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Acute Kidney Injury

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ABSTRACT

Acute kidney injury (AKI) is defined as the sudden loss of kidney function. AKI is part of a group of diseases collectively called acute kidney disease and disorder (AKD), in which a slow decline in kidney function or persistent kidney dysfunction is associated with irreversible loss of nephrons (functional units of kidney), which can eventually lead to chronic kidney disease (CKD). New biomarkers to detect injury before loss of function await clinical application. AKI and AKD is a major concern worldwide. Infections and hypovolemic shock are the main causes of AKI in low- and middle-income countries. In high-income countries, AKI occurs most often in hospitalized elderly patients and is associated with sepsis, medications, or invasive procedures. Infections and trauma-induced AKI are common in all regions. The broad spectrum of AKI involves different pathophysiological mechanisms. Management of AKI in the intensive care setting is complex, including appropriate volume management, careful monitoring of nephrotoxic drugs, and choice of renal replacement therapies. Fluid and electrolyte management is essential. Because AKI can be fatal, renal replacement therapy is often necessary. AKI generally has a poorer prognosis in critically ill patients due to various reasons. Long-term consequences of AKI and

AKD include chronic kidney disease and morbidity due to cardiovascular disease. Therefore, early detection and prevention of AKI are quintessential.

Key words: Acute kidney injury; Chronic kidney disease; Dialysis; Nephrotoxins; Renal replacement therapy

INTRODUCTION

Acute kidney injury (AKI) remains a major problem in clinical medicine today.[1] It occurs in about 1-5% of all hospitalized patients. The incidence increases significantly as the severity of the underlying cause progresses: up to 50% of patients treated in the intensive care unit develop AKI, in many cases secondary to disseminated infection or sepsis.[2,3] The term acute kidney injury replaced acute renal failure, emphasizing that the progression of kidney damage begins long before it is possible to measure adequate excretion of renal function by standard laboratory tests. The term also refers to a continuum of predictions where an increase in mortality is associated with even a small increase in serum creatinine and a further increase in mortality as creatinine levels rise. The prognosis has not significantly improved in the last 20-30 years, although significant progress has been made in the field of intensive care and dialysis treatment.[4,5] In the mid-1970s, 70% of all patients with AKI died. Mortality decreased moderately in the early 1990s (30-50%) and has remained stable for the last 20 years. The poor prognosis is due in part to the disease itself that causes AKI, but also to the complications associated with AKI. Thus, the invention of more effective therapeutic interventions remains an important goal of the field of nephrology research.

Definition of AKI

AKI is defined as an acute impairment of renal function manifested by an increase in serum creatinine[6]. In most patients (70%), urine production also decreases. The definition of the syndrome is refined from time to time, and according to the latest KDIGO guidelines, AKI can be diagnosed if the following criteria are met: (I) an increase in serum creatinine of more than 0.3 mg/dL within 48 hours, or (II) a 1.5-fold increase in serum creatinine within a seven day period (compared to a known or suspected baseline) and/or (III) a decrease in urine output below 0.5 ml/kg per day for at least 6 hours.[7,8] It should not be forgotten that serum creatinine is a poor parameter of renal function, because its concentration begins to increase late in AKI, when at least 60% of renal function is lost. The severity of AKI varies, and several scores can be used to distinguish certain degrees of acute kidney failure. The RIFLE criteria distinguish risk (R), injury (I), failure (F), loss (L), and end-stage kidney disease (E) depending on the relative increase in serum creatinine and/or relative decrease in urine production.[9,10] It should be noted that stage E can only be diagnosed if the renal dysfunction lasts more than 3 months. Such criteria may not be important from a therapeutic point of view, but from a prognostic point of view, since the prognosis significantly worsens with the severity of kidney damage.

