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ACUTE KIDNEY INJURY IN THE CRITICALLY ILL PATIENT: A REVIEW STUDY

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Abstract:

Objective: *A comprehensive review of the literature to provide a focused and thorough update on the issue of acute kidney injury (AKI) in the surgical patient.*

Methods: *A PubMed and Medline search was performed and keywords included AKI, renal failure, critically ill patients.*

Findings: *A common clinical problem encountered in critically ill patients is AKI. The recent consensus definitions for the diagnosis and classification of AKI (i.e., Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease/Acute Kidney Injury Network) have enabled us to standardize the severity of AKI and facilitate strategies for prevention. These strategies as well as treatment modalities of AKI are discussed. We provide a concise overview of the issue of renal failure.*

Conclusions: *Acute kidney injury is a common problem in the critically ill patient and is associated with worse clinical outcomes. A standardized definition and staging system has led to improved diagnosis and understanding of the pathophysiology of AKI. There are many trials leading to improved prevention and management of the disease.*

Key words: *Acute kidney injury, renal failure, critically ill, renal replacement therapy.*

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INTRODUCTION:

Acute kidney injury (AKI) is a significant morbidity encountered in the critically ill patient both in medical and surgical intensive care units (ICUs). Approximately 6% of critically ill patients with AKI are treated with some form of renal replacement therapy (RRT) during their ICU stay. [1] These patients often have a prolonged hospital course; longer days spent in the ICU, and may go on to require dialysis after discharge. [2] The intensivists who care for these patients must have the fundamental knowledge of the principles related to AKI to understand important strategies for both the prevention and treatment of AKI. This article will aim to provide a review of the pathophysiology of AKI, go over the most recent diagnosis and classification systems, describe specific causes of AKI in the intensive care setting, review fluids chosen for resuscitation, and discuss timing and modes of RRT based on recent evidence.

Epidemiology of AKI:

The incidence of AKI varies depending on the population studied. It accounts for 1% of hospital admissions in the United States. This review will focus on hospital acquired AKI, which has an incidence of 5% to 7%. [3,4] there are a number of causes of AKI in the critical care setting, with acute tubular necrosis remaining the most common. The process is often multifactorial including sepsis, nephrotoxic drugs, contrast agents, and postsurgical. [4] Approximately 5% to 20% of ICU patients will develop some AKI, of whom approximately 6% will require some form of RRT during their ICU stay. [1,2] The incidence of ICU-related AKI has increased over the last decades and this is probably due to the increasing incidence of sepsis-related hospital admissions.

Pathophysiology:

Intrinsic Causes of AKI:

The pathogenesis of AKI involves a complex relationship among vascular, tubular, and inflammatory factors. [2,5] The AKI secondary to septic shock is predominantly thought to involve a reduction in renal blood flow secondary to systemic arterial vasodilation and concomitant intrarenal vasoconstriction. This results in renal hypo perfusion and ischemia. The kidneys receive higher blood flow per unit mass compared to any other organ in the body but the actual fraction of extracted oxygen is less. This makes the kidney very sensitive to conditions of hypo perfusion. Ischemia and toxins result in vasoconstriction, endothelial injury, and the activation of innate and acquired inflammatory immune responses. [2,5] The oxygen supply to the renal tissues can be impaired due to acute blood loss from trauma or during acute hemodilution during resuscitation with large quantities of crystalloids in trauma or septic shock. [6] The AKI that results then triggers a cascade of inflammatory processes both locally and systemically. This systemic inflammatory response syndrome is initially characterized by a systemic release of pro inflammatory cytokines followed by a counter anti-inflammatory response syndrome. This anti-inflammatory response is aimed at controlling and limiting the inflammatory process. [7] Uremia in the setting of AKI can disrupt this natural sequence of events and this has been thought to play a key role in the pathogenesis of multi organ failure.

Extra renal Causes of AKI:

Intra-abdominal hypertension. The kidneys have a unique relationship with other vital organs. Diseases and processes that affect one organ will often affect another. An example of a process that can lead to the development of AKI is the presence of intra-abdominal hypertension (IAH). In a critically ill patient, normal intra-abdominal pressure (IAP) is approximately 5 to 7 mm Hg. Intra-abdominal hypertension is defined by a sustained or repeated elevation of IAP 12 mm Hg. A common clinical scenario in which this may occur is with excessive fluid resuscitation due to inflammation. [8,9] the combination of large fluid volumes inflammation-induced capillary leak results in fluid sequestration in extracellular compartments, which leads to visceral edema, and subsequent IAH. [11]

Mechanical Ventilation and Pulmonary Causes:

As renal function is closely related to other organs, it is also affected by interventions used in the critically ill patient. There are very close lung–kidney interactions including renal effects of acute lung injury and mechanical ventilation. There is a known entity called ventilator-induced kidney injury. The investigators demonstrated that those treated with a lung-protective lower tidal volume technique had fewer days with AKI. [12] The physiologic impact of positive pressure ventilation (PPV) and its effects on renal perfusion are well documented. [12-14] The PPV results in decreased renal perfusion and function by 2 main mechanisms. The first is the hemodynamic effects, which is illustrated by decreased cardiac output as a result of reduced venous return from the increase in intrathoracic pressures. This can also lead to hypotension and fluid responsive shock. All of this has been shown to correlate with decrease in renal blood flow, glomerular filtration rate, and urine output during PPV. A recent review by van den Akker et al showed that invasive mechanical

ventilation was associated with a 3-fold increase in the odds of developing AKI in the critically ill patients. [13] The PPV has also been shown to alter various neurohormonal systems including increased sympathetic outflow, which in turn activates the renin–angiotensin axis resulting in decreased renal blood flow, fluid retention, and oliguria. [14]

Definition and Classification:

In the past, it was thought that a major impediment to good comparative research in acute renal failure was the lack of a uniform definition. It was believed this might explain differences in reported incidence and outcomes of AKI in the literature. As a result, in 2004, the Acute Dialysis Quality Initiative workgroup developed a consensus definition known as the Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease (RIFLE) classification. [2,15-17] This classification was based on 2 main parameters, changes in serum creatinine (SCr) from baseline and urine output. The severity of the renal failure was determined by the more severe of the 2 parameters.

