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Acute Kidney Injury in Burn Patients: Clinically Significant Over the Initial Hospitalization and 1 Year After Injury:

An Original Retrospective Cohort Study

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Abstract

Objective—To examine the development of acute kidney injury (AKI) after burn injury as an independent risk factor for increased morbidity and mortality over initial hospitalization and 1-year follow-up.

Background—Variability in fluid resuscitation and difficulty recognizing early sepsis are major barriers to preventing AKI after burn injury. Expanding our understanding of the burden AKI has on the clinical course of burn patients would highlight the need for standardized protocols.

Methods—We queried the Healthcare Cost and Utilization Project State Inpatient Databases in the states of Florida and New York during the years 2009 to 2013 for patients over age 18 hospitalized with a primary diagnosis of burn injury using ICD-9 codes. We identified and grouped 18,155 patients, including 1476 with burns >20% total body surface area, by presence of AKI. Outcomes were compared in these cohorts via univariate analysis and multivariate logistic regression models.

Results—During initial hospitalization, AKI was associated with increased pulmonary failure, mechanical ventilation, pneumonia, myocardial infarction, length of stay, cost, and mortality, and also a lower likelihood of being discharged home. One year after injury, AKI was associated with development of chronic kidney disease, conversion to chronic dialysis, hospital readmission, and long-term mortality.

Conclusions—AKI is associated with a profound and severe increase in morbidity and mortality in burn patients during initial hospitalization and up to 1 year after injury. Consensus protocols for initial burn resuscitation and early sepsis recognition and treatment are crucial to avoid the consequences of AKI after burn injury.

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Keywords

acute kidney injury; burn injury; chronic kidney disease; dialysis; mortality; resuscitation; sepsis

Acute kidney injury (AKI) is common, especially in the intensive care unit (ICU). It remains a significant problem after burn injury and is responsible for considerable morbidity and mortality.¹ AKI is associated with an increased risk of chronic kidney disease (CKD), particularly in older patients, and studies have shown that AKI increases the long-term risk of death even without renal replacement therapy (RRT) and after complete recovery of renal function.² An appreciation of the etiologies and consequences of AKI can help to minimize its occurrence and progression to CKD. However, prevention of AKI in the care of burn patients is complicated by underlying processes that are unique to the pathophysiology of burn injuries.³ Development of AKI after burn injury has been broadly classified into 2 categories: early AKI and late AKI.⁴ Early AKI occurs less than 5 days after the burn and is commonly associated with inadequate fluid replacement during initial burn resuscitation.⁵ Late AKI occurs more than 5 days after the burn, and, while multifactorial in origin, is usually secondary to sepsis.⁶ Despite our growing knowledge of the causes of AKI in burn patients, there remains a need for improvements in burn resuscitation and early identification and treatment of sepsis.

Fluid resuscitation has long been recognized as the cornerstone of initial care for burn injury.⁷ Appropriate fluid resuscitation is necessary to avoid hypovolemic shock, early AKI, and multiple organ dysfunction (MODS).⁸ Although there have been many formulas and approaches to resuscitation, the Parkland formula⁹ remains the most commonly used. Over time, patients have been receiving progressively more fluid than that predicted by the Parkland formula.^{10,11} This phenomenon is known as “fluid creep,”¹² and although there are many potential reasons for this (narcotics, sedation, greater use of intubation and mechanical ventilation, a departure from colloids, and provider inattention), there are ongoing efforts to cut back on the volume of resuscitation and avoid the complications associated with excessive resuscitation.¹³

Acute kidney injury can occur later in the hospitalization, with sepsis being the leading cause of late AKI after burn injury.⁶ Early treatment of sepsis is critical and has been shown to improve outcomes and decrease mortality.¹⁴ The Surviving Sepsis Campaign Guidelines¹⁵ and recent Third International Consensus Definitions for Sepsis and Septic Shock¹⁶ have done a great deal to guide early sepsis recognition and treatment. However, the persistent systemic inflammatory response characteristic of significant burn injury has handicapped efforts at defining and identifying sepsis after burn injury, and the 2007 guidelines¹⁷ are in need of updating.

