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Review

# Acute kidney injury after burn

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ABSTRACT

Acute kidney injury (AKI) is a common and morbid complication after severe burn, with an incidence and mortality as high as 30% and 80%, respectively. AKI is a broad clinical condition with many etiologies, which makes definition and diagnosis challenging. The most recent Kidney Disease: Improving Global Outcomes (KDIGO) consensus guidelines defined stage and severity of AKI based on changes of serum creatinine and urine output (UOP) across time. Burn-related kidney injury is typically classified as early (0–3 days after injury) or late (4–14 days after injury). Early burn AKI is typically due to hypovolemia, poor renal perfusion, direct cardiac suppression from TNF-alpha, and precipitation of denatured proteins, while late AKI is often due to sepsis, multi-organ failure, and nephrotoxic drugs. Diagnosis can be difficult as UOP and biochemical markers can be relatively normal even with significant renal injury. A sensitive and specific biomarker for the early diagnosis of AKI is sorely needed, and multiple potential biomarkers are being investigated. For treatment, the reversal of the underlying cause is the first intervention. The advent of renal replacement therapy has significantly improved the mortality of burn patients with AKI and should be initiated early if injury progresses despite initial maneuvers. Unfortunately, no beneficial pharmacologic agents have been identified, despite multiple investigations. Of burn patients who survive AKI, the vast majority do not receive long-term hemodialysis and they are generally thought to have a good renal prognosis although this view is shifting. Preliminary data in the burn population suggest that AKI may confer an increased risk of end-stage renal disease and long-term all-cause mortality, but further research is needed.

*Abbreviations:* AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; CKD, chronic kidney disease; CRRT, continuous renal replacement therapy; CVVH, continuous venovenous hemofiltration; ESRD, end-stage renal disease; FeNa, fractional excretion of sodium; GFR, glomerular filtration rate; IHD, intermittent hemodialysis; KDIGO, Kidney Disease: Improving Global Outcomes; NGAL, neutrophil gelatinase-associated lipocalin; RIFLE, risk, injury, failure, loss, end-stage renal disease; RRT, renal replacement therapy; sCr, serum creatinine; SLED, sustained low-efficiency dialysis; TBSA, total body surface area; TNF, tumor necrosis factor; UOP, urine output.

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## 1. Introduction

Acute kidney injury (AKI) is a frequent and very serious complication of burns, with an incidence of up to 30% depending on the definition utilized. Even with the advent of continuous renal replacement therapy (CRRT), AKI in burned patients portends a poor prognosis with a mortality rate as high as 80% [1–4]. Before 1965, no survivors were reported from AKI after burns [5]. Advances have been made in the understanding of AKI pathobiology in these patients; however, this has not translated to significant advances in treatment or an improvement in mortality outcome until recently. Prevention and mitigation of nephrotoxicity are likely the best strategies to attenuate AKI risk or progression, although AKI is often unavoidable in severely burned patients. In this article, we will review the current definitions, etiology, pathophysiology, diagnosis, treatment, and long-term effects of AKI in burn patients.

## 2. Definitions and classification

AKI is conventionally defined as an abrupt decrease in kidney function [6]. This clinical syndrome has many etiologies and encompasses both direct injury to the kidney and acute impairment in kidney function, or either individually [7].

The early detection of AKI leads to effective avoidance of nephrotoxicity and adequate fluid management and therefore improvement in post-AKI outcomes, which highlights the importance of a standardized definition of AKI that incorporates both classic and novel markers of kidney function and damage [7]. For many years, no consensus existed for the definition of AKI. More than 30 different definitions have been used in the literature, making comparisons between studies and drawing conclusions from them extremely difficult [8]. The first combined effort to standardize the definition of renal insufficiency was the Risk, Injury, Failure; Loss, End-Stage Renal Disease (RIFLE) criteria that used absolute and relative changes in estimated glomerular filtration rate (GFR), serum creatinine (sCr) or urine output (UOP) to characterize AKI severity stages (Table 1). RIFLE has good prognostic accuracy for mortality as there is an independent and stepwise increase in mortality as AKI severity increases, but this classification system does have some major limitations. One is that a baseline sCr is necessary to define and classify AKI in this system. This baseline value is often unknown and then has to be estimated using age, gender, and race. The RIFLE criteria also does not account for patients receiving renal replacement therapy (RRT) and therefore has less accuracy in predicting mortality in this population [9]. Lastly, it may not identify patients with slight, but clinically significant, changes in sCr.

In an attempt to address these weaknesses and incorporate a time component for changes in sCr, the Acute Kidney Injury Network (AKIN) criteria were created with a classification of AKI based on sCr and UOP changes. The AKIN criteria do not include changes in GFR and do not need a baseline sCr. Instead, they define AKI as a sudden decrease (within 48 h) of renal function defined by an increase in sCR by $\geq$0.3 mg/dL or 1.5x initial value. They also classify injury into three stages. Stage 1 corresponds to the risk class in RIFLE (but considers a sCr increase of $\geq$0.3 mg/dL). Stage 2 and 3 correspond to injury and failure classes, respectively. Stage 3 also includes patients receiving RRT independently of sCr or UOP prior to initiation [10]. The major criticism of the AKIN criteria is that they do not allow the identification of AKI when sCr elevation occurs in a time frame longer than 48 h.

Both RIFLE and AKIN have been validated in multiple studies in both medical and burn ICUs, and both show that increased severity of AKI based on these criteria correlate closely with mortality and adverse renal outcomes [11–15]. Comparisons of these two definitions, in burn and non-burn patients, have not shown a clear benefit of one classification system over the other [14,16]. In 2010, in an attempt to combine these two criteria, increase sensitivity, and simplify the diagnosis and grading of AKI, The Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines established a consensus definition of AKI incorporating both sCr and UOP parameters, and staging the severity of AKI from 1 to 3 [6]. In this system, AKI is defined as any of the following: an increase in sCr $\geq$0.3 mg/dL within 48 h, an increase in sCr $\geq$1.5 times baseline (or first measurement), or a UOP $<$0.5 mL/kg/h for 6 h. The major advantages of these criteria is that they incorporate smaller sCr changes, which was the weakness of