There are 3 stages described in RIFLE, which include Risk, Injury, and Loss all of which have increasing prognostic significance based on the increase in SCr from baseline (see Table 1). After data emerged demonstrating that even small alterations in renal function led to adverse outcomes, the Acute Kidney Injury Network (AKIN) modified the RIFLE classification system in 2007. [15,16,18] This network replaced the term acute renal failure with AKI in an attempt to standardize both the definition and staging of kidney injury and it has facilitated improved risk stratification in critical AKI. The AKIN workgroup defined AKI as a reduction in kidney function occurring over no more than 48 hours with an absolute increase in SCr level 0.3 mg/dL or more or a relative increase in SCr 1.5- to 2-fold, or documented oliguria less than 0.5 mL/kg/h for more than 6 hours despite adequate fluid resuscitation. [18] There have been multiple studies, which have shown really no difference between the 2 in predicting mortality, but they have allowed for a more uniform classification [15,19] (see Table 2).

The Kidney Disease Improving Global Outcomes Network addresses both of these classification systems within their guidelines as both have been validated. However, they do note that there are limitations with both and they recommend that patients should be staged according to the criteria that give them the highest stage.

Table 1. RIFLE Classification

	Cr/GFR Criteria	Urine Output (UO) Criteria
Risk	creased Cr 1.5 or GFR	UO <0.5 mL/kg/h 6 h UO
Injury	decreases >25%	<0.5 mL/kg/h 12 h
Failure	creased Cr 2 or GFR	Ↄ <0.3 mL/kg/h 24 h or
Loss	decreases >50%	anuria 12 h
ESRD	creased Cr 3 or GFR decreases >75% or Cr 4 mg/dL (with a cute rise of 0.5 mg/dL) Persistent ARF ¼ complete los s End-stage renal disease	of renal function for >4 weeks

Abbreviations: ARF, acute renal failure; Cr, tion rate; RIFLE, Risk, Injury, Failure, Loss of ki ney disease. reatinine; GFR, glomerular filtradney function, and End-stage kid-

Table 2. AKIN Classification.

	Cr Criteria	Urine Output (UO) Criteria
Stage 1	creased Cr 1.5 or 0.3 mg/dL	UO <0.5 mL/kg/h 6 h
Stage 2	Increased Cr 2	UO <0.5 mL/kg/h 12 h

Stage 3	creased Cr 3 or Cr 4 mg/dLↃ (with acute rise of 0.5 mg/dL)	<0.3 mL/kg/h 24 h or anuria 12 h

Fluids for Resuscitation and AKI:

A major part of the acute management of critically ill patients is centered about fluid resuscitation and the uses of crystalloids versus colloids have been studied and debated both in the medical and surgical literature. Crystalloids and colloids have different benefits and risks related to outcomes including renal dysfunction in the critically ill patients, and in the most recent update for the Surviving Sepsis Guidelines there is a section dedicated to the choice of fluids and how they related to kidney injury. These studies relating to the choice of fluids and how they relate to renal failure will be outlined next.

Specifically, the Crystalloids Morbidity Associated with severe Sepsis (CRYSTMAS) study was a multicenter RCT that compared the hemodynamic effects and safety of the lower molecular-weight HES to normal saline for hemodynamic stabilization in patients with severe sepsis. They hypothesized that the use of colloids would reduce the amount of fluid required to reach hemodynamic stability. Their safety variables were kidney function categorized according to the RIFLE and AKIN classifications. The study did correlate that less colloid was needed compared to crystalloid to reach hemodynamic stability and there was no difference in mortality. This study was an underpowered study with fewer than 200 patients.

Timing of Initiation of RRT:

The mainstay of treatment for AKI is RRT and there is a paucity of data to guide the optimal timing to initiate and mode of therapy. There are a number of indications for the initiation of RRT including acid/base derangements, volume overload, various electrolyte abnormalities, and uremia. [2,4,6,16,20] As the primary goal of RRT is to compensate for loss of renal function and the associated sequelae such as fluid overload and clearance of toxins, the conventional markers for the initiation of RRT include SCr, blood urea nitrogen (BUN), and oliguria < 200 mL in 12 hours. As a matter of fact, these parameters traditionally have served to guide our involvement of nephrologists with decisions regarding RRT.

CONCLUSIONS:

In summary, AKI has been linked to sepsis and inflammation, as the kidney is very sensitive to hypo perfusion. The kidney is also sensitive to many of our interventions, such as mechanical ventilation and excessive fluid resuscitation. Positive pressure ventilation can lead to hemodynamic changes and also the systemic release of cytokines that can impact renal function. Fluid therapy during resuscitation can also result in renal impairment, including all forms of fluid therapy. Crystalloids and colloids in the form of albumin are considered equally safe, however. Crystalloids are first-line therapy followed by 5% albumin for large volume resuscitation. The initiation of RRT should be considered early and there are data supporting early RRT in the setting of oliguria versus the traditional parameters including azotemia, fluid overload, electrolyte changes, and acidosis.

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