Variability in fluid resuscitation and difficulty recognizing early sepsis are major barriers to preventing AKI after burn injury. Expanding our understanding of the burden AKI has on the clinical course of burn patients would highlight the need for standardized protocols. Whereas AKI has been strongly associated with increased morbidity and mortality in certain patient populations,¹ the literature on AKI in burn patients is comparatively incomplete. Studies of AKI after burn injury have addressed etiology³ and incidence,¹⁸ and have also

demonstrated a strong association with mortality,^{19,20} though study populations have generally been small and there remains a need to investigate long-term outcomes.²¹ In view of the paucity of epidemiological data concerning long-term prognosis and renal outcomes for burn patients with AKI, we sought to clearly define the impact that development of AKI has on burn outcomes using statewide databases to analyze a much larger population of burn patients than has been reported in the past. Specifically, we aimed to examine whether AKI after burn injury is an independent factor in the development of early and late complications during initial hospitalization and up to 1 year after injury.

Methods

Overview of Study Design

This retrospective cohort study was designed to examine differences in clinical outcomes associated with the development of AKI among all patients hospitalized with a burn injury in 2 states over a 4-year period. Databases provided by the Agency for Healthcare Research and Quality (AHRQ) were utilized to provide information about each burn patient's initial hospital stay and any stays 1 year thereafter. Our Institutional Review Board has deemed our study, which relies on de-identified and publicly available data, exempt from review.

Data Sources

The Healthcare Cost and Utilization Program (HCUP) State Inpatient Databases (SIDs) are administrative, all-payer databases that provide de-identified and protected data on over 100 clinical and nonclinical variables²² in the 47 participating states. The HCUP SIDs were sponsored by the AHRQ to help inform health-related decisions. Additionally, HCUP provides cost-to-charge ratio (CCR) files that provide a yearly ratio between the average real cost and the total charge to insurance for each individual hospital. These files are used to estimate actual cost of hospital visits in the SIDs. For this study, we utilized the Florida and New York SIDs for the years 2009 to 2013.

Study Population

Patients who were admitted to the hospital with a burn injury as their primary diagnosis in the states of Florida and New York between the years 2009 and 2013 were included in the study. This analysis was restricted to the states of Florida and New York due to the availability of HCUP Supplemental Variables for Revisit Analysis, allowing for measurement of 1-year outcomes.²³ In addition, Florida and New York provided a useful population for the study of population-level outcomes as a result of their diverse populations and health systems.²⁴ Patients were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes (see Supplemental Table 1, <http://links.lww.com/SLA/B90>). Patients were excluded if they were under the age of 18 because the use of HCUP revisit analyses has not been validated in that population, preventing the measurement of 1-year outcomes in that group.

Definition of Variables

Relevant variables in the SIDs included patient age, sex, and presence of Elixhauser comorbidities (see "Statistical Analysis" subsection). Burns were characterized by both

severity (presence of second or third-degree burns) and total body surface area (TBSA). Presence of AKI at the time of initial burn treatment was identified based on presence of relevant ICD-9-CM diagnosis codes (see Supplemental Table 1, <http://links.lww.com/SLA/B90>) at the time of the initial hospital stay.

Outcomes

Clinical outcomes included complications during the initial treatment of the burn injury and complications that arose within 1 year after injury. For the initial hospitalization, we also examined hospital length of stay (LOS), estimated cost of care, and discharge disposition.

The complications at the time of initial burn that we probed for included pulmonary failure, need for mechanical ventilation, pneumonia, wound infection, myocardial infarction, Deep venous thrombosis, and death. These complications must not have been present at the time of admission, thus ensuring only patients who developed these complications as part of their burn recovery were included in the relevant analyses. LOS and discharge disposition for the initial burn injury were pulled directly from the SIDs. Estimated cost of care was calculated with the aid of the CCR files, as per previously validated methodology stated above.

The complications we monitored for development up to 1 year after initial burn admission included development of severe CKD (defined as stage 3–5 CKD), conversion to chronic dialysis, pneumonia, hospital readmission, postdischarge mortality, and total 1-year mortality. A 30-day rate for readmission was calculated to better compare results with similar studies. Patients with CKD or preexisting dialysis status at the time of initial burn injury were excluded from being grouped with those who developed CKD or converted to chronic dialysis within the follow-up window.

