are defined by either changes in serum creatinine or urine output. The assignment of the corresponding changes in serum creatinine and changes in urine output to the same strata are NOT based on evidence. The serum creatinine criteria stronger predictor of ICU mortality.

- The change in serum creatinine during acute renal failure does not directly correlate with the actual change in glomerular filtration rate, which alters the assignment of that patient to a particular RIFLE level.

- It is impossible to calculate the change in serum creatinine in patients who present with ARF but without a baseline measurement of serum creatinine.
AKI-AKIN Criteria

- **AKIN DIAGNOSTIC CRITERIA** —

  - Abrupt (within 48 hours) absolute increase in the serum creatinine concentration of $\geq 0.3 \text{ mg/dL}$ from baseline, a percentage increase in the serum creatinine concentration of $\geq 50$ percent, or oliguria of less than 0.5 mL/kg per hour for more than six hours.

  - An absolute change in serum creatinine of $\geq 0.3 \text{ mg/dL}$ is based on data that an 80 percent increase in mortality risk associated with changes in serum creatinine concentration of as little as 0.3 to 0.5 mg/dL.

  - Time constraint of 48 hours is based on data that poorer outcomes were associated with small changes in the creatinine when the rise in creatinine was observed within 24 to 48 hours.

  - Two additional caveats:
    - The diagnostic criteria is valid only after volume status had been optimized.
    - Urinary tract obstruction ruled out if oliguria is the sole diagnostic criterion.
AKI

- Some definitions
  - Azotemia - a build up of nitrogenous wastes
  - Uremia - constellation of sx from build up of uremic toxins
  - Oliguria - uop < 400 cc/day
  - Oligoanuric - uop < 100 cc/day
  - Polyuria - uop > 3 L/day
AKI

- Epidemiology
  - More common in inpatient setting
  - Incidence of 7.2%
  - Most common cause prerenal azotemia
  - Overall mortality was 19.4%
AKI-classification

- Prerenal azotemia - reduced renal blood flow/perfusion pressure
- Intrinsic renal azotemia - direct parenchymal injury
  - Vascular, glomerular, interstitial, tubular
- Postrenal azotemia - obstruction to urine flow
Case

- 58 yo male with h/o HTN and DM presents to the ER with nausea/vomiting, diarrhea.
  - Patients medications include lisinopril, HCTZ, metformin
  - Sodium 132, K 5.5, Cl 113, Hco3 20, Bun 40, Cr 2.0
  - U Na 15 meq/L, Ucreat 100 mg/dL, Uurea 50 mg/dL
  - Renal u/s shows medical renal disease
Juxtaglomerular Apparatus
AKI-prerenal

- Kidneys receive 25% of cardiac output → 0.75 L plasma flow per minute
  - Needed to maintain GFR, renal oxygenation and solute transport

- True intravascular volume depletion - hemorrhage, diuretics, GI loss etc
  - Decreased intravascular volume causes release of renin, vasopressin, catecholamines, endothelin
  - While these hormones act to increase BP to keep organs perfused, they can cause renal vasoconstriction
  - Therefore if they are unable to normalize BP, they can be detrimental
AKI

- Effective circulatory insufficiency- CHF, cardiac disease, cirrhosis, sepsis, autonomic failure,
  - HRS is a classic example- low peripheral resistance, low renal perfusion, UNa<10 meq/L, Uosm 100mosm> than plasma
  - Will need to rule out true hypovolemia

- Renal artery disease- RAS

- Altered intrarenal hemodynamics-
  - Afferent vasoconstriction- NSAIDs, calcineurin inhibitors, hypercalcemia
  - Efferent vasoconstriction- ACEI/ARB
AKI-Prerenal

- Autoregulation - This capacity can be impaired in
  - the elderly,
  - in those with significant arterial disease or renal artery stenosis,
  - in the presence of volume depletion,
  - in those taking vasodilatory prostaglandin inhibitors (e.g. non steroidal anti-inflammatory drugs [NSAIDs]), cyclooxygenase (COX) inhibitors, angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs)
AKI-Prerenal

- Increased COX2 at macula densa increases renin production
- Limited to severe volume depleted states
- Increased COX2 in Medulla results increases natriuresis
- In volume overload states helps excretion of NaCl
AKI-Prerenal

- Rule out parenchymal disease

- With volume depletion and prerenal disease tubules avidly reabsorb water and sodium

- Therefore urine UNa will be lower than 20meq/L and urine Osm will be high

- FENa = UNa x Scr/SNa x Ucr X100  FENa <1%

- In patients on diuretics
  - FEUrea = Urea x Scr/Surea x Ucr X100  FEUrea < 35%

