Post Cardiac Surgery Acute Kidney Injury: evidence for early recognition and timely support

Manal Alasnag
22/02/11
Acute renal failure
Acute renal dysfunction
Acute kidney injury
Overview

- Background
- Classification & staging
- Early Biomarkers
- Early vs late RRT
Prevalence

Depending on the definition:

- 5% of all patients admitted to hospital
- 1-25% of ICU patients
- 30-40% (post cardiotomy adult patients)
  - 1-5% require dialysis
  - 80% mortality

Schneider, Crit Care Med 2010 Vol 38, No 3
Prevalence

- 2.5-4.5% (critically ill children)
  - Mortality 8-89%

- 10% (cardiac surgical infants & children)
  - Mortality rates 15% to 60%

Schneider, Crit Care Med 2010 Vol 38, No 3
Sinning et al.
Renal Function Predicts Mortality After TAVI

SHA22
Risk Factors

- Pre-existing renal dysfunction
- Ventricular dysfunction
- Prolonged CPB time
- Multiple staged procedures
Natural history of AKI

Cerdá J et al. CJASN 2008;3:881-886
Acute Kidney Injury

- glomerular filtration rate
- changes in urine output
- azotemia and oliguria
Acute Kidney Injury

• NOT creatinine and urine output

• BUT changes in creatinine and urine output
Acute Dialysis Quality Initiative

• (ADQI) 2004:
  – a standard definition
  – multilevel classification system
  – stratify the severity
RIFLE Criteria for Acute Kidney Dysfunction

- **Risk**
  - Increased creatinine x 1.5 or GFR decrease > 25%

- **Injury**
  - Increased creatinine x 2 or GFR decrease > 50%
  - Increase creatinine x 3 or GFR dec > 75% or creatinine ≥ 4mg/dl (Acute rise of ≥ 0.8 mg/dl)

- **Failure**
  - UO < 0.5 ml/kg/h x 6 hrs
  - UO < 0.5 ml/kg/h x 12 hrs
  - UO < 0.3 ml/kg/h x 24 hrs or anuria x 12 hrs

- **Loss**
  - Persistent AKD*** = complete loss of renal function > 4 weeks

- **ESRD**
  - End Stage Renal Disease

*www.ADQI.net*

<table>
<thead>
<tr>
<th>Category</th>
<th>Glomerular filtration rate criteria</th>
<th>Urine output criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk</strong></td>
<td>Serum creatinine x 1.5</td>
<td>&lt; 0.5ml/kg/h x 6h</td>
</tr>
<tr>
<td><strong>Injury</strong></td>
<td>Serum creatinine x 2</td>
<td>&lt; 0.5ml/kg/h x 12h</td>
</tr>
<tr>
<td><strong>Failure</strong></td>
<td>Serum creatinine x 3 or Serum creatinine &gt; 4 mg/dl with acute rise &gt; 0.5 mg/dl</td>
<td>&lt; 0.3ml/kg/h x 24 h or Anuria x 12h</td>
</tr>
<tr>
<td><strong>Loss</strong></td>
<td>Persistent loss of kidney function &gt; 4 weeks</td>
<td></td>
</tr>
<tr>
<td><strong>End-stage</strong></td>
<td>Persistent loss of kidney function &gt; 3 months</td>
<td></td>
</tr>
</tbody>
</table>
RIFLE on PICU

- 150 mechanically ventilated PICU patients
- Incidence of AKI = 82%
- 11.1% overall mortality
- 14.6% mortality in AKI group

RIFLE on PICU

3983 patient admissions

Overall mortality: 6.4%

3396 patients

587 exclusions:
ESRD
Chronic Renal Failure
Renal transplant
<1 month, >21 years old

No AKI: 3057 pts
Mortality: 3.7%

AKI During PICU: 339 pts (10% incidence)

AKI on Admission: 194 pts (5.7% incidence)

R: 111 (3.3%)
I: 101 (3%)
F: 127 (3.7%)

Mortality: 30%

R: 57 (1.7%)
I: 56 (1.6%)
F: 81 (2.4%)

