# Management and Outcomes of Acute Kidney Injury due to Burns: A Literature Review

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ABSTRACT

Acute kidney injury (AKI), a common and severe complication following burn injuries, presents a significant challenge due to its broad clinical manifestations and diverse etiologies. AKI, previously known as acute renal failure, can present abruptly following burns or thermal injuries, causing detrimental health outcomes such as progressive kidney dysfunction, increased hospital length of stay, and requirement of renal replacement therapy (RRT). AKI affects the maintenance of homeostasis of fluid and electrolytes, elimination of metabolic wastes and byproducts, and acid–base balance. Aggressive nutritional support is particularly necessitated in burn patients to prevent protein-energy wasting and a negative nitrogen balance. Understanding the pathogenesis of AKI in burns and improving its prevention and early diagnosis are active areas of research in this field. Despite the potential benefits, the optimal timing and threshold for RRT initiation in burn patients with AKI remain unclear, warranting further studies. Ongoing investigations focus on refining RRT techniques, evaluating biomarkers for early detection of AKI, and exploring adjunctive therapies to enhance renal recovery. The aim of this study is to review the etiology, diagnostic tools, and interventions that improve outcomes associated with AKI in burn-related settings.

Lay Summary

Acute kidney injury occurs in nearly one-quarter of people with severe burns and leads to increased mortality rates. Burn injuries can be associated with numerous complications, such as hypermetabolic response, hypovolemia, hypotension, and sepsis, and involves early burn- and late burn-related complications. Validated metrics for classifying the extent of burn injuries, such as the Abbreviated Burn Severity Index on admission, Sequential Organ Failure Assessment Score on admission, Modified Marshall Score, baseline blood urea nitrogen, and serum creatinine all serve to discriminate the risk of acute kidney injury. With no current consensus on predictive energy equations or ideal nutritional goals, optimal nutritional support in burn patients with acute kidney injury largely relies on the burn severity, individual presentation of malnourishment, and timely resuscitation. Although novel biomarkers such as plasma and urinary NGAL levels, KIM-1, and IL-18 are still being investigated as diagnostic tools for acute kidney injury in both the early and late burn periods, and artificial intelligence/machine learning may soon be incorporated as an efficacious assessment tool in the future. Renal replacement therapy is often indicated in the setting of acute kidney injury due to severe burns, especially if the metabolic and fluid disturbances due to acute kidney injury are not adequately managed with fluid resuscitation, diuretics, electrolyte repletion, and other supportive measures. However, with over a third of all burn-related acute kidney injury patients requiring some form of renal replacement therapy, elevated mortality rates remain a cause for concern.

**Key words:** acute kidney injury; burns; thermal injury; renal replacement therapy.

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## INTRODUCTION

Burn-related injuries can cause adverse complications such as acute kidney injury (AKI),[1] where the dysregulation of kidney function presents a dangerous physiological problem.[2] The kidneys, serving as primary regulators of fluid homeostasis,[3] metabolite equilibrium,[4] and pH balance,[5] become subject to a series of nephrotoxic attacks and cellular disruptions due to the immediate effects of a burn injury. Understanding the pathophysiology of AKI due to burns allows for prompt diagnosis with early and aggressive management, reducing the progression of kidney injury, in-patient mortality rates, and post-AKI-related consequences.[6] Studies into AKI's risk factors and clinical features suggest that even mild AKI due to

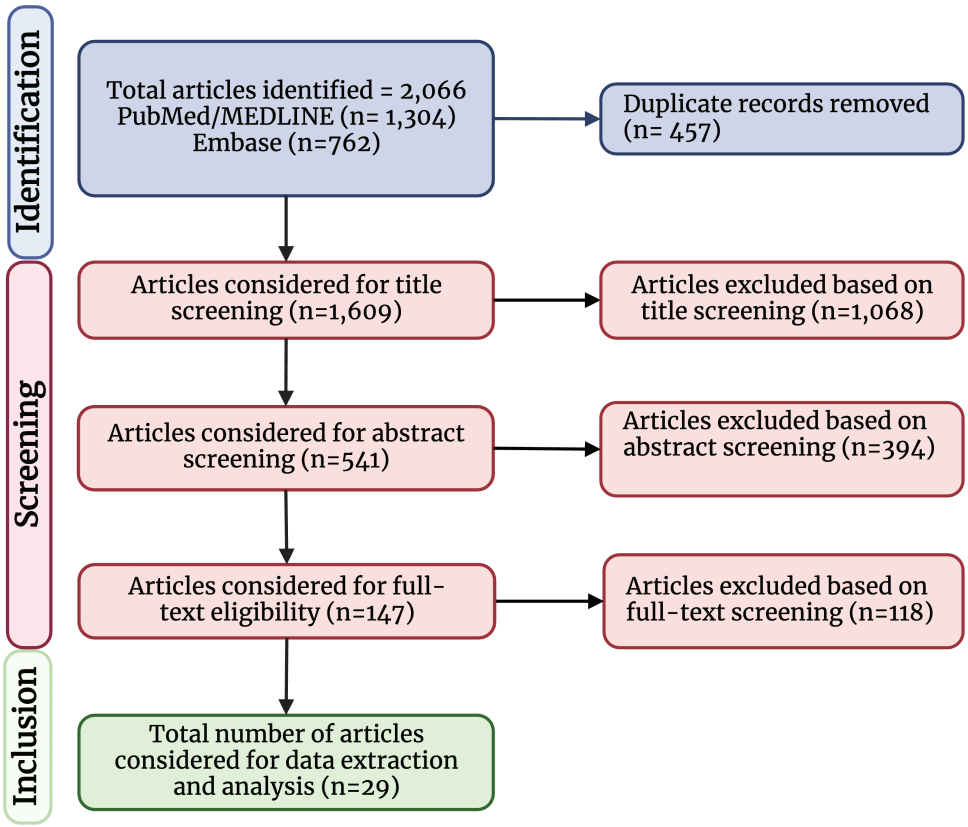


**Figure 1.** Presents a flow chart summarizing the literature search results

underlying critical illness can be associated with lasting renal damage and functional loss.[7–9] In this article, we review current classifications, epidemiology, pathophysiology, diagnostic criteria, and the efficacy of various supportive and dialytic interventions for ameliorating AKI in burn-related settings.

## DATA SELECTION AND REVIEW

The literature search was conducted across PubMed/MEDLINE and EMBASE databases to identify all studies relevant to AKI in burn-related settings, published from 2000 until October 2022. Medical subject headings (MeSH terms) utilized in the search included "acute kidney injury," "burns," "burn injuries," "renal replacement therapy," and "renal failure." Our search strategy encompassed burn patients across all age groups, irrespective of burn severity or AKI classification, and regardless of the need for renal replacement therapy (RRT). Only studies published in English were considered, including prospective, retrospective, case-controlled, and cohort studies. Two independent investigators reviewed the titles, abstracts, and full texts of the retrieved studies. Any disagreements concerning inclusion criteria or study selection were resolved via a consensus of the 2 authors or by a third independent reviewer.

A total of 2061 articles were retrieved, and after duplicate removal and screening, 29 articles were deemed eligible for data extraction (Figure 1). Studies assessing burn parameters reported the frequency and severity of burn injury via TBSA, the proportion of inhalational injuries, and mortality. Frequently reported adverse outcomes among burn patients with AKI-included sepsis, need for mechanical ventilation, and the duration of the hospital or intensive care unit (ICU) stay. The need for RRT was reported in 20 of the collected studies, including RRT incidence and modality. All relevant publications were considered for data extraction, and tables were created summarizing the results of the included studies.

## CLINICAL STAGING

Classification and assessment of AKI vary broadly internationally, with one report suggesting over 200 definitions of AKI across Europe,[10] emphasizing the need for consistent and widely accessible diagnostic criteria. Among the most used measures are the Acute Kidney Injury Network (AKIN) and Risk, Injury, Failure, Loss, End-Stage Renal Disease (RIFLE) classifications. Published in 2004, the RIFLE criteria stratify AKI into high-sensitivity groups: risk, injury, and failure, with progressive renal disease beyond this point classified into complete loss and ESRD.[11,12] The RIFLE system identifies changes in serum creatinine, glomerular filtration rate (GFR), and urine output (UOP) to detect and stage AKI. Since these biomarkers are analyzed with relative ease and are known predictors of renal function, the following evaluations are simple and cost-effective. Despite this, the reliance of the RIFLE criteria on frequently unobtainable baseline levels and the time lag between kidney dysfunction and noticeable

fluctuations in serum creatinine underscored the imperative to improve AKI staging criteria.[13,14] In 2007, the AKIN classification system modified the RIFLE criterion by using a 0.3 mg/dL increase in serum creatinine within 48 hours as an additional indication of stage 1 disease. Furthermore, AKIN removed the complete loss of renal function and ESKD, adding RRT to the staging criteria.[12]

Released in 2012, The Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines were designed to unify the AKIN and RIFLE scoring systems. KDIGO-defined AKI utilizes absolute and relative increases in serum creatinine, potential administration of RRT, or a decline in urinary output (UOP) to stage the severity of AKI.[15] The KDIGO diagnostic criteria have been widely used in critically ill patients revealing a greater sensitivity for AKI than previous classifications.[16,17] However, a single-center prospective observational study that used various approaches to implement the KDIGO criteria showed AKI incidence varying between 28% and 75% in the same critically ill cohort.[18] Despite multiple iterations of clinically and temporally defined stages of AKI, recent studies have widely adopted KDIGO guidelines to assess the progression, morbidity, and mortality of kidney injury in the burn population.[19–21]

## EPIDEMIOLOGY

The incidence of AKI in burn patients is nearly 30%–40%, increasing with burn severity.[19,22,23] Mortality rates among these patients are frequently reported, ranging from nearly 40%,[24] to as high as 80%.[25] A cohort analysis including 304 patients over 5 years with severe burns (>10% TBSA) revealed that 26.6% (81 patients) developed AKI (diagnosed by RIFLE criteria). These patients were noted to be more likely to be female and have sepsis.[15] In this study, 60% of patients had stage 1 AKI, and progression through AKI stages was associated with increases in mortality rates. In some instances, the incidence rate of AKI development can even be higher. A retrospective cohort study by Clark et al. examined 1040 ICU patients suffering from thermal burns, with 58% developing AKI.[22] In their study, patients were graded with the KDIGO SCr-based criteria, and nearly 10% of patients required RRT for AKI stage 3. Incidence for RRT increased to 20% when TBSA burn severity was greater than 40.[22] The proportion of patients requiring RRT increased with severe burn injuries, reaching an incidence of 20% in patients with TBSA >40%.[22] Similarly, mortality rates are also understood to rise as the severity of burn injuries and AKI increases.

Another study noted that AKI occurred in as many as 28% of patients with severe burns, with an associated mortality rate as high as 88.0% in patients with severe burn-related AKI.[26] As such, mortality rates are understood to rise as the severity of burn injuries and AKI increases. While individual figures of in-hospital mortality vary, a comprehensive view of AKI incidence approaches 40%. The cumulative incidence rate of AKI is tabulated in Table 1. Despite study-specific fluctuations in mortality data, this literature review presents the detrimental outcomes due to burns and mortality rates in patients with AKI across various studies in Table 2.

