Acute Kidney Injury

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Acronyms

- AKI/ARF – Acute Kidney Injury/Acute Renal Failure
- ATN – Acute Tubular Necrosis
- TGF – tubuloglomerular feedback
- RRT – Renal Replacement Therapy – Dialysis
- SCr – Serum Creatinine
- UO – Urine Output
- FENa – Fractional Excretion of Sodium
- FEUrea – Fractional Excretion of Urea

Objectives

- Define AKI/ARF and progression
- Evaluation
- Implications of kidney injury
- Management

Cases are from patients I have seen in the last year. Names, places, and birthdates are abstracted for anonymity.

Why does AKI Matter?

- AKI is expensive
- Mortality risk increased both short and long-term
  - Worse for those who survived an ICU stay[1]
  - Most commonly cardiovascular disease and cancer
- Increases in MACE, HF, Coronary events, HTN[2]
- Increased risk of recurrent AKI
- Increased risk of long-term CKD and increased risk of dialysis needs.
- Death

Epidemiology

- 1 % of all hospital admissions have AKI on admission
- Incidence of in-hospital AKI 2%-5%
- Up to 2/3 of ICU patients develop AKI

Cost

- Based on 2012 NHANES data, when there were >30 million hospital stays
- AKI was associated with a cost increase of $7933
- If 1-3% of all hospitalizations: $2.4b-$7b
- If we include the costs of dialysis related to AKI, this increases to >$24b

Case 1

- 55 yo W presented to the ER with abdominal pain, admitted to the ICU with necrotizing pancreatitis.
- History of longstanding alcohol use disorder, 10+ standard drinks daily
- Baseline renal function with normal SCr 0.9 3 months prior

- Hospital Day 2, urine output declining (<500cc/24 hours), SCr 2. Electrolytes controlled

Evaluation of AKI

- Metabolic panel
- Urine microscopic assessment
- Fractional Excretion of Sodium (FENa)
- Fractional Excretion of Urea (FEUrea)
- Imaging

Renal Function assessment Day 2

- SG >1.030, no blood, no protein, no leukocyte esterase
- FENa 1%
- FEUrea 15%
- Retroperitoneal US: 9.5 cm in length bilaterally, mild cortical echogenicity, no hydronephrosis

Diagnosis?

- HRS
- ATN
- Crescentic Glomerulonephritis
- Acute Interstitial Nephritis
- Ischemic/Hemodynamic AKI

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Acute Kidney Injury

Decrease in filtration/homeostatic ability less than 3 months in duration

What do we use to define kidney injury?

- Serum creatinine trends
- Urine output
- Urinary biomarkers – largely investigational
- Cystatin C
- Imaging

- Severity classification
  - RIFLE
  - AKIN

AKI definitions

- AKIN vs RIFLE criteria
- Define subgroups of AKI severity
- Used in research
- Used to help predict inclement need for RRT

RIFLE Criteria

- Developed in 2004 by Acute Dialysis Quality Initiative
- Defined by SCr and urine output
- Risk
- Injury
- Failure
- Loss of Kidney Function
- End-stage disease

RIFLE

Class	GFR	UO
Risk	↑ SCr × 1.5 or ↓ GFR >25%	<0.5 mL/kg/h × 6 h
Injury	↑ SCr × 2 or ↓ GFR >50%	<0.5 mL/kg/h × 12 h
Failure	↑ SCr × 3 or ↓ GFR >75% or if baseline SCr ≥353.6 μmol/L (≥4 mg/dL) ↑ SCr >44.2 μmol/L (>0.5 mg/dL)	<0.3 mL/kg/h × 24 h or anuria × 12 h
Loss of kidney function	Complete loss of kidney function >4 weeks	
End-stage kidney disease	Complete loss of kidney function >3 months	

[a]GFR, glomerular filtration rate; UO, urine output; SCr, serum creatinine.

- Adapted from Lopes JA and Jorge S. The RIFLE and AKIN classifications for acute kidney injury: a critical and comprehensive review. *Clin Kidney J*. 2013; **6**: 8-14

AKIN Criteria

- Developed in 2007 by Acute Kidney Injury Network
- Similarly uses SCr and urine output
- Modification of the RIFLE criteria
- Increases sensitivity and specificity of AKI diagnosis
- Stages 1, 2, 3/HD

AKIN

Stage	SCr	UO
1	↑ SCr ≥26.5 μmol/L (≥0.3 mg/dL) or ↑SCr ≥150 a 200% (1.5 a 2×)	<0.5 mL/kg/h (>6 h)
2	↑ SCr >200 a 300% (>2 a 3×)	<0.5 mL/kg/h (>12 h)
3[b]	↑ SCr >300% (>3×) or if baseline SCr ≥353.6 μmol/L (≥4 mg/dL) ↑SCr ≥44.2 μmol/L (≥0.5 mg/dL)	<0.3 mL/kg/h (24 h) oranuria (12 h)

[a]SCr, serum creatinine; UO, urine output.
[b]Stage 3 also includes patients requiring RRT independent of the stage (defined by SCr and/or UO) they are in at the moment they initiate RRT.

