Chapter 32
Approach to Acute Kidney Injury (AKI) in Critically Ill Patients in the ICU

32.1 Introduction

32.1.1 Definition and Significance of AKI

Acute kidney injury (AKI) is a sudden decline in kidney function. This leads to the buildup of waste products like urea and creatinine in the blood and causes imbalances in fluids and electrolytes. In critically ill patients, AKI is a serious complication associated with high rates of illness and death. It is common in the intensive care unit (ICU) because patients there are exposed to multiple risk factors such as severe infections (sepsis), medications that can harm the kidneys (nephrotoxins), and unstable blood flow (hemodynamic instability). The KDIGO (Kidney Disease: Improving Global Outcomes) guidelines provide a standard definition of AKI based on increases in serum creatinine and decreases in urine output.

AKI is significant not only because it affects the kidneys but also because it can impact other organ systems. In critically ill patients, AKI often indicates underlying problems like septic shock or heart failure. It can worsen other organ failures due to mechanisms like fluid overload and increased urea levels. AKI also leads to longer ICU stays, higher healthcare costs, and can negatively affect long-term patient outcomes [1] [Ref: Algorithm 32.1].

32.2 Epidemiology: How Common Is AKI in the ICU?

AKI occurs in about 30% to 60% of ICU patients. This wide range is due to differences in patient populations and how AKI is diagnosed. The KDIGO criteria have helped standardize AKI diagnosis by emphasizing increases in serum creatinine and low urine output (oliguria) for early detection. However, in critically ill patients,

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factors like low blood volume (hypovolemia), fluid shifts, and muscle wasting can affect urine output and creatinine levels, making diagnosis challenging.

ICU patients are particularly prone to AKI because of the severity of their illnesses, exposure to multiple nephrotoxic drugs, and the invasive procedures they often undergo. AKI can also be part of multi-organ dysfunction syndrome, complicating the clinical picture. When AKI is present, it usually indicates a worse prognosis, including higher rates of needing mechanical ventilation and renal replacement therapy (RRT) [2].

32.3 Impact on Short- and Long-Term Health

In the short term, AKI increases the risk of longer ICU stays, the need for RRT, and higher in-hospital mortality rates. Mortality rates for ICU patients with AKI can exceed 50%, especially for those requiring RRT. AKI often leads to fluid overload, which can worsen heart function, lung mechanics, and overall blood flow. This increases the likelihood of multiple organ failure and the need for advanced life-support measures.

In the long term, many patients who survive AKI do not fully regain kidney function, leading to chronic kidney disease (CKD). Persistent AKI—kidney dysfunction lasting more than 48 h—has a particularly poor prognosis. Survivors are also at increased cardiac risk, recurrent AKI episodes, and eventually needing long-term dialysis. This underscores the importance of early recognition, prevention strategies, and long-term follow-up for patients with AKI during critical illness [3].

32.4 Pathophysiology of AKI

32.4.1 Different Types and How They Present

AKI is a complex condition with various causes and presentations, known as phenotypes. The main types are:

- **Prerenal AKI:** Caused by reduced blood flow to the kidneys without direct kidney damage. Common causes include dehydration, low blood volume, or low blood pressure due to sepsis. It is often reversible if treated promptly.
- **Intrinsic (Intrarenal) AKI:** Results from direct damage to the kidney tissues, such as acute tubular necrosis (ATN), inflammation of the kidney (nephritis), or diseases affecting the kidney's filtering units (glomerulonephritis). Causes include prolonged ischemia, sepsis, and exposure to nephrotoxins.
- **Post-renal AKI:** Occurs due to blockage in the urinary tract (e.g., kidney stones or tumors), causing backpressure and impairing kidney function.

In critically ill patients, these types can overlap. For example, a patient might have decreased kidney blood flow (prerenal) and also direct kidney damage from toxins (intrinsic) [4].