- Easier formula is renal failure index
  - UNa X (Pcr/Ucr) X100  <1% suggestive of prerenal state

- Persistent prerenal azotemia can lead to ischemic ATN
Case

- 68 yo with h/o peripheral vascular disease, DM, HTN admitted for STEMI s/p PCI. Two weeks later presents with oliguria
  - Sodium 135, K 5.0, Cl 110, Hco3 19
  - BUN 50/Creat 3.0 (baseline normal)
  - Low C3/C4
  - + urinary eosinophils
  - UA bland
  - Urine sodium 50 meq/L, Ucreat 60mg/dL
AKI-Intrinsic-vascular

- Vascular injury (large or medium size)-
  - Thrombosis of the renal artery in a single functioning kidney or with bilateral disease,
  - Embolism from the heart or atherosclerotic plaque in aorta
  - Dissection from trauma or collagen vascular disease
    - Present with flank pain, fever, hematuria and oligoanuria
    - Elevated LDH, urinalysis + for blood
  - large and medium vessel vasculitis
    - Takayasu’s arteritis, Giant cell arteritis
AKI-vascular

- Vascular disease-
  - Embolization of atheroemboli (debris from ulcerated plaques in the aorta, cholesterol) to interlobar, arcuate and interlobular arteries
  - Causes a giant cell reaction in surrounding interstitium,
  - This occurs usually after invasive procedures such as PCI or vascular surgery
  - However, thrombolytic therapy or anticoagulation can precipitate this by disrupting the fibrous cap on an ulcerated plaque
  - Patients usually present with abrupt onset of severe HTN, acute kidney injury, livedo reticularis, digital/limb ischemia, signs of ischemia to other organs

red, non-blanchable (doesn't turn white when pressed) network-pattern (reticulated) in the skin
AKI-vascular

- Lab findings include eosinophilia, eosinophiluria, hypocomplementemia, elevated ESR
- UA is bland
- Differentiate from contrast nephropathy which develops after 48 hrs and peaks within a week and recovers over the next few days
- Cholesterol emboli follows a more delayed onset, rarely recovers, can lead to permanent damage and ESRD
- ? Benefit from steroids, no randomized clinical trials
AKI-vascular

- Arteriole- medium/small vessel damage
  - Polyarteritis nodosa- typically idiopathic can be associated with HepB
  - Presents with severe HTN and kidney injury
  - Diagnosed with renal arteriogram showing beading in the arterial tree
  - It can effect arterial beds in other organs

- Scleroderma - uncontrolled accumulation of collagen and widespread vascular lesions characterized by thickening of the vascular wall and narrowing of the vascular lumen
  - Multiple organs involved, lungs, heart, GI tract, skin
  - Scleroderma renal crisis develops in approximately 10 to 20 percent of patients with the diffuse cutaneous form of systemic sclerosis
  - presents with AKI, severe HTN and flare of dz
  - ACEI are used to treat this entity
AKI-vascular

- Renal vein thrombosis- in setting of significant proteinuria/nephrotic syndrome
  - Usually with membranous nephropathy
  - Loss of anticoagulants (ATIII, PAI) and increased procoagulants (tPA, fibrinogen)
  - AKI via raised intrarenal pressure and reduced perfusion
  - Anticoagulation, thrombolysis, treatment of proteinuria
Case

- 49 yo male with h/o DM, HTN, obesity admitted to the hospital with fever, productive cough. His BP on presentation was 90/60 mmHg.

- Baseline creat 1.1 mg/dL, on presentation had a creat of 2.0UA was bland, FENa 1.5%, FEUrea 45%

- Cessation of BP meds and fluid resuscitation failed to improve his BP

- Creatinine gradually increased to 3.0 and patient was transferred to the ICU on day #3 for pressors.

- Although uop improved with dopamine, creatinine did not improve and patient required 2 hemodialysis sessions for hyperkalemia and uremia

- At this point renal recovery ensued and he did not require any further dialysis
Acute tubular necrosis is the most common form of intrinsic AKI

Accounts for >80% of intrinsic AKI

Divided into

- Ischemic ATN 50%
- Nephrotoxic ATN other half
- Many instances both are present
- All result in tubular cell necrosis
AKI-Tubules

- Ischemic ATN - extension of severe uncorrected prerenal azotemia
- Prolonged renal hypoperfusion causes tubular cell injury which persists even after underlying hemodynamic insult is corrected
- Can be severe enough to cause cortical necrosis (atrophy of renal cortex)
- Various causes
  - Intra-op or post-op hypotension (with vascular or cardiac surgery)
  - Obstructive jaundice increases risk for ischemic ATN
  - Sepsis
  - Severe intravascular volume depletion
  - Cardiogenic shock
AKI-Tubules