In a 3-year retrospective study, AKI was noted to occur in only 5-20% of patients, a figure lower than that due to other critical illnesses (sepsis, post-surgery), with overall mortality disproportionately high at around 80%. These finding were consistent with a meta-analysis from 2010 determining the prevalence of RRT in all burn patients and in patients with AKI secondary to burn (3.2% and 27.1%, respectively), also identifying an 80% mortality of burn patients with RRT.[11,51]

**Table 1.** AKI Incidence in the ICU.

| Study by year | Number of patients in ICU | Incidence rate of AKI |
|---|---|---|
| Coca et al.[27] | 304 | 0.27 |
| Steinvall et al.[28] | 127 | 0.24 |
| Palmieri et al.[24] | 123 | 0.46 |
| Palmieri et al.[29] | 60 | 0.53 |
| Chung et al.[30] | 1973 | 0.33 |
| Hu et al.[31] | 396 | 0.38 |
| Hong et al.[32] | 45 | 0.24 |
| Yang et al.[33] | 66 | 0.47 |
| Yim et al.[34] | 97 | 0.41 |
| Kym et al.[35] | 85 | 0.56 |
| Queiroz et al.[36] | 293 | 0.26 |
| Rakkolainen et al.[37] | 19 | 0.47 |
| Kuo et al.[38] | 145 | 0.36 |
| Hundeshagen et al.[39] | 718 | 0.12 |
| Kimmel et al.[40] | 267 | 0.22 |
| Chun et al.[41] | 76 | 0.42 |
| Depret et al.[42] | 87 | 0.63 |
| Clark et al.[22] | 1040 | 0.58 |
| Total | 5921 | 0.38 |

Data on incidence rates of patients with AKI due to burn injuries in the ICU setting, compiled from 5921 patients.
Abbreviation: AKI: acute kidney injury

**Table 2.** Burn Characteristics and Adverse Outcomes.

| Study by year | Patients with AKI (*n*) | TBSA (%) | Inhalational injury (%) | Sepsis (%) | Placed on mechanical ventilator (%) | Length of stay (days) | Mortality (%) |
|---|---|---|---|---|---|---|---|
| Coca et al.[27] | 81 | 34 ± 19 | 43 | 49 | 69 | Hospital: 36.18 ± 29.2<br>ICU: 35.29 ± 25.52 | 28 |
| Steinvall et al.[28] | 31 | 47.2 ± 4.5 | - | 87 | 99 | Hospital: 67.3 ± 10.87 | 36 |
| Palmieri et al.[24] | 56 | 41.7 ± 17 | 26 | 38 | - | Hospital: 51 ± 40<br>ICU: 36.7 ± 36 | 9 |
| Palmieri et al.[29] | 32 | 45.2 ± 19 | - | 76 | - | ICU: 42.9 ± 27 | 34 |
| Chung et al.[30] | 656 | 25 (13–42) | 30 | - | - | Hospital: 24 (11–58)<br>ICU: 9 (3–28) | 21 |
| Hong et al.[32] | 11 | 69.6 ± 28.1 | 64 | n/a | 55 | Hospital: 31.1 ± 40.2<br>ICU: 16.9 ± 11.3 | 73 |
| Yang et al.[33] | 55 | 66.7 ± 21.1 | 45 | 49 | 85 | Hospital: 33.41 ± 40.55 | 51 |
| Yim et al.[34] | 40 | 54.2 ± 21.3 | 50 | 88 | - | - | 10 |
| Kym et al.[35] | 48 | 63.1 ± 19.4 | 44 | - | - | Hospital:37.9 ± 40.0 | 65 |
| Ren et al.[43] | 11 | 44.2 ± 22.4 | 64 | - | 46 | - | 36 |
| Rakkolainen et al.[37] | 9 | 45.6 ± 12.5 | 22 | 22 | 56 | ICU: 34.9 ± 21 | 22 |
| Kuo et al.[38] | 52 | 60.5 ± 3.3 | 5 | - | 75 | ICU: 43.6 ± 2.6 | 51 |
| Kimmel et al.[40] | 60 | 15 (12–20) | 33 | - | - | Hospital: 13.8 (8.9–19.8) | 8 |
| Chun et al.[41] | 32 | 68.9 ± 14.9 | 19 | 69 | - | - | 69 |
| Tremblay et al.[44] | 12 | 48 ± 16 | - | 100 | 100 | - | 50 |
| Akers et al.[45] | 17 | - | - | 18 | - | - | 35 |
| Demsey et al.[46] | 64 | 34 (18–50) | - | - | 98 | Hospital: 43 (22–63)<br>ICU: 15 (9–22) | 22 |
| Gille et al.[47] | 18 | 42.5 (33.3–52.5) | 33 | 94 | 94 | Hospital: 72.5 (49.25–96.5) | 11 |
| Holm et al. [48] | 48 | 48* | 79 | 75 | 100 | - | 85 |
| Leblanc et al.[9] | 16 | 58.0 ± 5.7 | - | - | - | Hospital: 24.2 ± 9.4 | 81 |
| Mustonen et al.[50] | 93 | 40.2 ± 17.7 | 23 | - | - | Hospital: 37.1 ± 22.6 | 44 |

Twenty-one studies identifying 1442 patients with AKI due to burn-related trauma and their associated rates of injury, sepsis, and mortality. Data are provided as mean ± SD or median (IQR).
*SD not provided.
Abbreviation: AKI: acute kidney injury.

Improved mortality rates have been observed in trials where early RRT was initiated for burn patients.[52] Additional data from the STARRT-AKI trial comparing early and standard timing of RRT initiation suggested that 8.2% of patients who survived for 90 days or more after hospitalization for AKI remained dependent on RRT.[52] Here, no statistically significant difference in mortality was observed between early and regular initiation of RRT for AKI. Although not specific to AKI in burn-related setting, these conflicting findings further reiterate the need for additional research to optimize RRT timing and delivery to improve prognostic outcomes.

Long-term outcomes for burn patients with AKI receiving RRT during their initial treatment have been studied scarcely in the literature. An epidemiological study of Finnish registries by Helantera et al. investigated 41 179 adults treated for burns between 1998 and 2011.[53] Of the 43 patients who developed ESRD following AKI-RRT, the authors considered burn injury to accelerate kidney deterioration rather than directly cause ESRD. This indicates an unlikely association between burn-induced AKI and long-term renal failure. These findings were supported by another retrospective study evaluating the incidence of long-term RRT following burn injuries, where 6.3% (2 out of 32 patients) of their surviving population developed ESRD requiring RRT greater than 3 months following burn injury.[54] However, in a retrospective cohort examination of burn patients who developed AKI, Thalji et al. displayed an increased incidence of severe CKD, hospital readmission, and mortality 1 year following the burn injury compared to non-AKI burn patients.[6] These conflicted findings suggest a need for further studies to include a longitudinal evaluation of adverse outcomes in burn-induced AKI patients and those requiring acute and chronic RRT.

## PATHOPHYSIOLOGY

Burn injuries can be associated with numerous complications, such as hypermetabolic response, hypovolemia, hypotension, and sepsis.[55] Early burn-related AKI (0–3 days after) may be prerenal (hypovolemia, poor renal perfusion) or intrinsic (prolonged and severe prerenal AKI resulting in acute tubular injury or tubular obstruction) in nature. Early burn-related AKI can be related to the degree of shock and under-resuscitation of shock in the early stages of the disease.[2] Previous studies have highlighted that the hypermetabolic response is preceded by a distinct initial hypometabolic phase in the first 48 hours.[56] Early burn-related AKI is also understood to be independently associated with rhabdomyolysis owing to direct tubular injury and oxidative stress.[15] Past reviews have associated hypovolemia, cardiac dysfunction, and ischemia with

early burn-related AKI, mediating biochemical and physiological alterations by proteins and signaling factors released from tissues after damage incurred from burns and other related injuries.[55]

A reduction in the overall perfusion of the kidneys causes prerenal AKI. Kidneys receive nearly 25% of cardiac output, and reduced kidney perfusion can be associated with vessel damage.[57] Here, "prerenal" restrictions in blood flow to the kidney are reflected in a decreased GFR, resulting in downstream physiological complications.[58] The characteristic decrease in GFR is due to renal hypoperfusion caused by hypovolemia and hypotension immediately after burn-related injuries.[59] Approaching the kidney on a functional level, intrinsic renal AKI is caused by damage to renal tubules, the interstitium, or the glomerulus. Damage to renal machinery may be associated with intrinsic renal pathology (glomerulonephritis, tubular obstruction) or prolonged prerenal injury.[60] In burn-related settings, this damage can be chemically induced by nephrotoxic drugs administered in the ICU or by an inability to perform timely, adequate fluid resuscitation.[61]

Burn-induced hypovolemia is characterized by reductions in intravascular fluid volume and damaging the proximal tubule and loop of Henle.[62,63] Hypovolemia is associated with the third-spacing of fluid due to widespread vasodilation and systemic inflammation, causing increased fluid in interstitial spaces and subsequently decreased renal perfusion pressures.[64] Ischemic injury induces the release of oxygen-free radicals and denatured cellular proteins and metabolites that exacerbate renal injury.[23] In the early stages, visceral vasoconstriction and low renal perfusion can also cause acute tubular necrosis (ATN) and oxidative damage.[2] Oxidative stress induced by reactive oxygen species (ROS) from burns elicits numerous biochemical pathways leading to inflammation and apoptosis, triggering renal tissue damage. Proinflammatory cytokines, such as IL-1β, IL-6, and TNF-α, are known for their immunosuppressive function and are associated with early burn-related AKI.[65] In addition, the oxidative stress response involves cytochrome-c release and caspase-3 activation mediating prolonged apoptosis.[66] A visual biochemical pathway of early AKI from burns due to oxidative stress is displayed in Figure 2.

Late burn-related AKI (4–14 days after) can result from sepsis, nephrotoxic drugs, multiorgan dysfunction, or prolonged shock.[11] This is often characterized by disseminated intravascular coagulation and ATN due to direct toxic damage from denatured tissue proteins. As such, progressive direct and indirect biological changes, along with interventions due to burn-related injuries, can induce highly toxic renal dysfunction. A visual schematic of the early and late causes of burn-related AKI is shown in Figure 3.

## RISK FACTORS AND CLASSIFICATION SCORES FOR AKI IN BURNS

Early detection of AKI in burn patients requires a high degree of clinical suspicion allowing for biomarker assessment, renal function tests, and UOP measures for early and accurate diagnosis.[67] A systematic review and meta-analysis of AKI in burns reveal multiple risk factors associated with worsened prognosis, including older age, greater burned TBSA, pronounced full-thickness TBSA, exposure to direct flames, and inhalational injuries.[2] Older age, diabetes mellitus, and chronic hypertension are understood to be associated with higher rates of AKI in the general population and burn populations.[55] The presence of sepsis,[68] blunt abdominal trauma,[69] rhabdomyolysis,[9] and the need for mechanical ventilation[70] have all been proven to be independently associated with an increased rate of developing AKI. Overall, examination of demographic and physiological data suggest that the severity of burn-related injuries, the extent of immediate and progressive renal damage, and variations in individual presentation of complications must be understood together to ensure efficient diagnosis and intervention.[55]

Predictive parameters, including scoring indices and standardized diagnostic criteria, can further aid in stratifying cases based on their risk profile, helping prevent the rapid illness progression often observed in the ICU.[71] Validated metrics for classifying the extent of burn injuries, such as the Abbreviated Burn Severity Index (ABSI) on admission, Sequential Organ Failure Assessment Score (SOFA score) on admission, Modified Marshall Score, baseline blood urea nitrogen (BUN), and serum creatinine all serve to discriminate the risk of AKI.[2] ABSI, SOFA, and Acute Physiology and Chronic Health Evaluation (APACHE II) mean scores at admission were found to be significantly greater in burn patients with AKI than those without AKI, indicating their use for early diagnosis.[72] These indices can be used for developing predictive models for adverse outcomes, as demonstrated by Moore et al., where APACHE III scores and full-thickness surface area (FTSA) were shown to predict mortality with better discrimination than either variable independently.[73] SOFA scores have also been considered a strong prognostic tool for patients with AKI undergoing continuous RRT. A study by Wang et al. displayed SOFA scores as better predictive models for 90-day mortality than APACHE II in univariate analysis.[74] These findings highlight the utility of comprehensive diagnostic criteria, encouraging further optimization of these criteria for baseline variations in burn-related hospital admissions. The extensive factors to consider when instituting a risk profile for AKI patients prompted by severe burns are provided in Figure 4. The heterogeneity and complexity of AKI-associated risk factors reiterate the need for further research into the physiological mechanisms that drive AKI pathogenesis and progression.

