Acute Kidney Injury: Why should you care?

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6/12/21
Consultant: CHF Solutions
AKI Foundation

I have no actual or potential conflict of interest with this presentation
AKI: Why should anyone care?

Outline

• AKI is common
• AKI is often missed
• AKI is bad: both short and long term
• AKI is preventable (to some degree)
Acute Kidney Injury or Acute Renal Failure?

- Previously > 30 definitions existed
- However, AKI ≠ ARF
  - Even small SCr rise is significant
  - Severity of AKI correlates with severity of outcomes
- Need for newer definitions
  - Grade AKI severity
  - Follow changes in kidney function
Kidney Disease: Improving Global Outcomes

<table>
<thead>
<tr>
<th>AKI STAGE</th>
<th>Serum creatinine criteria</th>
<th>Urine output criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Increase in SCr of $\geq 0.3$ mg/dL within 48 hours OR 1.5-1.9 X baseline</td>
<td>$&lt; 0.5$ ml/kg/hour for more than 6-12 hours</td>
</tr>
<tr>
<td>2</td>
<td>SCr 2-2.9 X baseline</td>
<td>$&lt; 0.5$ ml/kg/hour for more than 12 hours</td>
</tr>
<tr>
<td>3</td>
<td>SCr $&gt; 3$ X baseline OR SCr $&gt; 4$ mg/dL OR Start of RRT</td>
<td>$&lt; 0.3$ ml/kg/hour for 24 hours or anuria for 12 hours</td>
</tr>
</tbody>
</table>
Diagnosing AKI

Markers of filtration function
- Creatinine
- Cystatin C

Urine Output

Markers of Injury
- NGAL
- TIMP2 & IGFBP-7
- L-FABP, KIM-1, IL-18
Serum Creatinine

- Waste product of muscle metabolism
- Good marker in steady state conditions

**Drawbacks of SCr**
- Dependent on muscle mass
  - ↓production- acute/prolonged illness and sarcopenia
- Lags acute changes in kidney function
- Diluted in volume overload
Serum Cystatin C

- Produced by all nucleated cells
- Independent of muscle mass
- Does not cross placenta
- Drawbacks: Not available everywhere
- Slightly more expensive than creatinine
Urine Output

Correlates better with outcomes

- Not using UOP criteria leads to underdiagnosis
  - Upto 30% cases may be missed

Drawbacks

- Not reliably documented outside ICU setting
- May be charted as void counts and not actual volume
- Accurate measurement requires catheterization
Markers of kidney injury

**Urinary Neutrophil gelatinase-associated lipocalin (NGAL):**
- Elevated levels detected as early as 3 h after renal injury; peaks at 6-12 h
- Performance varies with context

**Urine TIMP-2 and IGFBP-7 (Nephrocheck™):** Cell cycle arrest markers
- POC device - FDA approved
- Robust prediction of progression of AKI

Others: L-FABP, IL-18, KIM-1, PenKid
<table>
<thead>
<tr>
<th>Structural Kidney Injury</th>
<th>No Damage</th>
<th>Damage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No SCR-based AKI</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>No kidney injury</td>
<td>&quot;Subclinical AKI&quot;</td>
<td>&quot;Clinical AKI&quot;</td>
</tr>
<tr>
<td>Yes SCR-based AKI</td>
<td>C</td>
<td>D</td>
</tr>
<tr>
<td>&quot;Hemodynamic AKI&quot;</td>
<td>&quot;Pre-renal Azotemia&quot;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&quot;Hepatorenal Syndrome&quot;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&quot;Cardiorenal Syndrome&quot;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&quot;RAAS Inhibition&quot;</td>
<td></td>
</tr>
</tbody>
</table>

- SCR Kinetics
- Decreased Production
- Renal Reserve
Outline

• AKI is common
  • AKI is often missed
  • AKI is bad: both short and long term
  • AKI is preventable (to some degree)
Epidemiology of Acute Kidney Injury in Critically Ill Children and Young Adults

Conclusions

Acute kidney injury is common and is associated with poor outcomes, including increased mortality, among critically ill children and young adults.

