Acute kidney injury in critical care unit

Masaomi Nangaku
Division of Nephrology and Endocrinology
the University of Tokyo Graduate School of Medicine, Japan
A 64-year-old woman was admitted to the hospital due to a severe asthma attack. On admission, her serum creatinine and serum urea nitrogen levels were 0.75 mg/dL (66.3 μmol/L) and 20.9 mg/dL, respectively. Intravenous therapy with dexamethasone was initiated for treatment of the asthma attack. The next day, serum creatinine level increased to 4.63 mg/dL (409.3 μmol/L).
Case

Extensive examinations were performed, but only serum creatinine level supported the diagnosis of AKI (serum urea nitrogen was 14.9 mg/dL, urine volume was preserved, and urinalysis was normal).

What is your diagnosis?
1. pre-renal AKI
2. renal AKI
3. post-renal AKI
4. pseudo-AKI
Later, we learned that the blood sample had been drawn by a physician in training and was obtained from the patient’s left cubital vein, with tourniquet applied, at the same time that dexamethasone was being infused into the left dorsal hand vein.
Pseudo–AKI secondary to intravenous dexamethasone

Dexamethasone contains creatinine as a buffer. Thus, approximately 1 hour later, a new blood sample was obtained from the patient’s right arm; serum creatinine level was normal in this sample.

Drugs that can cause pseudoelevation in serum creatinine concentration

Sources of Extrinsic Creatinine
8 mg creatinine in dexamethasone, 3.3 mg
16 mg creatinine in hydrocortisone, 100 mg
37.5 mg creatinine in azasetron hydrochloride, 10 mg

Analytical Interference
5-Fluorocytosine
Cefoxitin

● Increase in SCr by $\geq 0.3$ mg/dl ($\geq 26.5$ lmol/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 $\leq 0.5$ ml/kg/h for 6 hours.
<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum creatinine</th>
<th>Urine output</th>
</tr>
</thead>
</table>
| 1     | 1.5–1.9 times baseline  
OR  
≥0.3 mg/dl (≥26.5 μmol/l) increase | <0.5 ml/kg/h for 6–12 hours |
| 2     | 2.0–2.9 times baseline | <0.5 ml/kg/h for ≥12 hours |
| 3     | 3.0 times baseline  
OR  
Increase in serum creatinine to  
≥4.0 mg/dl (≥353.6 μmol/l)  
OR  
Initiation of renal replacement therapy  
OR, In patients <18 years, decrease in eGFR to <35 ml/min per 1.73 m² | <0.3 ml/kg/h for ≥24 hours  
OR  
Anuria for ≥12 hours |
Retooling the Cr clearance equation to estimate kinetic GFR when the plasma Cr is changing acutely

\[ KeGFR = \frac{SSP_{Cr} \times CrCl}{MeanP_{Cr}} \times \left(1 - \frac{24 \times \Delta P_{Cr}}{\Delta Time(h) \times Max\Delta P_{Cr}/Day}\right) \]

- **Serum creatinine**
- **Clearance equation**
- **Kinetic eGFR formula**
risk is greatest when patients meet both the serum creatinine level and urine output criteria for AKI

Kellum et al. JASN 2015
targeted approach for AKI

AKI therapy
Requirement for renal replacement therapy or dialysis

Frusemide to prevent acute deterioration in renal function

<table>
<thead>
<tr>
<th>Study</th>
<th>Frusemide</th>
<th>Control</th>
<th>Frusemide (95% CI)</th>
<th>Control (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hager</td>
<td>0/62</td>
<td>0/59</td>
<td>0.47 (0.24 to 0.86)</td>
<td>Not estimable</td>
</tr>
<tr>
<td>Lassnig</td>
<td>2/41</td>
<td>0/40</td>
<td>4.35 (0.14 to 0.78)</td>
<td>4.08 (0.46 to 3.59)</td>
</tr>
<tr>
<td>Solomon</td>
<td>1/25</td>
<td>0/28</td>
<td>0.90 (0.46 to 0.7)</td>
<td>Not estimable</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>128</td>
<td>127</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 3 (frusemide), 0 (placebo)
Test for heterogeneity: $\chi^2 = 0.03$, df = 1, $P = 0.86$, $I^2 = 0$
Test for overall effect: $z = 1.27$, $P = 0.21$