## DIAGNOSIS OF AKI IN BURNS

To optimize its diagnosis and treatment, AKI is primarily defined as the rapid and often abrupt decline in renal function reflected by the GFR, serum creatinine, and blood urea nitrogen (BUN).[75] A decline in the GFR, a measure of plasma filtration in the glomeruli, has been considered a standard and direct measure of renal function decline in AKI.[76] Practical difficulties in measuring GFR[77] have led to an emphasis on using downstream increases in serum creatinine and BUN as more accessible indicators of AKI.[78–80] Despite recent advances in diagnostic definitions of AKI using serum creatinine and BUN, these renal markers may remain normal in the early stages of injury, proving diminished clinical utility. The earliest symptom of AKI can be an abrupt decline in the volume of

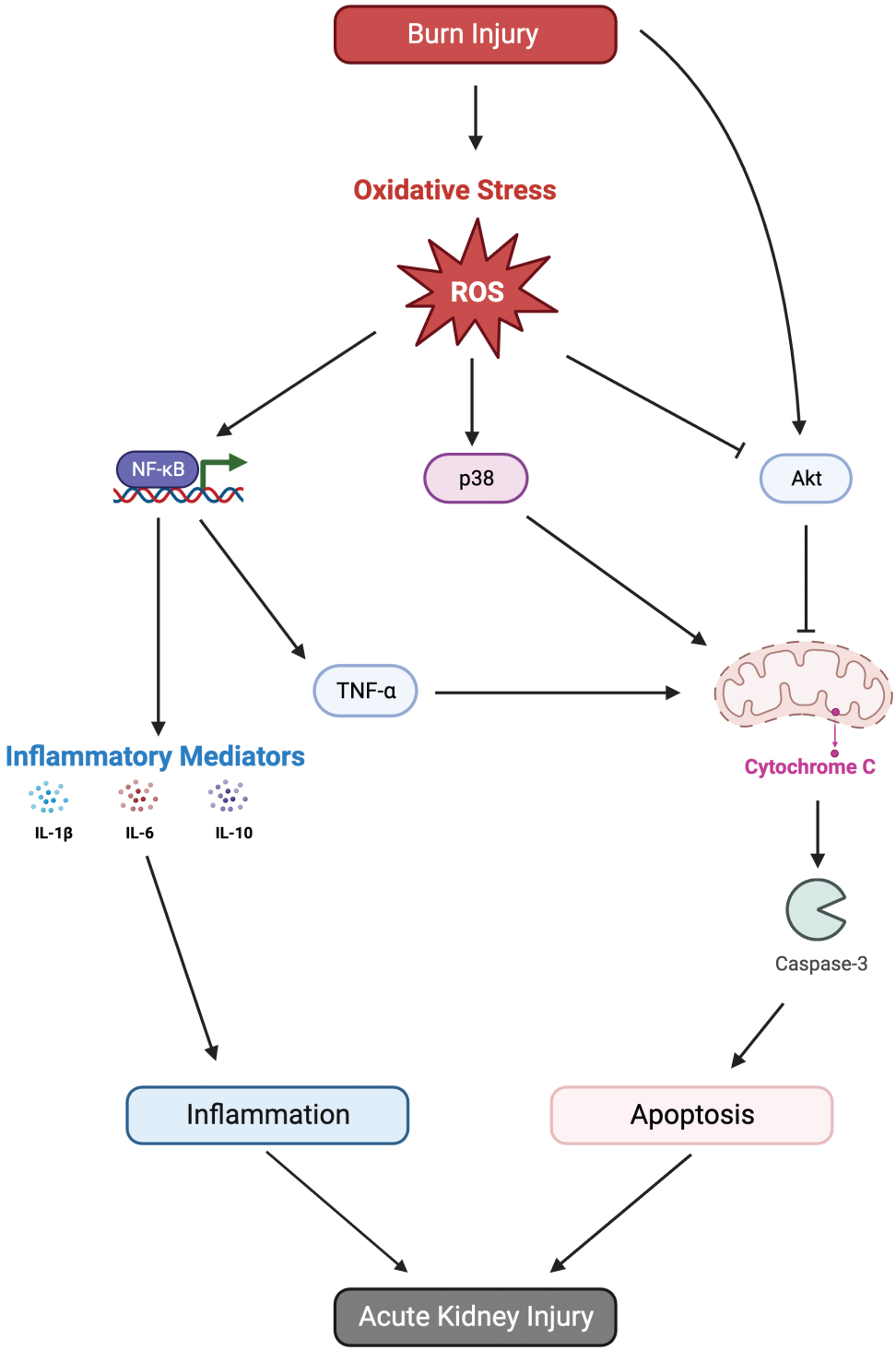


**Figure 2.** Provides a flow diagram for the damaging of renal tissue in burn-induced AKI following inflammation and apoptosis under oxidative stress. NF-kB and p38 are activated by reactive oxygen species (ROS), releasing cytochrome c, and activating the caspase-3 apoptotic pathway

urine produced, thereby causing electrolyte imbalances, retention of water, and accumulation of metabolic byproducts and toxins.[60] Identification of these predictive biomarkers and their use throughout disease progression holds the potential to improve management and reduce adverse outcomes in affected patients.

Serum creatinine (1.5× or greater from baseline) and elevated levels of BUN are used to classify AKI, and Emami et al. displayed an AUC of 0.73 and 0.71 for serum creatinine and BUN, respectively, in predicting early and late AKI from burns using RIFLE criteria.[35] However, both BUN and serum creatinine have several notable limitations in their evaluation

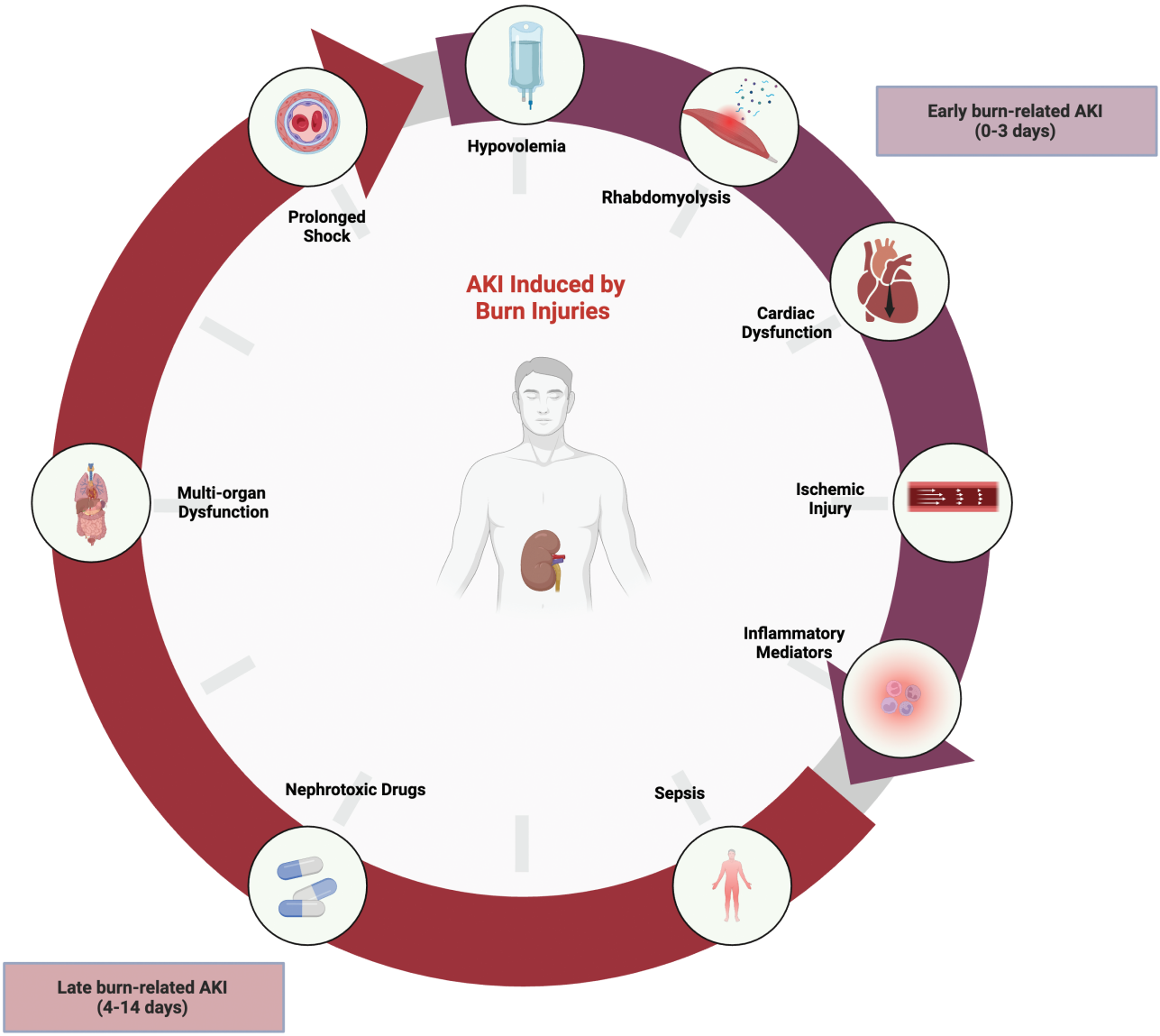


**Figure 3.** Depicts the early (0–3 days) and late (4–14) stages of burn injuries with pre-, intrinsic-, and postrenal complications correlated to direct reductions in renal functions to prompt AKI diagnosis

of renal function in the setting of burns. Hypercatabolic-induced urea overproduction and states of rhabdomyolysis can independently elevate BUN and serum creatinine levels, respectively. Second, the GFR can be preserved to an extent (and thus serum creatinine levels) during kidney injury due to the renal reserve. Moreover, fixed rates of creatinine and BUN production influence their levels in AKI.[35] In fact, serum creatinine remains unaffected until the GFR decreases by 30%–40%.[81] Factors such as sepsis, catabolic state, dehydration, and hypovolemic shock can further complicate serum creatinine levels and, thus, its reliability as a biomarker in AKI due to burns. BUN has shown mixed results in its strength as a predictive biomarker, likely due to its modification by factors such as burn size, sex, and age.[82]