Mortality: 32%
## Staging System for Acute Kidney Injury modified from the RIFLE

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum creatinine criteria</th>
<th>Urine output criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Increase in serum creatinine of $\geq 0.3 \text{ mg/dl}$ or increase to $\geq 150%$ to $200%$ (1.5 to 2-fold) from baseline</td>
<td>$&lt;0.5 \text{ ml/kg/h}$ for more than 6 hours</td>
</tr>
<tr>
<td>2</td>
<td>Increase in serum creatinine to $&gt; 200%$ to $300%$ ($&gt;2$ to $3$ fold) from baseline</td>
<td>$&lt;0.5 \text{ ml/kg/h}$ for more than 12 hours</td>
</tr>
<tr>
<td>3</td>
<td>Increase in serum creatinine to $&gt;300%$ ($3$ fold) from baseline (or serum creatinine of $\geq 4.0 \text{ mg/dl}$ with an acute increase of at least $0.5 \text{ mg/dl}$)</td>
<td>$&lt;0.3 \text{ ml/kg/h}$ for 24 hours or anuria for 12 hours</td>
</tr>
</tbody>
</table>

Acute kidney injury is defined as an abrupt deterioration in kidney function, currently defined as an absolute increase of at least $0.5 \text{ mg/dl}$ or a relative increase of at least $50\%$.
Creatinine

- Depends on age, muscle mass, ...
- Slow increase
  - up to 50% kidney function loss not reflected
  - measures renal injury over days
- After cardiac surgery $\rightarrow$ diluted
## Markers for acute injury

<table>
<thead>
<tr>
<th>Year</th>
<th>Acute Myocardial Infarction</th>
<th>Acute Kidney Injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>1960</td>
<td>LDH</td>
<td>creatinine</td>
</tr>
<tr>
<td>1970</td>
<td>CPK, Myoglobin</td>
<td>creatinine</td>
</tr>
<tr>
<td>1980</td>
<td>CK-MB</td>
<td>creatinine</td>
</tr>
<tr>
<td>1990</td>
<td>Troponin-T</td>
<td>creatinine</td>
</tr>
<tr>
<td>2000</td>
<td>Troponin-I</td>
<td>creatinine</td>
</tr>
</tbody>
</table>
Figure 2. 1-Year Outcome According to Baseline Serum Creatinine

Survival rate according to quartiles (Qs) of baseline serum creatinine (mg/dL).
Q1: <1.08 mg/dL, Q2: 1.08 to 1.24 mg/dL, Q3: 1.25 to 1.57 mg/dL, Q4: ≥1.58 mg/dL.
A CONCEPTUAL FRAMEWORK OF ACUTE KIDNEY INJURY

Normal → Increased risk → Damage → ↓ GFR → Kidney failure → Death

Complications

Antecedents
Intermediate Stage
Stage
AKI
Outcomes

Lameire N et al. NDT Plus 2008;1:392-402
Biomarkers

- Neutrophil Gelatinase-Associated Lipocalin (NGAL)
- Kidney Injury Molecule-1
- Cystatin-C
- Interleukin 18
- N-acetyl-B-d-glucosaminidase (NAG)
- Albumin
• 25 kDa protein
• Bound to gelatinase from human neutrophils
• Expressed at low concentrations
  – kidney
  – trachea
  – lungs
  – stomach
  – colon
• Induced very early after ischaemia
NGAL in AKI

• Upregulated in ischemic acute injury
• Accumulates in proximal tubules
• Proliferating epithelial cells
  – Regulator of epithelial morphogenesis
  – Iron-transporting protein
  – Exogenous NGAL → improved survival in mice
Mishra et al, NGAL as biomarker for aki after cardiac surgery, Lancet, April 2005
NGAL

• Early biomarker for AKI
  – Precedes increase in serum creatinine by 1-3 days

• Urinary results
  – Advantages
    • Less invasive, less interfering proteins
  – Problems
    • Severe oliguria
    • Fluid overall status / diuretic therapy
    • Sensitivity and specificity
RRT: Timing