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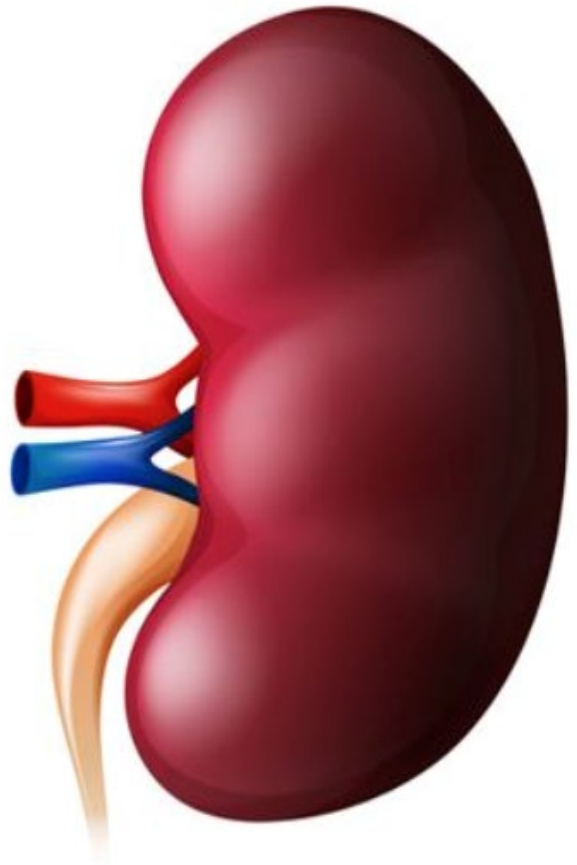
Differential Diagnosis of Acute Kidney Injury

Pre-Renal

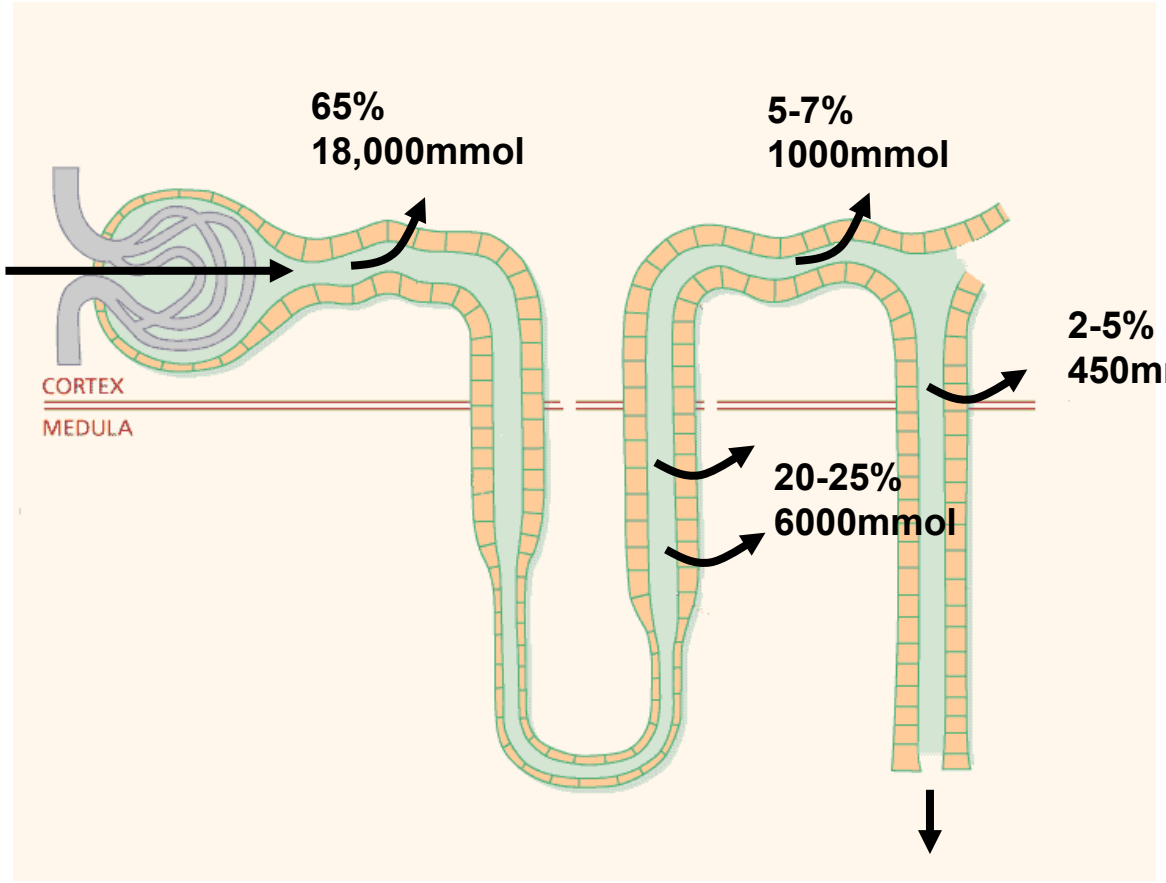
Renal

Post-Renal



Normal sodium reabsorption (99+%)