Recent studies have attempted to identify neutrophil gelatinase-association lipocalin (NGAL) as an early onset biomarker for AKI in burn patients that can be elevated as early as 4 hours after renal injury and remains elevated till 48 hours after injury.[83] NGAL is released by epithelial cells and neutrophils in areas such as the lungs, renal tissue, tracheal tissue, and the intestine, where plasma NGAL levels are understood to correspond to levels of distal tubular injury.[84] Elevated plasma and urine NGAL levels were also noted to be associated with higher 48-hour mortality rates in patients with severe burns.[33] A correlation between serum NGAL levels and TBSA ($r$ = .572, $P$ = .001) by Lee et al. determined its prospective use as a severity marker in burn patients. Kim et al. found that urinary NGAL was a higher predictor as a biomarker of AKI in burn patients compared to serum NGAL.[81] They attributed these differences to factors such as acute respiratory distress syndrome (ARDS), sepsis, and systemic inflammatory response system (SIRS) which impact plasma NGAL more than urinary NGAL. Notably, the study also found serum creatinine to be superior to urinary NGAL

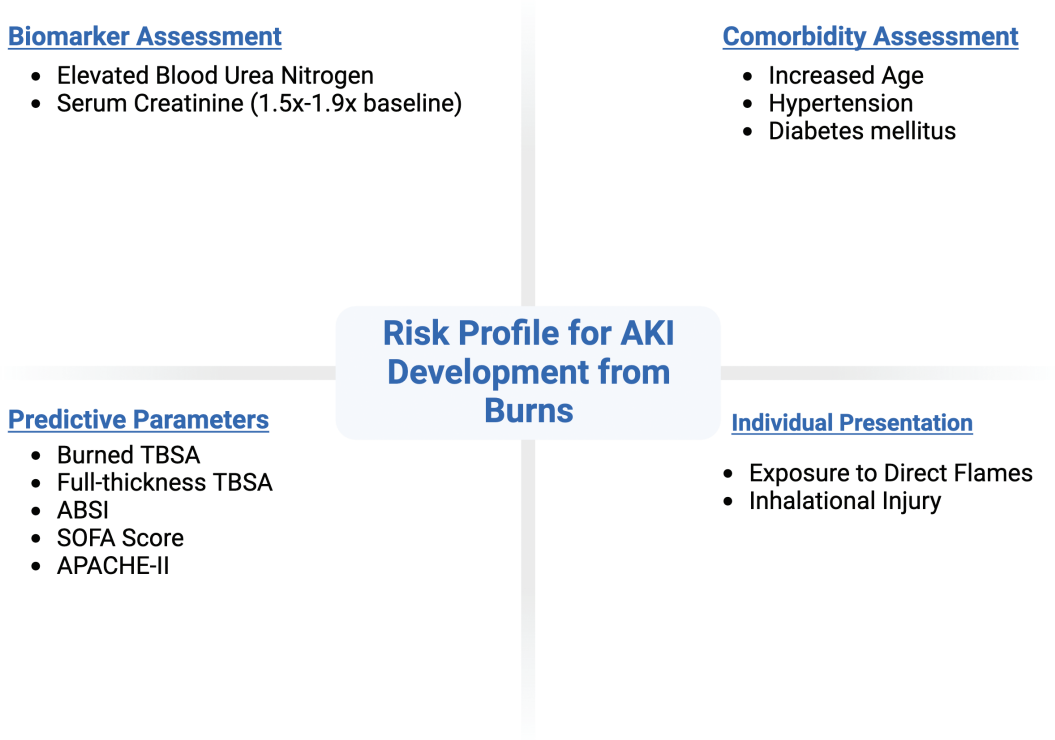


**Figure 4.** Outlines varying clinical measures available, to be used alongside the individual patient presentation, when establishing a risk profile for moderate to severe burn-related AKI patients. Abbreviations: ABSI: A Body Shape Index; SOFA: Sequential Organ Failure Assessment; APACHE: Acute Physiology and Chronic Health Evaluation

in the first week of AKI. This may be explained by differences in the staging of AKI. Early AKI involves volume alterations and potential fluid resuscitations, whereas late AKI is associated with multiorgan failure, nephrotoxic agents, and sepsis. Thus, different biomarkers may need to be considered for different stages of AKI.

On the other hand, Yim et al. have noted that in patients admitted to the ICU with burns and AKI, serum cystatin-C levels have been useful in detecting late-onset AKI.[34] This was confirmed in their study with an AUC of ROC curve for predicting AKI with serum cystatin-C of 0.908 (0.843–0.973) on day 14 postburn, which was greater than that of serum creatinine at 0.790 (0.692–0.888).[34] These patients have significantly elevated cystatin-C at a mean of postburn day 14 and developed AKI at a mean of postburn day 17.[34] Cystatin C is notably not influenced by protein intake, gender, age, or muscle composition unlike serum creatinine levels. Studies have typically considered cystatin C a stronger indicator of burn-induced AKI than creatinine due to various factors, such as its shorter half-life. However, Kim et al. found serum creatinine to be a superior predictor and attributed this difference to factors such as systemic inflammation, which is associated with burn patients who have a higher risk of infection and can alter the levels of certain biomarker.[81]

A prospective cohort study investigated serum creatinine, serum cystatin C, and plasma and urinary NGAL levels as diagnostic tools for AKI in both the early and late burn periods.[33] They found that all 4 of these biomarkers were reliable predictors of early AKI and death. Notably, urinary and serum NGAL levels increased at the time of admission, whereas cystatin C and creatinine did not increase until 12 hours after admission. More specifically, urine NGAL was the first biomarker to increase, followed by serum NGAL, cystatin C, and serum creatinine levels. However, both urinary and serum NGAL levels were increased in patients with greater surface area burns. Thus, the percent TBSA (% TBSA) may help determine which biomarkers are most influential in early AKI burn patients. They also found that only urine and plasma NGAL levels were statistically significant in predicting late AKI and deaths within 6 hours of admission, although they were unable to distinguish this from patients who would not develop AKI and thus survive. NGAL was a poor predictor in instances of high % TBSA.[33]

Other biomarkers, such as urinary kidney injury molecule-1 (KIM-1) and interleukin-18 (IL-18), have also been noted to be elevated among patients developing AKI following burn injuries. Ren et al. found that combined KIM-1 and IL-18 levels might be superior biomarkers to serum creatinine and BUN in early-stage AKI due to burns.[43] In fact, their values increase within 2 hours of renal injury allowing for rapid detection of AKI. Their study determined urinary KIM-1 levels had a positive correlation with increasing severity of burn injury, determined by factors such as % TBSA and the presence of rhabdomyolysis. They found that both urinary KIM-1 and IL-18 levels were strongly correlated with serum creatinine and BUN levels and detected earlier than serum creatinine elevations. Combining both urinary KIM-1 and IL-18 levels for evaluation, rather than looking at one or the other, improved the ability to predict AKI.[43]

While more analysis is warranted to understand the prognostic efficacy of these novel biomarkers in the setting of burns, it is possible to develop a model to predict AKI in these settings. Artificial intelligence/machine learning (AI/ML) algorithms have recently been developed and tested for their efficacy in diagnosing AKI in burn patients, where Tran et al. developed a k-nearest neighbor ML model to identify AKI risk in burn patients with 90%–100% accuracy.[85] A pilot comparison by Rashidi et al. utilized NGAL, creatinine, UOP, and N-terminal pro B-type natriuretic peptide (NT-proBNP) to successfully predict AKI following severe burns 61.8 ± 32.5 hours in patients faster than KDIGO criteria.[86] The potential for AI/ML to be used in diagnostic capabilities compared to the current workflow is shown in Figure 5.

## NUTRITION IN BURN PATIENTS WITH AKI

Malnutrition is seen in 24%–60% of hospitalized AKI patients, demonstrating significant protein-energy wasting and negative nitrogen balance.[87] Severe burn-related trauma is likewise associated with metabolic derangements in the ICU setting, exacerbated by AKI. Directly following severe burn injury, patients observe an "ebb" phase characterized by a decrease in tissue perfusion and metabolic rate lasting 2 to 3 days. In the subsequent persistent hypermetabolic response, inflammatory mediators and catecholamines effectuate severe catabolism for a prolonged period.[88] A clinical trial encompassing 668 children with burns revealed a significant difference in mortality associated with those receiving early versus late enteral nutrition (8.5% vs. 12%, $P < .05$).[89] This poses an adverse outcome as protein breakdown is not limited to just muscle tissue but affects all organs in burn patients, where large protein and energy debts become a predictor for multiple organ dysfunction (MODS) and mortality. The catabolic persistence in burn victims aggravated by AKI involves the wasting of lean body mass, and dietary recommendations suggest enteral nutrient supplementation with high protein diets for adults (1.5 to 2 g/kg/day) and children (2.5–4.0 g/kg/day).[90] A prospective crossover trial by Hart et al. determined that carbohydrate-rich diets (82% carbohydrates, 15% protein, and 3% fat) given during the hypermetabolic phase decreased protein breakdown ($P < .01$) and increased endogenous insulin levels in pediatric burn patients compared to high-fat diets ($P = .01$).[91]