Frusemide to treat acute renal failure

<table>
<thead>
<tr>
<th>Study</th>
<th>Frusemide</th>
<th>Control</th>
<th>Frusemide (95% CI)</th>
<th>Control (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown</td>
<td>28/28</td>
<td>27/28</td>
<td>47.31 (0.97 to 1.1)</td>
<td>1.04 (0.02 to 0.96)</td>
</tr>
<tr>
<td>Karayannopoulos</td>
<td>1/10</td>
<td>7/10</td>
<td>1.16 (0.02 to 0.8)</td>
<td>Not estimable</td>
</tr>
<tr>
<td>Kleinknecht</td>
<td>31/33</td>
<td>31/33</td>
<td>42.66 (0.88 to 1.13)</td>
<td>1.00 (0.40 to 1.54)</td>
</tr>
<tr>
<td>Shilliday</td>
<td>10/32</td>
<td>12/30</td>
<td>7.96 (0.48 to 0.71)</td>
<td>99.10 (0.71 to 1.26)</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>103</td>
<td>101</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 70 (frusemide), 77 (placebo)
Test for heterogeneity: $\chi^2 = 21.68$, df = 3, $P < 0.0001$, $I^2 = 86.2$
Test for overall effect: $z = 0.39$, $P = 0.69$

Total (95% CI)

Total events: 73 (frusemide), 77 (placebo)
Test for heterogeneity: $\chi^2 = 13.95$, df = 5, $P = 0.02$, $I^2 = 64$
Test for overall effect: $z = 0.12$, $P = 0.91$

favors furosemide  favors control

Ho & Sheridan. BMJ 2006
low dose dopamine

Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group

Kaplan-Meier curve of time to recovery of normal renal function

Bellomo et al. Lancet 2000
meta-analysis of hANP after surgery

Nigwekar et al. CJASN 2009

<table>
<thead>
<tr>
<th>Study</th>
<th>ANP n/N</th>
<th>Control n/N</th>
<th>OR (random) 95% CI</th>
<th>Weight</th>
<th>OR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>6/6</td>
<td>6/6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kuse 1996</td>
<td>5/7</td>
<td>4/4</td>
<td>2.17</td>
<td>42.49</td>
<td>Not estimable</td>
</tr>
<tr>
<td>Meyer 1997</td>
<td>0/7</td>
<td>6/7</td>
<td>17.73</td>
<td>0.97</td>
<td>Not estimable</td>
</tr>
<tr>
<td>Meyer 1999</td>
<td>28/85</td>
<td>21/58</td>
<td>11.14</td>
<td>0.28</td>
<td>[0.09, 0.91]</td>
</tr>
<tr>
<td>Rahman 1994</td>
<td>7/30</td>
<td>12/23</td>
<td>11.45</td>
<td>0.30</td>
<td>[0.09, 0.94]</td>
</tr>
<tr>
<td>Sward 2004</td>
<td>6/29</td>
<td>14/30</td>
<td>42.49</td>
<td>0.34</td>
<td>[0.12, 0.96]</td>
</tr>
<tr>
<td>Subtotal</td>
<td>162</td>
<td>128</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events: 52 (ANP), 63 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: Chi² = 8.23, df = 3 (P = 0.04), I² = 63.6%</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Total (95% CI) = 0.824 (P = 0.04)</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>ANP n/N</th>
<th>Control n/N</th>
<th>OR (random) 95% CI</th>
<th>Weight</th>
<th>OR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lewis 2000</td>
<td>109/248</td>
<td>108/256</td>
<td>23.42</td>
<td>57.51</td>
<td>0.97 [0.52, 1.46]</td>
</tr>
<tr>
<td>Meyer 1999</td>
<td>69/108</td>
<td>86/114</td>
<td>19.63</td>
<td>0.52</td>
<td>[0.29, 0.94]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>385</td>
<td>428</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events: 190 (ANP), 217 (Control)</td>
<td></td>
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</tr>
<tr>
<td>Test for heterogeneity: Chi² = 4.72, df = 2 (P = 0.09), I² = 57.6%</td>
<td></td>
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<tr>
<td>Test for overall effect: Z = 0.52 (P = 0.60)</td>
<td></td>
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</tr>
<tr>
<td>Total (95% CI) = 0.824 (P = 0.04)</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>ANP n/N</th>
<th>Control n/N</th>
<th>OR (random) 95% CI</th>
<th>Weight</th>
<th>OR (random) 95% CI</th>
</tr>
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<td></td>
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<tr>
<td></td>
<td>242</td>
<td>280</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events: 242 (ANP), 280 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: Chi² = 16.89, df = 6 (P = 0.010), I² = 64.5%</td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 1.80 (P = 0.07)</td>
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</tr>
</tbody>
</table>
Glutaraldehyde EPO protects kidney in ischemia/reperfusion injury without increasing red blood cell production

