Acute Renal Failure

Acute Kidney Injury (AKI)

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Acute Kidney Injury
Overview

• Definition and epidemiology

• Classification

• Clinical course and workup

• Management
Acute Kidney Injury (formerly acute renal failure): definition

- Loss of kidney function (GFR) within hours/days
- Frequently accompanied by decreased urinary output (oliguria or rarely anuria)

Note: the definition is based on creatinine and/or urine output criteria
Section 2: AKI Definition

2.1.1: AKI is defined as any of the following (Not Graded):

- Increase in SCr by $\geq 0.3\text{ mg/dl} \ (\geq 26.5\text{ }\mu\text{mol/l})$ within 48 hours; or
- Increase in SCr to $\geq 1.5$ times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume $< 0.5\text{ ml/kg/h}$ for 6 hours.

2.1.2: AKI is staged for severity according to the following criteria (Table 2). (Not Graded)

Table 2 | Staging of AKI

<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 times baseline OR $\geq 0.3\text{ mg/dl} \ (\geq 26.5\text{ }\mu\text{mol/l})$ increase</td>
<td>$&lt; 0.5\text{ ml/kg/h}$ for 6–12 hours</td>
</tr>
<tr>
<td>2</td>
<td>2.0–2.9 times baseline</td>
<td>$&lt; 0.5\text{ ml/kg/h}$ for $\geq 12$ hours</td>
</tr>
<tr>
<td>3</td>
<td>3.0 times baseline OR Increase in serum creatinine to $\geq 4.0\text{ mg/dl} \ (\geq 353.6\text{ }\mu\text{mol/l})$ OR Initiation of renal replacement therapy OR In patients $&lt; 18$ years, decrease in eGFR to $&lt; 35\text{ ml/min per 1.73 m}^2$</td>
<td>$&lt; 0.3\text{ ml/kg/h}$ for $\geq 24$ hours OR Anuria for $\geq 12$ hours</td>
</tr>
</tbody>
</table>
Changes in GFR and serum creatinine after injury to the kidney

![Graph showing changes in GFR and serum creatinine over 28 days. GFR (mL/min) and serum creatinine (mg/dL) are plotted against days. GFR decreases sharply at day 0 and rises gradually over time. Serum creatinine increases to a peak at day 14 and then decreases.](image-url)
Epidemiology

• General population
  – no renal replacement therapy: 5/1000/y
  – Renal replacement therapy: 250 PMP

• Hospital admissions
  – 2-3% of all admissions have AKI
  – In hospital development: 5-7%
  – In ICU development: 30%

• Mortality: 20-50%
  – Depending on cause and comorbidity

• Increased risk for later chronic kidney disease
Prognosis

Mortality, %

- All cases
- ICUs
- Medical
- Surgical
- Nephrol

*P<0.001 respect to all cases
Acute Kidney Injury
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Classification of acute kidney injury

Prerenal

Postrenal

Intrinsic renal

Glomerular disease
- glomerulonephritis

Tubular injury
- Ischemic
- Sepsis
- Toxic

Interstitial nephritis

Vascular disease
- Vasculitis
- HUS/TTP
- Obstruction (emboli, thrombosis)
Causes of AKI in hospitals setting

- Acute tubular necrosis
- Acute interstitial nephritis
- Obstruction
- Acute-on-chronic renal failure
- Prerenal
- RPGN
- Vascular
Prerenal (functional) acute kidney injury

- Functional GFR decrease due to hemodynamic changes leading to decreased intraglomerular pressure (no true renal parenchymal disease)
  - Hypovolaemia, hypotension, preglomerular vasoconstriction etc.

- Renal failure may resolve after eliminating the hemodynamic trigger

- If sustained may lead to intrinsic renal failure (acute tubular necrosis)

- Increased risk in patients with baseline chronic kidney disease
Prerenal AKI: causes

- **Extracellular fluid loss**
  - bleeding, decreased fluid intake, diarrhea, vomiting, excessive diuresis

- **Decreased effective circulating volume + edema**
  - Heart failure, nephrosis syndrome, cirrhosis

- **Decreased effective circulating volume + vasodilation**
  - sepsis, anaphylaxis

- **Glomerular autoregulatory failure**
  - **Afferent artery vasoconstriction:**
    - NSAI, hepatorenal syndrome, cyclosporin A, adrenalin, hyperkalcemia, sepsis
  - **Efferent artery vasodilation:**
    - ACEI, ARB
Autoregulation of the glomerular circulation

- Afferent arteriole
- Increased vasodilatory prostaglandins
- Increased angiotensin II
- Normal GFR maintained
Prerenal AKI: clinical features