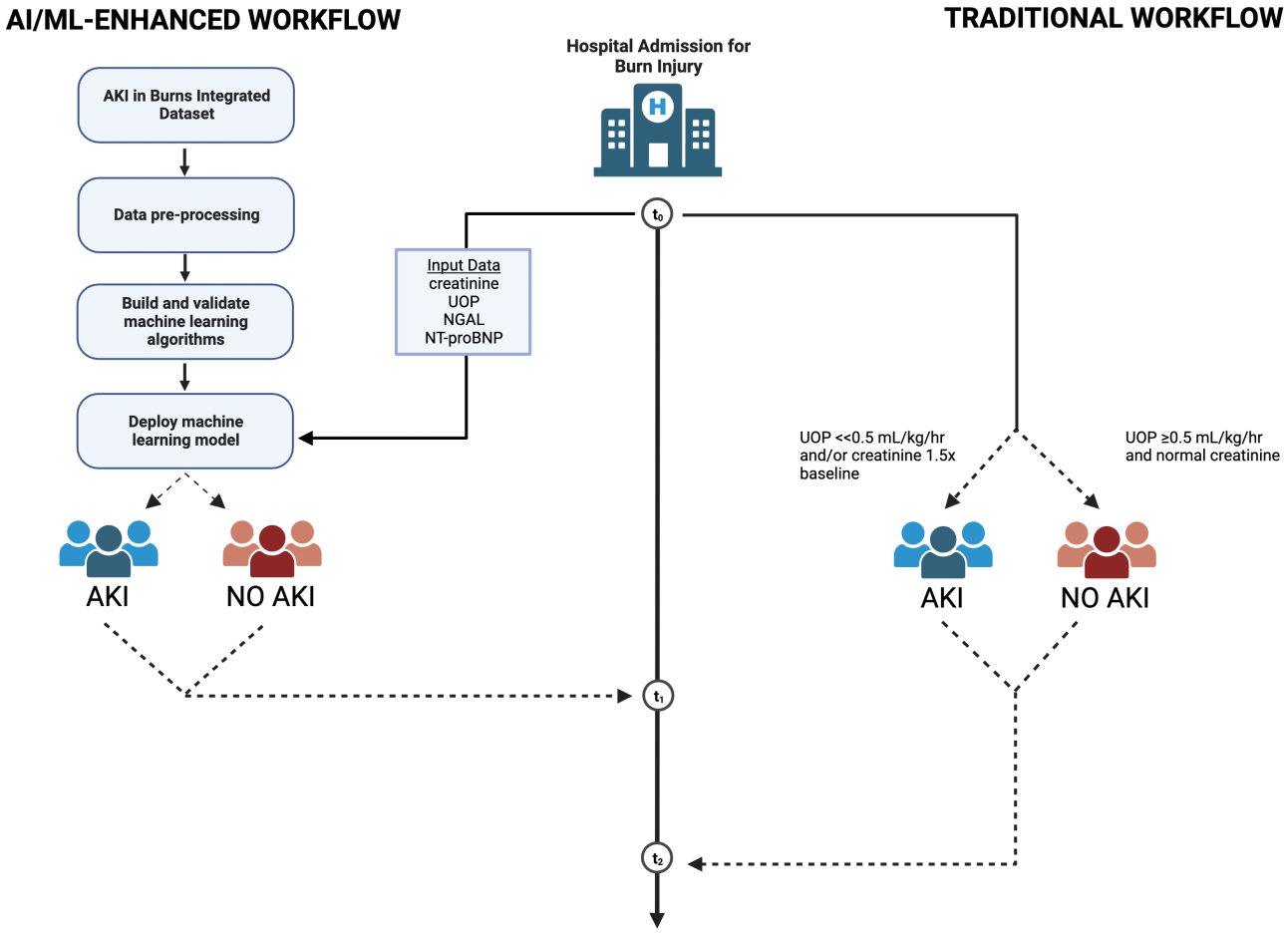


**Figure 5.** Outlines a conceptual model for the use of AI/ML-enhanced workflow toward diagnosing acute kidney injury (AKI) in burn patients. Integrated datasets, using patient electronic medical records, laboratory values, physiological parameters, and medications, are used to develop an ML model to diagnose AKI in burn patients. Data are received from the time of admission ($t_0$), and AI/ML algorithms can predict AKI ($t_1$) earlier than traditional methods ($t_2$)

Accurate assessments of the diminished nutritional status in burn-induced AKI patients are further complicated by nutrient clearance during RRT. A prospective study by Oh et al. identified significant reductions in amino acids and micronutrients following various modalities of acute RRT such as intermittent hemodialysis (IHD), sustained low-efficiency diafiltration (SLEDf), and continuous veno-venous hemofiltration (CVVH).[92] Their results displayed the most significant loss in plasma amino acids due to CVVH, followed by SLEDf and IHD ($P < .001$). In addition, patients with severe burns display exudative losses of trace elements, also found depleted in the effluent following RRT.[92] This is a severe concern in burn-induced AKI patients requiring RRT, as these trace elements are also cofactors in critical enzymes involved with antioxidant defense, immune response, and wound healing.[93] With no current consensus on predictive energy equations or ideal nutritional goals, optimal nutritional support in burn patients with AKI largely relies on the burn severity, individual presentation of malnourishment, and timely resuscitation. However, these findings may also provide a basis for considering a patient's nutritional status and necessary dietary supplementation toward RRT initiation.

## MANAGEMENT OF BURN INJURIES AND ACUTE KIDNEY INJURY

Hypovolemia and hypotension complicate burn injuries, resulting in poor perfusion and fluid volume instability within internal organs. Burn patients with reduced perfusion are prone to develop AKI and subsequent complications. Since the underlying pathology of AKI is reduced renal perfusion, management should involve aggressive and early crystalloid resuscitation, utilizing Lactated Ringers (LR). Although the "gold-standard" was the Parkland Formula, it has been recognized that patients may have been over-resuscitated, leading to the more recent adoption of the American Burn Association Consensus Formula.

Parkland's formula for resuscitation is as follows:

Fluid requirement (in mL) = 4 mL × Body weight (kg) × TBSA Burn (%)

(First half given over 8 hours and next half given over 16 hours)

American Burn Association Consensus Formula:

Fluid requirement for adults (in mL) = 2 mL × Body weight (kg) × TBSA Burn (%)

Fluid requirement for pediatrics (in mL) = 3 mL × Body weight (kg) × TBSA Burn (%)

Excessive fluid resuscitation with volumes exceeding 250 mL/kg in 24 hours—known as the "Ivy Index" is associated with increased mortality.[94] Newer studies have aimed at using colloids such as Fresh Frozen Plasma or Albumin, as these allow for resuscitation of intravascular volumes alone, sparing the interstitial/extravascular compartments and thereby preventing iatrogenic edema.[95]

Negative consequences that consist due to the management of burns and AKI early in the treatment course substantially impact hospital expenditures and patient outcomes. Non-dialytic treatment of AKI in burn patients involves close monitoring of antimicrobial medications such as aminoglycosides, vancomycin, some cephalosporins, and many other known nephrotoxic drug agents.[96] Palmieri et al. identified the use of nephrotoxic drugs to the progression of the highest RIFLE class, increasing their rate of sepsis and mortality.[29] Another retrospective review by Hundeshagen et al. associated the coadministration of vancomycin and piperacillin-tazobactam (PT) with increased renal dysfunction in pediatric and adult burn patients.[39] In their study, vancomycin and PT treatment relative to vancomycin treatment alone led to higher serum creatinine levels (0.26 ± 0.62 mg/dl vs. 0.05 ± 0.10 mg/dl, $P < .01$), lower creatinine clearance (−26 ± 39 mL/min vs. −10 ± 28 mL/min, $P < .001$), and a greater need for RRT (3% vs. 0%, $P = .03$). Drug-induced tubular injury can be worsened with exposure to multiple nephrotoxins and underlying comorbidities, suggesting use only when pharmacokinetically monitored and administrated in appropriate intervals.

Later complications of burns include sepsis and MODS. Management of these complications involves both fluid management and appropriate antimicrobial therapy. This goal-directed management of sepsis, often referred to as Early Goal Directed therapy (EGDT), has decreased morbidity associated with critical illnesses, including burns.[97] EGDT involves fluid resuscitation with crystalloids as the first step and subsequent use of vasoactive agents or blood transfusions if necessary. The principal purpose behind EGDT is to ensure an early approach with infectious foci control before they disseminate pathogens that may complicate AKI.

Some studies have suggested that the use of Dopamine-1 receptor agonist medications such as Fenoldopam has a role in managing AKI. A retrospective review of 16 studies spanning 1290 patients who received Fenoldopam for preventing or managing AKI caused by critical illnesses suggests that Fenoldopam use can reduce the need for RRT in patients with AKI.[98] Another retrospective analysis of 758 severely burned patients admitted to a Burns Intensive Care Unit (BICU) showed an improvement in UOP, serum creatinine, and systolic blood pressure in patients treated with low-dose Fenoldopam, and this effect was sustained for over 48 hours among most of the 77 patients who received the drug.[99] While Fenoldopam has shown promise in treating AKI, randomized controlled trials are warranted to better understand the true applicability of such medications. If renal function continues to decline despite resuscitative efforts, introducing RRT may be the next best step.

## ROLE OF RRT IN THE MANAGEMENT OF AKI IN BURNS

Over the last 2 decades, burn treatment centers have employed a range of RRT modalities to address significant metabolic and fluid balance derangements. Continuous RRT (CRRT) has become standard practice for patients with severe burns, particularly when initial management such as fluid resuscitation, diuretics, electrolyte replenishment, and other supportive measures are insufficient. Despite advancements in RRT techniques and burn care, AKI secondary to burn injuries is associated with increased mortality remaining near 50%–60%.[100,101] Duan et al. found an increased risk of RRT and AKI with an increased TBSA, with the highest rates of RRT in the TBSA ≥40% group.[102] A cohort study noted that prompt initiation of Continuous Venovenous Hemofiltration

**Table 3.** RRT Modalities and Outcomes Following Burn-Induced AKI.

| Study by year | Patients with AKI (*n*) | RRT initiated (%) | Length on RRT (days) | Mode of RRT | Mortality of patients on RRT (%) |
|---|---|---|---|---|---|
| Coca et al.[27] | 81 | 37 | 20 ± 24 | RRT | 73 |
| Steinvall et al.[28] | 31 | 13 | - | Dialysis | 75 |
| Hong et al.[32] | 11 | 45 | - | Intermittent and continuous HD | 80 |
| Yang et al.[33] | 55 | 40 | 5.82 ± 4.89 | CRRT | 77 |
| Yim et al.[34] | 40 | 58 | - | CRRT | - |
| Kym et al.[35] | 48 | 46 | - | CRRT | - |
| Ren et al.[43] | 11 | 45 | - | CRRT | 80 |
| Rakkolainen et al.[37] | 9 | 22 | - | RRT | 0 |
| Kuo et al.[38] | 52 | 17 | - | RRT | - |
| Chun et al.[41] | 32 | 63 | - | CRRT | 95 |
| Tremblay et al.[44] | 12 | 100 | 14 ± 13 | CVVHDF/CVVH/CVVHD | 50 |
| Akers et al.[45] | 38 | 87 | - | CVVH | 58 |
| Damkat-Thomas et al.[103] | 17 | 29 | - | RRT | 40 |
| Demsey et al.[46] | 64 | 28 | - | CVVHDF/IHD | 39 |
| Soltani et al.[104] | 38 | 87 | 10.3 (1–44) | HD | 70 |
| Gille et al.[47] | 18 | 100 | - | CVVHDF | 11 |
| Haberal et al.[105] | 19 | 100 | - | PD/HD | 79 |
| Holm et al.[48] | 48 | 100 | 10.5* | CAVH | 85 |
| Leblanc et al. [49] | 16 | 10 | 12.5 ± 1.7 | CAVH/CAVHDF/CVVHDF | 50 |
| Mustonen et al.[50] | 93 | 34 | 20.9 ± 60.3 | CRRT/HD/PD | 63 |

Baseline data on RRT treatment modality, prevalence, and mortality due to AKI in burn patients. Data are presented as mean ± SD or median (IQR).
*No SD.
Abbreviations: CVVH: continuous venovenous hemofiltration; CVVHDF: continuous venovenous hemodiafiltration; CAVH: continuous arteriovenous hemofiltration; IHD: intermittent hemodialysis; AKI: acute kidney injury; RRT: renal replacement therapy.

(CVVH) in severely burned patients yielded better outcomes in the form of reduced 28-day mortality rate, overall in-hospital mortality rates, decreased dependence for vasopressors, and better recovery in cases with shock.[25] This retrospective analysis of early RRT compared to standard treatment in historical controls suggested the potential for improved outcomes, raising questions about the appropriate timing and thresholds for initiating RRT in AKI. RRT modalities and associated adverse healthcare outcomes from identified studies are presented in Table 3.

Hill et al. also observed CVVH as an effective means for improving survival in burn patients requiring vasoactive medications.[33] In their study, CVVH alone did not significantly improve mortality, but a difference was noted in the subset of their population receiving vasopressors with CVVH (54% vs. 37%, $P = .032$).[33] Timely initiation of RRT in critically ill, burn patients with AKI, along with aggressive treatment options, advocates as the best course for intervention. Published studies showed that burned patients' average time from injury to dialysis was approximately 15 days.[44] Analysis of a multinational, controlled trial (STARRT-AKI trial) identified the results of early vs. standard initiation of RRt. Composite events such as mortality rate at 90 days were comparable at 43.9% in the early treatment group and 43.7% in the standard treatment group. Among patients who survived, continued reliance on RRT was seen in 10.4% of patients in the accelerated therapy group, and 6% in the standard treatment group (Relative risk of 1.74, 95% CI, 1.24 to 1.43).[52] While analysis of RRT modalities and outcomes in burns is still underway (ClinicalTrials.gov Identifier: NCT01213914), at present, CRRT seems to be preferred as the first-line RRT from this trial. A clear-cut timeline for the administration of CRRT in the setting of burn-associated AKI has yet to be established; however, some data suggest that serum creatinine levels may be used to help in the decision-making process.[106] The pathophysiology of the disease may also be a more robust indicator for initiating RRT rather than renal function, while discontinuation of RRT is generally associated with the return of serum creatinine and UOP to normal levels.[106] More recently, Zhang et al. looked into using furosemide stress testing (FST) to help predict the timing of CRRT initiation in AKI patients.[107] UOP 2 hours after receiving furosemide was analyzed and found to be superior to NGAL in determining progression from stages 1 and 2 to stage 3 AKI.

