Acute Kidney Injury

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Clinical Significance of Acute Kidney Injury (AKI)$^1$

- Common yet underrecognized syndrome (1.2 Million people/year)
- Heterogenous
- Costly
  - Increased length of stay
  - Increased risk of mortality
  - Increased risk of chronic kidney disease (CKD)

$^1$Lewington AJ et al., 2013, Kidney international, 84(3):457-67
Definition of AKI

Sudden Deterioration of renal function
  • What is sudden?
  • What is deterioration?

Consensus Guidelines
  • RIFLE: Risk, Injury, Failure, Loss, ESRD
  • AKIN: Acute Kidney Injury Network
  • KDIGO: Kidney Disease Improving Global Outcomes
Diagnostic Criteria of AKI

1) Reduction in urinary output
2) Increased serum creatinine

• Either of these criteria can be used to define the 3 stages of AKI
# Urine Output - Diagnostic Criteria of AKI

<table>
<thead>
<tr>
<th>AKI Stage</th>
<th>Urine Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt; 0.5 mL/kg/h for 6–12 hours</td>
</tr>
<tr>
<td>2</td>
<td>&lt; 0.5mL/kg/h for ≥ 12 hours</td>
</tr>
<tr>
<td>3</td>
<td>&lt;0.3mL/kg/h for ≥ 24 hours</td>
</tr>
<tr>
<td></td>
<td>OR Anuria for ≥ 12 hours</td>
</tr>
</tbody>
</table>

# Serum Creatinine - Diagnostic Criteria of AKI

<table>
<thead>
<tr>
<th>Stage&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Serum Creatinine Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Increased by x1.5 (within 7 days) OR ≥ 0.3 mg/dL (≥26.5 μmol/L) (within 48hrs)</td>
</tr>
<tr>
<td>2</td>
<td>Increased by x2</td>
</tr>
<tr>
<td>3</td>
<td>Increased by x3 or ≥ 4.0 mg/dL (≥353.6 μmol/L) or initiation of RRT Or &lt;18 years, a decrease in eGFR &lt; 35 mL/minute/1.73 m&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Clinical Decision Support for AKI

Study by Al-Jaghbeer et al.³

- **Mortality**: 0.8% reduction
- **Length of stay**: 0.3 days reduction
- **Dialysis Use**: 2.7% reduction

³Al-Jaghbeer M et al., 2018; Journal of the American Society of Nephrology, 29(2):654-60
Clinical Management

- Discontinue or dose-adjust nephrotoxic drugs
- Treat the underlying disease
- Treat electrolyte disturbances
- Optimize fluid balance and hemodynamics

## Risk Factors for AKI²

<table>
<thead>
<tr>
<th>Exposures</th>
<th>Susceptibilities</th>
</tr>
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<tbody>
<tr>
<td>Sepsis</td>
<td>Dehydration or volume depletion</td>
</tr>
<tr>
<td>Critical illness</td>
<td>Advanced age</td>
</tr>
<tr>
<td>Circulatory shock</td>
<td>Female Gender</td>
</tr>
<tr>
<td>Burns</td>
<td>Black Race</td>
</tr>
<tr>
<td>Trauma</td>
<td>CKD</td>
</tr>
<tr>
<td>Cardiac surgery (especially with cardiopulmonary bypass)</td>
<td>Chronic diseases (heart, lung, liver)</td>
</tr>
<tr>
<td>Major noncardiac surgery</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>Nephrotoxic Drugs</td>
<td>Cancer</td>
</tr>
<tr>
<td>Radiocontrast agents</td>
<td>Anemia</td>
</tr>
<tr>
<td>Poisonous plants and animals</td>
<td></td>
</tr>
</tbody>
</table>

The Problem with Serum Creatinine

• Delayed Marker: >50% renal function loss for increase in creatinine\(^4\)
• Good for epidemiological studies, difficult to apply at the bedside
• How often is serum creatinine measured in AKI evaluation?
  • High risk: Measure at least daily\(^2\)

\(^4\)Najafi M et al., 2014, World journal of cardiology, 6(9):1006
Small Changes in Kidney Function

- Associated with significant short & long-term outcomes
  - An increase of 0.1 mg/dL is associated with increased risk\(^5\)
  - In patients with histopathologic evidence, 1/3 of patients could not diagnosed based on KIDGO criteria\(^6\)

\(^5\) Newsome BB et al., 2008, Archives of internal medicine, 168(6):609-16
\(^6\) Chu R et al, 2014; Clinical Journal of the American Society of Nephrology, CJN-06150613
Future of AKI Diagnosis: From Reactive to Proactive

- Asymptomatic
  - Increasing Risk
- Symptomatic
  - Kidney Failure
    - eGFR
    - Serum creatinine

Proactive Measures

Reacting to Manage the Damage
Other Markers of AKI

**Tubular Stress/Injury**
- TIMP2
- IGFBP-7
- NGAL
- L-FABP
- IL-18

**Decreased Glomerular Filtration**
- Creatinine, Serum
- Cystatin, Serum
## Kinetics of Urinary Markers of AKI

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Kinetics</th>
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<tr>
<td>KIM-1</td>
<td>Detected within 12-24h post injury, peaks at 48-72h</td>
</tr>
<tr>
<td>IL-18</td>
<td>Detected within 6h post injury, peaks at 12-18h</td>
</tr>
<tr>
<td>TIMP-2 + IGFBP-7</td>
<td>Detected within 12h post injury</td>
</tr>
<tr>
<td>NGAL</td>
<td>Detected within 3h post injury, peaks at 6h</td>
</tr>
<tr>
<td>L-FABP</td>
<td>Detected within 1h post injury, peaks within 6h</td>
</tr>
</tbody>
</table>

Hertzberg D et al., 2017, Clinical Kidney Journal, 10(3):323-31
Impact of New AKI Markers

1. Promising Research
   • Need more clinical outcomes

2. Timing and frequency for biomarker measurements is unclear
   • Exposure specific?

3. How will AKI be addressed in the context of pre-existing chronic kidney disease?
Conclusion/Summary

- AKI is defined by changes in serum creatinine and urinary output – KDIGO Guidelines
- A syndrome that is highly variable in severity, etiology, and timing of the acute insult
- Early indications of AKI by novel markers to enable optimal management
References


Disclosures/Potential Conflicts of Interest

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