All complications were identified via ICD-9-CM diagnostic and procedure codes as outlined in Supplemental Table 1 (<http://links.lww.com/SLA/B90>). The specific ICD-9 codes we used were chosen based on their prior validated uses in other studies after the same complications in the HCUP databases.^{25,26}

Statistical Analysis

We compared clinical outcomes in the population of hospitalized burn patients using development of AKI as the primary independent variable for univariate analysis. Pearson chi-square test was used to evaluate categorical variables (presence or absence of subsequent complications), and the Student *t* test was used to evaluate continuous variables (LOS and estimated cost). Categorical data were reported using proportions, and continuous data were reported using arithmetic means with standard deviation.

To further assess the degree to which AKI was associated with our many clinical outcomes, multivariate analysis was performed to control for the influence of patient characteristics and comorbidities through the use of the Elixhauser approach. The Elixhauser approach makes use of a collection of patient comorbidities designated via ICD-9 codes that have been found to independently affect clinical outcomes and have been shown to be a valid way to control for their influence on an examined outcome in database studies.²⁷ We further controlled for patient age, sex, burn size, and burn severity in our modeling. Logistic regression data were

reported using odds ratios (ORs) with 95% confidence intervals (CIs). To perform the analysis on costs and LOS, patients were grouped into quartiles based on the value of the variable. Presence in the highest quartile was the measured outcome.

For all statistical analyses, a *P* value <0.05 was set as the measure for statistical significance. All statistical analyses were conducted using STATA version 13 (StataCorp LP, College Station, TX).

Results

Patient Characteristics

The study population included 18,155 unique burn patients with a mean age of 47.3, who were hospitalized in New York and Florida between 2009 and 2013 (Table 1). Of these, 14,546 had burns less than 10% TBSA (80.12%) and 1476 (8.13%) had burns covering at least 20% TBSA (Table 2). AKI was observed in 4.64% of all hospitalized burn patients and 20.73% of those with burns >20% TBSA. Age, burn size, and number of comorbidities were significantly greater in patients with AKI in both groups.

Outcomes During Hospitalization

Univariate analysis of the incidence of 10 different outcomes during initial burn treatment (Table 3) showed a significantly higher rate of all negative outcomes if a patient developed AKI. Pulmonary failure, mechanical ventilation, pneumonia, Myocardial infarction (MI), and mortality were all found to have a 10 to 20× greater incidence with AKI development in all burn patients, and a 2 to 3× greater incidence in patients with >20% TBSA burns. Rate of discharge home, LOS, and total costs likewise showed vast significant differences associated with AKI in both populations.

Multivariate analysis of the association between AKI and these outcomes (Table 4) showed that AKI was associated with significantly increased odds of all but 2 negative outcomes, and also lower odds of discharge to home.

Outcomes After Hospitalization

Univariate analysis of the incidence of development of severe CKD, conversion to chronic dialysis, pneumonia, hospital readmission, and mortality (both total and postdischarge mortality) up to 1 year after the initial burn injury (Table 5) showed a significant increase in the rate of all negative outcomes if a patient developed AKI. Patients with >20% TBSA burns experienced a significant increase in hospital readmission and mortality; however, given the limitations in reporting based on sample size, we were unable to report on progression to CKD, need for hemodialysis, and postdischarge mortality in this group.

Multivariate analysis of the association of AKI on the same clinical outcomes up to 1 year after initial burn hospitalization (Table 6) showed AKI was independently associated with increased odds of development of severe CKD, conversion to chronic dialysis, hospital readmission, and total 1-year mortality.

Discussion

In this study—one of the largest population based studies examining AKI after burn injury—we found that AKI was associated with a significant increase in morbidity and mortality during initial hospitalization, and also a significant increase in development of severe CKD, conversion to chronic dialysis, hospital readmission, and mortality 1 year after burn injury.