Epidemiology

The global mortality burden of AKI far exceeds mortality from breast cancer, heart failure, or diabetes, and mortality has remained high for the past 50 years.[11,12] Generally, the incidence of AKI is reported as either

community-acquired or hospital-acquired AKI. In high-income countries (HICs), AKI is mostly hospital-acquired, while community-acquired AKI is more common in low-income countries. In HIC, AKI patients are generally elderly, have multiple co-morbidities, and have access to dialysis and intensive care when needed. The main causes of AKI in HIC are postoperative or diagnostic interventions or iatrogenic factors. However, there are many community-acquired causes in poor environments, including sepsis, body volume depletion, poisons (bites, drugs) and pregnancy.[13,14] Patients tend to be younger than those with HIC, access to treatment is more difficult, and women are underrepresented in the patient population.

Risk factors of AKI

Risk factors for AKI include environmental, socioeconomic and/or cultural factors, as well as factors related to the treatment process, acute exposure and patients themselves.[15,16] Environmental factors include inadequate drinking water and sewage systems, inadequate infectious disease control, and inadequate health care delivery systems. Patient-related factors may be modifiable, such as volume depletion, hypotension, anemia, hypoxia, and use of nephrotoxic medications, or nonmodifiable, such as chronic kidney, heart, liver, or gastrointestinal disease, diabetes, and serious infections and sepsis.[17-19] Less common causes are genetic predisposition to myoglobinuria, hemoglobinuria and urolithiasis. Other important risk factors for AKI are serious illness, acute infections, sepsis, malaria, severe trauma, hypovolemia, old age, pre-existing chronic kidney disease, acute organ failure, major surgery (including heart surgery), intensive care unit stay with exposure to nephrotoxic medications and acquiring opportunistic infections, cancer chemotherapy, delayed kidney transplant graft function, autoimmune diseases with rapidly progressive kidney damage, cholesterol crystal embolism, and urinary tract obstruction.[20-23] Although severe AKI occurs more often in association with hospital-associated risk factors such as major surgery, hemorrhage, septic shock, or drug intoxication in elderly patients with multiple diseases, milder forms of AKI can also occur in the community. In contrast, in low- and middle-income countries (LMICs), community-acquired AKI affects younger, previously healthy individuals, and the incidence of sepsis and obstetric complications is relatively high. COVID-19 remains a major risk factor for AKI worldwide.[24,25]

Kidney physiology and mechanisms of AKI

Renal Physiology and Renal Lifespan

The kidneys maintain the homeostasis of body fluids, electrolytes, osmolality and pH, excrete metabolic waste products and secrete hormones and bioactive molecules. Because AKI disrupts homeostasis, severe AKI is potentially fatal if renal replacement therapy (RRT) does not maintain homeostasis until renal function is restored. AKI in multiorgan failure is often fatal despite RRT.

The kidneys consist of nephrons, small independent functional units whose glomerular part filters fluids and small molecules from the blood, and a single tubule that reabsorbs most of the filtered molecules and excretes metabolic waste products, producing 1-2 liters of urine each day. The number of nephrons is determined at birth and decreases

gradually with age after about 25 years.[26] Because metabolic activity also declines with age, healthy 70-year-olds can do well with only half the original number of nephrons without adaptation. However, low nephron count at birth or loss of nephrons after normal aging shortens renal lifespan. Therefore, the incidence of chronic kidney disease and kidney failure requiring RRT increases in the elderly. AKI and CKD are linked because AKI can cause irreversible nephron loss at any stage of life, thereby shortening kidney life.[27,28] Thus, AKI is an important risk factor for chronic diseases, especially in the aging population.

The pathogenesis of inflammatory diseases of the renal parenchyma, such as glomerulonephritis and vasculitis, is complex and involves almost all aspects of the innate inflammatory system and mechanisms mediated by antibodies and immune cells.[29-31] In this review, we focus on acute kidney injury due to prerenal factors, because this form is the most common in developed countries, in hospitals, and especially in critically ill patients. Much of our understanding of the pathophysiology of prerenal acute kidney injury comes from animal studies.[32] Studies in models of acute ischemia induced by acute renal artery occlusion reveal the many pathways and mechanisms of organ injury likely involved. The coagulation system is locally activated, leukocytes infiltrate the kidney, the endothelium is damaged and adhesion molecules are expressed, cytokines are released, toll-like receptors are induced, intrarenal vasoconstrictor pathways are activated, and apoptosis is induced. It appears that kidney injury can trigger organ injury elsewhere (so-called organ crosstalk) through obscure pathways, further emphasizing the complexity of the biological response to acute kidney injury.