<u>Na Filtered</u>:
GFR: 180L/d
180 x 140 = 25,000mmol

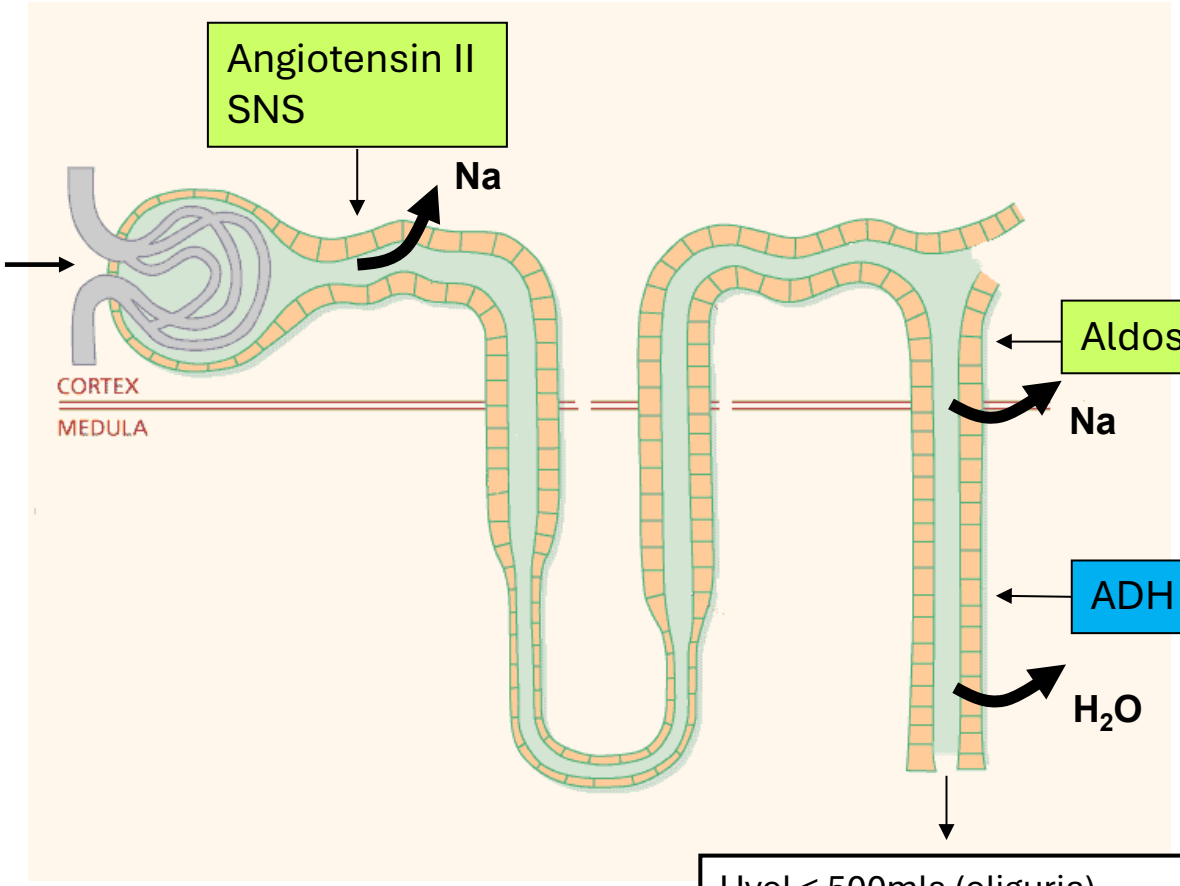


<u>Na excreted</u>
1.5L urine containing 150mmol Na

Note: 125mls/min x 1440mins = 180L

Increased Na and H_2O reabsorption in pre-renal AKI

↓GFR 14mls/min
= 20L/d
2800 mmol Na filtered



Uvol < 500mls (oliguria)
Uosm > 500 **(ADH)**
U_{Na} < 10 mmol/L, FENa < 1%
(RAAS)

Fractional Excretion of Sodium (FENa)

