KDIGO Clinical Guidelines for Management of AKI

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Disclosure

• Gambro:
  – Expert Panel
  – Fellowship Funding
An independently incorporated nonprofit foundation, governed by an international board, with the stated mission to:

‘Improve the care and outcomes of kidney disease patients worldwide through promoting coordination, collaboration, and integration of initiatives to develop and implement clinical practice guidelines.’
Guiding Principles for KDIGO Guideline Development

• Scientific and methodological rigor
• Interdisciplinary approach
• Independence of work groups
• Transparency of the guideline development process
Published Clinical Practice Guidelines

• Prevention, Diagnosis, Evaluation, and Treatment of Hepatitis C in CKD
  – Published in Kidney International in April, 2008

• Diagnosis, Evaluation, Prevention, and Treatment of CKD-MBD
  – Published in Kidney International in July, 2009

• Care of Kidney Transplant Recipients
  – Published in the American Journal of Transplantation in October, 2009; Executive Summary published in Kidney International in December, 2009

Kidney Disease: Improving Global Outcomes
Why KDIGO guidelines on AKI management?

- AKI is common.
- AKI imposes a heavy burden of illness (morbidity and mortality).
- The cost per person of managing AKI is high.
- AKI is amenable to early detection and potential prevention.
- There is considerable variability in practice to prevent, diagnose, treat, and achieve outcomes of AKI.
- Clinical practice guidelines in the field have the potential to reduce variations, improve outcomes, and reduce costs.
- Formal guidelines do not exist on this topic.
<table>
<thead>
<tr>
<th>Grade</th>
<th>Patients</th>
<th>Clinicians</th>
<th>Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1 “We recommend”</td>
<td>Most patients in your situation would want the recommended course of action and only a few would not.</td>
<td>Most patients should receive the recommended course of action.</td>
<td>The recommendation can be evaluated as a candidate for developing a policy or performance measure.</td>
</tr>
<tr>
<td>Level 2 “We suggest”</td>
<td>The majority of patients in your situation would want the recommended course of action but many would not.</td>
<td>Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with his or her values and preferences.</td>
<td>The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined.</td>
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</tbody>
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2.1.2: AKI is staged for severity according to the following criteria (Table 2). (Not Graded)

2.1.3: The cause of AKI should be determined whenever possible. (Not Graded)
## Staging of AKI Severity

<table>
<thead>
<tr>
<th>Stage</th>
<th>Δ Serum creatinine</th>
<th>Urine output</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5-1.9 X baseline or ≥ 26.5 μmol/l (0.3 mg/dl) increase</td>
<td>&lt;0.5 ml/kg/h for 6-12 hrs</td>
</tr>
<tr>
<td>2</td>
<td>2.0-2.9 X baseline</td>
<td>&lt;0.5 ml/kg/h for ≥ 12 hrs</td>
</tr>
<tr>
<td>3</td>
<td>3.0 X baseline or Increase in serum creatinine to ≥ 353.6 μmol/l or Initiation of RRT or in patients &lt;18 yrs, decrease in eGFR to &lt; 35 ml/min per 1.73 m</td>
<td>&lt;0.3 ml/kg/h for ≥ 24 hrs Or Anuria for ≥ 12 hrs</td>
</tr>
</tbody>
</table>
Relationship between Acute and Chronic Kidney Disease

AKD  AKI  CKD
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Stages defined by creatinine and urine output are surrogates

GFR

Complications

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

Antecedents
Intermediate Stage
AKI
Outcomes

Markers such as NGAL, KIM-1, and IL-18 are surrogates
## Causes of AKI and Diagnostic Tests

<table>
<thead>
<tr>
<th>Selected causes of AKI requiring immediate diagnosis and specific therapies</th>
<th>Recommended diagnostic tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased kidney perfusion</td>
<td>Volume status and urinary diagnostic indices</td>
</tr>
<tr>
<td>Acute glomerulonephritis, vasculitis, interstitial nephritis, TTP/HUS</td>
<td>Urine sediment examination, serologic testing and hematologic testing</td>
</tr>
<tr>
<td>Urinary obstruction</td>
<td>Kidney ultrasound</td>
</tr>
</tbody>
</table>
2.2.1: We recommend that patients be stratified for risk of AKI according to their susceptibilities and exposures. (1B)