Mortality

Acute kidney injury was associated with profound increases in mortality during initial hospitalization and up to 1 year after burn injury in all burn patients, and also patients with >20% TBSA burns. Mortality is the most frequently studied outcome in studies researching AKI in burn patients,^{19,20,28} though our study is the first to report on mortality rates 1 year after hospitalization. Burn patients with AKI experienced a 1-year mortality rate of 36.10% for all burn patients and 63.07% for burns >20% TBSA, compared with 3.16% and 20.00% for those without AKI. This is not too dissimilar to what has been observed in other populations that develop AKI, such as a 1-year mortality rate of 50.4% in general ICU patients²⁹ and 23.7% after major cardiac surgery with ICU admission.³⁰ It is without question, therefore, that the development of AKI has a grave effect on the prognosis of critically ill patients. Our data suggest that when the inciting injury is a burn, the stakes are likely even higher—highlighting the dire need for improved monitoring and prevention of AKI in this population.

Cardiopulmonary Function

Among all burn patients, AKI was associated with a 10-fold increase in the rates of pulmonary failure, mechanical ventilation, and pneumonia. Among >20% TBSA burn patients (a population that already has a high rate of pulmonary complications), AKI was associated with more than double the rates of these pulmonary complications. These findings are consistent with current research on AKI and its detrimental effects on lung function.^{31,32} This association is particularly important because it has been shown that concomitant respiratory failure and AKI leads to skyrocketing mortality rates.³³ Interestingly, these pulmonary complications have also been linked to excessive fluid administration during resuscitation.¹³ One possible repercussion of this association is that an overconservative administration of fluid (with the intent of avoiding pulmonary edema and failure) may lead to AKI and then to the same pulmonary complications when the kidneys are unable to perform their function. It is clear that burn patients are at risk for serious pulmonary sequelae after both under and over-resuscitation. A more precise and standardized system to provide appropriate fluid requirements would help alleviate these morbidities.

Our data demonstrate an association between AKI and MI in all burn patients, and also in those with >20% TBSA burns. A causal effect of burn injury on MI is well-documented³⁴ as is a causal effect of MI on development of AKI.³⁵ A logical explanation for the increased rate of MI in the AKI groups in our study is that these patients developed an MI as a consequence of their burn injury, which further decreased renal perfusion and increased their risk for AKI.

Hospital Costs, LOS, Discharge, and Readmission

Acute kidney injury was associated with an increase in both unadjusted and multivariate-adjusted mean hospital costs and LOS in all burn patients and those with >20% TBSA. AKI has previously been associated with an increase in hospital costs and LOS in the recovery of a variety of conditions and surgical operations.^{36,37} Ours are the first data that attempt to characterize the increased cost of AKI, specifically in the burn population, and we found these differences to be quite large. The OR that a burn patient's cost of care would be in the highest quartile was 1.898 in AKI versus non-AKI patients. The unadjusted difference translated to an average increase of \$85,660 in all burn patients and \$93,022 in >20% TBSA patients. These increases in costs are enormous when compared with a study finding an average increase of \$10,680 in all-hospitalized patients who develop AKI,³⁶ and another that found a \$14,000 average increase in general postsurgery patients.³⁷ LOS was likewise increased compared with other studied populations. Our average increase of 23.0 days in AKI versus non-AKI burn patients was larger than the 3.5 days found among all hospitalized patients³⁸ and the 3.5 days found in general ICU patients.³⁹ Therefore, whereas cost and LOS are increased when any patient develops AKI, the difference is even greater when that patient is a burn victim.

In addition to LOS and cost, discharge home is one mark of a good outcome for many conditions. Discharge disposition has been shown to have a major impact on the risk of death after hospitalization for traumatic injuries including burns.⁴⁰ Our data are the first to examine the rates of discharge home for a large number of burn patients with and without AKI. Importantly, the odds of a burn patient with AKI going home after hospitalization are one-third that of a non-AKI patient.