- Decreased spot urine Na-concentration (<20 mmol/l)
  - Unless the patient is on a diuretic
- Fracional excretion of sodium (FE_{Na}) < 1%
- Concentrated urine (osmolarity usually above 500mosm/l)
- Specific gravity usually >1.020
- Increase in BUN usually > increase in creatinine
- Negative urinary sediment (sometimes hyline casts)
Intrinsic renal acute kidney injury
Intrinsic AKI: causes

- Acute tubular necrosis ~ 70-80%
  - Ischemic
  - septic
  - Toxic (exogenous vs endogenous substances)

- Acute tubulointerstitial nephritis ~ 5-6%
  - Drugs - allergic, sarcoidosis, SLE
  - Infectious (acute pyelonephritis, CMV EBV)

- Glomerular damage ~ 4-5%
  - Acute glomerulonephritis
  - Vasculitis (ANCA pozitíve)

- Vascular damage ~ 2-3%
  - Renal artery occlusion, renal vein thrombosis
  - Cholesterol embolisation
  - Thrombotic microangiopathy (e.g. hemolytic uremic syndrome, preeclampsia etc.)
Some endogenous toxins that may cause acute tubular necrosis

- Sepsis
- Pigment: haemolysis, rhabdomyolysis
- uric acid,
- „tumor lysis syndrome” (uric acid, phosphate)
- Oxalate
- Calcium
- light chains
Some exogenous toxins that may cause acute tubular necrosis

- Iodinated contrast media
- Intoxication: ethylene glycol
- Heavy metals: arzenic, cadmium, mercury, lead
- Antimicrobials: acyclovir, aminoglicosides, amphotericin B, indinavir, pentamidin, vancomycin,
- Chemotherapeutics: cisplatin, carboplatin, ifosfamid,
- Amphetamin
- Herbs
- Animal toxins (wasp, spider, snake bites)
The outer medulla is susceptible to hypoxia due to low oxygen delivery and high oxygen consumption.
GFR decrease in ATN

- Inflammation
- Tubular obstruction
- Tubuloglomerular feed-back
- Backleak
Akut tubularis necrosis: damage
Akut tubular necrosis: restitution
Clinical features of acute tubular necrosis

• Urinary Na concentration usually above 20 mmol/l
• $FE_{Na} > 2-3\%$
• Urinary osmolarity $\cong$ serum
• Urine specific gravity $\sim 1.010$
• Sediment: muddy brown granular
  ATN casts
Biomarkers in intrinsic AKI
The troponins of the kidney?

Potential urinary biomarkers for early diagnosis of AKI
- NAG
- β2M
- α1M
- RBP
- Cystatin C
- KIM-1
- Clusterin
- Microalbuminuria

NGAL
CYR-61
IL-18
OPN
FABP
NHE3
Fetuin A

Delayed biomarkers for kidney injury
- ↑ Serum creatinine
- ↑ Blood urea nitrogen

Normal epithelium
Ischemia/reperfusion
Toxicity
Damage
Necrosis
Apoptosis
Cell death
↓ GFR

Comprehensive Clinical Nephrology, 2010
Contrast induced nephropathy

Risk factors

• Chr. Kidney disease
• Diabetic nephropathy
• Heart failure
• Volume depletion
• Proteinuria

• High osmolarity contrast agent
• Large volume of contrast agent

Prevention

• Pre and postprocedural hydration:
  - isotonic NaCl or Nabicarb, urine flow 150-200ml/h)

• Use of non-ionic, iso-osmolar contrast agent
• Low volume of contrast agent

• Acetil cystein: 600mg t.i.d pre/post
Tumor lysis syndrome

AKI after chemotherapy of large tumor burden (e.g. hematologic) and cell lysis

Rarely after:
- steroid threatment of lymphoproliferative diseases
- radiotherapy
- interferon

Features:
- hyperuricemia
- hyperphosphatemia
- hypocalcemia
- hyperkalemia

Risk factor:
- volume depletion,
  chr. kidney disease

Prevention:
- hydration (Saline),
- allopurinol 600-900mg
- febuxostate 120mg
- uricase (UA→allantoin)

Akute kidney injury
- ATN+ tubular crystal obstruction+ inflammation

Uric acid crystals
• AKI due to cholesterol embolisation into small renal arterioles and glomerular capillaries

• AKI following intraarterial procedures

• Increased risk in patients with widespread atherosclerosis

• Immediate but also after after a few days
Atheroembolic acute kidney injury (cholesterol embolisation)

- **Multisystemic disease**
  - kidney: AKI
  - skin: livedo reticularis
  - toes: small emboly „blue toe”
  - intestines: ischemia

- Eozinofiluria
- Low complement
Postrenal acute kidney injury
Postrenal acute kidney injury