Recent interest in blood endotoxin and inflammatory cytokine removal via extracorporeal methods has shown to be effective through various pathways after a long period of CRRT. High levels of pro- and anti-inflammatory mediators are released into the bloodstream during the early stages of burns, indicating a need for nonconventional prompt treatments in AKI to control early-onset sepsis and septic shock.[108] CRRT utilized in these patients suffering from severe burns with concurrent sepsis effectively mitigates the build-up of urea and various organic acids. These nephrotoxic compounds have the potential to impede the wound-healing process and destabilize hemodynamics.[109] A meta-analysis of 538 deep burn patients with 274 receiving CVVH/continuous venovenous hemodiafiltration (CVVHDF) blood purification presented a significant reduction in 28-day mortality and sepsis ($P < .05$); however, their results were inconclusive of other vital signs and the use of CVVH/CVVHDF in more severe complications.[110] A study on administering CVVH rather than dialysis found

decreased vasopressor requirements in AKI related to burn injury. They postulated that cytokine removal was associated with improved hemodynamic homeostasis. You et al. recently discovered that the early utility of high-volume hemofiltration (HVHF), resulted in the substantial elimination of cytokines in patients with sepsis and concurrent burn injuries.[102,111] Furthermore, an increased survival rate, diminished sepsis rate, improved immunologic response, and improved arterial oxygen partial pressure ratios to a fraction of inspired oxygen were found. However, the RESCUE study, which looked at shock resolution through HVHF, found no changes in cytokines such as interferon-γ, IL6, IL8, IL10, and IL12, or tumor necrosis factor-α over 48 hours in this instance. Thus, other metabolic mechanisms should also be considered to explain the improvement of symptoms. The studies suggest future research and therapy may be directed at removing damage-associated molecular patterns (DAMPs), as they are increased in burn injury and associated with monocyte activation and inflammation.[102]

Interestingly, Bellomo et al. looked at the differences in the delivery of caloric intake (DCI) in patients with AKI receiving RRT.[112] Using data from patients receiving CRRT, they found the mean caloric intake was 11 Kcal/Kg/day, and 90-day mortality was similar for patients with a DCI above or below the median. Thus, there was no independent association between 90-day mortality and DCI. However, the authors mention a DCI of 25–35 Kcal/Kg/day is recommended for patients with AKI, although more RCTs needs to be collected to solidify these recommendations. Another study recently looked at the effects of regional citrate anticoagulation (RCA) as a means to mitigate the inflammatory response in patients receiving CRRT.[113] More specifically, it functions through lowering expression of CD11b, an integrin found on neutrophils, and plasminogen activator inhibitor-1 (PAI-1) levels, enhancing fibrinolysis activity. Although stables levels of complements c3b and c5a were found in patients receiving RCA, more data need to be acquired.

## COMPREHENSIVE CARE OF BURN PATIENTS WITH AKI

The comprehensive management of burn-related injuries requires a team of integrated healthcare professionals collaborating across multiple specialties. The burn care team, often consisting of a burn surgeon/specialist, intensivist, anesthesiologist, respiratory therapy, occupational/physical therapy, nursing staff, dietician, pharmacy, psychology/psychiatry social work/case management, and chaplain services, among others, must work together to address their patient's physical and psychosocial needs.[114] The size of the burn team, the composition of professionals, and the scope of their work rely on the extent of injuries in the burn patient.[115] Burn-related injuries requiring acute RRT must utilize precision medicine to guide resource-intensive intervention promptly, allowing for an individualized approach to monitoring clinical status. The American Society of Nephrology Acute Kidney Injury Advisory Group advocates for the need for a nephrologist in the ICU setting, using their expertise in AKI diagnosis and RRT modalities to facilitate the homeostasis of fluids and electrolytes in burn victims.[116] A single-center retrospective study by Rhee et al. demonstrated that the use of a specialized CRRT intervention team in the ICU decreased CRRT initiation time ($P = .027$) and the rate of in-hospital mortality ($P = .007$).[117] These findings support using a multidisciplinary team to treat burns patients with AKI, ensuring high-quality care delivery in the ICU.

## CONCLUSIONS

AKI is a common complication of burn injuries, with its incidence rising as the severity of burns, presence of high-risk scores, and pre-existing comorbidities increase. Renal injuries can be caused by poor perfusion, nephrotoxic drug insults, rhabdomyolysis, tubular injury, and among others. There is a lack of one uniform classification system that can grade kidney injury. However, a consistent pattern of increasing mortality and morbidity is seen as the severity of AKI rises across all systems. We note that AKI diagnosis shows promise, with the emergence of novel biomarkers that appear to show encouraging results in both early diagnosis of AKI and providing an accurate functional analysis of renal reserve and function. The management of AKI in the setting of burn injuries remains similar to that of AKI alone due to other causes centered around fluid resuscitation to improve renal perfusion, antibiotic, supportive management to treat associated conditions, and resorting to RRT if inadequate renal function remains. While no one modality of RRT has been deemed universally superior to others, CRRT is the preferred modality among clinicians and is the current topic of multiple trials.

### REFERENCES

1. Nielson CB, Duethman NC, Howard JM, Moncure M, Wood JG. Pathophysiology of systemic complications and current management. J Burn Care Res. 2017;38(1):e469–e481. https://doi.org/10.1097/bcr.0000000000000355
2. Clark A, Neyra JA, Madni T et al. Acute kidney injury after burn. Burns. 2017;43(5):898–908. https://doi.org/10.1016/j.burns.2017.01.023
3. Guyton AC. Blood pressure control--special role of the kidneys and body fluids. Science. 1991;252(5014):1813–1816. https://doi.org/10.1126/science.2063193
4. Rhee EP. A systems-level view of renal metabolomics. Semin Nephrol. 2018;38(2):142–150. https://doi.org/10.1016/j.semnephrol.2018.01.005
5. Rajkumar P, Pluznick JL. Acid-base regulation in the renal proximal tubules: using novel pH sensors to maintain homeostasis. Am J Physiol Renal Physiol. 2018;315(5):F1187–F1190. https://doi.org/10.1152/ajprenal.00185.2018
6. Thalji SZ, Kothari AN, Kuo PC, Mosier MJ. Acute kidney injury in burn patients: clinically significant over the initial hospitalization and 1 year after injury: an original retrospective cohort study. Ann Surg. 2017;266(2):376–382. https://doi.org/10.1097/sla.0000000000001979
7. Aikawa N, Wakabayashi G, Ueda M, Shinozawa Y. Regulation of renal function in thermal injury. J Trauma. 1990;30(12 Suppl):S174–S178. https://doi.org/10.1097/00005373-199012001-00035
8. Jeschke MG, Barrow RE, Wolf SE, Herndon DN. Mortality in burned children with acute renal failure. Arch Surg. 1998;133(7):752–756. https://doi.org/10.1001/archsurg.133.7.752
9. Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. N Engl J Med. 2009;361(1):62–72. https://doi.org/10.1056/NEJMra0801327
10. Ricci Z, Ronco C, D'Amico G et al. Practice patterns in the management of acute renal failure in the critically ill patient: an international survey. Nephrol Dial Transplant. 2006;21(3):690–696. https://doi.org/10.1093/ndt/gfi296
11. Brusselaers N, Monstrey S, Colpaert K, Decruyenaere J, Blot SI, Hoste EAJ. Outcome of acute kidney injury in severe burns: a systematic review and meta-analysis. Intensive Care Med. 2010;36(6):915–925. https://doi.org/10.1007/s00134-010-1861-1