Chattong et al. Br J Pharmacol 2013
Ischemia is a common pathway in a variety of AKI

Reduction in renal blood flow

- Intravascular volume depletion and hypotension
  - Gastrointestinal tract, renal, dermal losses
  - Hemorrhage
- Decreased effective intravascular volume
  - Congestive heart failure
  - Cirrhosis
  - Nephrosis
  - Peritonitis
- Medications
  - Cyclosporin A
  - Tacrolimus
  - Angiotensin-converting enzyme inhibitors
  - Nonsteroidal antiinflammatory drugs
  - Radiocontrast agents
  - Amphotericin
- Sepsis
- Hepatorenal syndrome

Acute kidney injury

- No reflow phenomenon


Renal vascular disease
- Large vessel
  - Renal artery thrombosis
  - Arterial occlusion during surgery
  - Renal artery stenosis
- Small vessel
  - Vasculitis
  - Preeclampsia
  - Sickle cell anemia
  - Hypercalcemia
  - Transplant rejection
Kidney requires large amounts of oxygen

Weight: 0.3% of body weight

Blood flow: 20-25% of cardiac output

O$_2$ consumption:

28% of total body consumption

O$_2$ (cortex): 50-100mmHg

O$_2$ (medulla): 9.8-21.8mmHg
Cellular responses against hypoxia
Hypoxia Inducible Factor (HIF)

Oxygen transport (EPO, Transferrin)
Vascular regulation (VEGF, adrenomedullin, HO-1)
Glucose uptake and glycolysis (Glut-1, Aldolase A)
Anti-oxidative enzymes (SODs, catalase)

Protection of the kidney against ischemia by constitutively active HIF

Manotham, Nangaku et al.
Kidney Int 2005
HIF activation therapy
Preconditioning in an ischemia-reperfusion model

Positive correlation between creatinine and tubular injury

Inhibition of HIF activation in tubular cells by hyperglycemia via oxidative stress!

HIF activation in diabetic kidneys is enhanced by anti-oxidants

Rosenberger a et al. Kidney Int 2008
Impaired adaptive response against hypoxia under hyperglycemic conditions

**Normoxia**

- HIF-α
- OH
- pVHL

Proteosomal degradation

**Process**

- Succinate → CO₂
- 2-oxoglutarate → O₂
- Prolyl hydroxylase
- Fe

**HIF-α**

- HIF-1b

**Gene expression**

- MGO
- p300

**MGO**

- Gene expression
When to start RRT

Section 5: Dialysis Interventions for Treatment of AKI

5.1.1: Initiate RRT emergently when life-threatening changes in fluid, electrolyte, and acid-base balance exist.

5.1.2: Consider the broader clinical context, the presence of conditions that can be modified with RRT, and trends of laboratory tests—rather than single BUN and creatinine thresholds alone—when making the decision to start RRT.
“Absolute” indications for CKD/ESRD should be avoided in AKI

1. Consider other organ injuries especially the lungs
2. Increased catabolism and adequate nutritional protein
3. Fluid space for intravenous medications
4. more sensitive to metabolic derangements (acid-base and electrolyte status)
Earlier initiation is better for AKI?

- Meta-analysis of 2 RCT, 4 pro-, 9 retrospective

![Forest plot of 15 studies](image)

Favors Early  Favors Late

Karvellas & Bagshaw. Crit Care 2011
Earlier initiation is better for AKI?

- **NSARF** (National Taiwan University Hospital Study group on Acute Renal Failure)

  **Post-major abdo surgery AKI**
  
  (n=98)
  

  **Septic AKI** (n=370)
  
  Crit Care. 2011;15:R134
Earlier initiation is better for AKI?

- **NSARF** (National Taiwan University Hospital Study group on Acute Renal Failure)

Post-surgery AKI (n=648), *Plos One* 2012;7:e42952

Duration of time between ICU admission and RRT initiation:
- **Early** = 0–1 day
- **Intermediate** = 2–3 day
- **Late** = ≥ 4 day
HD does not protect the poorly functioning kidney against CI-AKI: meta-analysis