Unfortunately, this ischemic model has little clinical relevance in diseases such as sepsis. Sepsis is the most common cause of acute kidney injury in hospitalized and intensive care patients.[33] The model also has little relevance for periods of reduced perfusion that may occur during major surgery, as 80% renal artery occlusion for 2 h does not cause permanent renal dysfunction. Thus, many of the principles that physicians use to understand acute kidney injury are questionable for patients in modern hospitals or intensive care units. The most common causes of acute kidney injury in such patients are sepsis, major surgery (especially open heart surgery), and acute decompensated heart failure.[34,35] The renal artery is not blocked in any of these situations. More appropriate models are needed.

Neurohormonal mechanisms

Activation of the sympathetic system and neurohormonal responses specific to the kidney are activated in acute kidney injury.[36] The renin-angiotensin-aldosterone system, the renal sympathetic system and the tubulo-glomerular feedback system are activated. Knowing these changes led to further understanding of how people can develop acute kidney injury. This framework suggests that in sepsis-like situations, infection leads to nitric oxide synthase induction and nitric oxide-mediated vasodilation, which in turn leads to arterial hypoperfusion and baroreceptor activation.[37] These circulatory changes trigger activation of the sympathetic system, which increases renin-angiotensin-aldosterone system (RAAS) activity and renal vasoconstriction. At the same time, arginine vasopressin is released and promotes water retention.

Hepatorenal syndrome (HRS) is perhaps the most widely studied form of acute kidney injury in terms of neurohormonal changes and provides useful mechanistic insights.[38] In this syndrome, as in experimental sepsis, acute kidney injury occurs without histopathological renal changes and is thus functional in nature. Severe renal vasoconstriction associated with significant RAAS activation is a characteristic finding in patients with hepatorenal syndrome, suggesting that neurohormonal events drive the development of the disease. Although the mechanisms leading to such activation are debated, the central event is thought to be a decrease in systemic blood pressure due to splanchnic vasodilation.[39] The neurohormonal response to such vasodilation supports systemic blood flow, but renal blood flow may be adversely affected. It is not known whether a similar condition occurs in other diseases associated with hypotension and systemic vasodilation (eg, inflammation and sepsis). Thus, elevations in noradrenaline, renin, and angiotensin II may contribute to other forms of acute kidney injury, suggesting that, at least in some settings, neurohormonal renal vasoconstriction may underlie the loss of excretory function.

Clinical manifestations

AKI patients do not suffer from clinical symptoms more or less specific to the disease. On the other hand, they may indicate symptoms of some underlying disease (eg heart failure, sepsis, systemic vasculitis, thrombotic microangiopathy). Urine production is reduced in 70% of AKI and can result in fluid retention with worsening blood pressure and heart failure with pulmonary edema.[40] Due to the reduction in the secretion of electrolytes and endogenous/exogenous residues, the whole body is affected. The term uremia describes such poisoning and is associated with a variety of heterogeneous symptoms, including pruritus, neurological manifestations, nausea and vomiting, diarrhea, anorexia and loss of appetite, cardiac arrhythmias, and insomnia.[41,42] In addition, patients have an increased risk of infections and abnormal bleeding complications (due to platelet dysfunction). The presence of uremia is important because in most cases dialysis therapy becomes mandatory. Polyuria after initial oliguria usually indicates the onset of kidney function, but can cause significant loss of water, sodium and potassium. The latter can cause heart rhythm abnormalities.[43] If the kidney recovery takes more than 3 months, it means AKI is transformed to CKD.

