Sepsis and AKI: bidirectional and synergistic relationship?

Dept. of Internal Medicine I, Charles University Medical School and Teaching Hospital Plzen Czech Republic
Sepsis as a cause of AKI

47%

46%

42%
<table>
<thead>
<tr>
<th>Study</th>
<th>AKI definition</th>
<th>Population</th>
<th>Number of pts</th>
<th>Incidence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoste</td>
<td>S-cr &gt; 177</td>
<td>Surgical</td>
<td>185</td>
<td>16</td>
</tr>
<tr>
<td>Yengenaga</td>
<td>S-cr &gt; 177</td>
<td>Mixed</td>
<td>257</td>
<td>11</td>
</tr>
<tr>
<td>Oppert</td>
<td>S-cr x 2</td>
<td>Mixed</td>
<td>401</td>
<td>41</td>
</tr>
<tr>
<td>Neveu</td>
<td>S-cr &gt; 310 and/or S-urea &gt; 36</td>
<td>Mixed</td>
<td>157</td>
<td>46</td>
</tr>
</tbody>
</table>

Sepsis → AKI: a serious issue in the ICU
<table>
<thead>
<tr>
<th>Study</th>
<th>AKI definition</th>
<th>Population</th>
<th>Number of pts</th>
<th>Sepsis AKI incidence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levy</td>
<td>Scr &gt; 177</td>
<td>CI-AKI</td>
<td>47</td>
<td>45</td>
</tr>
<tr>
<td>Thakar</td>
<td>RRT</td>
<td>Cardiac surgery</td>
<td>318</td>
<td>34</td>
</tr>
<tr>
<td>Hoste</td>
<td>RRT</td>
<td>Mixed</td>
<td>647</td>
<td>80 (infection)</td>
</tr>
<tr>
<td>Mehta (PICARD)</td>
<td>ΔScr&gt;44 if Scr &lt; 133 ΔScr&gt;88 if Scr 133-442</td>
<td>Mixed</td>
<td>611</td>
<td>40</td>
</tr>
</tbody>
</table>
Sepsis and AKI: complex interconnections

AKI plays a role both in response to and development of sepsis.
AKI: predictor of bad outcome
Outcome of sepsis: AKI vs non-AKI

Mortality %

<table>
<thead>
<tr>
<th></th>
<th>AKI</th>
<th>Non-AKI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoste</td>
<td>57</td>
<td>28</td>
</tr>
<tr>
<td>Yengenaga</td>
<td>72</td>
<td>24</td>
</tr>
<tr>
<td>Oppert</td>
<td>67</td>
<td>43</td>
</tr>
<tr>
<td>Bagshaw</td>
<td>58</td>
<td>35</td>
</tr>
<tr>
<td>SOAP</td>
<td>41</td>
<td>23</td>
</tr>
<tr>
<td>BEST</td>
<td>70</td>
<td>52</td>
</tr>
</tbody>
</table>
Septic AKI unique

Bagshaw et al, CC 2008
Severity of SA-AKI and mortality: a graded relationship

Bagshaw et al, CC 2008
Sepsis as a consequence of AKI

Mehta R et al, ICM, 2011
Sepsis and AKI bidirectional

Sepsis

AKI

Mortality

Sepsis

AKI

Sepsis

AKI

Mortality
Distinct population?

- Sicker
- More alterations in acute physiology
- Higher need for MV

- Sicker
- Higher need for dialysis
- Persistent fluid overload
- Non-surgical procedures

Bagshaw et al, CJASN 2007, CC 2008
Mehta R et al, ICM, 2011
An independent effect on mortality?

- Neveu et al. NDT 1996
  - Hospital mortality
  - OR 2.51; 95% CI, 1.44-4.39

- Bagshaw et al. CJASN 2007
  - Hospital mortality
  - OR 1.48; 95% CI, 1.17-1.89

- Bagshaw et al. CC 2008
  - Hospital mortality
  - OR 1.54; 95% CI, 1.45-1.64

- Oppert et al. NDT 2008
  - Hospital mortality
  - OR 2.11; 95% CI, 1.27-3.52
Why does AKI in sepsis increase mortality (even if there is RRT)?

high-risk group that „failed stress test“?

„genetic make-up“ predisposing these patients to bad outcome?

*Parikh et al., JASN 2009*
Elevated Plasma Concentrations of IL-6 and Elevated APACHE II Score Predict Acute Kidney Injury in Patients with Severe Sepsis

Figure 1. Kaplan-Meier estimates of remaining free of acute kidney injury (AKI) on the basis of IL-6 quartile.
What discriminates AKI from non-AKI in sepsis?
Early abnormal host immune response appears to be the major pathobiological factor predicting the development of septic AKI.
Acute kidney injury in non-severe pneumonia is associated with an increased immune response and lower survival.
Why does AKI increase mortality (even if there is RRT)?

"genetic make-up" predisposing these patients to bad outcome
"failed stress test"

Kidney as "motor" of sepsis and MODS
Kidney as „motor“ of sepsis and MODS

[Image of the diagram showing the kidney as the central point affecting various organs like brain, heart, lung, liver, and gastrointestinal tract, with indications of changes like increased permeability, leukocyte trafficking, and altered liver enzymes.]
Pre-existing Renal Disease Promotes Sepsis-induced Acute Kidney Injury and Worsens Sepsis Outcome via Multiple Pathways

Kent Doi, M.D., Ph.D., Asada Leelahavanichkul, M.D., Xuzhen Hu, Karen L. Sidransky, Yan Qin, M.D., Christoph Eisner, M.D., Jurgen Schnermann, M.D., Peter S. T. Yuen, Ph.D., and Robert A. Star, M.D.

FA-induced KI + CLP after 2 weeks

Veh + CLP

Identified pathomechanisms:

- increased capillary permeability
- increased plasma VEGF
- decreased bacteria clearance
- splenocyte apoptosis

Impaired monocyte cytokine production in critically ill patients with acute renal failure

Jonathan Himmelfarb, Phuong Le, Jennifer Klenzak, Stephanie Freedman, M. Elizabeth McMenamin, T. Alp Ikizler, and the PICARD Group

Oxidative Stress Is Increased in Critically Ill Patients with Acute Renal Failure

SA-AKI: driving force accelerating the downward spiral toward bad outcome
Postulated mechanisms underlying the bidirectional relationship between sepsis and AKI

Matejovic et al. Contrib Nephrol. 2011