- Nephrotoxic ATN
- Via changes in intrarenal hemodynamics, direct toxic effect or both
- Organic and nonorganic substances
  - Heavy metals (lead, cadmium, mercury)
  - Aminoglycosides-pinocytosed back into cells and cause ATN
  - AmphotericinB- destroys cellular membrane through sterol interaction
  - Contrast- by both ischemic and nephrotoxic (causes reactive oxygen species production and osmotic cellular injury)
  - Adefovir/cidofovir/tenofovir- mitochondrial disruption
  - Pigment nephropathy- heme pigment or myoglobinuria (rhabdo) inhibit nitric oxide production, promote reactive oxygen species and reduce renal perfusion
AKI-Tubules

- Crystal deposition in tubular lumens- underlying renal disease and volume depletion predispose to this form of ATN
  - Uric acid nephropathy- tubular obstruction from urate crystals (tumor lysis syndrome)
  - Certain meds
    - Acyclovir- large IV doses
    - Indinavir- volume contraction and urine pH>5.5
    - Foscarnet and methotrexate
    - Large doses of vitamin C (systemic oxalosis)
- Cast nephropathy of multiple myeloma
  - Monoclonal light chains precipitate in the tubular lumen resulting in obstruction and injury
AKI-Tubules

- Osmotic nephrosis
  - Induction of tubular swelling, cell disruption and occlusion of tubular lumen
  - Hyperosmolar substances (sucrose, dextran, mannitol)
    - Filtered and then reabsorbed by the tubules™ cause a water shift given high osmolality
Case

- 56-year-old woman presented with nausea, vomiting, anorexia.
- PMH: chronic GERD, endometriosis, mitral valve prolapse, migraine headache, and well-controlled mild Crohn disease.
- Thirteen days before this presentation, the patient underwent a colonoscopy to evaluate recent abdominal pain and changing bowel habit, 2 doses of oral Fleet Phospho-soda (45 mL each) were administered in the evening before and the morning of the procedure.
- Meds: estrogens, omeprazole, bupropion, atenolol, calcium supplement.
- Physical examination nonfocal, with a blood pressure of 160/75 mm Hg. Laboratory tests: Electrolytes normal, uric acid normal.
- The patient did not have hypertension previously and, 5 months before this admission, her renal function was normal, with a serum creatinine of 0.8 mg/dL.
- The serum creatinine was 3.8 mg/dL and the blood urea nitrogen was 30 mg/dL.
- Urinalysis was normal, CT urogram negative for obstruction.
AKI-Tubules

- Acute phosphate nephropathy (new KID on the block)

- A form of acute kidney injury that is associated with deposits of calcium-phosphate crystals in the renal tubules that may result in permanent renal function impairment. Formation of phosphate crystals within the renal tubules.

- Occurs following the ingestion of oral sodium phosphate laxatives such as C.B. Fleet's Phospho soda and Salix's Visocol taken for bowel cleansing prior to a colonoscopy.

- The risk of this complication is increased with age, dehydration, or in the presence of hypertension or if the patient is taking an ACE inhibitor or angiotensin receptor blocker.

- On bx findings are typical of nephrocalcinosis: diffuse tubular injury with calcium phosphate crystal deposition.
(a) abundant intraluminal and intracellular calcifications in distal tubules. (Hematoxylin and eosin, original magnification × 400.)

(b) A positive histochemical reaction with the von Kossa stain confirms that the tubular concretions are composed of calcium phosphate (original magnification × 400).
AKI-Glomerular

- Glomerular disease can present with AKI
  - RPGN- immune complex, pauci immune and antiGBM disease
    - AKI with active urine sediment (red cell casts, dysmorphic red cells), HTN, edema
  - Thrombotic microangiopathy (HUS/TTP/pre-eclampsia)
    - Endothelial injury, platelet deposition and thrombosis of arterioles and glomerular capillaries
    - Can present with active urine sediment
    - Key features- microangiopathic hemolytic anemia and thrombocytopenia
AKI-Intersitium

- Acute interstitial nephritis
  - Hallmark—presence of cellular infiltrate (lymphocyte, monocyte, eosinophils or plasma cells) and the edema (fibrosis) in the interstitium
  - Glomeruli and vasculature is normal
  - Triad of fever, rash and eosinophilia/eosinophiluria only present in 1/3 (most common cause of eosinophiluria is UTI)
  - Urinalysis may reveal mild proteinuria, leukocyturia, ± hematuria
  - Diagnosis made on bx otherwise follow clinical presentation
  - Galium scan may be of some utility if bx contradicated
  - Steroids can be helpful (shorten course of injury and hasten recovery)  Gonzalez et al. Kidney Int. 2008 Apr;73(8):940-6.
AKI-Intersitium

