About Acute Kidney Injury

The Need For Clarity

Acute kidney injury (AKI) is a complex and increasingly prevalent condition associated with high mortality in critically ill patients. Although it occurs quickly (over the course of hours), there is commonly a challenge in risk assessment due to the inadequate tools currently available to physicians. Failure to recognize and manage AKI in the early stages can lead to devastating outcomes for patients and increased costs to the healthcare system.

The burden of AKI extends far beyond short-term clinical outcomes and financial consequences: it can last a lifetime. Many patients who survive AKI require ongoing care for chronic kidney disease and incur the long-term risk of developing end-stage renal disease.\(^1\)

The Kidney Disease Improving Global Outcomes (KDIGO) foundation is a preeminent group of physicians, researchers and policy makers working to improve the outcomes of kidney disease patients worldwide. Through a variety of activities, KDIGO promotes the need to recognize and manage AKI early in order to improve outcomes and mitigate the need for dialysis. In its Clinical Practice Guideline for Acute Kidney Injury, KDIGO notes the importance of ongoing assessment of high-risk patients until risk has subsided.\(^2\)

More About Acute Kidney Injury

How the Kidneys Work

The primary function of the kidneys is to maintain fluid and electrolyte balance within the body and excrete a variety of wastes as urine. They also play a central role in controlling blood pressure and in the formation of new red blood cells.

Disease Classifications

*Kidney disease* is classified in two distinct groups: Acute Kidney Injury (AKI) and Chronic Kidney Disease (CKD).

**Acute Kidney Injury (AKI):** A potentially reversible loss of kidney function that develops over hours to days. AKI ranges from mild impairment to complete organ failure. Due to a lack of symptoms, it can often be a stealth condition, resulting in what some experts have called a “kidney attack.”\(^3\)

**Chronic Kidney Disease (CKD):** A permanent loss of kidney function that progresses over months or years.

Incidence

AKI affects up to seven percent of hospitalized patients. With more than 36 million annual admissions to U.S. hospitals,\(^4\) well over 1 million patients are affected by AKI annually.

The incidence of AKI is much higher among critically ill patients, with up to half developing some degree of AKI during their illness, leading to a concomitant increase in mortality.\(^5,6,7,8,9\) In the largest study to date examining the epidemiology of AKI, defined by RIFLE criteria, in the ICU setting (n=41,972 patients), 36 percent developed AKI.\(^10\) One in five of these patients progressed to renal failure requiring renal replacement.

Causes and Risk Factors

Most hospitalized patients are being treated for some other acute medical issue when they develop AKI. These issues include sepsis, respiratory failure, heart failure, trauma, major surgery, burns and toxic insults to the kidney from medications and/or iodinated contrast material used for CT imaging. Sepsis is a common cause of AKI in the intensive care unit, accounting for roughly one-third of all hospitalized patients with AKI.\(^11\)

Risk factors for the development of AKI include advanced age, female gender, ethnicity and a number of comorbidities including diabetes, hypertension, vascular disease and obesity.

Symptoms

AKI most commonly develops without overt symptoms. Although AKI patients often have decreased urine output, it is not a universal finding in such patients, nor is it specific to AKI. When it is present, it may develop hours to days after the kidney injury takes place.
Biomarkers and Assessing Risk

Today, the diagnosis of AKI is universally made on the basis of laboratory test results. Measurements of serum creatinine and urea concentrations remain the “gold standard.” This methodology has not changed in many decades, and there is growing consensus that better diagnostic tools are desperately needed to reduce the burden of AKI. Although some newer biomarker-based tests have recently become available, they are also considered insufficient for risk assessment of AKI.

Serum creatinine (SCr). Creatinine is a waste product formed by the normal breakdown of muscle cells that is freely filtered out of the blood by the kidney. When kidney function declines, serum concentrations of creatinine increase proportionally. Rises in serum creatinine may not be apparent for 24 to 48 hours after kidney injury occurs. By that time as much as 50 percent of kidney function can be lost. In addition, serum creatinine is elevated in CKD, making it difficult to detect AKI in these patients. Finally, serum creatinine levels can change with factors unrelated to renal disease, such as age, race, gender, diet, muscle mass, metabolism, strenuous exercise and hydration status.

Urine output is used in conjunction with serum creatinine tests to assess for AKI. As mentioned above, it also has a number of significant limitations. A minimum of 12 hours must pass to determine moderate or severe AKI by urine output criteria, which gives fast-moving AKI too much of a head start. In addition, urine output may not be measured frequently enough to provide a timely indicator of injury. Finally, urine output is affected by a number of other physiologic variables as well as hydration status and medications such as diuretics.

Management

Management options for AKI are limited. The KDIGO Clinical Practice Guideline for Acute Kidney Injury sets the standard for the direction of AKI patient management. In addition to treating the underlying illness, management options include fluid therapy, vasopressors and/or inotropes, and renal replacement therapy (RRT).

A 2009 report out of the United Kingdom looking at the diagnosis and treatment of AKI found vast room for improvement in recognition of the disease, risk assessment and overall care. According to the report, over 30 percent of the hospital acquired AKI patients suffered from an avoidable kidney injury. Failure to recognize AKI leads to suboptimal clinical management and a delay in the involvement of a nephrologist.

Mortality

The mortality associated with severe AKI (i.e., patients requiring RRT) in the ICU setting is staggering. Although it varies significantly according to associated organ system failure and comorbidity status, mortality rates for AKI patients requiring RRT are approximately 50 to 60 percent.

Costs

It is estimated that each year AKI is a factor in more than 1 million hospitalizations in the United States resulting in $10 billion in excess costs to the healthcare system. AKI is associated with increased hospital length of stay, which increases the total cost of care. One study showed that after cardiac surgery, the average patient without AKI required an average of 1.4 days of hospitalization at a cost of $13,838. Similar surgical patients who experienced AKI required hospital stays of between 2.4 to 5.4 days, with a cost of $21,775 to $49,328, depending on the severity of the kidney injury.

Improving Outcomes

It is believed that continued biomarker research can help meet clinicians’ needs for improved diagnostic and risk assessment. The identification of novel AKI biomarkers has been designated a top priority by the American Society of Nephrology.

Important properties of clinically relevant AKI biomarkers should include:

- accuracy, reliability and rapid turnaround time;
- measurement from non-invasive sources, such as blood or urine;
- ability to perform either at bedside or in a standard clinical laboratory;
- validation by prospective studies demonstrating high predictive ability;
- cost-efficacy.
References