2.2.2: Manage patients according to their susceptibilities and exposures to reduce the risk of AKI (see relevant guideline sections). (Not Graded)

2.2.3: Test patients at increased risk for AKI with measurements of SCr and urine output to detect AKI. (Not Graded) Individualize frequency and duration of monitoring based on patient risk and clinical course. (Not Graded)
## Causes of AKI: exposures and susceptibilities for non-specific AKI

<table>
<thead>
<tr>
<th>Exposures</th>
<th>Susceptibilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>Dehydration or volume depletion</td>
</tr>
<tr>
<td>Critical illness</td>
<td>Advanced age</td>
</tr>
<tr>
<td>Circulatory shock</td>
<td>Female gender</td>
</tr>
<tr>
<td>Burns</td>
<td>Black race</td>
</tr>
<tr>
<td>Trauma</td>
<td>CKD</td>
</tr>
<tr>
<td>Cardiac surgery (especially with CPB)</td>
<td>Chronic diseases (heart, lung, liver)</td>
</tr>
<tr>
<td>Major noncardiac surgery</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Nephrotoxic drugs</td>
<td>Cancer</td>
</tr>
<tr>
<td>Radiocontrast agents</td>
<td>Anemia</td>
</tr>
<tr>
<td>Poisonous plants and animals</td>
<td></td>
</tr>
</tbody>
</table>

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3.1.1: In the absence of hemorrhagic shock, we suggest using isotonic crystalloids rather than colloids (albumin or starches) as initial management for expansion of intravascular volume in patients at risk for AKI or with AKI. (2B)

3.1.2: We recommend the use of vasopressors in conjunction with fluids in patients with vasomotor shock with, or at risk for, AKI. (1C)

RESEARCH RECOMMENDATIONS

- There is a need to examine physiologic electrolyte solutions vs. saline in the prevention of AKI.
- Compare different types of vasopressors and different BP goals for prevention and treatment of AKI in hemodynamically unstable patients.
Discontinue all nephrotoxic agents when possible
Ensure volume status and perfusion pressure
Consider functional hemodynamic monitoring
Avoid hyperglycemia
Consider alternatives to radiocontrast procedures

Non-invasive diagnostic workup
Consider invasive diagnostic workup

Check for changes in drug dosing
Consider Renal Replacement Therapy
Consider ICU admission

Avoid subclavian catheters if possible
3.4.1: We recommend not using diuretics to prevent AKI. (1B)

3.4.2: We suggest not using diuretics to treat AKI, except in the management of volume overload. (2C)

3.5.1: We recommend not using low-dose dopamine to prevent or treat AKI. (1A)

RESEARCH RECOMMENDATION

- Given the potential to mitigate fluid overload but also to worsen renal function and possibly cause kidney injury, further study is required to clarify the safety of loop diuretics in the management of patients with AKI.

The SPARK Study: a phase II randomized blinded controlled trial of the effect of furosemide in critically ill patients with early acute kidney injury.

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3.8.1: We suggest not using aminoglycosides for the treatment of infections unless no suitable, less nephrotoxic, therapeutic alternatives are available. (2A)

3.8.2: We suggest that, in patients with normal kidney function in steady state, aminoglycosides are administered as a single dose daily rather than multiple-dose daily treatment regimens. (2B)

3.8.3: We recommend monitoring aminoglycoside drug levels when treatment with multiple daily dosing is used for more than 24 hours. (1A)

3.8.4: We suggest monitoring aminoglycoside drug levels when treatment with single-daily dosing is used for more than 48 hours. (2C)

3.8.5: We suggest using topical or local applications of aminoglycosides (e.g., respiratory aerosols, instilled antibiotic beads), rather than i.v. application, when feasible and suitable. (2B)
3.8.6: We suggest using lipid formulations of amphotericin B rather than conventional formulations of amphotericin B. (2A)