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year published</th>
<th>Study design</th>
<th>Radiocontrast agent</th>
<th>Technique</th>
<th>Duration of extracorporeal treatment (hour)</th>
<th>Dialyzer</th>
<th>Blood flow (mL/min)</th>
<th>Dialysate flow (mL/min)</th>
<th>RR for CI-AKI (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lehnert et al. [61]</td>
<td>1998</td>
<td>RCT</td>
<td>Iopentol</td>
<td>HD</td>
<td>63 ± 6 min after radiocontrast procedure</td>
<td>Fresenius P50</td>
<td>139 ± 8</td>
<td>500</td>
<td>1.33 (95% CI 0.64–2.91)</td>
</tr>
<tr>
<td>Sterner et al. [62]</td>
<td>2000</td>
<td>RCT</td>
<td>Iohexol, iodixanol, and ioxaglate</td>
<td>HD</td>
<td>Maximum 3 hrs after radiocontrast procedure</td>
<td>Low-flux cellulose acetate or diacetae</td>
<td>200</td>
<td>500</td>
<td>1.70 (95% CI 0.59–4.90)</td>
</tr>
<tr>
<td>Vogt et al. [63]</td>
<td>2001</td>
<td>RCT</td>
<td>Nonionic low osmolarity</td>
<td>HD</td>
<td>Median 120 min (range 50–280) after radiocontrast procedure</td>
<td>Fresenius P50, F60</td>
<td>180</td>
<td>500</td>
<td>1.27 (95% CI 0.80–2.01)</td>
</tr>
<tr>
<td>Berger et al. [64]</td>
<td>2001</td>
<td>RCT</td>
<td>Iopromide</td>
<td>HD</td>
<td>108 ± 25 min after radiocontrast procedure</td>
<td>Fresenius P6</td>
<td>220</td>
<td>500</td>
<td>3.43 (95% CI 0.43–25.98)</td>
</tr>
<tr>
<td>Frank et al. [65]</td>
<td>2005</td>
<td>RCT</td>
<td>Iomeprol</td>
<td>HD</td>
<td>Simultaneously with radiocontrast procedure</td>
<td>Fresenius F60</td>
<td>200</td>
<td>500</td>
<td>Total clearance of contrast media was significantly increased and the area under curve (AUC) of contrast media concentration was significantly lower in the HD group when compared with control group. However, the authors did not report incidence of CI-AKI</td>
</tr>
<tr>
<td>Gaburri et al. [48]</td>
<td>2003</td>
<td>Prospective cohort</td>
<td>Ioversol</td>
<td>CVVHD1</td>
<td>Simultaneously with radiocontrast procedure</td>
<td>Prisma MR400</td>
<td>150</td>
<td>Replacement and dialysate 2,000 mL/h</td>
<td>1.56 (95% CI 0.66–3.72)</td>
</tr>
<tr>
<td>Mareszzi et al. [49]</td>
<td>2003</td>
<td>RCT</td>
<td>Iopentol</td>
<td>CVVH</td>
<td>Initiated 4–6 hrs before, interrupted during, and resumed after radiocontrast procedure</td>
<td>Renaflow H1700</td>
<td>100</td>
<td>Replacement 1,000 mL/hour; no dialysate</td>
<td>0.12 (95% CI 0.05–0.32)</td>
</tr>
<tr>
<td>Heidt et al. [66]</td>
<td>2005</td>
<td>Retrospective cohort</td>
<td>Iopromide</td>
<td>HD</td>
<td>As soon as technically feasible</td>
<td>AM-Bio HX90</td>
<td>200</td>
<td>500</td>
<td>0.33 (95% CI 0.01–7.72)</td>
</tr>
</tbody>
</table>
# Timing of RRT in AKI

## Potentially influencing factors for starting RRT

<table>
<thead>
<tr>
<th>Category</th>
<th>Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-specific</td>
<td>Kidney function/reserve</td>
</tr>
<tr>
<td></td>
<td>Co-morbid disease and physiologic reserve</td>
</tr>
<tr>
<td></td>
<td>Primary diagnosis: severity of illness and trajectory</td>
</tr>
<tr>
<td></td>
<td>Acute kidney injury: severity and trend</td>
</tr>
<tr>
<td>Clinician-specific</td>
<td>Goals of therapy</td>
</tr>
<tr>
<td></td>
<td>Clinician threshold for initiation</td>
</tr>
<tr>
<td></td>
<td>Local practice patterns, Prescribing service</td>
</tr>
<tr>
<td>Organizational</td>
<td>Country/institution, Health costs</td>
</tr>
<tr>
<td></td>
<td>ICU type</td>
</tr>
<tr>
<td></td>
<td>Machine and nursing availability</td>
</tr>
</tbody>
</table>

Bagshaw et al. Critical Care 2009
Timing of RRT in AKI

Research recommendations by KDIGO AKI-GL

• Determine reproducible criteria for starting RRT in AKI.

