Acute Kidney Injury

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SpR Endo/ Hon. Lecturer
Introduction

• We will look at the definition, incidence, mechanisms and management of acute kidney injury (AKI).

• Newer terminology for acute renal failure

• Incidence – about 1% of hospital admissions are complicated by AKI and 7% of hospitalised patients develop AKI during the course of their hospital stay.

• More importantly it complicates about 30% of intensive care admissions
Definition – AKIN criteria

• An abrupt (within 48 hours) reduction in kidney function currently defined as

• An absolute increase in serum creatinine of $\geq 26.4 \mu\text{mol/l}$, a percentage increase in serum creatinine of more than or equal to 50% (1.5-fold from baseline),

• or

• A reduction in urine output (documented oliguria of less than 0.5 ml/kg per hour for more than six hours).

• This assumes adequate volume repletion and no obstruction or easily reversible cause of urinary retention.

Mehta et al Crit Care. 2007;11(2):R31
## Stages of renal injury

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum creatinine (SCr) criteria</th>
<th>Urine output criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SCr increase ≥ 26 μmol/L or SCr increase ≥ 1.5- to 2-fold from baseline</td>
<td>&lt;0.5 mL/kg/hr for &gt; 6 consecutive hrs</td>
</tr>
<tr>
<td>2</td>
<td>SCr increase ≥ 2 to 3-fold from baseline</td>
<td>&lt;0.5 mL/kg/hr for &gt; 12 hrs</td>
</tr>
<tr>
<td>3</td>
<td>SCr increase ≥ 3-fold from baseline or SCr increase 354 μmol/L with an acute increase of more than 44 μmol/L or Commenced on renal replacement therapy (RRT) irrespective of stage</td>
<td>&lt;0.3 mL/kg/hr for &gt; 24 hrs or anuria for 12 hrs</td>
</tr>
</tbody>
</table>

AKIN staging – Mehta et al Critical Care 2007 11: R31
Comparison between RIFLE and AKIN

**RIFLE**

- **Risk**: Increased Cr x 1.5 or GFR decreases >25%
- **Injury**: Increased Cr x 2 or GFR decreases >50%
- **Failure**: Increased Cr x 3 or GFR decreases >75% or Cr ≥ 4 mg/dl (with acute rise of ≥ 0.5 mg/dl)
- **Loss**: Persistent ARF = complete loss of renal function for > 4 weeks
- **ESRD**: End Stage Renal Disease

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<th>Urine Output (UO) Criteria</th>
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<td>UO &lt; 0.5 ml/kg/hr x 6 hr</td>
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<tr>
<td>UO &lt; 0.3 ml/kg/hr x 24 hr</td>
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**AKIN**

- **Stage 1**: Increased Cr x 1.5 or ≥ 0.3 mg/dl
- **Stage 2**: Increased Cr x 2
- **Stage 3**: Increased Cr x 3 or Cr ≥ 4 mg/dl (with acute rise of ≥ 0.5 mg/dl)

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Patients who receive renal replacement therapy (RRT) are considered to have met the criteria for stage 3 irrespective of the stage that they are in at the time of commencement of RRT.

Aetiology

• Broadly divided into pre-renal, intrinsic renal and post renal
• Pre-renal – Volume depletion due to any cause.
• Commonest cause of ARF
• Intrinsic renal problems such as acute tubular necrosis, glomerulonephritides, acute interstitial nephritis
• Post – renal: Mainly obstructive
• Can also be classified as oliguric and non-oliguric

Oliguria <400ml urine/day; anuria - <100ml urine/day
Pre-renal causes

• **Volume depletion**
  – Renal losses (diuretics, polyuria)
  – GI losses (vomiting, diarrhoea)
  – Cutaneous losses (burns, Stevens-Johnson syndrome)
  – Haemorrhage
  – Pancreatitis

• **Decreased cardiac output**
  – Heart failure
  – Pulmonary embolus
  – Acute myocardial infarction
  – Severe valvular disease
  – Abdominal compartment syndrome (tense ascites)

• **Systemic vasodilation**
  – Sepsis
  – Anaphylaxis
  – Anaesthetics
  – Drug overdose