12. Lin CY, Chen YC. Acute kidney injury classification: AKIN and RIFLE criteria in critical patients. World J Crit Care Med. 2012;1(2):40–45. https://doi.org/10.5492/wjccm.v1.i2.40
13. Lopes JA, Jorge S. The RIFLE and AKIN classifications for acute kidney injury: a critical and comprehensive review. Clin Kidney J. 2013;6(1):8–14. https://doi.org/10.1093/ckj/sfs160
14. Cruz DN, Ricci Z, Ronco C. Clinical review: RIFLE and AKIN--time for reappraisal. Crit Care. 2009;13(3):211. https://doi.org/10.1186/cc7759
15. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract. 2012;120(4):c179–c184. https://doi.org/10.1159/000339789
16. Luo X, Jiang L, Du B, Wen Y, Wang M, Xi X; Beijing Acute Kidney Injury Trial (BAKIT) Workgroup. A comparison of different diagnostic criteria of acute kidney injury in critically ill patients. Crit Care. 2014;18(4):R144. https://doi.org/10.1186/cc13977
17. Zhou J, Liu Y, Tang Y et al. A comparison of RIFLE, AKIN, KDIGO, and Cys-C criteria for the definition of acute kidney injury in critically ill patients. Int Urol Nephrol. 2016;48(1):125–132. https://doi.org/10.1007/s11255-015-1150-6
18. Wiersema R, Jukarainen S, Eck RJ et al. Different applications of the KDIGO criteria for AKI lead to different incidences in critically ill patients: a post hoc analysis from the prospective observational SICS-II study. Crit Care. 2020;24(1):164. https://doi.org/10.1186/s13054-020-02886-7
19. You B, Yang Z, Zhang Y et al. Late-onset acute kidney injury is a poor prognostic sign for severe burn patients. Front Surg. 2022;9:842999. https://doi.org/10.3389/fsurg.2022.842999
20. Martins J, Nin N, Muriel A et al. Early acute kidney injury is associated with in-hospital adverse outcomes in critically ill burn patients: an observational study. Nephrol Dial Transplant. 2022:gfac339. https://doi.org/10.1093/ndt/gfac339.
21. Kim HY, Kong YG, Park JH, Kim Y-K. Acute kidney injury after burn surgery: Preoperative neutrophil/lymphocyte ratio as a predictive factor. Acta Anaesthesiol Scand. 2019;63(2):240–247. https://doi.org/10.1111/aas.13255
22. Clark AT, Li X, Kulangara R et al. Acute kidney injury after burn: a cohort study from the parkland burn intensive care unit. J Burn Care Res. 2019;40(1):72–78. https://doi.org/10.1093/jbcr/iry046
23. Bellomo R, Ronco C, Kellum JA et al. Acute renal failure - definition, outcome measures. Animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care. 2004;8(4):R204–R212. https://doi.org/10.1186/cc2872
24. Palmieri T, Lavrentieva A, Greenhalgh D. An assessment of acute kidney injury with modified RIFLE criteria in pediatric patients with severe burns. Intensive Care Med. 2009;35(12):2125–2129. https://doi.org/10.1007/s00134-009-1638-6
25. Chung KK, Lundy JB, Matson JR et al. Continuous venovenous hemofiltration in severely burned patients with acute kidney injury: a cohort study. Crit Care. 2009;13(3):R62. https://doi.org/10.1186/cc7801
26. Witkowski W, Kawecki M, Surowiecka-Pastewka A, Klimm W, Szamotulska K, Niemczyk S. Early and late acute kidney injury in severely burned patients. Med Sci Monit. 2016;22:3755–3763. https://doi.org/10.12659/msm.895875
27. Coca SG, Bauling P, Schifftner T, Howard CS, Teitelbaum I, Parikh CR. Contribution of acute kidney injury toward morbidity and mortality in burns: a contemporary analysis. Am J Kidney Dis. 2007;49(4):517–523. https://doi.org/10.1053/j.ajkd.2006.12.018
28. Steinvall I, Bak Z, Sjoberg F. Acute kidney injury is common, parallels organ dysfunction or failure, and carries appreciable mortality in patients with major burns: a prospective exploratory cohort study. Crit Care. 2008;12(5):R124. https://doi.org/10.1186/cc7032
29. Palmieri T, Lavrentieva A, Greenhalgh DG. Acute kidney injury in critically ill burn patients. Risk factors, progression and impact on mortality. Burns. 2010;36(2):205–211. https://doi.org/10.1016/j.burns.2009.08.012
30. Chung KK, Stewart IJ, Gisler C et al. The Acute Kidney Injury Network (AKIN) criteria applied in burns. J Burn Care Res. 2012;33(4):483–490. https://doi.org/10.1097/BCR.0b013e31825aea8d
31. Hu JY, Meng XC, Han J et al. Relation between proteinuria and acute kidney injury in patients with severe burns. Crit Care. 2012;16(5):R172. https://doi.org/10.1186/cc11649
32. Hong DY, Lee JH, Park SO, Baek KJ, Lee KR. Plasma neutrophil gelatinase-associated lipocalin as early biomarker for acute kidney injury in burn patients. J Burn Care Res. 2013;34(6):e326–e332. https://doi.org/10.1097/BCR.0b013e31827d1f36
33. Yang HT, Yim H, Cho YS et al. Assessment of biochemical markers in the early post-burn period for predicting acute kidney injury and mortality in patients with major burn injury: comparison of serum creatinine, serum cystatin-C, plasma and urine neutrophil gelatinase-associated lipocalin. Crit Care. 2014;18(4):R151. https://doi.org/10.1186/cc13989
34. Yim H, Kym D, Seo DK et al. Serum cystatin C and microalbuminuria in burn patients with acute kidney injury. Eur J Clin Invest. 2015;45(6):594–600. https://doi.org/10.1111/eci.12452
35. Kym D, Cho YS, Yoon J, Yim H, Yang H-T. Evaluation of diagnostic biomarkers for acute kidney injury in major burn patients. Ann Surg Treat Res. 2015;88(5):281–288. https://doi.org/10.4174/astr.2015.88.5.281
36. Queiroz LF, Anami EH, Zampar EF, Tanita MT, Cardoso LTQ, Grion CMC. Epidemiology and outcome analysis of burn patients admitted to an Intensive Care Unit in a University Hospital. Burns. 2016;42(3):655–662. https://doi.org/10.1016/j.burns.2015.08.002
37. Rakkolainen I, Vuola J. Plasma NGAL predicts early acute kidney injury no earlier than s-creatinine or cystatin C in severely burned patients. Burns. 2016;42(2):322–328. https://doi.org/10.1016/j.burns.2015.11.006
38. Kuo G, Yang SY, Chuang SS et al. Using acute kidney injury severity and scoring systems to predict outcome in patients with burn injury. J Formos Med Assoc. 2016;115(12):1046–1052. https://doi.org/10.1016/j.jfma.2016.10.012
39. Hundeshagen G, Herndon DN, Capek KD et al. Co-administration of vancomycin and piperacillin-tazobactam is associated with increased renal dysfunction in adult and pediatric burn patients. Crit Care. 2017;21(1):318. https://doi.org/10.1186/s13054-017-1899-3
40. Kimmel LA, Wilson S, Walker RG, Singer Y, Cleland H. Acute kidney injury: It's not just the "big" burns. Injury. 2018;49(2):213–218. https://doi.org/10.1016/j.injury.2017.11.016
41. Chun W, Kim Y, Yoon J et al. Assessment of plasma neutrophil gelatinase-associated lipocalin for early detection of acute kidney injury and prediction of mortality in severely burned patients. J Burn Care Res. 2018;39(3):387–393. https://doi.org/10.1097/BCR.0000000000000605
42. Dépret F, Boutin L, Jarkovský J et al. Prediction of major adverse kidney events in critically ill burn patients. Burns. 2018;44(8):1887–1894. https://doi.org/10.1016/j.burns.2018.08.007
43. Ren H, Zhou X, Dai D et al. Assessment of urinary kidney injury molecule-1 and interleukin-18 in the early post-burn period to predict acute kidney injury for various degrees of burn injury. BMC Nephrol. 2015;16:142. https://doi.org/10.1186/s12882-015-0140-3
44. Tremblay R, Ethier J, Querin S, Béroniade V, Falardeau P, Leblanc M. Veno-venous continuous renal replacement therapy for burned patients with acute renal failure. Burns. 2000;26(7):638–643. https://doi.org/10.1016/s0305-4179(00)00010-3
45. Akers KS, Cota JM, Chung KK, Renz EM, Mende K, Murray CK. Serum vancomycin levels resulting from continuous or intermittent infusion in critically ill burn patients with or without continuous renal replacement therapy. J Burn Care Res. 2012;33(6):e254–e262. https://doi.org/10.1097/BCR.0b013e31825042fa
46. Demsey D, Mordhorst A, Griesdale DEG, Papp A. Improved outcomes of renal injury following burn trauma. Burns. 2019;45(5):1024–1030. https://doi.org/10.1016/j.burns.2019.04.001
47. Gille J, Sablotzki A, Malcharek M, Raff T, Mogk M, Parentin T. Regional citrate anticoagulation for continuous renal replacement therapy in severe burns-a retrospective analysis of a protocol-guided approach. Burns. 2014;40(8):1593–1601. https://doi.org/10.1016/j.burns.2014.01.028
48. Holm C, Horbrand F, von Donnersmarck GH, Mühlbauer W. Acute renal failure in severely burned patients. Burns. 1999;25(2):171–178. https://doi.org/10.1016/s0305-4179(98)00144-2
49. Leblanc M, Thibeault Y, Querin S. Continuous haemofiltration and haemodiafiltration for acute renal failure in severely burned patients. Burns. 1997;23(2):160–165. https://doi.org/10.1016/s0305-4179(96)00085-x
50. Mustonen KM, Vuola J. Acute renal failure in intensive care burn patients (ARF in burn patients). J Burn Care Res. 2008;29(1):227–237. https://doi.org/10.1097/BCR.0b013e31815f3196
51. Putra ON, Saputro ID, Diana D. Rifle criteria for acute kidney injury in burn patients: prevalence and risk factors. Ann Burns Fire Disasters. 2021;34(3):252–258.
52. Bagshaw SM, Wald R, Adhikari NKJ et al. Timing of initiation of renal-replacement therapy in acute kidney injury. N Engl J Med. 2020;383(3):240–251. https://doi.org/10.1056/NEJMoa2000741
53. Helantera I, Koljonen V, Finne P, Tukiainen E, Gissler M. The risk for end-stage renal disease is increased after burn. Burns. 2016;42(2):316–321. https://doi.org/10.1016/j.burns.2015.10.027
54. Rakkolainen I, Mustonen KM, Vuola J. Long-term outcome after renal replacement therapy in severe burns. J Burn Care Res. 2020;41(4):866–870. https://doi.org/10.1093/jbcr/iraa034
55. Wu G, Xiao Y, Wang C et al. Risk factors for acute kidney injury in patients with burn injury: a meta-analysis and systematic review. J Burn Care Res. 2017;38(5):271–282. https://doi.org/10.1097/bcr.0000000000000438
56. Xu H, Yu YM, Ma H et al. Glucose metabolism during the early "flow phase" after burn injury. J Surg Res. 2013;179(1):e83–e90. https://doi.org/10.1016/j.jss.2012.02.037