Long-term consequences of AKI

Irreversible nephron loss, fibrosis and CKD

Depending on the severity of AKI, few, many, or most nephrons remain irreversibly destroyed and lost, resulting in post-AKI CKD and shortened renal lifespan.[44] Albuminuria after AKI is a clinical indicator of CKD, even when GFR appears to have fully recovered. The impact of AKI on renal life expectancy is most evident in older adults, where AKI-related nephron loss increases age-related nephron loss and often chronic kidney disease from previous injuries or chronic nephropathies, known as AKI in CKD. Therefore, since ATN means nephron loss, the severity of

ATN determines the effect on kidney lifespan. In extreme cases, severe ATN can lead to kidney failure and continuous need for RRT.

Hypertension and risk of cardiovascular disease

AKI survivors may have hypertension, which may be a sign of subclinical CKD. A retrospective cohort study showed a 22% increased risk of blood pressure >140/90 mmHg in patients with AKI compared to those without AKI.[45] CKD after AKI is associated with increased cardiovascular and cerebrovascular morbidity and mortality.[46-48] It is not clear whether this increase is related to effects on the cardiovascular system during an episode of AKI or to an increased risk of CKD after AKI.

Mortality

AKI survivors face increased post-hospital mortality. Long-term mortality in AKI patients may also be increased. In a study of heart surgery patients, the increase in mortality risk was independent of improvement in kidney function at hospital discharge and did not begin until 4 to 5 years after surgery.[49] The most common causes of death are cardiovascular disease (28%) and cancer (28%), and the corresponding standardized mortality rates are nearly six and eight times higher than those in the general population. Cancers were mostly hematological or urogenital. An episode of AKI predicts the risk of later development of kidney cancer, and an episode of AKI after partial nephrectomy for kidney cancer increases the risk of cancer recurrence, probably because kidney damage causes DNA damage and clonal expansion of mutated cells during the healing phase.[50,51] Indeed, renal progenitors that leads to tubular regeneration can become tumor cells after ischemic ATN and trigger monoclonal lesions in the papillary renal cell adenoma-carcinoma sequence.

Diagnosis, screening and prevention

Unlike myocardial infarction and other acute organ failure, AKI does not cause immediately alarming symptoms such as chest pain, shortness of breath, paralysis or blindness; therefore, diagnosis requires special technical assessments. The best overall index of kidney function is GFR, but direct measurement of GFR is difficult. Generally, GFR is estimated using serum levels of endogenous filtration markers such as creatinine. Several studies have shown that small increases in serum creatinine are associated with worse outcomes in AKI.[52] In addition, urine output is a sensitive parameter of renal function and a biomarker of tubular damage. However, the relationship between urine output, GFR and tubular injury is very complex.

Diagnostic and classification criteria

There is evidence to suggest that acute and mild declines in renal function, as manifested by changes in blood chemistry and urine output, are associated with worse outcome in AKI. In contrast to the old term acute kidney failure, the Risk, Injury, Failure, Loss of kidney function and End-Stage Renal Disease (RIFLE) and Acute Kidney Injury Network (AKIN) classifications have provided updated definitions of AKI that cover the entire spectrum of

syndrome from slight increase in serum creatinine to the need for active treatment.[53] The RIFLE and AKIN classifications have three degrees of severity based on changes in serum creatinine or urine output, with the worse of the two criteria being used to determine the grade. RIFLE and AKIN thus provided a conceptual framework for the diagnosis and staging of AKI, but further modifications were necessary to respond to the clinical complexity of AKI, especially outside the intensive care unit (ICU) or hospital settings.