- The fractional excretion of a substance is the percentage of the filtered substance that is excreted in the urine.
- FENa is more accurate than UNa alone, as it accounts for the abstraction of water by ADH.
- FENa <1% suggests prerenal disease, FENa >2% suggests ATN

$$FENa = \frac{excreted\ Na^+}{filtered\ Na^+}\ X\ 100$$

$$Excreted\ \ Na^+ = (U_{Na})(V)$$

$$Filtered\ Na^+ = (P_{Na})(GFR) = P_{Na}\left(\frac{(U_{creat})(V)}{P_{creat}}\right)$$

$$FENa = \frac{(U_{Na})(V)(P_{creat})}{P_{Na}(U_{creat})(V)}\ X\ 100$$

$$\boldsymbol{FENa = \frac{(U_{Na})(P_{creat})}{P_{Na}(U_{creat})}\ X\ 100}$$

FENa and FEUrea

- Assessment of how avidly the kidneys are reabsorbing volume
  - Is the patient currently hypovolemic?
- Asking specifically whether there is a possibly reversible hemodynamic injury
- Original studies included small numbers of people
- Dramatic variability over time
- If hemodynamic injury persists, can progress to iATN
- Predominantly of value in oliguric patients[4]

Variables in fractional excretion

LOW URINE SODIUM NOT DUE TO PRERENAL AKI	HIGH URINE SODIUM NOT DUE TO ATN
normal renal funciton with low salt intake	Normal renal function with excessive salt intake
Acute GN	Normal renal funciton after administration of sodium-containing IV fluids
Acute urinary obstruction	Resolving urinary obstruction
	Bicarbonaturia and other anion-uria (toluene)
	Glucosuria (SGLT2i, hyperglycemia)
LOW URINE SODIUM DESPITE ATN	**HIGH URINE SODIUM DESPITE PRERENAL AKI**
AKI with liver failure or CHF	Administration of sodium-containing IV fluids
Recent iodinated radiocontrast exposure	Active diuretics
Early sepsis-associated AKI	CKD
Pigment nephropathy	Glucosuria (SGLT2i, hyperglycemia)
	Bicarbonaturia and other anion-uria (toluene)
	Salt-wasting nephropathies (Bartter/Gitelman)

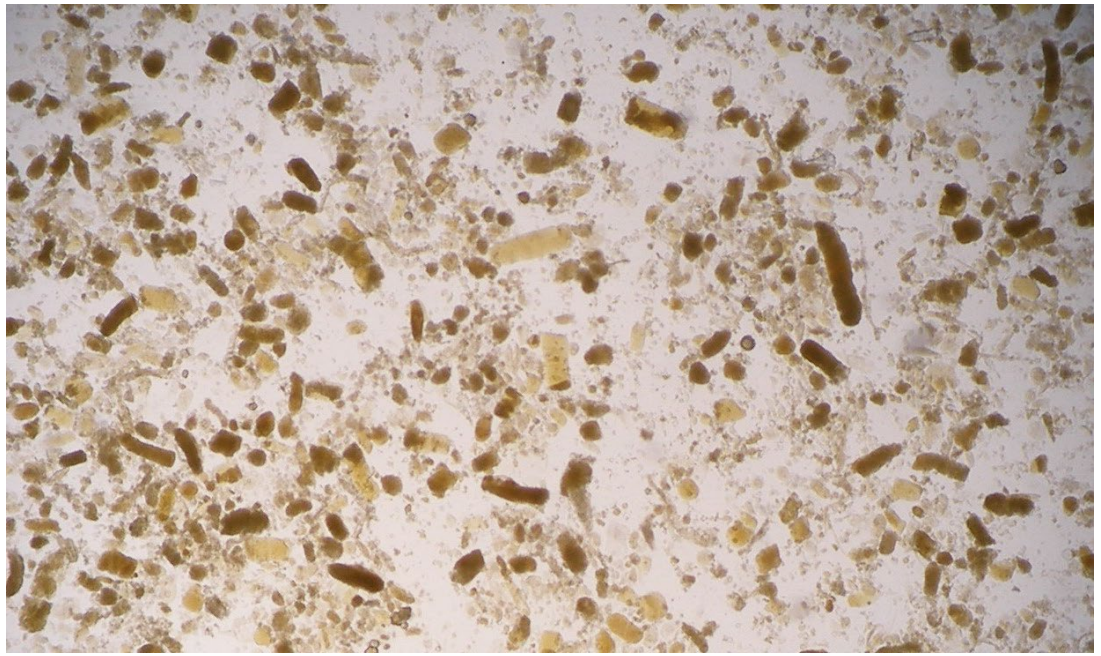
Adapted from Aron A and Amatruda J, citation 5

Case 1 continued

- On hospital day 7
- Renal function deteriorating, with SCr 5 mg/dL
- Hyperkalemia 5.2mEq/L
- Oligo-anuria (<150cc/24 hr)