57. Manzoor H, Bhatt H. Prerenal kidney failure. In: StatPearls. StatPearls Publishing Copyright © 2022; 2022.
58. Blantz RC, Singh P. Analysis of the prerenal contributions to acute kidney injury. Contrib Nephrol. 2011;174:4–11. https://doi.org/10.1159/000329027.
59. Molitoris BA. Low-flow acute kidney injury: the pathophysiology of prerenal azotemia, abdominal compartment syndrome, and obstructive uropathy. Clin J Am Soc Nephrol. 2022;17(7):1039–1049. https://doi.org/10.2215/cjn.15341121
60. Gameiro J, Fonseca JA, Outerelo C, Lopes JA. Acute kidney injury: from diagnosis to prevention and treatment strategies. J Clin Med. 2020;9(6):1704. https://doi.org/10.3390/jcm9061704
61. Perazella MA. Drug use and nephrotoxicity in the intensive care unit. Kidney Int. 2012;81(12):1172–1178. https://doi.org/10.1038/ki.2010.475
62. Myers BD, Moran SM. Hemodynamically mediated acute renal failure. N Engl J Med. 1986;314(2):97–105. https://doi.org/10.1056/nejm198601093140207
63. Kitiwan BK, Vasunilashorn SM, Baer HJ, Mukamal K, Juraschek SP. The association of urine osmolality with decreased kidney function and/or albuminuria in the United States. BMC Nephrol. 2021;22(1):306. https://doi.org/10.1186/s12882-021-02478-9
64. Er RE, Ulusal Okyay G, Aygencel BKG et al. Comparison Between RIFLE, AKIN, and KDIGO: acute kidney injury definition criteria for prediction of in-hospital mortality in critically Ill patients. Iran J Kidney Dis. 2020;14(5):365–372.
65. Alsawaf S, Alnuaimi F, Afzal S et al. Plant flavonoids on oxidative stress-mediated kidney inflammation. Biology (Basel). 2022;11(12):1717. https://doi.org/10.3390/biology11121717
66. Zhuang S, Demirs JT, Kochevar IE. p38 mitogen-activated protein kinase mediates bid cleavage, mitochondrial dysfunction, and caspase-3 activation during apoptosis induced by singlet oxygen but not by hydrogen peroxide. J Biol Chem. 2000;275(34):25939–25948. https://doi.org/10.1074/jbc.M001185200
67. Xiao Z, Huang Q, Yang Y et al. Emerging early diagnostic methods for acute kidney injury. Theranostics. 2022;12(6):2963–2986. https://doi.org/10.7150/thno.71064
68. Peerapornratana S, Manrique-Caballero CL, Gómez H, Kellum JA. Acute kidney injury from sepsis: current concepts, epidemiology, pathophysiology, prevention and treatment. Kidney Int. 2019;96(5):1083–1099. https://doi.org/10.1016/j.kint.2019.05.026
69. Haines RW, Lin SP, Hewson R et al. Acute kidney injury in trauma patients admitted to critical care: development and validation of a diagnostic prediction model. Sci Rep. 2018;8(1):3665. https://doi.org/10.1038/s41598-018-21929-2
70. Hepokoski ML, Malhotra A, Singh P, Crotty Alexander LE. Ventilator-induced kidney injury: are novel biomarkers the key to prevention? Nephron. 2018;140(2):90–93. https://doi.org/10.1159/000491557
71. Kes P, Basić Jukić N. Acute kidney injury in the intensive care unit. Bosn J Basic Med Sci. 2010;10(Suppl 1):S8–12. https://doi.org/10.17305/bjbms.2010.2639
72. Kuvvet Yoldas T, Atalay A, Balci C, Demirağ K, Uyar M, Çankayalı I. Acute kidney injury in burns in the intensive care unit: A retrospective research. Ulus Travma Acil Cerrahi Derg. 2023;29(3):321–326. https://doi.org/10.14744/tjtes.2022.95048
73. Moore EC, Pilcher DV, Bailey MJ, Cleland H, McNamee J. A simple tool for mortality prediction in burns patients: APACHE III score and FTSA. Burns. 2010;36(7):1086–1091. https://doi.org/10.1016/j.burns.2010.03.013
74. Wang H, Kang X, Shi Y et al. SOFA score is superior to APACHE-II score in predicting the prognosis of critically ill patients with acute kidney injury undergoing continuous renal replacement therapy. Ren Fail. 2020;42(1):638–645. https://doi.org/10.1080/0886022X.2020.1788581
75. Thomas ME, Blaine C, Dawnay A et al. The definition of acute kidney injury and its use in practice. Kidney Int. 2015;87(1):62–73. https://doi.org/10.1038/ki.2014.328
76. Molitoris BA, Reilly ES. Quantifying glomerular filtration rates in acute kidney injury: a requirement for translational success. Semin Nephrol. 2016;36(1):31–41. https://doi.org/10.1016/j.semnephrol.2016.01.008
77. Seegmiller JC, Eckfeldt JH, Lieske JC. Challenges in measuring glomerular filtration rate: a clinical laboratory perspective. Adv Chronic Kidney Dis. 2018;25(1):84–92. https://doi.org/10.1053/j.ackd.2017.10.006
78. Edelstein CL. Biomarkers of acute kidney injury. Adv Chronic Kidney Dis. 2008;15(3):222–234. https://doi.org/10.1053/j.ackd.2008.04.003
79. Waikar SS, Bonventre JV. Creatinine kinetics and the definition of acute kidney injury. J Am Soc Nephrol. 2009;20(3):672–679. https://doi.org/10.1681/asn.2008070669
80. Uchino S, Bellomo R, Goldsmith D. The meaning of the blood urea nitrogen/creatinine ratio in acute kidney injury. Clin Kidney J. 2012;5(2):187–191. https://doi.org/10.1093/ckj/sfs013
81. Kim Y, Cho YS, Kym D et al. Diagnostic performance of plasma and urine neutrophil gelatinase-associated lipocalin, cystatin C, and creatinine for acute kidney injury in burn patients: A prospective cohort study. PLoS One. 2018;13(6):e0199600. https://doi.org/10.1371/journal.pone.0199600
82. Emami A, Javanmardi F, Rajaee M et al. Predictive biomarkers for acute kidney injury in burn patients. J Burn Care Res. 2019;40(5):601–605. https://doi.org/10.1093/jbcr/irz065
83. Nath CK, Rajkhowa P, Barman B et al. Plasma neutrophil gelatinase-associated lipocalin (NGAL): a candidate biomarker to detect early acute kidney injury (AKI) for at-risk intensive care admissions. J Family Med Prim Care. 2022;11(7):3681–3686. https://doi.org/10.4103/jfmpc.jfmpc_2316_21
84. Matsa R, Ashley E, Sharma V, Walden AP, Keating L. Plasma and urine neutrophil gelatinase-associated lipocalin in the diagnosis of new onset acute kidney injury in critically ill patients. Crit Care. 2014;18(4):R137. https://doi.org/10.1186/cc13958
85. Tran NK, Sen S, Palmieri TL et al. Artificial intelligence and machine learning for predicting acute kidney injury in severely burned patients: a proof of concept. Burns. 2019;45(6):1350–1358. https://doi.org/10.1016/j.burns.2019.03.021
86. Rashidi HH, Sen S, Palmieri TL, Blackmon T, Wajda J, Tran NK. Early recognition of burn- and trauma-related acute kidney injury: a pilot comparison of machine learning techniques. Sci Rep. 2020;10(1):205. https://doi.org/10.1038/s41598-019-57083-6
87. Meyer D, Mohan A, Subev E, Sarav M, Sturgill D. Acute kidney injury incidence in hospitalized patients and implications for nutrition support. Nutr Clin Pract. 2020;35(6):987–1000. https://doi.org/10.1002/ncp.10595
88. Clark A, Imran J, Madni T, Wolf SE. Nutrition and metabolism in burn patients. Burns Trauma. 2017;5:11. https://doi.org/10.1186/s41038-017-0076-x
89. Khorasani EN, Mansouri F. Effect of early enteral nutrition on morbidity and mortality in children with burns. Burns. 2010;36(7):1067–1071. https://doi.org/10.1016/j.burns.2009.12.005
90. Williams FN, Branski LK, Jeschke MG, Herndon DN. What, how, and how much should patients with burns be fed? Surg Clin North Am. 2011;91(3):609–629. https://doi.org/10.1016/j.suc.2011.03.002
91. Hart DW, Wolf SE, Zhang XJ et al. Efficacy of a high-carbohydrate diet in catabolic illness. Crit Care Med. 2001;29(7):1318–1324. https://doi.org/10.1097/00003246-200107000-00004
92. Oh WC, Mafrici B, Rigby M et al. Micronutrient and amino acid losses during renal replacement therapy for acute kidney injury. Kidney Int Rep. 2019;4(8):1094–1108. https://doi.org/10.1016/j.ekir.2019.05.001
93. Pantet O, Stoecklin P, Charriere M, Voirol P, Vernay A, Berger MM. Trace element repletion following severe burn injury: a dose-finding cohort study. Clin Nutr. 2019;38(1):246–251. https://doi.org/10.1016/j.clnu.2018.01.025
94. Chung KK, Wolf SE, Cancio LC et al. Resuscitation of severely burned military casualties: fluid begets more fluid. J Trauma Inj Inf Criti Care. 2009;67(2):231–7; discussion 237. https://doi.org/10.1097/TA.0b013e3181ac68cf
95. van den Brink DP, Kleinveld DJB, Sloos PH et al. Plasma as a resuscitation fluid for volume-depleted shock: potential benefits and risks. Transfusion. 2021;61(Suppl 1):S301–S312. https://doi.org/10.1111/trf.16462
96. Perazella MA, Rosner MH. Drug-induced acute kidney injury. Clin J Am Soc Nephrol. 2022;17(8):1220–1233. https://doi.org/10.2215/CJN.11290821
97. Chen ZH, Jin CD, Chen S et al. The application of early goal directed therapy in patients during burn shock stage. Int J Burns Trauma. 2017;7(3):27–33.
98. Gillies MA, Kakar V, Parker RJ, Honoré PM, Ostermann M. Fenoldopam to prevent acute kidney injury after major surgery-a systematic review and meta-analysis. Crit Care. 2015;19:449. https://doi.org/10.1186/s13054-015-1166-4
99. Simmons JW, Chung KK, Renz EM et al. Fenoldopam use in a burn intensive care unit: a retrospective study. BMC Anesthesiol. 2010;10:9. https://doi.org/10.1186/1471-2253-10-9.
100. Kellum JA, Hoste EAJ. Acute kidney injury: epidemiology and assessment. Scand J Clin Lab Invest. 2008;68(sup241):6–11. https://doi.org/10.1080/00365510802144813
101. Uchino S, Kellum JA, Bellomo R et al. Acute renal failure in critically ill patients: a multinational, multicenter study. JAMA. 2005;294(7):813–818. https://doi.org/10.1001/jama.294.7.813
102. Duan Z, Cai G, Li J, Chen FK, Chen XM. Meta-analysis of renal replacement therapy for burn patients: incidence rate, mortality, and renal outcome. Front Med (Lausanne). 2021;8:708533. https://doi.org/10.3389/fmed.2021.708533
103. Damkat-Thomas L, Black CE, Bedi A. Acute kidney injury and the burned patient: progression and outcomes. Burns. 2011;37(1):175–176. https://doi.org/10.1016/j.burns.2010.06.013

104. Soltani A, Karsidag S, Garner W. A ten-year experience with hemodialysis in burn patients at Los Angeles County + USC Medical Center. J Burn Care Res. 2009;30(5):832–835. https://doi.org/10.1097/BCR.0b013e3181b480eb
105. Haberal M, Ozdemir A, Bayraktar U, Oner Z, Bilgin N. Gastrointestinal and renal complications in burned patients. Eur J Plastic Surg. 1993;16(1):17–21. https://doi.org/10.1007/BF00192700
106. Lavrentieva A, Depetris N, Moiemen N, Joannidis M, Palmieri TL. Renal replacement therapy for acute kidney injury in burn patients, an international survey and a qualitative review of current controversies. Burns. 2022;48(5):1079–1091. https://doi.org/10.1016/j.burns.2021.08.013
107. Zhang K, Zhang H, Zhao C et al. The furosemide stress test predicts the timing of continuous renal replacement therapy initiation in critically ill patients with acute kidney injury: a double-blind prospective intervention cohort study. Eur J Med Res. 2023;28(1):149. https://doi.org/10.1186/s40001-023-01092-9
108. Linden K, Stewart IJ, Kreyer SF et al. Extracorporeal blood purification in burns: a review. Burns. 2014;40(6):1071–1078. https://doi.org/10.1016/j.burns.2014.01.013
109. Maroz N, Simman R. Wound healing in patients with impaired kidney function. J Am College Clin Wound Special. 2013;5(1):2–7. https://doi.org/10.1016/j.jccw.2014.05.002
110. Zhang G, Liu W, Li J, Wang D, Duan J, Luo H. Efficacy and safety of blood purification in the treatment of deep burns: a systematic review and meta-analysis. Medicine (Baltim). 2021;100(5):e23968. https://doi.org/10.1097/MD.0000000000023968
111. You B, Zhang YL, Luo GX et al. Early application of continuous high-volume haemofiltration can reduce sepsis and improve the prognosis of patients with severe burns. Crit Care. 2018;22(1):173. https://doi.org/10.1186/s13054-018-2095-9
112. Bellomo R, Cass A, Cole L et al. Calorie intake and patient outcomes in severe acute kidney injury: findings from The Randomized Evaluation of Normal vs. Augmented Level of Replacement Therapy (RENAL) study trial. Crit Care. 2014;18(2):R45. https://doi.org/10.1186/cc13767
113. Kaewdoungtien P, Tachaboon S, Kangsumrith N, Srisawat N. Immunomodulation effect of regional citrate anticoagulation in acute kidney injury requiring renal replacement therapy. Blood Purif. 2023;52(5):474–482. https://doi.org/10.1159/000529350
114. Butler DP. The 21st century burn care team. Burns. 2013;39(3):375–379. https://doi.org/10.1016/j.burns.2013.01.004
115. Al-Mousawi AM, Mecott-Rivera GA, Jeschke MG, Herndon DN. Burn teams and burn centers: the importance of a comprehensive team approach to burn care. Clin Plast Surg. 2009;36(4):547–554. https://doi.org/10.1016/j.cps.2009.05.015
116. Askenazi DJ, Heung M, Connor MJ, Jr et al. Optimal role of the nephrologist in the intensive care unit. Blood Purif. 2017;43(1-3):68–77. https://doi.org/10.1159/000452317
117. Rhee H, Jang GS, Han M et al. The role of the specialized team in the operation of continuous renal replacement therapy: a single-center experience. BMC Nephrol. 2017;18(1):332. https://doi.org/10.1186/s12882-017-0746-8