3.8.7: In the treatment of systemic mycoses or parasitic infections, we recommend using azole antifungal agents and/or the echinocandins rather than conventional amphotericin B, if equal therapeutic efficacy can be assumed. (1A)

RESEARCH RECOMMENDATIONS

- RCTs should be conducted comparing lipid complex with liposomal Amphoteracin B in patients with systemic mycosis, with the rate of AKI as a primary or secondary end-point.
- Markers of early nephrotoxicity and mechanisms to avoid nephrotoxicity with amphotericin B formulations need to be studied further in clinical investigations.
4.1: Define and stage AKI after administration of intravascular contrast media (Not Graded)

4.1.1: In individuals who develop changes in kidney function after administration of intravascular contrast media, evaluate for CI-AKI as well as for other possible causes of AKI. (Not Graded)

4.2.1: Assess the risk for CI-AKI and, in particular, screen for pre-existing impairment of kidney function in all patients who are considered for a procedure that requires intravascular (i.v. or i.a.) administration of iodinated contrast medium. (Not Graded)

4.2.2: Consider alternative imaging methods in patients at increased risk for CI-AKI. (Not Graded)

4.3.1: Use the lowest possible dose of contrast medium in patients at risk for CI-AKI. (Not Graded)

4.3.2: We recommend using either iso-osmolar or low-osmolar iodinated contrast media, rather than high-osmolar iodinated contrast media in patients at increased risk of CI-AKI. (1B)
4.4.1: We recommend i.v. volume expansion with either isotonic sodium chloride or sodium bicarbonate solutions, rather than no i.v. volume expansion, in patients at increased risk for CI-AKI. (1A)

4.4.2: We recommend not using oral fluids alone in patients at increased risk of CI-AKI. (1C)

4.4.3: We suggest using oral NAC, together with i.v. isotonic crystalloids, in patients at increased risk of CI-AKI. (2D)

4.4.4: We suggest not using theophylline to prevent CI-AKI. (2C)

4.4.5: We recommend not using fenoldopam to prevent CI-AKI. (1B)

4.5.1: We suggest not using prophylactic intermittent hemodialysis (IHD) or hemofiltration (HF) for contrast-media removal in patients at increased risk for CI-AKI. (2C)
Renal Replacement Therapy
5.1.1: Initiate RRT emergently when life-threatening changes in fluid, electrolyte, and acid-base balance exist. (Not Graded)

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 urea and creatinine thresholds alone—when making the decision to start RRT. (Not Graded).

5.2.1: Discontinue RRT when it is no longer required, either because intrinsic kidney function has recovered to the point that it is adequate to meet patient needs, or because RRT is no longer consistent with the goals of care. (Not Graded).

5.2.2: We suggest not using diuretics to enhance kidney function recovery, or to reduce the duration or frequency of RRT. (2B)
Fluid Overload in Children with AKI

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RESEARCH RECOMMENDATIONS

• Determine reproducible criteria (e.g., fluid overload, biomarker level, severity score) to inform the decision to start RRT in adult and pediatric AKI patients. Such criteria may also permit the identification of patients who will ultimately require RRT and hence limit uncertainty around whether to begin therapy.

• Determine whether early vs. late start of RRT, based on the above-mentioned criteria, results in improved clinical outcomes (e.g., mortality, evolution to CKD Stage 5) of AKI patients.
5.3.1: In a patient with AKI requiring RRT, base the decision to use anticoagulation for RRT on assessment of the patient’s potential risks and benefits from anticoagulation. (Not Graded)

5.3.1.1: We recommend using anticoagulation during RRT in AKI if a patient does not have an increased bleeding risk or impaired coagulation and is not already receiving systemic anticoagulation. (1B)
For patients without an increased bleeding risk or impaired coagulation and not already receiving effective systemic anticoagulation, we suggest the following:

5.3.2. For anticoagulation in intermittent dialysis, we recommend using either unfractionated or low-molecular-weight heparin, rather than other anticoagulants. (1C)