• Determine whether early vs. late start of RRT results in improved clinical outcomes.
Online HDF in septic AKI provides better removal of VEGF and other cytokines

prospective randomized controlled study in 28 septic AKI patients

Chancharoenthana et al. Ther Apher Dial 2013
Online HDF in septic AKI is associated with better renal outcome

Chancharoenthana et al. Ther Apher Dial 2013
High-volume hemofiltration for septic AKI: a systematic review and meta-analysis

Pooled analysis for 28-day mortality did not show any difference between HVHF compared with control HF

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>HVHF Events</th>
<th>HVHF Total</th>
<th>Control HF Events</th>
<th>Control HF Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boussekey et al.</td>
<td>3</td>
<td>9</td>
<td>5</td>
<td>10</td>
<td>5.7%</td>
<td>0.50 [0.08, 3.21]</td>
<td></td>
</tr>
<tr>
<td>Joannes-Boyau et al.</td>
<td>25</td>
<td>66</td>
<td>29</td>
<td>71</td>
<td>33.2%</td>
<td>0.88 [0.44, 1.75]</td>
<td></td>
</tr>
<tr>
<td>Sanchez et al.</td>
<td>2</td>
<td>15</td>
<td>7</td>
<td>15</td>
<td>6.0%</td>
<td>0.18 [0.03, 1.07]</td>
<td></td>
</tr>
<tr>
<td>Zhang et al.</td>
<td>81</td>
<td>141</td>
<td>81</td>
<td>139</td>
<td>55.1%</td>
<td>0.97 [0.60, 1.55]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>231</td>
<td>235</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>0.82 [0.52, 1.28]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>111</td>
<td></td>
<td>122</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.04; Chi² = 3.55, df = 3 (P = 0.31); I² = 16%
Test for overall effect: Z = 0.88 (P = 0.38)
AKI prognosis
AKI is worse than AMI

Veterans Affairs database

Long-term risk of coronary events after AKI


DM (+)/AKI (+)
DM (+)/AKI (-)
DM (-)/AKI (+)
DM (-)/AKI (-)
Long-term risk of mortality after septic AKI

Patients with AKI

Patients without AKI

Lopes et al. BMC Nephrol 2010
CKD worsens septic AKI by releasing High Mobility Group Box Protein-1

Leelahavanichkul et al. Kidney Int 2011
The Nexus of Acute Kidney Injury, Chronic Kidney Disease, and World Kidney Day 2009

Mark D. Okusa,* Glenn M. Chertow,† and Didier Portilla,‡ for the Acute Kidney Injury Advisory Group of the American Society of Nephrology

Editorial

AKI: No CKD Progression

AKI: CKD Progression

AKI on CKD: CKD Progression
Association of complete recovery from AKI with incident CKD

Retrospective cohort study using the Intermountain Healthcare Enterprise Data Warehouse

<table>
<thead>
<tr>
<th></th>
<th>Crude</th>
<th>Propensity-stratified analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n=3,090)</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>AKI (n=719)</td>
<td>5.93 (4.49-7.84)</td>
<td>3.82 (2.81-5.19)</td>
</tr>
</tbody>
</table>

CKD after AKI: a systematic review and meta-analysis

Hazard ratio for CKD

8.8 (95%CI 3.1-25.5)

Hazard ratio for ESRD

3.1 (95%CI 1.9-5.0)
Repair after AKI

A variety of growth factors probably contribute to the restoration of a normal tubular epithelium.

**Dedifferentiation phase:**
- loss of apical-basal polarity
- lack of tight junctions
- decreased expression of epithelial cell markers N-cadherin, E-cadherin, and ZO-1
- increased expression of mesenchymal cell markers vimentin, α-SMA, and FSP-1

**Proliferation and redifferentiation phase:**
- regain of apical-basal polarity
- presence of tight junctions
- increased expression of epithelial cell markers N-cadherin, E-cadherin, and ZO-1
- decreased expression of mesenchymal cell markers vimentin, α-SMA, and FSP-1
- restored function of tubular epithelial cells

How does AKI progress to CKD?