Kaddourah A, Basu RK, Bagshaw S, Goldstein SL for the AWARE Investigators

@menonshina
Incidence and outcomes of neonatal acute kidney injury (AWaken): a multicentre, multinational, observational cohort study

AKI in non ICU population

- Only 17% had > 2 SCr measurements
  - AKI present in 30% of those
- Conclusion: AKI occurs in at least 5% of all noncritically ill hospitalized children

Outline

• AKI is common
• AKI is often missed
• AKI is bad: both short and long term
• AKI is preventable (to some degree)
• 2009 Kids Inpatient Database: >4000 hospitals in 44 states
• AKI identified using ICD-9 codes
• Of ~2.6 million children, ~10000 developed AKI
• Incidence: 3.9/1000 admissions (~0.4%)
AKI in non ICU population

- Only 17% had ≥ 2 SCr measurements
  - AKI present in 30% of those
- Conclusion: AKI occurs in at least 5% of all noncritically ill hospitalized children

Community acquired AKI in the ED

Retrospective Single center

1 mth- 18 yrs
15,486 patients

CA-AKI
239 (1.5%)

AKI identification:
• ED clinician: 46/239
• Inpatient team: 123/239
• Never recognized: 74/239

Better recognition:
• Admission
• Older children
• More severe AKI

Neonatal AKI Documentation at Discharge: Findings from the AWAKEN Cohort

2162 Neonates Enrolled in AWAKEN Study

140 participants had <2 serum creatinine measurements and no urinary output data

2022 Neonates eligible for secondary analysis

605 infants with AKI (30.0%)

1417 infants without AKI (70.0%)

78 with documented AKI (12.9%)

527 with undocumented AKI (87.1%)

Infants with AKI Poorly Identified at Discharge

Chmielewski J, et al. Abstract presented at PAS 2021; slide courtesy Dr MC Starr
Chmielewski J, et al. Abstract presented at PAS 2021; slide courtesy Dr MC Starr

AKI discharge documentation rate? 13%

Factors associated with missing documentation?
- AKI diagnosed on UOP
- Stage 1 AKI
Outline

• AKI is common
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• AKI is preventable (to some degree)
# Short term outcomes with AKI

<table>
<thead>
<tr>
<th>Outcome</th>
<th>All Pts n=156</th>
<th>No AKI</th>
<th>Stage 2/3 AKI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical Vent days</td>
<td>2 (0, 7)</td>
<td>2 (0, 6)</td>
<td>6 (3, 15)</td>
</tr>
<tr>
<td>CRRT use (%)</td>
<td>6 (85.7)</td>
<td>0</td>
<td>6 (100)</td>
</tr>
<tr>
<td>Organ failure days</td>
<td>3 (1, 8)</td>
<td>3 (1, 7)</td>
<td>7 (3, 16)</td>
</tr>
<tr>
<td>Hospital LOS (days)</td>
<td>17 (8, 34)</td>
<td>16 (8, 30)</td>
<td>38 (16, 69)</td>
</tr>
<tr>
<td>ICU LOS (days)</td>
<td>6 (3, 12)</td>
<td>6 (3, 12)</td>
<td>8 (6, 18)</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>9 (7.1)</td>
<td>6 (4)</td>
<td>3 (20)</td>
</tr>
</tbody>
</table>

- ICU stay
- Duration of mechanical ventilation
- Mortality among critically ill patients

Retrospective case control study

100 patients with NTMx-AKI matched with patients who received NTMx but did not develop AKI

Chart review at ≥ 6 months post AKI/exposure
  - Nephrology clinic visit (y/n)
  - Serum creatinine/Cystatin C
  - Presence of hypertension
  - Urine for protein and creatinine
### Acute Kidney Injury Associated with High Nephrotoxic Medication Exposure Leads to Chronic Kidney Disease after 6 Months

Shina Meron, MD, Eric S. Kirkendall, MD, Hovı Nguyen, MPH, and Stuart L. Goldstein, MD

<table>
<thead>
<tr>
<th>eGFR (ml/min/1.73m²)</th>
<th>Before AKI N=100</th>
<th>Hospital DC N=92</th>
<th>6 months post N=77</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;90</td>
<td>0</td>
<td>24% (Including 5 &lt;60)</td>
<td>23% (Including 2&lt; 60)</td>
</tr>
<tr>
<td>90-150</td>
<td>100%</td>
<td>76%</td>
<td>65%</td>
</tr>
<tr>
<td>&gt;150</td>
<td>0</td>
<td>0</td>
<td>12%</td>
</tr>
</tbody>
</table>

**At 6 months post-AKI**

- 37% patients with hypertension
- 20% seen by a nephrologist
- Only 42% with complete CKD assessment: renal function, BP, urine protein

(J Pediatr 2014;165:522-7)
## Long term outcomes

<table>
<thead>
<tr>
<th>Population</th>
<th>Follow up (yrs)</th>
<th>Proteinuria</th>
<th>Htn</th>
<th>eGFR&lt; 90</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cooper, et al Cardiac surg N=51</td>
<td>7</td>
<td>3.9%</td>
<td>21%</td>
<td>14.3%</td>
</tr>
<tr>
<td>Mammen, et al PICU</td>
<td>1-3</td>
<td>9.5%</td>
<td>3.2%</td>
<td>39%</td>
</tr>
<tr>
<td>Askenazi, et al Non ICU N=29</td>
<td>3-5</td>
<td>27.6%</td>
<td>20.7%</td>
<td>14%</td>
</tr>
<tr>
<td>Slack, et al Septic shock N=12</td>
<td>4.2</td>
<td>18%</td>
<td>25%</td>
<td>25%</td>
</tr>
</tbody>
</table>
"This means something but I can't remember what!"
AKI-CKD continuum