32.5 How AKI Happens: Key Mechanisms

1. **Ischemia (Lack of Blood Flow):** Reduced blood flow leads to oxygen deprivation in kidney cells, causing cell injury or death, especially in areas like the proximal tubules. This is common in shock, heart failure, or major surgeries.
2. **Sepsis:** Severe infections cause systemic inflammation, leading to endothelial dysfunction and altered renal blood flow. Inflammatory substances can directly damage kidney cells. AKI from sepsis can occur even without significant drops in blood pressure.
3. **Nephrotoxicity (Drug-Induced Damage):** Certain medications and substances can harm kidney cells by causing oxidative stress and cell death. Common nephrotoxins include some antibiotics (like aminoglycosides), contrast dyes used in imaging, and NSAIDs. Critically ill patients are at higher risk due to multiple medications and other factors like dehydration.
4. **Inflammation:** The body's immune response can contribute to kidney damage through the release of inflammatory substances, activation of white blood cells, and production of harmful free radicals. This can worsen kidney injury from other causes [5].

32.6 From AKI to Chronic Kidney Problems

The concept of acute kidney disease (AKD) bridges the gap between AKI and CKD. AKD refers to kidney dysfunction lasting between 7 and 90 days. Even if AKI seems to resolve, there may be ongoing damage leading to CKD.

Key factors in the progression from AKI to CKD include:

- Incomplete healing of kidney tissues.
- Persistent inflammation.
- Development of scar tissue (fibrosis).
- Loss of renal functional reserve.

Patients with persistent AKI are at higher risk for CKD. Risk factors for progression include preexisting kidney problems, repeated episodes of AKI, and ongoing exposure to factors that harm the kidneys.

32.7 Classification and Diagnosis

32.7.1 KDIGO Criteria: How AKI Is Staged

The KDIGO guidelines provide a standardized way to diagnose and stage AKI using two main measures:

1. Serum Creatinine:
   - An increase of ≥0.3 mg/dL (26.5 μmol/L) within 48 h.
   - Or an increase to ≥1.5 times the baseline level, occurring within the prior 7 days.
2. Urine Output:
   - Less than 0.5 mL/kg/h for 6 h.

32.7.2 Staging of AKI

Stage 1:

- Serum Creatinine: 1.5–1.9 times baseline or increase of ≥0.3 mg/dL.
- Urine Output: <0.5 mL/kg/h for 6–12 h.

Stage 2:

- Serum Creatinine: 2.0–2.9 times baseline.
- Urine Output: <0.5 mL/kg/h for ≥12 h.

Stage 3:

- Serum Creatinine: 3.0 times baseline or increase to ≥4.0 mg/dL.
- Urine Output: <0.3 mL/kg/h for ≥24 h or anuria for ≥12 h.
- Initiation of renal replacement therapy (RRT).

These criteria help identify patients at risk and guide treatment decisions.

32.7.3 Transient vs. Persistent AKI

- Transient AKI: Kidney dysfunction that resolves within 48 h. Often due to reversible factors like dehydration. Patients usually have a better prognosis if treated promptly.
- Persistent AKI: Lasts more than 48 h and often involves direct kidney damage. Associated with higher risks of complications, progression to AKD, and development of CKD.

Distinguishing between transient and persistent AKI is important because persistent AKI requires more intensive management and monitoring for long-term kidney health.

32.8 Challenges in Diagnosing AKI in the ICU

Diagnosing AKI in critically ill patients can be difficult due to limitations of traditional markers:

- **Serum Creatinine:**
  - Rises late in AKI—only after significant kidney damage.
  - Affected by factors like muscle mass (which may be low in ICU patients due to muscle wasting) and fluid status (dilution from fluid overload can lower creatinine levels).
- **Urine Output:**
  - Can be influenced by diuretics, fluid resuscitation, and other factors unrelated to kidney function.
  - Oliguria may not always reflect the severity of kidney injury.