## Disaster nephrology

### Table 2 | Earthquakes associated with mortality > 5000 since 1985

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>Magnitude</th>
<th>Deaths</th>
<th>Crush syndrome</th>
<th>Dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michoacan, Mexico</td>
<td>1985</td>
<td>8.0</td>
<td>9500</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Spitak, Armenia</td>
<td>1988</td>
<td>6.7</td>
<td>25,000</td>
<td>600</td>
<td>225-385</td>
</tr>
<tr>
<td>Western Iran</td>
<td>1990</td>
<td>7.4</td>
<td>50,000</td>
<td>Unknown</td>
<td>156</td>
</tr>
<tr>
<td>Latur-Killari, India</td>
<td>1993</td>
<td>6.2</td>
<td>9748</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td><strong>Kobe, Japan</strong></td>
<td>1995</td>
<td><strong>6.9</strong></td>
<td><strong>5000</strong></td>
<td><strong>372</strong></td>
<td><strong>123</strong></td>
</tr>
<tr>
<td>Marmara, Turkey</td>
<td>1999</td>
<td>7.6</td>
<td>17,118</td>
<td>639</td>
<td>477</td>
</tr>
<tr>
<td>Gujarat, India</td>
<td>2001</td>
<td>7.6</td>
<td>20,085</td>
<td>35</td>
<td>33</td>
</tr>
<tr>
<td>Bam, Iran</td>
<td>2003</td>
<td>6.6</td>
<td>31,000</td>
<td>124</td>
<td>96</td>
</tr>
<tr>
<td>Sumatra, Indonesia</td>
<td>2004</td>
<td>9.1</td>
<td>227,898</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Kashmir, Pakistan</td>
<td>2005</td>
<td>7.6</td>
<td>86,000</td>
<td>118</td>
<td>65</td>
</tr>
<tr>
<td>Sumatra, Indonesia</td>
<td>2006</td>
<td>6.3</td>
<td>5749</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Sichuan, China</td>
<td>2008</td>
<td>7.9</td>
<td>87,587</td>
<td>229</td>
<td>113</td>
</tr>
<tr>
<td>Port au Prince, Haiti</td>
<td>2010</td>
<td>7.0</td>
<td>316,000</td>
<td>Unknown</td>
<td>79</td>
</tr>
<tr>
<td><strong>Tohoku, Japan</strong></td>
<td>2011</td>
<td><strong>9.0</strong></td>
<td><strong>20,896</strong></td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

Disaster nephrology

1. AKI treatment: Crush syndrome

2. Treatment of dialysis patients at afflicted areas
AKI due to rhabdomyolysis

Myoglobin released from muscle injure the kidney in three ways:
● Tubular obstruction, possibly in association with uric acid
● Direct proximal tubular cell injury
● Vasoconstriction, which results in a reduction in blood flow in the outer medulla
Treatment of AKI due to rhabdomyolysis

Use of bicarbonate for hydration and alkalization of urine

urine pH above 6.5 may prevent heme-protein precipitation with Tamm-Horsfall protein, intratubular pigment cast formation, and uric acid precipitation; correct metabolic acidosis; and reduce hyperkalemia
Treatment of AKI due to rhabdomyolysis

Use of bicarbonate for hydration and alkalinization of urine

the administration of intravenous fluid should be adjusted to maintain the urinary output at approximately 200 to 300 mL/hour
Treatment of AKI due to rhabdomyolysis

Use of bicarbonate for hydration and alkalinization of urine

Warning: excessive alkalemia (pH>7.5, $\text{HCO}_3^->30\text{mEq/L}$) may induce suppression of respiration and aggravation of hypocalcemia
Treatment of AKI due to rhabdomyolysis

Use of bicarbonate for hydration and alkalinization of urine => When to stop

CK < 5000 U/L
Mb < 5000 ng/mL
Disappearance of myoglobinuria

Mb has a short half life and decreases rapidly compared with CK.
Dialysis therapy

Hyperkalemia with ECG abnormalities
Oliguria
=>
Start dialysis immediately
Treatment of AKI due to rhabdomyolysis

Dialysis therapy

Molecular weight of Mb is 180 kDa, which can be removed by hemofiltration. Based on the Cochrane review, CRRT therapy was associated with improved serum creatinine, BUN, and potassium levels; reduced duration of the oliguria phase; and was associated with reduced time in hospital.

Dialysis therapy

However, no significant differences were found in mortality rates in patients treated with CRRT compared with conventional therapy (RR 0.17, 95% CI 0.02 to 1.37).

Acute kidney injury due to rhabdomyolysis and renal replacement therapy: a critical review

Nadezda Petejova* and Arnost Martinek

the decision to initiate renal replacement therapy in clinical practice should not be made on the basis of the myoglobin or creatine phosphokinase serum concentrations
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