Proteinuria
Hypertension
AKI Recovery
Loss of renal reserve
Non-Recovery
Acute Kidney Injury
Healthy Kidneys
Complete Recovery
Proteinuria
Hypertension
Chronic Kidney Disease
Low renal reserve/ CKD
Non-Recovery
Follow up after AKI

- Monitor for long term dysfunction
  - Creatinine/Cystatin C
  - Proteinuria
  - Blood pressure
- Educate parents/patients about AKI
  - Higher risk for repeat episodes
- AKI Clinic - Established in June 2016
  - Systematically follow children with AKI
Outline

• AKI is common
• AKI is often missed
• AKI is bad: both short and long term
• AKI is preventable (to some degree)
Prevention

• Primary: Identify patients with increased AKI risk before exposure to any injurious agent
  • Documentation of AKI; awareness of CKD

• Secondary: Following exposure
  • Identify the existence or extent of injury early (NINJA)

• Tertiary: After AKI onset ➔ avoiding further complications
  • E-alerts and Clinical Decision Support Systems
Secondary Prevention: Nephrotoxic medication (NTMx) Surveillance

- Prospective NTMx-AKI surveillance program
- Started as a single center program at Cincinnati Children’s
- Uses the EHR to identify non ICU patients exposed to ≥ 3 NTMx
- Intervention: SCr monitoring
AKI intensity decreased in Year 1 by 42%

Associated with 908 AKI days avoided in one year
A prospective multi-center quality improvement initiative (NINJA) indicates a reduction in nephrotoxic acute kidney injury in hospitalized children

Stuart L. Goldstein1,2, Devesh Dahale1,2, Eric S. Kirkendall1,2, Theresa Mottes1,2, Heather Kaplan1,2, Stephen Muething1,2, David J. Askenazi3, Traci Henderson7, Lynn Dill7, Michael J.G. Somers4, Jessica Kerr5, Jennifer Gilarde4, Joshua Zaritsky5, Valerie Bica6, Patrick D. Brophy6, Jason Misurac6, Richard Hackbarth7, Julia Steinke7, Joann Mooney7, Sara Ogrin3, Vimal Chadha3, Bradley Warady4, Richard Ogden8, Wendy Hoebing5, Jordan Symons9, Karyn Yonekawa9, Shina Menon1, Lisa Abrams9, Scott Sutherland10, Patricia Weng1, Fang Zhang11,12,13 and Kathleen Walsh12

see commentary on page 458
Tertiary prevention

If AKI occurs, try to avoid associated complications

Using Clinical Decision Support Systems including Electronic alerts
Acute Kidney Injury in the Era of the AKI E-Alert

Jennifer Holmes,* Timothy Rainer,† John Geen,‡ Gethin Roberts,§ Kate May,* Nick Wilson,* John D. Williams,¶ and Aled O. Phillips,* on behalf of the Welsh AKI Steering Group

Utility of Electronic Medical Record Alerts to Prevent Drug Nephrotoxicity

Melissa Martin¹ and F. Perry Wilson²,³

Utility of electronic AKI alerts in intensive care: A national multicentre cohort study

Jennifer Holmes, MSc, Gethin Roberts, MD, John Geen, PhD, Alan Dodd, PhD, Nicholas M. Selby, MD, Andrew Lewington, MD, Gareth Scholey, MD, John D. Williams, MD, Aled O. Phillips, MD, On behalf of the Welsh AKI steering group

Identification of Patients Expected to Benefit from Electronic Alerts for Acute Kidney Injury

Aditya Biswas,¹ Chirag R. Parikh,¹,² Harold I. Feldman,³,⁴,⁵ Amit X. Garg,⁶ Stephen Latham,⁷ Haiqun Lin,¹ Paul M. Palevsky,⁸,⁹ Ugosuchwu Ugwuowo,¹ and F. Perry Wilson¹,²

The incidence of pediatric acute kidney injury is increased when identified by a change in a creatinine-based electronic alert

Jennifer Holmes¹, Gethin Roberts¹, Kate May¹, Kay Tyerman¹, John Geen¹, John D. Williams⁵ and Aled O. Phillips¹; on behalf of the Welsh AKI Steering Group

¹Welsh Rare Disorder Network, Cwm Taf University Health Board; ²Department of Clinical Biochemistry, Huwidda University Health Board; ³Department of Paediatric Nephrology, Leeds Teaching Hospital NHS Trust; ⁴Department of Clinical Biochemistry, Cwm Taf University Health Board and Faculty of Life Sciences and Education, University of South Wales; and ⁵Institute of Nephrology, Cardiff University School of Medicine, Cardiff, UK
Do electronic alerts improve outcomes in patients with acute kidney injury?