• Advantages:
  – Restores dry body weight
  – Swings in intravascular volume are avoided
  – BP is maintained
  – Decreases activation of neurohormones
  – Minimizes treatment-associated renal injury
  – Metabolic control
  – Allows aggressive nutritional support
<table>
<thead>
<tr>
<th>Author</th>
<th>Patient numbers</th>
<th>CRRT Initiated early (average days)</th>
<th>CRRT Initiated late (average days)</th>
<th>Medications at CRRT initiation</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elahi et al. [15]</td>
<td>64 cardiac surgery patients needing CRRT</td>
<td>0.78 ± 0.2 days</td>
<td>2.55 ± 2.2 days</td>
<td>Dopa 6 out of 58 Adre 20 out of 44 Amin 11 out of 53 Frus 27 out of 37</td>
<td>Retrospective study</td>
</tr>
<tr>
<td>Bent et al. [16]</td>
<td>65 cardiac surgery patients needing CRRT</td>
<td>2.38 days</td>
<td>N/A</td>
<td>IABP = 32.3% Ventilation = 58.5% Hypotension despite inotropes = 40%</td>
<td>Retrospective study</td>
</tr>
<tr>
<td>Luckraz et al. [19]</td>
<td>98 cardiac surgery patients needing CRRT</td>
<td>2.08 ± 1.66</td>
<td>N/A</td>
<td>IABP = 40% Tracheostomy for prolonged ventilation = 32%</td>
<td>Retrospective study</td>
</tr>
<tr>
<td>Settings et al. [17]</td>
<td>100 trauma patients needing CRRT</td>
<td>10.5 since hospital admission</td>
<td>19.4 since hospital admission</td>
<td>Survival rate significantly increased among early starters compared to late starters (39.0 vs 20.0%, p = 0.041)</td>
<td>Retrospective study</td>
</tr>
</tbody>
</table>
RRT: Timing

• Association between small serum creatinine changes after cardiac surgery and mortality
  – Changes within 48-hrs and 30-day mortality

• Decrease in serum creatinine
  – 2.6% mortality

• Increase in serum creatinine
  – 8.9% mortality

Elevated creatinine may be an independent indicator for risk of death
RRT in children

- Pediatric bone marrow transplant recipients
  - ≥10% weight gain from baseline (fluid overload) predictor of death

- Fluid overload on PICU an independent risk factor for death

### RRT in children


<table>
<thead>
<tr>
<th>Variable</th>
<th>All, n</th>
<th>Survivors, n</th>
<th>Nonsurvivors, n</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>9.6 (2.5, 14.3), 113</td>
<td>8.5 (2.5, 14.6), 69</td>
<td>9.9 (2.2, 13.9), 44</td>
<td>.92</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>31.2 (15.9, 55.3), 112</td>
<td>35.5 (20.0, 54.5), 68</td>
<td>27.3 (13.7, 56.3), 44</td>
<td>.33</td>
</tr>
<tr>
<td>PRISM III at CWW</td>
<td>13.0 (9.0, 17.0), 113</td>
<td>12.0 (8.0, 15.0), 69</td>
<td>15.5 (11.0, 18.5), 44</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hospital days before CWW</td>
<td>5.0 (1.0, 16.0), 113</td>
<td>3.0 (1.0, 7.0), 69</td>
<td>15.5 (4.0, 23.5), 44</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Days in ICU before CWW</td>
<td>2.0 (0.0, 4.0), 113</td>
<td>1.0 (0.0, 3.0), 69</td>
<td>3.0 (1.0, 5.0), 44</td>
<td>.03</td>
</tr>
<tr>
<td>GFR at CWW</td>
<td>21.7 (13.7, 41.4), 105</td>
<td>20.1 (12.6, 36.7), 65</td>
<td>27.0 (16.8, 55.8), 40</td>
<td>.08</td>
</tr>
<tr>
<td>P/F ratio at CVVH</td>
<td>173 (140, 295), 74</td>
<td>187 (155, 309), 40</td>
<td>163 (125, 227), 34</td>
<td>.13</td>
</tr>
<tr>
<td>%FO before CVVH</td>
<td>10.9 (2.8, 22.1), 94</td>
<td>7.8 (2.0, 16.7), 52</td>
<td>15.1 (4.9, 23.9), 42</td>
<td>.02</td>
</tr>
<tr>
<td>ICU %FO before CVVH</td>
<td>5.2 (1.9, 13.0), 75</td>
<td>5.0 (1.3, 10.6), 42</td>
<td>8.1 (2.5, 14.1), 33</td>
<td>.15</td>
</tr>
<tr>
<td>% Intubated</td>
<td>70.8, 113</td>
<td>58.0, 69</td>
<td>90.9, 44</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>% With vasoactive infusions</td>
<td>69.9, 113</td>
<td>60.9, 69</td>
<td>84.1, 44</td>
<td>.009</td>
</tr>
<tr>
<td>% With abnormal GFR</td>
<td>92.4, 105</td>
<td>93.9, 61</td>
<td>90.0, 40</td>
<td>.48</td>
</tr>
</tbody>
</table>
Fluid overload:

- A marker for severity of illness
- A threshold for therapeutic intervention
- Can we extrapolate from adult studies
Conclusion

- Identifying risk factors for AKI before PICU admission
- Directing therapy that will prevent worsening grades of kidney injury
- Earlier identification of AKI
- Earlier intervention may improve patient outcome on PICU
Thank You