• **Afferent arteriolar vasoconstriction**
  – Hypercalcaemia
  – Drugs (NSAIDs, amphotericin B, calcineurin inhibitors, norepinephrine, radiocontrast agents)
  – Hepatorenal syndrome

• **Efferent arteriolar vaso-dilation**
  • ACEIs or ARBs

• **Renal artery occlusion**
Pre-renal

• Reversible and by definition does not include parenchymal tissue damage
• Can progress to include intrinsic elements if not treated adequately and results in ischaemic acute tubular necrosis (ATN)
• Results from inadequate perfusion of the kidneys from volume depletion, heart failure, afferent arteriolar vasoconstriction or efferent arteriolar vasodilatation.
• In the background of volume depletion, drugs such as ACEI and ARB can induce pre-renal RF.
Pre-renal AKI

Hypoperfusion

- Activation of sympathetic system
- Activation of RAAS
- ADH release

Efferent arteriolar vaso-constriction
Splanchnic vasoconstriction
Retention of Na and water in the tubules
Stimulation of thirst

Maintenance of GFR
Compensation

- As detailed in the diagram, compensatory mechanisms are activated.
- If hypoperfusion becomes more severe (or if patient is on ACEI, ARBs or NSAIDs), the mechanisms overload and intrinsic renal damage results.

- Hepato-renal syndrome is a special form of pre-renal ARF in cirrhosis
Differentiating between pre-renal and intrinsic

- Urine specific gravity and osmolality will be higher in pre-renal since there is active conservation of Na and water
- Hence urine Na excretion will also be lower.
- However this is not true if there is glycosuria or in case of myoglobinuria or contrast induced nephropathy causing intrinsic renal failure. Hence the use of fractional excretion of sodium

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<th>Pre-renal</th>
<th>Intrinsic renal</th>
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<tr>
<td>Urine specific gravity</td>
<td>&gt;1.020</td>
<td>&lt;1.010</td>
</tr>
<tr>
<td>Urine osmolality</td>
<td>&gt;500 mOsm/l</td>
<td>&lt;350mOsm/L</td>
</tr>
<tr>
<td>Urine Na</td>
<td>&lt;20 mmol/l</td>
<td>&gt;40 mmol/l</td>
</tr>
<tr>
<td>Fractional Na excretion</td>
<td>&lt;1%</td>
<td>&gt;1%</td>
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\[
FENa = \frac{UrNa}{PjNa} + \frac{UrCr}{PjCr} \times 100
\]
Treatment of pre-renal RF

• If due to hypovolaemia – replacement with appropriate fluid is the solution.

• Since there might be underlying intrinsic componentent this must be done carefully monitoring the fluid status (JVP, BP, HR, urine output; if necessary use CVP monitoring)

• If this is due to cardiogenic reasons careful fluid resuscitation and inotropes/other cardiac support may be necessary.
Intrinsic AKI

• **Tubular (Acute Tubular Necrosis) (commonest cause)**
  
  – Ischaemic
  
  – Cytotoxic
    
    • Haeme pigment (rhabdomyolysis, intravascular haemolysis)
    
    • Crystals (tumour lysis syndrome, ethylene glycol poisoning, acyclovir, methotrexate)
    
    • Drugs (**radiocontrast agents**, aminoglycosides, lithium, amphotericin B, cisplatin, ifosfamide,)

• **Interstitial (Acute Interstitial Nephritis)**
  
  – Drugs (penicillins, cephalosporins, **NSAIDs**, **proton-pump inhibitors**, allopurinol, rifampicin etc)
  
  – Infection (pyelonephritis, viral nephritides)
  
  – Systemic disease (Sjögren syndrome, sarcoid, lupus, lymphoma, leukaemia, tubulonephritis, uveitis)
Intrinsic AKI

• Glomerular (Acute Glomerulo Nephritis and RPGN or crescentic GN)
  – Post –Streptococcal GN and other acute GN
  – Anti–GBM disease -Goodpasture syndrome
  – ANCA-associated GN - Wegener granulomatosis, Churg-Strauss syndrome, microscopic polyangiitis
  – Immune complex GN (SLE, Primary MPGN, post-infection cryoglobulinaemia)

