Acute Kidney Injury (AKI) is Prevalent, Costly and Deadly

INCIDENCE
- 7.18% of hospitalized patients.
- 200,000 people die each year from AKI in the US.
- Up to 50% of critically ill patients develop some stage of AKI.

MORBIDITY & MORTALITY
- 9-times higher risk of development of Chronic Kidney Disease.
- 2-times higher risk of premature death.
- In Europe, the mortality rate for AKI ranges from 17.2 to 26.3%.

Cost
- Estimated annual costs to US healthcare system attributable to hospital-acquired AKI is > $10 billion.
- In the UK, “The annual AKI-related cost is estimated as £1.12 billion per year.”
- Length of stay increase between 1.1 days and 3.2 days.

AKI is twice as deadly as a myocardial infarction (MI)

You might also be interested in a Selection of Publications on the “risk assessment of Acute Kidney Injury using novel biomarkers”

AKI: Acute Kidney Injury

For a typical 400-bed community hospital, the incremental resources consumed by AKI in the ICU often exceed $20M and 8,500 bed days annually.

A study of over 36,000 hospitalized veterans demonstrated that patients who developed AKI without myocardial infarction (MI) had a higher mortality than those who suffered a MI without developing AKI.

A PIc of Acute Kidney Injury

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AKI: Acute Kidney Injury
Acute Kidney Injury (AKI), is an abrupt loss of kidney function that develops within 7 days. It was previously known as Acute Renal Failure. It is a global public health concern impacting ~13.3 million patients per year.

**Etiology of AKI in the ICU**

- Sepsis
- Major surgery
- Low cardiac output
- Hypovolemia
- Nephrotoxic Medications
- Antibiotics
- Angiotensin-converting enzyme inhibitor
- Angiotensin II receptor blockers
- Radiocontrast dye
- Chemotherapeutic agents

**Recommended management of AKI**

**KDIGO Consensus Guideline for AKI**

<table>
<thead>
<tr>
<th>AKI Stage</th>
<th>High Risk</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Discontinue all nephrotoxic agents when possible</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Ensure volume status and perfusion pressure</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Consider functional hemodynamic monitoring</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Monitor serum creatinine and urine output</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Avoid hyperglycemia</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Consider alternatives to radiocontrast procedures</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Non-invasive diagnostic workup</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Consider invasive diagnostic workup</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Check for changes in drug dosing</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Consider renal replacement therapy</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Consider ICU admission</strong></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Avoid subclavian catheters if possible</strong></td>
<td>✔</td>
<td>✔</td>
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</tr>
</tbody>
</table>

KDIGO highlights that in accordance with your current practice, these particular actions could be considered when patients are at risk for AKI.

**FIVE MOST COMMON CAUSES OF AKI IN THE ICU**

- Infection
- Major surgery
- Low cardiac output
- Hypovolemia

**OTHER COMMON CAUSES OF AKI IN THE ICU**

- Hepatorenal syndrome
- Trauma
- Cardiopulmonary bypass
- Abdominal compartment syndrome
- Rhabdomyolysis
- Obstruction

**With Novel Biomarkers, you can predict kidney stress BEFORE damage occurs. Serum Creatinine and Urine Output are NOT SPECIFIC to Kidney Stress.**

**KDIGO**

Adapted from KDIGO Guidelines 2012.

**Invasive diagnostic studies performed to identify biomarkers of early AKI risk assessment**

<table>
<thead>
<tr>
<th>Biomarkers</th>
<th>AUC (with 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMP-2</td>
<td>0.7</td>
</tr>
<tr>
<td>IGFBP7</td>
<td>0.8</td>
</tr>
<tr>
<td>NGAL</td>
<td>0.6</td>
</tr>
<tr>
<td>Cystatin C</td>
<td>0.5</td>
</tr>
<tr>
<td>KIM-1</td>
<td>0.7</td>
</tr>
<tr>
<td>Pi-GST</td>
<td>0.8</td>
</tr>
<tr>
<td>L-FABP</td>
<td>0.9</td>
</tr>
</tbody>
</table>

**Symptomatic (Diagnosis)**

Functional Biomarkers: Serum Creatinine, Urine Output

**Serum Creatinine**

- Lagging indicator
- Minimum of 6 hours must pass to determine urine output
- Affected by healthcare-associated infections

**Urine Output**

- Lagging indicator
- Maximum of 6 hours must pass to determine urine output
- Tedium to measure
- Affected by healthcare-associated infections

**Risk Assessment of AKI: Biomarkers**

- **Kidney stress is a precursor of AKI.**

**SAPPHIRE Study**

- 35 sites: 20 US and 15 Europe
- 744 patient cohort
- Identify the best biomarker among 340 proteins

Urinary IGFBP7 and TIMP-2 were the best-performing markers in the discovery study.

**Tubular Cell Cycle Arrest Biomarkers**

- TIMP-2 and IGFBP7 are:
  - Biomarkers of cellular stress in the early phase of tubular cell injury caused by a wide variety of insults (inflammation, ischemia, oxidative stress, drugs, and toxins)
  - Involved in G1 cell-cycle arrest that prevents cells from dividing until damage can be repaired
  - Both biomarkers appear as "alarm" proteins for other nearby cells

**Adapted from Kellum and al.**

**Diagnosis of AKI: Functional Biomarkers**

- Serum Creatinine and Urine Output are NOT SPECIFIC to Kidney Stress.

**Normal vs Increased Risk vs Damage vs Decreased GFR vs Kidney Failure**

**AUC (Area under the curve)**

<table>
<thead>
<tr>
<th>AUC (with 95% CI)</th>
<th>0.5</th>
<th>0.6</th>
<th>0.7</th>
<th>0.8</th>
<th>0.9</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Creatinine</strong></td>
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<tr>
<td><strong>Urine Output</strong></td>
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**Adapted from Kellum and al.**

**References**

1. [Acute Kidney Injury (AKI)](https://www.atsjournals.org/content/142/1S/14)
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