The latest KDIGO guidelines defined the diagnostic criteria for AKI. Contrary to previous recommendations, the KDIGO criteria no longer require adequate fluid resuscitation and exclusion of urinary tract obstruction before using the criteria. Patients with CKD are particularly prone to AKI, as CKD is an independent risk factor for AKI. However, the diagnosis of AKI in patients with CKD is difficult because these patients have impaired renal function and changes in serum creatinine levels after AKI are partially confounded with baseline renal function levels. The KDIGO criteria use decreased urine output, but decreased urine output is also a physiological mechanism in response to decreased fluid intake or fluid loss that readily responds to fluid intake and usually does not indicate tubular damage. Damaged tubules no longer respond to diuretics due to the loss of necessary sodium transporters; thus, a single bolus of a loop diuretic that is not followed by a significant increase in urine output, called the furosemide stress test, indicates tubular injury.[54] In fact, the incidence of AKI is significantly higher when both urine output and serum creatinine are abnormal, compared with abnormal serum creatinine alone (62.1% vs. 17.7%).

Screening and risk assessment with biomarkers

About half of patients with stage 1 acute kidney injury have elevated serum biomarkers and histological abnormalities on renal biopsy, whereas most of those with stage 3 AKI have both.[55] Serum creatinine level and urine output are two functional biomarkers with several limitations. The specificity of urine production is low because several factors can affect this parameter, including hypovolemia and the use of diuretics.[56] In contrast, serum creatinine sensitivity in previously healthy kidneys is low because serum creatinine levels rise only when at least 50% of functional nephrons are lost. In patients with a low baseline GFR, small changes in kidney function can lead to a increase in serum creatinine of 0.3 mg/dL, which defines AKI. Although novel biomarkers such as IL-18 or kidney injury molecule 1 (KIM-1) are available and most of them have a very good predictive value, there are limitations, including poor predictive power when the timing of kidney injury is unknown; therefore, they are only inconsistently applied in clinical practice.

Preventive measures

In LMIC, prevention of volume depletion alone is thought to have a large impact on the incidence of AKI. In addition to preventing volume depletion and nephrotoxin exposure or overdose, new biomarkers may identify patients at high risk of AKI. This approach can be used to stratify patient populations and implement different interventions to prevent the development of AKI. Implementation of the "KDIGO bundle" consisting of volume and hemodynamic optimization, avoidance of nephrotoxic drugs and prevention of hyperglycemia in patients with high risk of AKI identified by biomarkers can prevent AKI after cardiac surgery.[57-59] In a Quality Initiative program,

implementation of supportive measures in biomarker-positive patients reduced the incidence of moderate and severe AKI after cardiac surgery and the incidence of AKI in abdominal surgery patients.[60] Despite these data, only about 5% of high-risk patients receive these supportive measures.

Management

Management of AKI is often suboptimal. The first step in managing AKI is to identify its causes, such as prerenal causes (hypovolemia), intrinsic renal causes, or postrenal causes (outflow obstruction). Further treatment is influenced by the clinical situation, location and history of the patient.

Volume status

Volume depletion may cause impairment of kidney function, but does not damage the kidney by itself unless it is severe and persistent. However, volume depletion can contribute to several causes of AKI, and fluid resuscitation is the cornerstone of treatment. Patients with AKI in the community may become dehydrated, as may hospitalized patients receiving diuretics or dehydrating from injuries or drainage. A hospitalized patient should never become severely dehydrated; however, correcting dehydration by giving inappropriate fluids without properly assessing patients with AKI can lead to fluid overload, which can have significant detrimental effects.[61] Patients requiring intravenous fluid resuscitation should be under direct physician supervision and treatment will benefit from guidelines for hemodynamic monitoring. In addition, the sudden need for fluid resuscitation requires measures to determine its cause (for example, occult bleeding or sepsis). It should be noted that patients can develop oliguria from AKI and then become fluid overloaded with injudicious administration of intravenous fluids in addition to fluids from medications and nutritional support. Importantly, fluid overload has been identified as a major cause of AKI, as venous congestion can compromise circulation and cause direct damage to the renal parenchyma.