• Vascular (large and small vessel)
  – Renal artery obstruction (thrombosis, emboli, dissection, vasculitis, atheromatous)
  – Renal vein obstruction (thrombosis)
  – Microangiopathy (TTP, haemolytic uremic syndrome [HUS], DIC, preeclampsia)
  – Malignant hypertension
  – Scleroderma renal crisis , Transplant rejection
Acute Tubular Necrosis

- Ischaemia and toxins (drugs, crystals, pigment)
  - Due to intra-renal vasoconstriction
  - Tubular cell injury due to hypoxia
- Tubular cells can recover once the underlying cause is reversed
- Initially oliguria is seen. (Isosthenuria)
- After 1-3 weeks recovery can occur with polyuria initially due to defective tubular reabsorption
Investigations

• Hyperkalemia, hyponatremia and metabolic acidosis - common (↑K, ↓Na, ↑pH)

• ABG, FBC, clotting, U&E, urinalysis and culture, calcium, LFT, ECG and CXR initially

• Urinalysis – Look for casts – Granular muddy brown cast or tubular cell casts are suggestive

• Urine dip positive for haeme but no RBCs in urine + reddish brown (‘cola coloured’ urine) suggests myo/haemo globinuria
Investigations

• Renal ultrasound
• Complement level, ANA, ANCA
• Further investigations depend on possible aetiology
  • (myoglobinuria and contrast nephropathy – two intrinsic causes in which FENa is low)
  • (Emerging markers urine NGAL, serum cystatin etc)

NGAL - neutrophil gelatinase associated lipocalin
Treatment

• Treatment is largely supportive
• Appropriate fluid replacement if the cause is hypovolaemia
• Correct hyperkalaemia and hypocalcaemia as well as severe metabolic acidosis
• If there is fluid overload iv diuretics such as frusemide can be tried
• Stop all nephrotoxic drugs
Dialysis

• No agreed criteria on when to start dialysis
• Haemodialysis, CVVHD or haemofiltration or peritoneal dialysis can be used.
• If there is haemodynamic instability haemofiltration or CVVHD may be preferred
• During recovery phase polyuria is often seen
Contrast induced nephropathy

- Risk in – people with
  - Diabetes and diabetic nephropathy
  - Previous decline in GFR
  - Volume depleted individuals
- Develops 24-48 hours after contrast use
- Low FENa
- Prevention- N- Acety cysteine, adequate volume repletion prior to procedure and occasionally NaHCO3 or theophylline
- In diabetics stop metformin 48 hours prior to the procedure and restart 24-48 hours post
Acute Interstitial Nephritis

• Mainly allergic – NSAIDs, antibiotics, PPI are the main causes. Cholesterol emboli is another major cause
• Peripheral eosinophilia is the main feature
• Rash may be seen. Fever occasionally
• AIN due to NSAIDs may present with nephrotic range proteinuria, in other cases it is negligible
• Occasionally due to HIV, hanta virus and CMV
Acute Glomerulonephritis

• Acute renal failure is seen only in RPGN (crescentic GN where 50% glomeruli are involved)
• Rare cause of AKI
• RBC casts in urine is pathognomonic of PSGN

• (see earlier slides for other causes of RPGN)
Post-Renal

- Tubular obstruction from crystals (uric acid, oxalate, sulfa, myeloma light chain, acyclovir, methotrexate)
- Ureteric obstruction
  - stones, tumour, fibrosis, ligation during pelvic surgery
- Bladder neck obstruction
  - benign prostatic hypertrophy [BPH], cancer of the prostate, neurogenic bladder, tricyclic antidepressants, ganglion blockers, bladder tumour, stone disease, haemorrhage/clot
- Urethral obstruction
  - strictures, tumour, phimosis
- Intra-abdominal hypertension
  - tense ascites
- Renal vein thrombosis
Treatment

• Removal of obstruction and supportive management
• Polyuric phase is often seen during recovery
Questions
Thank You