Urine Assessment day 7

- SG 1.020, Trace protein, no glucose, no ketones, no blood
- + granular casts
- FENa 3.02%
- FEUrea 35 %



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Acute Tubular Necrosis

- Most commonly caused by ischemic events
- Caused by:
  - Afferent arteriolar vasoconstriction in response to TGF
  - Back-leak of glomerular filtrate
  - Tubular obstruction
- 4 phases:
  - Initiation
  - Extension
  - Maintenance
  - Recovery

Haniff MO, Bali A, Ramphul K. Acute Tubular Necrosis. *StatPearls*. 2025(1). Accessed 7/2025. <https://www.ncbi.nlm.nih.gov/books/NBK507815/>

BUT

- ATN is a histologic diagnosis

Improving ATN diagnosis

- Urine microscopy
- Presence and number of casts
- Consistently demonstrated good diagnostic and prognostic performance
- Especially useful in differentiating established ATN from prerenal AKI

Urine Microscopy in ATN

Bagshaw et al

Repeated Urine Microscopy

- Further studies have indicated benefit from repeat examinations
- Performed two or three times over 10 days
- Improves the sensitivity of ATN diagnosis

Case 2

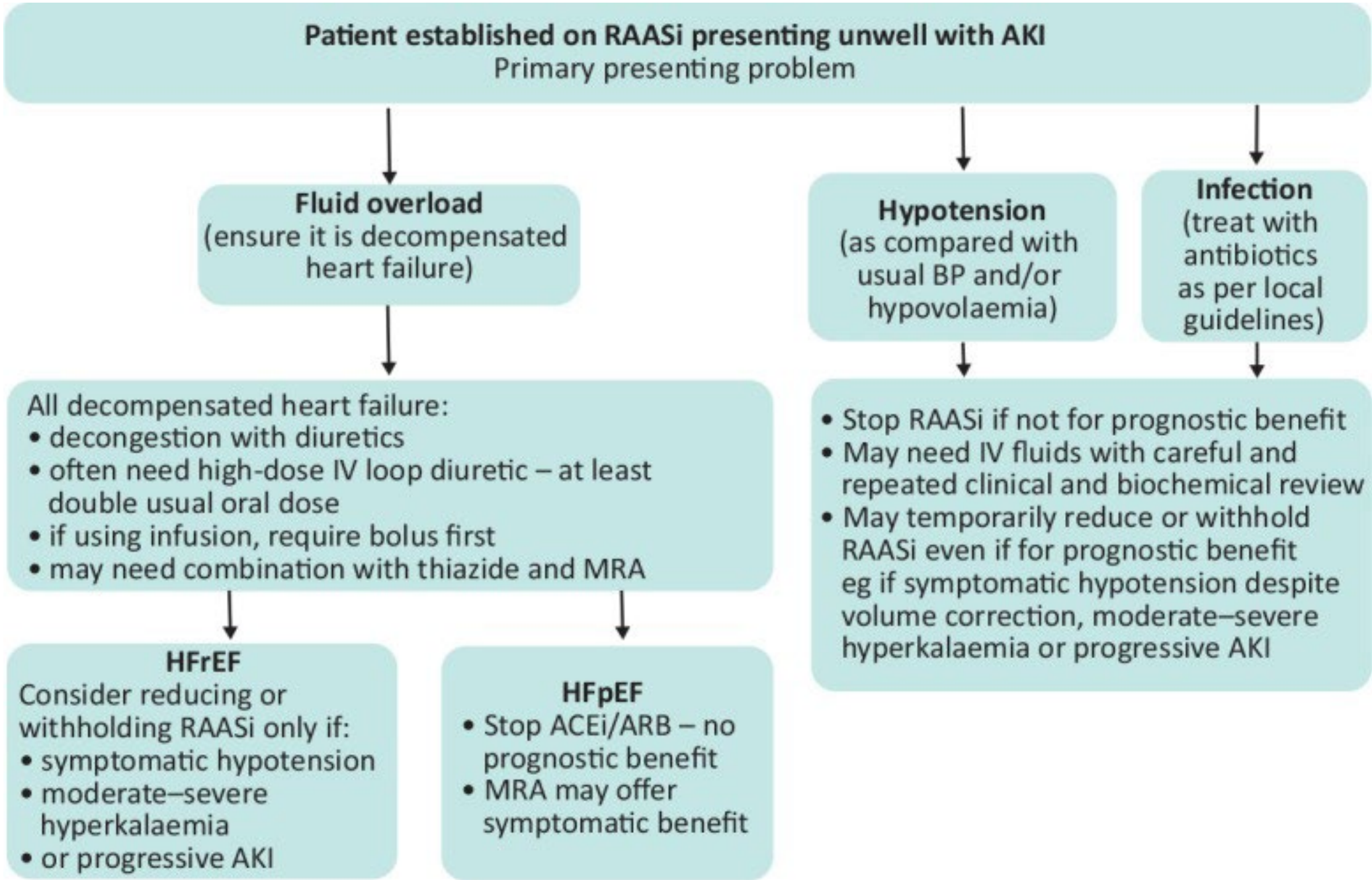
- 65 M with history HFrEF EF 35%, CAD with prior 3 vessel CABG presents with decompensation
- On lisinopril, empagliflozin, carvedilol, furosmide
- Baseline Cr 2mg/dL, on admission 4.3mg/dL
- Exam reveals BP 135/90, edematous with pulmonary rales