32.9 Biomarkers and Early Detection

Established Biomarkers

- Neutrophil Gelatinase-Associated Lipocalin (NGAL):
  - Released by damaged kidney cells.
  - Detectable in blood and urine within a few hours of injury.
  - Helps distinguish between prerenal and intrinsic AKI.
- Tissue Inhibitor of Metalloproteinases-2 (TIMP-2) and Insulin-Like Growth Factor Binding Protein 7 (IGFBP-7):
  - Indicators of cell stress in the kidneys.
  - Combined as the [TIMP-2]*[IGFBP7] test.
  - Predict risk of developing severe AKI within 12 h.

Emerging Biomarkers

- Kidney Injury Molecule-1 (KIM-1):
  - Appears on kidney cells after injury.
  - Useful for detecting early tubular damage.

- Cystatin C:
  - A protein filtered by the kidneys, less affected by muscle mass.
  - May provide a more accurate estimate of kidney function in critically ill patients.
- Proenkephalin (PenKid):
  - Reflects real-time kidney function.
  - Less influenced by external factors like fluid status.

Others
Uromodulin, Calprotectin, IgG, Nephrin, Podocalyxin, Podocin, Transferrin, IL-18, Vanin 1, Galactin 3, PDGF.

Using Technology: Machine Learning and AI
- Machine learning (ML) and artificial intelligence (AI) can analyze large amounts of patient data to predict AKI risk.
- AI models use factors like vital signs, lab results, and patient history to generate risk scores.
- These tools can provide early warnings to clinicians, potentially improving patient outcomes.

32.10 Management Strategies

Preventing AKI
- Fluid Management: Balance is key—avoid both dehydration and fluid overload.
- Hemodynamic Monitoring: Use tools to assess and maintain adequate blood flow and pressure.
- Avoiding Nephrotoxins: Minimize exposure to harmful medications; monitor levels when use is necessary.

Optimizing Blood Flow to the Kidneys
- Maintain Adequate Blood Pressure: Aim for a mean arterial pressure (MAP) of at least 65 mmHg, adjusted based on individual patient needs.
- Use of Vasopressors and Inotropes: Medications that support blood pressure and heart function can help maintain kidney perfusion.

Fluid Management Approaches
- Restrictive Fluid Therapy: Limiting fluids to prevent overload, which can worsen outcomes.

- Liberal Fluid Therapy: More generous fluid administration; may be needed in cases of hypovolemia.
- Individualized Care: The best approach depends on the patient's condition; careful monitoring is essential.

Renal Replacement Therapy (RRT)
- When to Start: Indications include severe electrolyte imbalances, acid-base disturbances, fluid overload, and signs of uremia.
- Timing: Early initiation is debated; some studies suggest waiting until it is absolutely necessary, while others advocate for starting sooner.

32.11 Special Considerations in Critically Ill Patients

AKI in Sepsis

Mechanisms:

- Hemodynamic Changes: Sepsis can cause low blood pressure and poor kidney perfusion.
- Inflammation: Release of cytokines damages kidney tissues.
- Microcirculatory Dysfunction:
- Management Challenges:
- Fluid Resuscitation: Necessary but can lead to fluid overload.
- Vasopressors: Support blood pressure but may reduce kidney blood flow if overused.
- Balancing Treatments: Requires careful monitoring to support circulation without harming the kidneys.

Impact of Mechanical Ventilation and Blood Pressure Instability

Mechanical Ventilation:

- High PEEP Levels: intrathoracic pressure reducing venous return to the heart and kidney perfusion.
- Neurohormonal Activation: Triggers systems that can constrict blood vessels in the kidneys.
- Hemodynamic Instability:
- Hypotension: Low blood pressure reduces kidney perfusion.
- Vasopressors: Necessary to raise blood pressure but can cause renal vasoconstriction.
- Monitoring: Continuous assessment of blood pressure and kidney function is vital.