Hospital readmissions are a major contributor to healthcare costs and a marker of quality of care. Studies have only recently begun to examine the effect that AKI has on rates of readmission. Among all burn patients, we found a 30-day readmission rate of 29.93% with AKI versus 11.51% without AKI. This is somewhat similar to a study of ICU patients, which found a 20.0% versus 12.3% difference between AKI and non-AKI patients,⁴¹ but a much greater difference than that observed in a study of general hospital patients, which reported a 15% versus 11% difference.⁴² The non-AKI readmission rate is similar among our study and the others mentioned. However, our higher observed readmission rate for burn patients with AKI suggests that the development of AKI after burn injury and the numerous associated complications associated differs from other conditions requiring critical care or hospital admission.

CKD and Dialysis

Among all burn patients, AKI was associated with a significantly increased rate of severe CKD and conversion to chronic dialysis in the year after burn injury. These associations held strong even after controlling for a multitude of other patient factors. These findings are consistent with recent studies in other select patient populations touting a relationship between AKI and CKD,^{43,44} or End Stage Renal Disease (ESRD)⁴⁵ or both.⁴⁶ These other studies examined AKI in the older population, in nonsurgical patients, or after unspecified surgical procedures. Because the pathophysiology of AKI in burn injury is different than that

of other surgical or nonsurgical conditions,³ our data provide evidence of the relationship between AKI and subsequent kidney dysfunction that can be better generalized to the population of burn patients.

There is currently only 1 other study on the relationship between AKI and subsequent dialysis treatment in the burn population.⁴⁷ This recent study found an odds of dialysis of 2.40 in burn patients who developed AKI compared with the general Finnish population. Our study expands on these findings by directly comparing dialysis conversion in burn patients with and without AKI (4.58% vs 0.33%), rather than the general population, and thus serving as a better control. Our data create an opportunity to better generalize burn patients' risk of conversion to chronic dialysis if they were to develop AKI.

We discovered a study that questioned whether we can conclude that AKI causes CKD, citing that the risk factors are the same and the relationship may not be causal.⁴⁸ However, our multivariate analysis provides evidence that AKI is associated with CKD and dialysis-requiring ESRD development even after controlling for the risk factors proposed in that study.

Incidence of AKI

We recorded the incidence of AKI in our patient population to compare it with previous studies as an external measure of validity for our data. The majority of previous studies report incidence rates of AKI for >20% TBSA burn patients. The rate of our data of 20.73% is consistent with the consensus of 10% to 30% that has been reported previously.^{3,18} Other studies have found somewhat higher incidence rates (ranging from 24.4% to 26.6%).^{19,49} However, these studies differed from ours in that they were prospective studies that diagnosed AKI using direct measurement of serum creatinine levels, allowing them a more sensitive probe than the ICD-9 billing codes in our retrospective database study. Additionally, these studies worked with a much smaller sample size (126–304 burn patients) than the 18,155 patients we were able to capture. We found only 1 study that reported an AKI incidence that differed greatly from ours (53.3%) in a sample of 60 patients.²⁸ Interestingly, our data revealed that African Americans were more likely, and Hispanics were less likely, to develop AKI. The difference in incidence of AKI by race indicates an important population-level health disparity. Given the impact of AKI on both short and long-term outcomes, this difference in incidence suggests an important population-level health disparity that warrants further study.

Limitations and Moving Forward

Although our population-based analysis of all recorded burn patients treated in 2 states over a 4-year period has many strengths, as a retrospective database review, our data cannot be used to draw conclusions about cause and effect between AKI and the studied outcomes. This would be better addressed with a prospective study designed to better capture AKI through serum creatinine (sCr) and urine output data. It is certainly possible that confounders, including the development of sepsis, could explain some of the adverse outcomes associated with AKI. Additionally, our methodology for probing patient outcomes (using ICD-9 codes) limited the sensitivity for detecting AKI. It is possible that patients who

experienced minor renal impairment during their recovery were not assigned a code for AKI and were thus missed. Other studies on AKI utilized directly measured sCr to define AKI according to The Acute Kidney Injury Network or RIFLE criteria, which allowed inclusion of patients with even minor increases in sCr. Similarly, we were unable to assess urine output and capture periods of oliguria. Thus, our incidence of AKI may likely underestimate the true incidence of AKI, as many cases of mild AKI may have gone unrecorded.