Do you stop the ACEi?

Are RAASi “nephrotoxic”?

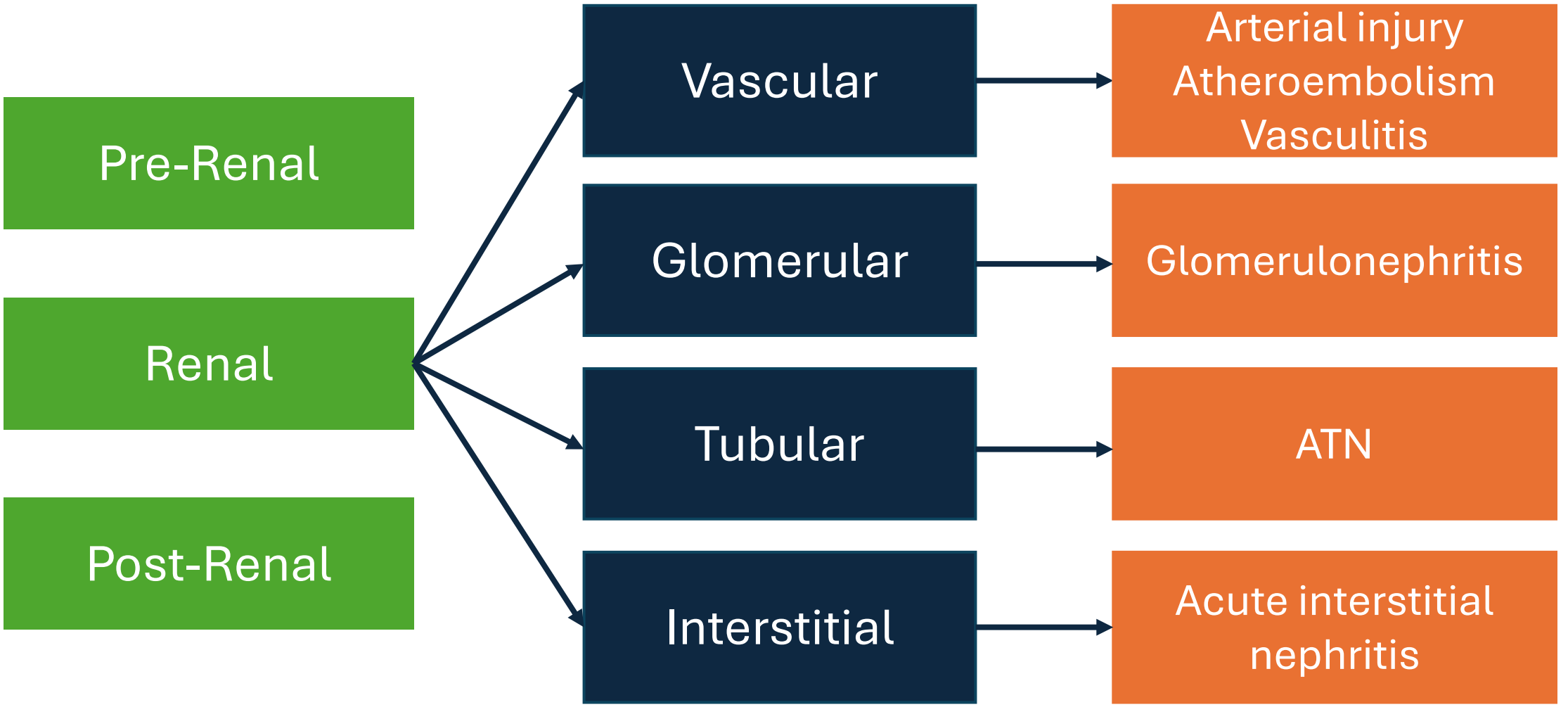
Congestion vs renal function

- Studies have shown that patients with HF admission have their RAASI stopped, sometimes for upward of a year
- This has been shown to portend both in—hospital and 1 year survival decrement
- Decongestion is the primary goal of therapy
- RAASi if coupled with effective diuresis may worsen Cr
- Provided this remains at stage 1/asymptomatic, this is considered hemodynamic and not detrimental