32.12 Outcomes and Follow-Up

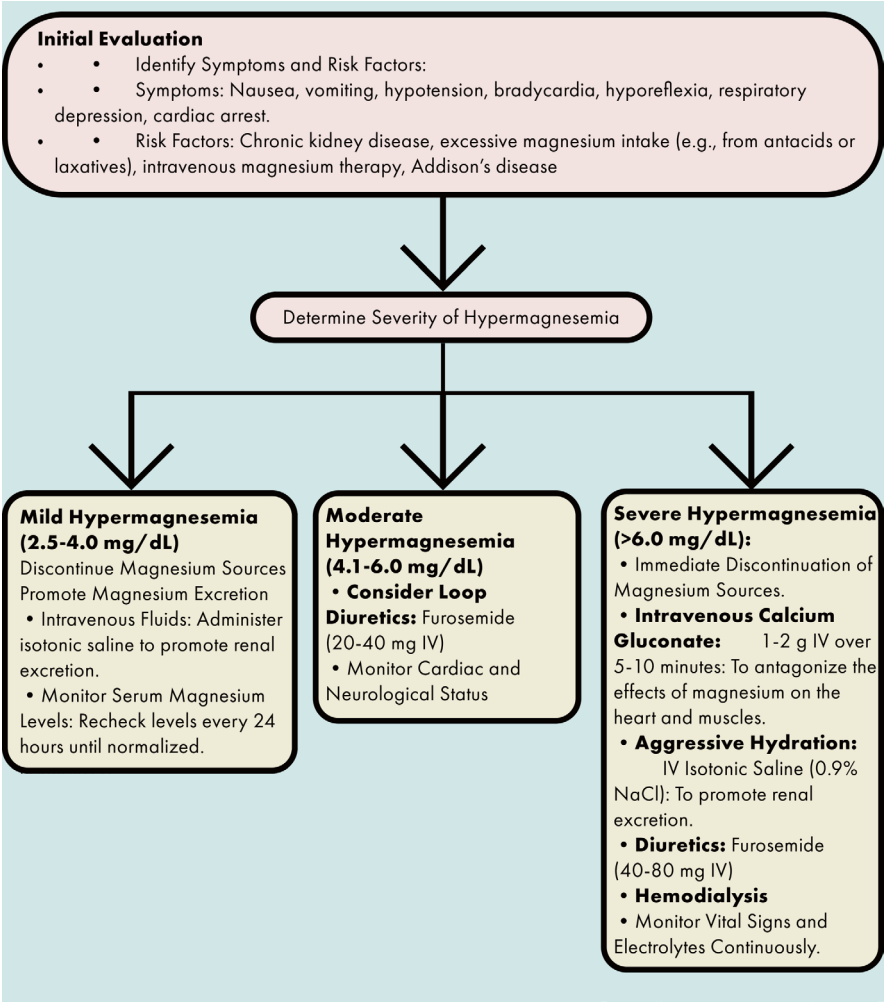
Long-Term Consequences
- Chronic Kidney Disease (CKD): Up to 30% of AKI survivors develop CKD.
- Major Adverse Kidney Events (MAKE):
- Mortality: Increased risk of death even after discharge.
- Need for RRT: Some patients require long-term dialysis.
- Decline in Kidney Function: Significant loss of kidney performance over time.

Importance of Follow-Up Care
- Regular Monitoring: Check renal function tests periodically.
- Multidisciplinary Approach: Involvement of nephrologists, primary care physicians, and other specialists.
- Risk Factor Management:
- Control Blood Pressure: Helps prevent further kidney damage.
- Avoid Nephrotoxins: Be cautious with medications that can harm the kidneys.
- Lifestyle Changes: Healthy diet, exercise, and smoking cessation can improve outcomes.
- Patient Education: Inform patients about the risk of recurrent AKI and signs to watch for.

32.13 Conclusion

Acute kidney injury is a frequent and severe complication in critically ill patients, significantly increasing morbidity and mortality. Early detection through standardized criteria and the use of biomarkers is crucial for timely and effective management. Preventive strategies focus on maintaining optimal fluid balance, ensuring adequate hemodynamic support, and minimizing exposure to nephrotoxic agents. Since AKI can lead to long-term kidney damage, follow-up care is essential to monitor for complications such as CKD and mitigate its progression.

Algorithm 32.1: Approach to acute kidney injury in the ICU (AKI) in Critically Ill Patients in the ICU



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Part III
Gastroenterology