For anticoagulation in CRRT, we suggest using regional citrate anticoagulation rather than heparin in patients who do not have contraindications for citrate. (2B)

For anticoagulation during CRRT in patients who have contraindications for citrate, we suggest using either unfractionated or low-molecular-weight heparin, rather than other anticoagulants. (2C)
5.3.4: In a patient with heparin-induced thrombocytopenia (HIT), all heparin must be stopped and we recommend using direct thrombin inhibitors (such as argatroban) or Factor Xa inhibitors (such as danaparoid or fondaparinux) rather than other or no anticoagulation during RRT. (1A)

5.3.4.1: In a patient with HIT who does not have severe liver failure, we suggest using argatroban rather than other thrombin or Factor Xa inhibitors during RRT. (2C)
5.4.1: We suggest initiating RRT in patients with AKI via an uncuffed nontunneled dialysis catheter, rather than a tunneled catheter. (2D)

5.4.2: When choosing a vein for insertion of a dialysis catheter in patients with AKI, consider these preferences (Not Graded):

- First choice: right jugular vein
- Second choice: femoral vein;
- Third choice: left jugular vein;
- Last choice: subclavian vein with preference for the dominant side.

5.4.3: We recommend using ultrasound guidance for dialysis catheter insertion. (1A)

5.4.4: We recommend obtaining a chest radiograph promptly after placement and before first use of an internal jugular or subclavian dialysis catheter. (1B)

5.4.5: We suggest not using topical antibiotics over the skin insertion site of a nontunneled dialysis catheter in ICU patients with AKI requiring RRT. (2C)
5.6.1: Use continuous and intermittent RRT as complementary therapies in AKI patients. (Not Graded)

5.6.2: We suggest using CRRT, rather than standard intermittent RRT, for hemodynamically unstable patients. (2B)

5.6.3: We suggest using CRRT, rather than intermittent RRT, for AKI patients with acute brain injury or other causes of increased intracranial pressure or generalized brain edema. (2B)

RESEARCH RECOMMENDATIONS

Large RCTs should compare SLED against other forms of RRT in patients with AKI. These trials should be standardized for treatment dose, buffer, membrane, anticoagulant, and timing of treatment.

The effects of different modalities of RRT on the long-term need for chronic dialysis, along with mortality, should be evaluated in prospective randomized trials.

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BEST Kidney Study: Recovery from dialysis dependence

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Continuous renal replacement therapy is associated with less chronic renal failure than intermittent haemodialysis after acute renal failure.
5.8.1: The dose of RRT to be delivered should be prescribed before starting each session of RRT. (Not Graded) We recommend frequent assessment of the actual delivered dose in order to adjust the prescription. (1B)

5.8.2: Provide RRT to achieve the goals of electrolyte, acid-base, solute, and fluid balance that will meet the patient’s needs. (Not Graded)

5.8.3: We recommend delivering a $\text{Kt/V}$ of 3.9 per week when using intermittent or extended RRT in AKI. (1A)

5.8.4: We recommend delivering an effluent volume of 20–25 ml/kg/h for CRRT in AKI (1A). This will usually require a higher prescription of effluent volume. (Not Graded).

In clinical practice, in order to achieve a delivered dose of 20–25ml/kg/h, it is generally necessary to prescribe in the range of 25–30ml/kg/h, and to minimize interruptions in CRRT.
Intensity of Renal Support in Critically Ill Patients with Acute Kidney Injury

The VA/NIH Acute Renal Failure Trial Network*

Intensity of Continuous Renal-Replacement Therapy in Critically Ill Patients

The RENAL Replacement Therapy Study Investigators*
ATN and RENAL Dosing Studies

- **ATN**
  - IHD Daily vs x 3 weekly
  - CRRT 20 vs 35 ml/kg/hr
  - Median CRRT duration: 21 hrs

- **RENAL**
  - CRRT 25 vs 40 ml/kg/hr
  - Mean filter duration: 25.8 hrs vs 28.6 hrs
Thank you for your attention!


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