Our risk-adjustment methods relied on using widely used comorbidity indexes. Some authors have raised the concern that they do not fully capture the extent of comorbid disease burden in burn patients.⁵⁰ Additional variables, including laboratory values, vitals, and more complete data on prior health encounters, would improve the estimation of baseline comorbidity; however, they are not available in HCUP.

Another limitation arose during analysis of 1-year outcomes. To detect outcomes, patients must have been admitted to a hospital for their visit to be recorded in the SIDs. Patients who may have developed a complication and were never admitted were missed by our analysis. The likely consequence is an underestimation of the true morbidity and mortality experienced with AKI after initial hospitalization for burn injury, although it is worth mentioning that the database captures readmissions to any hospital (not just the hospital where patients received their initial burn care). Similarly, we included only CKD stages 3 to 5 in our analysis because we did not detect more than a handful of stage 1 to 2 CKD patients. These patients are likely under-reported due to a lower incidence of hospitalization related to mild CKD. However, relevant studies on AKI and subsequent CKD development include only stages 3 to 5,^{43,44} so our ability to compare our results was not hampered.

This is the first study of AKI in burn patients to include such a large population. Moving forward, a study of this size utilizing sCr levels would allow more detailed insight into how AKI severity affects outcomes. Specifically, this would allow us to stratify patients by their degree of AKI to draw more precise conclusions about when to expect complications given a patient's renal status. Additionally, serial sCr levels would allow us to observe the timeframe of AKI in relation to subsequent complications. These data would increase comparability to other studies and increase the ability to generalize findings to patients in practice.

Finally, our findings are meant to emphasize the need for a better understanding of the mechanisms behind AKI development in burn patients. We know that inappropriate fluid resuscitation⁸ and sepsis⁶ are the leading causes of AKI during recovery after a burn injury. However, the burn community is still working on a true consensus as to the best way to resuscitate patients upon presentation with a burn. Likewise, although there is a current focus on research into early detection of sepsis, there is little research into the development of sepsis, specifically in burn patients who we know to have unique pathophysiology complicating the diagnosis.¹⁷ We hope that our data, which highlight the profound morbidity and mortality that follows AKI during recovery after burn injury, will spur increased interest into standardizing more effective ways to determine proper fluid resuscitation volume and early detection and treatment of sepsis in burn patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Singbartl K, Kellum JA. AKI in the ICU: definition, epidemiology, risk stratification, and outcomes. *Kidney Int.* 2012; 81:819–825. [PubMed: 21975865]
2. Hobson CE, Yavas S, Segal MS, et al. Acute kidney injury is associated with increased long-term mortality after cardiothoracic surgery. *Circulation.* 2009; 119:2444–2453. [PubMed: 19398670]
3. Emara S, Alzaylai A. Renal failure in burn patients: a review. *Ann Burns Fire Disasters.* 2013; 26:12–15. [PubMed: 23966893]
4. Schneider DF, Dobrowolsky A, Shakir IA, et al. Predicting acute kidney injury among burn patients in the 21st century: a classification and regression tree analysis. *J Burn Care Res.* 2012; 33:242–251. [PubMed: 22370901]
5. Mustonen KM, Vuola J. Acute renal failure in intensive care burn patients (ARF in burn patients). *J Burn Care Res.* 2008; 29:227–237. [PubMed: 18182927]
6. Chrysopoulou MT, Jeschke MG, Dziewulski P, et al. Acute renal dysfunction in severely burned adults. *J Trauma Acute Care Surg.* 1999; 46:141–144.
7. Monafo WW. Initial management of burns. *N Engl J Med.* 1996; 335:1581–1586. [PubMed: 8900093]
8. Lund T, Onarheim H, Reed RK. Pathogenesis of edema formation in burn injuries. *World J Surg.* 1992; 16:2–9. [PubMed: 1290261]
9. Baxter CR, Shires T. Physiological response to crystalloid resuscitation of severe burns. *Ann N Y Acad Sci.* 1968; 150:874–894. [PubMed: 4973463]
10. Cartotto RC, Innes M, Musgrave MA, et al. How well does the parkland formula estimate actual fluid resuscitation volumes? *J Burn Care Res.* 2002; 23:258–265.
11. Pruitt BA Jr. Protection from excessive resuscitation: “pushing the pendulum back”. *J Trauma Acute Care Surg.* 2000; 49:567–568.
12. Saffle JI. The phenomenon of “fluid creep” in acute burn resuscitation. *J Burn Care Res.* 2007; 28:382–395. [PubMed: 17438489]
13. Klein MB, Hayden D, Elson C, et al. The association between fluid administration and outcome following major burn: a multicenter study. *Ann Surg.* 2007; 245:622–628. [PubMed: 17414612]
14. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med.* 2001; 345:1368–1377. [PubMed: 11794169]
15. Levy MM, Rhodes A, Phillips GS, et al. Surviving sepsis campaign: association between performance metrics and outcomes in a 7.5-year study. *Intensive Care Med.* 2014; 40:1623–1633. [PubMed: 25270221]
16. Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of clinical criteria for sepsis: for the third international consensus definitions for sepsis and septic shock (sepsis-3). *JAMA.* 2016; 315:762–774. [PubMed: 26903335]
17. Greenhalgh DG, Saffle JR, Holmes JH 4th, et al. American burn association consensus conference to define sepsis and infection in burns. *J Burn Care Res.* 2007; 28:776–790. [PubMed: 17925660]
18. Holm C, Hörbrand F, von Donnersmarck GH, et al. Acute renal failure in severely burned patients. *Burns.* 1999; 25:171–178. [PubMed: 10208394]
19. Coca SG, Bauling P, Schiffner T, et al. Contribution of acute kidney injury toward morbidity and mortality in burns: a contemporary analysis. *Am J Kidney Dis.* 2007; 49:517–523. [PubMed: 17386319]