- Infections can promote AIN
  - Staphylococci, streptococci, mycoplasma, diptheroids, legionella
  - Viral infections such as CMV, EBV, HIV, Hantaan virus, parvovirus, rubeola
  - Rickettsia, leptospirosis, tuberculosis

- Systemic illnesses can cause AIN
  - Sarcoidosis promotes a lymphocytic interstitial nephritis at time associated with noncaseating granulomas
    - Can cause CKD, steroids helpful in decreasing the severity
  - SLE can cause interstitial nephritis in addition to glomerular dz (immune complex deposition in interstitium)
  - Sjogren’s disease
AKI-Intersitium

- Malignancy
  - Malignant infiltration of the kidney (leukemia and lymphoma)
  - Leukemic infiltration of the kidney causes nephromegaly, AKI and sometimes K+ wasting
  - Lymphomas can have distinct nodules in the kidney or diffuse infiltration
  - Lymphomas also cause renal enlargement
  - Chemo and XRT to treat the underlying disease is the treatment
Case

- 70 yo male with poor medical follow-up presents to the ER for fatigue, nausea and abdominal pain.
- PMH: Hypertension, hyperlipidemia, chronic allergies, BPH, OSA
- Meds: HCTZ, lisinopril, benadryl prn, simvastatin
- PSH: none
- Vitals: BP 165/90, P78
- Labs: Sodium 136, K+ 6.0, Cl- 110, Bicarb 18, BUN 80, Creat 5.0
- Previous labs from 3 years ago normal renal function
AKI- Postrenal

- Anatomic obstruction to urine flow
- The process causing postrenal AKI is called obstructive uropathy
- Hydronephrosis - dilation of the urinary collecting system
- For AKI to develop obstruction must effect both kidneys
- Obstruction may be complete (anuria) or partial (varying uop)
- Complete obstruction causes severe AKI with uremic signs/sxs
AKI - Postrenal

- Obstruction can occur anywhere starting at the renal calyces to urethra

- Most common cause of obstruction in the upper urinary tract (above bladder)
  - Stones
  - Retroperitoneal disease

- Most common cause of obstruction in the lower urinary tract (below the bladder)
  - BPH, bladder dysfunction

- History of stone, cancer, flank pain, neurogenic bladder, prostate disease

- Exam - palpable bladder, prostate enlargement
AKI - Postrenal

- Ureterocalyceal obstruction
  - Retroperitoneal disease (tumor, lymph node, fibrosis)
  - Papillary necrosis
  - Nephrolithiasis
  - Fungus balls
  - Blood clots
  - Strictures
    - Infection
    - Granulomatous disease
    - Prior instrumentation
AKI- Postrenal

- Bladder obstruction
  - Stones
  - Blood clots
  - Tumor
  - BPH
  - Functional
    - CVA
    - DM
    - Spinal cord injuries
    - Drugs
    - Neuropathic conditions

- Urethral obstruction
  - Urethral stricture, blood clots
AKI- Postrenal

- Imaging-
  - Ultrasound usually very sensitive/specific except for
    - Acute (<48 hrs) obstruction which does not allow time for urinary system to dilate
    - Superimposed volume contraction
    - Retroperitoneal disease involving the kidneys and ureters which encases the collecting system and blunts dilatation
    - Obese patients and overlying bowel gas can obscure imaging
  - CT urogram in above cases can be considered
  - If CT is negative and obstruction is still suspected then retrograde pyelogram may become necessary
AKI- Postrenal

- Post-void residual
  - volumes of 50 mL to 100 mL constitute the lower threshold defining abnormal residual urine volume.
  - Large PVRs are associated with UTIs, especially in persons at risk, such as children or patients with spinal cord injury or diabetes.
  - Very large PVRs (>300 mL) may be associated with an increased risk of upper urinary tract dilation and renal insufficiency.
**AKI- Postrenal**

- Early recognition and treatment is key as ongoing obstruction causes permanent damage
- Upper urinary tract obstruction is relieved by retrograde ureteral stent placement or nephrostomy tube
- Lower urinary tract obstruction is relieved via foley catheter
- Post-obstructive diuresis can occur specially in patients with bilateral complete obstruction
  - In part physiologic to remove excess sodium and water
  - Disturbed tubular function and tubular abn in water and salt reabsorption can last days or permanently
AKI- Postrenal

- Postobstructive diuresis is defined as diuresis of more than 200 mL/h for at least 2 hours.
- Patients with severe diuresis should receive intravenous fluid replacement in the form of half normal saline at 80% of the hourly urine volume for the first 24 hours, then 50%.