- **Extraureteral obstruction**
  - tumor
  - retroperitoneal fibrosis
  - ligation

- **Intraureteral obstruction**
  - Lithiasis, tumor
  - Blood clot

- **Bladder obstruction**
  - prostate hypertrophy, tumor
  - Bladder tumor
  - Pelvic tumor
  - Funkcional/neurologic

- **Urethral obstruction**
  - strikture, phymosis
Acute Kidney Injury
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• **Clinical course and workup**

• Management
Acute kidney injury - clinical course (characteristic for ATN)

- **Introductory phase**
  - s/s of the underlying disease

- **Olig-anuric, uremic phase (1-2 weeks)**
  - Volume and electrolyte pH disturbances ($K^+\uparrow$, $P\uparrow$, $Ca\uparrow\downarrow$, $Na\uparrow\downarrow$, $pH\downarrow$)
  - Uremia, encephalopathy
  - Complications
    - Haematologic (anaemia, throbocytopenia)
    - Frequent infections
    - Gastrointestinal (vomiting, diarrhea, gastric ulcers)
    - Cardiovascular (heart failure, arrhythmias, pericarditis)
    - Malnutrition

- **Polyuric phase (during restitution) 2-6 weeks**
  - May lead to 4-6 l/day urine output with electrolyte disturbances
Acute kidney injury – Workup (cause? complications?)

• **Medical history**
  - Previous kidney disease
  - Systemic disease (autoimmune, infection, diabetes etc)
  - Medication review (ACEI, NSAI, nephrotoxins, new drugs, OTC etc.)
  - Volume loss
  - Interventions
  - Urological/gynecological disease
  - Change in urine

• **Physical examination**
  - Volume status (BP, HR, jugular vein, skin, lung, edema)
  - Signs of systemic illnesses (rashes, arthritis, lymph nodes, hepatosplenomegaly etc)
  - Bladder percussion
Acute kidney injury – Workup (cause? complications?)

• **Laboratory**
  - BUN, creatinine
  - Blood count, electrolytes (Na, K, P, Ca, pH, bicarbonate, uric acid)
  - Immunology (dsDNA, ANCA complement etc.)
  - Urine output, protein, blood, Na, Fe\textsubscript{Na}, osmolarity/specific gravity
  - **Urinary sediment**
    - RBC dysmorphic (glomerular)
    - Hyalyne cast – prerenal
    - ATN cast – intrinsic renal
    - WBC cast - interstitial nephritis
    - RBC cast glomerulonephritis
    - Crystals (oxalat ethylene glycol poisoning)

• **Radiology** (ultrasound, chest Xray)

• **Renal biopsy**
  - If s/s suggestive of intrinsic renal, but not ATN
  - If ATN is not resolving within 2 weeks
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Prerenal postrenal acute kidney injury

• Volume depletion
  – Volume resuscitation (use crystalloids avoid starch)
  – Cessation of ACEI/ARB, NSAI, diuretic

• Effective volume depletion with edema (heart failure, nephrosis)
  – Na and volume restriction
  – Cessation of ACEI/ARB, NSAI
  – Step-up diuretic (furosemid+HCT)
  – Ultrafiltration
  – Optimize cardiac function

• Postrenal
  – Ensure urine flow (bladder catheter or transrenal drain)
Intrinsic renal acute kidney injury (ATN)

• Prevention
  – Avoid nephrotoxic drugs
  – Avoid hypoxia, prerenal disease, sepsis
  – Treat underlying disease (if known)

• Supportive care
  – Hypervolemia: furosemide rarely helps, dialysis
  – Acidosis: pH<7.2, HCO₃<17 Na-bicarbonate
  – Hyperkalemia: Ca-gluconate, glucose+insulin, NaHCO₃, resin, dialysis
  – Hyperphosphatemia: Ca-carbonat/acetat p.o.
  – Malnutrition: energy: 30-40 kcal/kg/day, protein restriction promotes catabolism
  – Infection control
  – Anemia treatment
  – Gastrointestinal profilaxis: PPI
Indications for renal replacement therapy

• Resistant hypervolemia
• Resistant hyperkalemia
• Resistant acidosis
• Uremic encephalopathy pericarditis
• Some intoxications (ethylene glicol, methanol, lithium)
• No set creatinine/BUN value but usually above 3-400/25-30

Methods
• Continuous v.s. intermittent (ICU)
• Hemodialysis, hemofiltration, hemodiafiltration
Acute Kidney Injury: summary

- Frequent disease with poor prognosis
- Most frequent types are the prerenal and acute tubular necrosis, but less frequent causes should not be forgotten
- Special attention to drug history, volume and urinary findings during workup
- Prevention and supportive care are key to ATN management