Hemodynamic control

Management of blood pressure and cardiac function in the setting of AKI (eg, septic shock or cardiac surgery) is complex and involves context-specific considerations, depending on the type of circulatory shock the patient is experiencing. Under normal conditions, most organs, including the kidneys, are adequately perfused with a mean arterial pressure (MAP) of 65 mmHg or above.[62] Studies examining whether MAP targets should be used in ICU patients have produced mixed results. Patients with severe (and perhaps poorly controlled) hypertension may benefit from a higher MAP in shock, but a fixed target cannot be recommended. Some findings suggest individualized blood pressure control by adjusting MAP targets based on the patient's typical blood pressure. Also, patients with elevated venous pressure (for example due to right-sided heart failure) may not achieve adequate renal perfusion pressure at a MAP of 65 mmHg. Studies using functional hemodynamic monitoring to guide hemodynamic management have shown promise in both cardiac surgery and sepsis. Noradrenaline is the first choice as a vasopressor in vasodilatory shock.[63,64] The other agents are generally reserved for shock requiring therapy or emergency situations, and none are generally more "kidney friendly."

Nephrotoxic drugs and substances

The risk of AKI increases with the number of nephrotoxic drugs used, and all potentially nephrotoxic agents that can be discontinued should be stopped.[65,66] If possible, careful monitoring of drug concentration is also mandatory (for example, in the case of vancomycin). The use of arteriolar contrast agents should be limited to situations where the therapeutic benefit outweighs the risk, and they should be used in the smallest amounts possible.

Stepwise management of AKI

The KDIGO AKI Guidelines emphasize the importance of AKI staging as a management guide. Prognosis is strongly correlated with the peak phase of AKI and the duration of AKI (transient versus persistent), so the urgency and invasiveness of diagnostic and therapeutic measures increase with the phase of AKI.[67] However, the stages of AKI must be interpreted in the context of baseline kidney function. For patients with preexisting normal renal function and stage 1 AKI, treatment primarily involves prompt identification of the likely cause of AKI and avoidance of secondary insults. Depending on baseline GFR, drug dosage adjustments usually become clinically relevant in stage 2 AKI. In stage 3 AKI, symptoms can be caused by a disturbance in the acid-base balance and electrolyte levels, as well as the accumulation of uremic toxins.[68] For example, patients may develop tachypnea not only due to fluid overload, but also due to metabolic acidosis. Acidosis removes potassium from cells, further exacerbating hyperkalemia. Even relatively moderate uremia can impair platelet function and increase the risk of bleeding. If treatment is ineffective or if the disorders are life-threatening, RRT is necessary.

In all stages of AKI, it is recommended to stop all potentially nephrotoxic drugs as soon as possible, because all drugs cause or contribute to AKI in most cases and are probably the most modifiable risk factors for AKI.[69,70] Volume control and hemodynamic monitoring are also required in all stages of AKI. Avoidance of hyperglycemia is important because filtered glucose increases tubular reabsorption workload and oxidative stress, a process that sensitizes renal tubules to damage. An important yet unresolved question so far is whether the various forms of acute kidney injury can be treated with approaches targeting the underlying causes. This strategy is possible in conditions such as obstructive uropathy or atypical hemolytic uremic syndrome, but other forms of AKI often have an unknown etiology. Current knowledge indicates that risk factors and risk modifiers such as medications, contrast agents, low cardiac output and overload should be reduced or eliminated. Even if the cause of an AKI episode is identifiable, this awareness may come too late to prevent the eventual common pathway of tubular toxicity, ischemia, and inflammation.