Patient established on RAASi presenting unwell with AKI
Primary presenting problem
Fluid overload
(ensure it is decompensated heart failure)
Hypotension
(as compared with usual BP and/or hypovolaemia)
Infection
(treat with antibiotics as per local guidelines)
All decompensated heart failure:
• decongestion with diuretics
• often need high-dose IV loop diuretic – at least double usual oral dose
• if using infusion, require bolus first
• may need combination with thiazide and MRA
• Stop RAASi if not for prognostic benefit
• May need IV fluids with careful and repeated clinical and biochemical review
• May temporarily reduce or withhold RAASi even if for prognostic benefit eg if symptomatic hypotension despite volume correction, moderate–severe hyperkalaemia or progressive AKI
HFrEF
Consider reducing or withholding RAASi only if:
• symptomatic hypotension
• moderate–severe hyperkalaemia
• or progressive AKI
HFpEF
• Stop ACEi/ARB – no prognostic benefit
• MRA may offer symptomatic benefit

Change in renal function compared with baseline	HFpEF (assuming no other prognostic indication)	HFrEF
Increase in serum creatinine by <30%	Consider stopping ACEi/ARB/ARNi Review MRA according to fluid status	Continue unless symptomatic hypotension
Increase in serum creatinine by 30–50%	Stop RAASi	Consider reducing dose or temporary withdrawal[a]
Increase in serum creatinine by >50%	Stop RAASi	Temporarily stop RAASi[a]
Severe renal dysfunction, for example, eGFR <20 mL/min/1.73 m^2	Stop RAASi	Stop RAASi if symptomatic uraemia irrespective of baseline function

Renal causes of AKI



Etiologies of ATN

Ischemic ATN	Nephrotoxic	Pigment-induced
Hemorrhage	Aminoglycosides	Myoglobin
Hypotension	Amphotericin	Hemoglobin
	Tenofovir	
	Cisplatin	

Treatment of ATN

- Treat the underlying condition!

- Prevent complications
  - Control volume overload
  - Dose medications appropriately
  - Avoid further nephrotoxic agents

- Supportive Care
  - Acute dialysis

Indications for acute HD

A – acidosis
E – electrolyte disorders
I – ingestions/intoxications
O – volume overload
U – uremia (uremic encephalopathy, pericarditis, bleeding, etc.)

Case 3: A 54-year-old man presents with low grade fever and nausea. He saw his PCP three weeks prior and was begun on a PPI for presumed GERD.

Physical Exam

T 38.2

Fatigued

1+ edema

Erythematous rash over trunk

Labs

BUN 68 mg/dl

Cr 3.8 mg/dl

Urine dipstick:

1+ protein, 1+ LE, trace blood

Urine microscopy:

Few WBCs, rare WBC cast

What would a renal biopsy be most likely to show?

A) Acute tubular necrosis

D) Acute glomerulonephritis

C) Acute interstitial nephritis

D) Obstructive uropathy

E) Urate nephropathy

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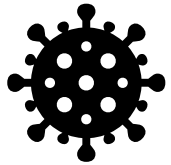
Acute Interstitial Nephritis: Common Causes

Drugs

Beta lactams
NSAIDs
PPIs
Sulfa
PD-1 inhibitors



Infection

Leptospirosis
Legionella
Viruses

Autoimmune

SLE
Sjögren’s
Sarcoidosis
IgG4 disease

AIN Features

- Immune-mediated: occurs in a small percentage of patients taking a given drug
- Not dose-dependent
- Extrarenal manifestations of hypersensitivity occur in 10-20%
- Recurs after re-exposure to the drug

AIN: key points

- Classic triad of fever, rash, eosinophilia is RARE (only 10%)
- Most important management is to STOP the offending agent
- Steroid use common but has not been studied in randomized trials

Case 3: 54 yo AA man presents to the hospital after a job fair Cr: 7
Denies recent medication use
Extensive personal and family of HTN with variable control

Physical Exam:
Thin, comfortable, NAD
BP 190/115 P 96 R 18
Lungs: scattered crackles
Heart: RRR S4S1S2 1-2/6 SM
Abd: Soft, no organomegaly

Labs:
Hct 29% with schistocytes on smear
Plts 95,000
Creatinine 2.1 mg/dl

Urine sediment: 2+ protein, large blood, + fragmented cells

Case 3 continued

- Given the thrombocytopenia with presence of at least MAHA/TMA, ADAMTs 13 was sent, resulted in 24 hours as 55%

What is the next step?