20. Mosier MJ, Pham TN, Klein MB, et al. Early acute kidney injury predicts progressive renal dysfunction and higher mortality in severely burned adults. *J Burn Care Res.* 2010; 31:83–92. [PubMed: 20061841]
21. Mason SA, Nathens AB, Finnerty CC, et al. Hold the pendulum: rates of acute kidney injury are increased in patients who receive resuscitation volumes less than predicted by the parkland equation. *Ann Surg.* 2016 Epub ahead of print.
22. HCUP databases. Rockville, MD: Agency for healthcare research and quality; Healthcare cost and utilization project (HCUP). Available at: <http://www.hcup-us.ahrq.gov/sidoverview.jsp> [Accessed February 25, 2016]
23. HCUP databases. Rockville, MD: Agency for healthcare research and quality; Healthcare cost and utilization project (HCUP). Available at: <https://www.hcup-us.ahrq.gov/toolssoftware/revisit/revisit.jsp> [Accessed February 25, 2016]
24. Chukmaitov A, Harless DW, Bazzoli GJ, et al. Delivery system characteristics and their association with quality and costs of care: Implications for accountable care organizations. *Health Care Manage Rev.* 2015; 40:92–103. [PubMed: 24566250]
25. Ray JJ, Satahoo SS, Meizoso JP, et al. Does obesity affect outcomes of adult burn patients? *J Surg Res.* 2015; 198:450–455. [PubMed: 25918008]
26. Hsu RK, McCulloch CE, Dudley RA, et al. Temporal changes in incidence of dialysis-requiring AKI. *J Am Soc Nephrol.* 2013; 24:37–42. [PubMed: 23222124]
27. Elixhauser A, Steiner C, Harris DR, et al. Comorbidity measures for use with administrative data. *Med Care.* 1998; 36:8–27. [PubMed: 9431328]
28. Palmieri T, Lavrentieva A, Greenhalgh DG. Acute kidney injury in critically ill burn patients. risk factors, progression and impact on mortality. *Burns.* 2010; 36:205–211. [PubMed: 19836141]
29. Bagshaw SM, Mortis G, Doig CJ, et al. One-year mortality in critically ill patients by severity of kidney dysfunction: a population-based assessment. *Am J Kidney Dis.* 2006; 48:402–409. [PubMed: 16931213]
30. Tsai H, Tsai F, Chen Y, et al. Impact of acute kidney injury on one-year survival after surgery for aortic dissection. *Ann Thorac Surg.* 2012; 94:1407–1412. [PubMed: 22939248]
31. Grams ME, Rabb H. The distant organ effects of acute kidney injury. *Kidney Int.* 2012; 81:942–948. [PubMed: 21814177]
32. Walcher A, Faubel S, Keniston A, et al. In critically ill patients requiring CRRT, AKI is associated with increased respiratory failure and death versus ESRD. *Ren Fail.* 2011; 33:935–942. [PubMed: 21910664]
33. Faubel S. Pulmonary complications after acute kidney injury. *Adv Chron Kidney Dis.* 2008; 15:284–296.
34. Abu-Sittah GS, Sarhane KA, Dibo SA, et al. Cardiovascular dysfunction in burns: review of the literature. *Ann Burns Fire Disasters.* 2012; 25:26–37. [PubMed: 23012613]
35. Goldberg A, Kogan E, Hammerman H, et al. The impact of transient and persistent acute kidney injury on long-term outcomes after acute myocardial infarction. *Kidney Int.* 2009; 76:900–906. [PubMed: 19657321]
36. Lahoti A, Nates JL, Wakefield CD, et al. Costs and outcomes of acute kidney injury in critically ill patients with cancer. *J Support Oncol.* 2011; 9:149–155. [PubMed: 21809520]
37. Hobson C, Ozrazgat-Baslanti T, Kuxhausen A, et al. Cost and mortality associated with postoperative acute kidney injury. *Ann Surg.* 2015; 261:1207–1214. [PubMed: 24887982]
38. Chertow GM, Burdick E, Honour M, et al. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol.* 2005; 16:3365–3370. [PubMed: 16177006]
39. Thakar CV, Christianson A, Freyberg R, et al. Incidence and outcomes of acute kidney injury in intensive care units: a Veterans Administration Study. *Crit Care Med.* 2009; 37:2552–2558. [PubMed: 19602973]
40. Davidson GH, Hamlat CA, Rivara FP, et al. Long-term survival of adult trauma patients. *JAMA.* 2011; 305:1001–1007. [PubMed: 21386078]
41. Horkan CM, Purtle SW, Mendu ML, et al. The association of acute kidney injury in the critically ill and postdischarge outcomes: a cohort study. *Crit Care Med.* 2015; 43:354–364. [PubMed: 25474534]