Management of the trajectory of AKI

Most patients with AKI who receive medical care and whose injury resolves on its own (such as surgery) or whose cause is resolved (such as stopping a nephrotoxic drug or treating an infection) begin to improve kidney function usually within 24-48 hours.[71] However, in 25–35% of patients, AKI persists for ≥72 hours. These patients have significantly worse outcomes. Thus, persistent AKI should prompt the clinician to reconsider their working

diagnosis regarding the cause of AKI. For example, in a patient who develops AKI after cardiac surgery, the volume status, hemodynamics, and medication list should be carefully reviewed and any problems corrected.[72]

Recurrence of AKI is common, especially in ICU patients.[73] Whether recurrence is due to multiple insults to kidney or recurrent renal failure due to damage from a single injury varies. It is best to assume that the recurrence may be due to a new cause that needs to be identified. Recovery after AKI is best assessed after hospital discharge, but follow-up of these patients has historically been poor. Patients may be discharged with unstable renal function and are therefore at greater risk of drug-related adverse events, since most receive drugs that are excreted by the kidneys.[74,75] Common reasons for hospital readmission are both treatment failure due to under dosing in patients with improving renal function and toxic effects due to overdose in patients with declining renal function. Therefore, patients should be referred to a nephrologist for evaluation of kidney function immediately after discharge from the hospital. Finally, even patients who appear to have fully recovered from AKI may be at increased risk of developing kidney damage over an unknown period of time.

Renal replacement therapy

The various aspects of RRT have advanced significantly over the years, making extracorporeal therapy safer and easier to implement. The time and choice of initiation of therapy remain controversial, often due to the heterogeneity of the populations studied. In a patient-centered evaluation based on the principles of precision medicine, life-threatening conditions are not the only indicators of the need to RRT but the prevention of clinical complications should also be considered.

Peritoneal dialysis has been used for many years and is still used in areas where access to more advanced techniques is limited or unavailable.[76,77] In the absence of evidence to support specific techniques, the choice of method should be based on pathophysiological considerations. In unstable and critically ill patients, continuous RRT is often preferred.[78] After the patient is discharged from the intensive care unit, intermittent methods such as continuous low-dose dialysis or daily intermittent hemodialysis can be safely used. Continuous veno-venous hemofiltration, continuous veno-venous hemodialysis, or continuous veno-venous hemodiafiltration are used according to center experience and staff training rather than evidence-based technique differences. A conceptual model of sequential extracorporeal therapy with early removal of endotoxins by polymyxin-B hemoperfusion followed by removal of cytokines and proinflammatory and anti-inflammatory mediators by absorbent devices has been proposed for patients with sepsis-related AKI.[79,80] The best time to initiate RRT in critically ill patients remains controversial, in part because of conflicting renal outcomes in relevant studies. In fact, best practices for RRT can vary in many ways, especially for certain populations.

Quality of life

There is no information on the quality of life of AKI patients in the intensive care unit, where many patients receive medication while on respiratory support. AKI-specific aspects would also be difficult to assess because the diseases are often complex. Existing research focuses on the long-term effects of AKI on health-related quality of life (HRQL) and functional status in critically ill survivors.[81-83] Most studies consistently show that survivors of AKI have significantly reduced HRQL compared to survivors of critical illness without AKI or the general population. HRQL was lower in patients who required intensive care for severe AKI than in those who did not. Among AKI survivors, 20–40% developed a new disability in at least one activity of daily living, and only 28–69% of AKI survivors with preexisting severe disease were able to return to work.[84] After one year of AKI requiring dialysis, 81.8% of survivors would agree to readmission to the ICU if necessary, but after four years that number dropped to 71.4.

Current and future perspective

To date improvements in the field of diagnosis and treatment of acute kidney injury remain unsatisfactory. From a diagnostic point of view, the introduction of a marker of kidney damage in clinical practice remains a priority compared to the current approach based on kidney function. Measurement of serum creatinine does not allow early diagnosis of AKI, which is essential to improve patient outcomes. Creatinine assessment also does not elucidate the extent to which subclinical episodes of AKI contribute to shortened renal lifespan and CKD. Recommendations from the 23rd ADQI Consensus Conference suggest that combining definitions of AKI based on serum creatinine and urinary excretion with biomarkers of kidney injury would improve the accuracy of predicting the course of AKI. [85] Future studies have yet to show the extent to which new biomarkers can help improve short- and long-term outcomes.

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