**METHODS**

- Multicenter
- Double blinded
- 6030 patients
- Acute kidney injury

**INTRODUCTION**

Multicenter, double blinded, 6030 patients with acute kidney injury were randomized to standard care or electronic alert.

**OUTCOMES**

<table>
<thead>
<tr>
<th>INTERVENTION</th>
<th>OUTCOMES</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Primary composite</td>
<td>20.9% (95% CI: -0.6 to 2.7)</td>
</tr>
<tr>
<td></td>
<td>AKI progression</td>
<td>15.5% (95% CI: -0.5 to 2.3)</td>
</tr>
<tr>
<td></td>
<td>Dialysis</td>
<td>3.1% (95% CI: -0.3 to 1.1)</td>
</tr>
<tr>
<td></td>
<td>Death</td>
<td>8.9% (95% CI: -0.3 to 1.1)</td>
</tr>
</tbody>
</table>

**RESULTS**

- Electronic alert: 21.3% (95% CI: -1.4 to 2.7)
- Standard care: 20.9% (95% CI: -0.6 to 2.7)

**Conclusion:** Alerts did not reduce the risk of our primary outcome among patients in hospital with AKI. The heterogeneity of effect across clinical centers should lead to a re-evaluation of existing alerting systems for AKI.

**Reference:** Wilson FP et al. Electronic health record alerts for acute kidney injury: multicenter, randomized clinical trial. BMJ. 2021. DOI: 10.1136/bmj.m4786

**Visual abstract:** Denisse Arellano, MD  
@denilise_am
Clinical Decision Support Systems

- Awareness of AKI is not enough
- ? a/w best practice guidelines to help with management
Impact of integrated clinical decision support systems in the management of pediatric acute kidney injury: a pilot study

Shina Menon, Rod Tarrago, Kristen Carlin, Hong Wu and Karyn Yonekawa

375 alerts recorded

- 264 alerts in 225 patients
  - 25 repeat alerts for increasing AKI
  - 239 unique episodes analyzed

- Baseline phase: 59 episodes in 56 patients
- CDS phase: 140 episodes in 130 patients
- Post CDS phase: 40 episodes in 39 patients

111: Removed from analysis

- 39: false-positive due to incorrect baseline
- 72: met exclusion criteria
  - 41 admitted to nephrology
  - 1 lab error
  - 5 palliative care
  - 13 recent transplant or nephrectomy
  - 12 CKD stage ≥4
## AKI Care Pathway: AEIOU

<table>
<thead>
<tr>
<th>When you see AKI, think “AEIOU”</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assess</strong> cause of AKI: prerenal, renal or post renal</td>
</tr>
<tr>
<td><strong>Evaluate</strong> drug doses: adjust medications; hold nephrotoxic drugs if not essential</td>
</tr>
<tr>
<td><strong>Intake</strong> and output charting</td>
</tr>
<tr>
<td><strong>Optimize</strong> volume status: ensure euvolemia; restrict fluids if oliguric</td>
</tr>
<tr>
<td><strong>Urine</strong> dipstick</td>
</tr>
</tbody>
</table>
Study

Conclusions

E-alerts improve the documentation, but it is still sub-optimal.

Better recognition of AKI enables providers to intervene early.

Multimodal CDS improve adherence with standard of care guidelines.

• Results in improved eGFR at discharge and follow up.
• Improvement not necessarily related to nephrology consultation
AKI: Why should you care?

Common complication of acute illness
- High mortality and morbidity
- Patients post stage 2-3 AKI at higher risk of subsequent CKD

Actual burden is still not well known
- Improved recognition and documentation of AKI may impact outcomes

Some AKI is preventable
- Increased awareness of risk factors
- Appropriate nephrotoxic medication use
Take Home Points

Be on the alert for AKI
• If you see AKI, call it by its name

Common sense measures
• Assess cause
• Evaluate drug doses
• I/O charting
• Optimize volume status
• Urine dipstick

If your patient develops AKI:
• Educate them
• Monitor for CKD
• AKI clinic
Division of Nephrology

- Joseph Flynn
- Jodi Smith
- Karyn Yonekawa

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- 🐦 @menonshina

Research

Mentors
- Stuart Goldstein
- Raj Basu

Collaborators:
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- Ari Pollack
- Hong Wu
- Kristen Carlin
- Tasha Murphy
- Alex Kula
- Michelle Starr