- Plasma Exchange
- Lisinopril
- Steroids
- Amlodipine
- Labetalol

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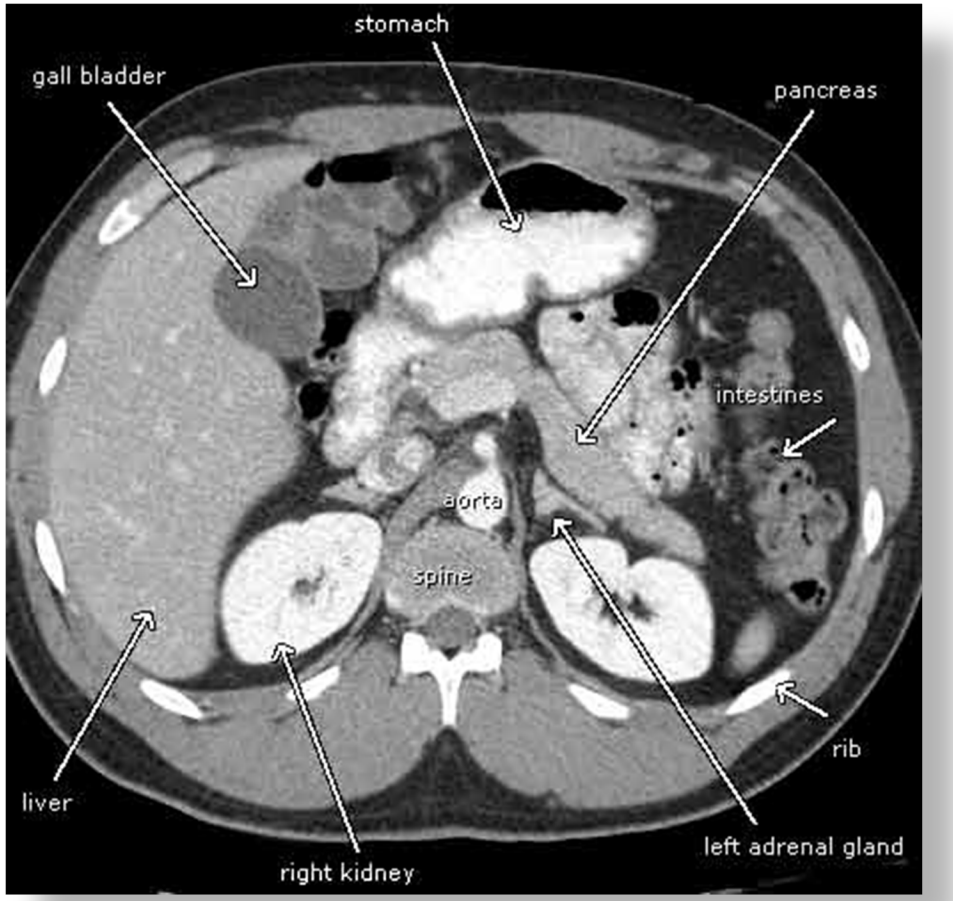
Contrast associated nephropathy

- Controversial?

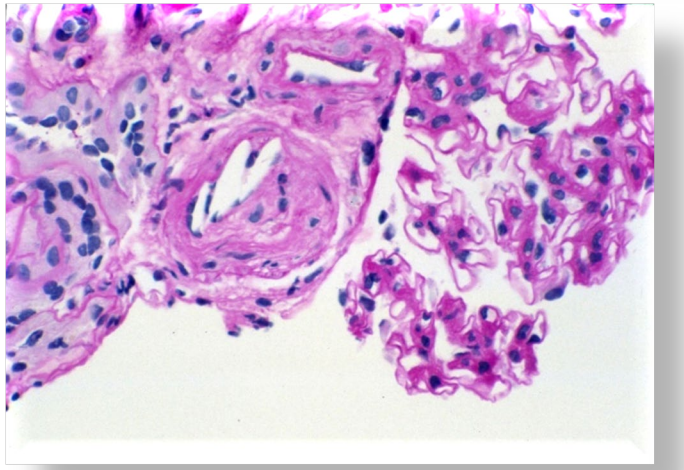
- Risk factors
  - Preexisting renal impairment (eGFR<30)
  - Volume depletion
  - Heart failure
  - Diabetes
  - Arterial vs venous contrast administration

- Prevention
  - Don’t withhold necessary imaging studies!
  - Limit amount of IV contrast
  - Avoid volume depletion
    - Hold diuretics
    - Isotonic fluids



Renal atheroembolism

- Clinical features
  - AKI
  - Digital infarcts
  - Livedo reticularis
  - Hypocomplementemia
  - Peripheral eosinophilia
- Management
  - ACEi
  - Statins
  - Avoid anticoagulation



Take-Home points

- AKI is expensive and associated with increased risks
- AKI is expensive
- Fractional excretion and urinalysis can be helpful for risk
- Dialyze if needed with AEIOU
- Higher SCr but drier is better
- AIN is dose independent
- Atheroembolism happens 2-8 weeks after vascular insult

References

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