Short-term Effects of Acute Kidney Injury

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KEYWORDS

• Acute kidney injury • Short term • Uremic toxins • Electrolytes
• Inflammatory mediators • Cytokines • Neutrophils • Immune system

KEY POINTS

- Acute kidney injury (AKI) is a systemic disease.
- Conventional short-term effects of acute kidney injury (eg, fluid, electrolytes, and acid-base abnormalities; and uremic toxin accumulation) respond well to renal replacement therapies. However, this approach is usually reserved for the severest stages of AKI.
- AKI modulates underlying processes by reducing cytokine clearance, triggering enhanced renal cytokine production and contributing to systemic inflammation.
- AKI negatively affects neutrophil recruitment and thereby worsens infections (experimental evidence).

INTRODUCTION

Acute kidney injury (AKI) occurs in more than 30% of critically ill patients.[1,2] Mounting epidemiologic evidence shows that AKI is an independent risk factor for mortality (ie, patients are dying because of, and not simply with, AKI).[1,3–5] This evidence does not only apply to the most severe form of AKI, for which patients are treated with renal replacement therapy (RRT). It also holds true for small declines in renal function, which in turn are associated with increased short-term mortality.[6,7] When the severity of AKI is classified according to current criteria,[8–10] a strong association between the severity of AKI and hospital mortality emerges.[11–14] AKI, at all stages, also affects other outcomes, including the length of hospital stay, readmission rates, and development of end-stage kidney disease.[15–18] These effects cannot solely be attributed to the loss of organ function, because it has been repeatedly been shown that the mortality of critically ill patients with end-stage renal disease is lower than that of patients with

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AKI, even when not requiring RRT.[19] Thus, despite extensive data showing the clinical impact of AKI, the exact underlying mechanisms remain largely unknown.

SHORT-TERM EFFECTS OF ACUTE KIDNEY INJURY: THE CONVENTIONAL PERSPECTIVE

The key acute consequences of AKI comprise electrolyte abnormalities, acidosis, and fluid overload (**Fig. 1**), but accumulation of uremic toxins has also been discussed as factor contributing to the increased mortality associated with AKI.[20–23]

Electrolyte Disturbance

Potassium homeostasis mainly relies on renal excretion, therefore hyperkalemia is a commonly encountered finding in AKI. Additional factors contributing to hyperkalemia in critical illness include pH-dependant shifts from the intracellular space and relative insulin resistance. Furthermore, rhabdomyolysis, hemolysis, and the adverse effects of certain drugs (eg, angiotensin-converting enzyme inhibitors, calcineurin inhibitors, cotrimoxazole) may also contribute to hyperkalemia. Hyperkalemia may induce or worsen metabolic acidosis by interfering with renal ammonium excretion ($NH4^+$).[24] Left untreated, hyperkalemia may be fatal, leading to severe cardiac arrhythmias, muscle weakness, paralysis, and change in mental status. Clinical symptoms are usually observed at potassium levels greater than 7.0 mEq/L in chronic hyperkalemia but may occur earlier with rapid changes in serum potassium occurring, which is often the case in AKI. Classic pharmacologic manipulation of potassium levels provides transitory improvement through intracellular potassium shifts. The only effective measures decreasing whole-body potassium load are diuretic therapy (as long as the kidney is responding), enteric potassium-binding resins, and RRT. A specific threshold for

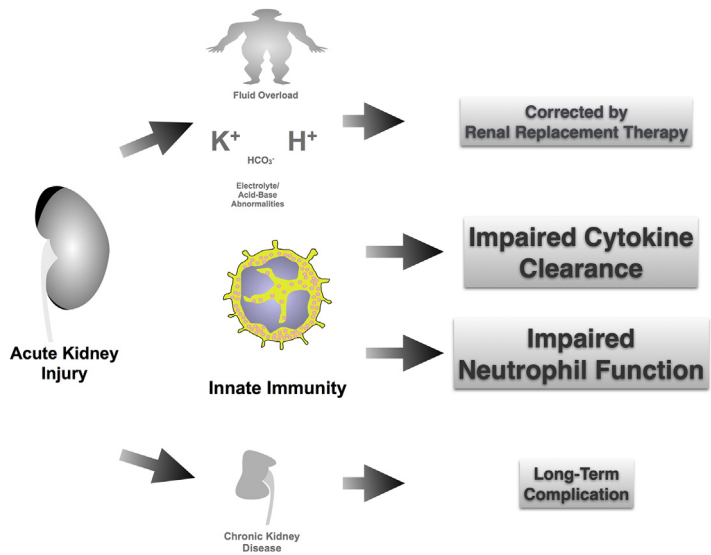

Fig. 1. Clinical effects of AKI. AKI has both short-term and long-term clinical effects. Fluid overload as well as acid-base and electrolyte imbalances are usually well controlled by RRT. The development of chronic kidney disease is a long-term effect of AKI. The effects of AKI on innate immunity have recently emerged as another important short-term factor in the pathophysiology of AKI.