42. Koulouridis I, Price LL, Madias NE, et al. Hospital-acquired acute kidney injury and hospital readmission: a cohort study. *Am J Kidney Dis.* 2015; 65:275–282. [PubMed: 25446018]
43. van Kuijk JP, Flu WJ, Chonchol M, et al. Temporary perioperative decline of renal function is an independent predictor for chronic kidney disease. *Clin J Am Soc Nephrol.* 2010; 5:1198–1204. [PubMed: 20430939]
44. Chawla LS, Amdur RL, Amodeo S, et al. The severity of acute kidney injury predicts progression to chronic kidney disease. *Kidney Int.* 2011; 79:1361–1369. [PubMed: 21430640]
45. Ishani A, Xue JL, Himmelfarb J, et al. Acute kidney injury increases risk of ESRD among elderly. *J Am Soc Nephrol.* 2009; 20:223–228. [PubMed: 19020007]
46. Coca SG, Singanamala S, Parikh CR. Chronic kidney disease after acute kidney injury: a systematic review and meta-analysis. *Kidney Int.* 2012; 81:442–448. [PubMed: 22113526]
47. Helanterä I, Koljonen V, Finne P, et al. The risk for end-stage renal disease is increased after burn. *Burns.* 2016; 42:316–321. [PubMed: 26620696]
48. Rifkin DE, Coca SG, Kalantar-Zadeh K. Does AKI truly lead to CKD? *J Am Soc Nephrol.* 2012; 23:979–984. [PubMed: 22460531]
49. Steinvall I, Bak Z, Sjöberg 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; 12:1.
50. Slocum CS, Goldstein R, DiVita MA, et al. Assessing the ability of comorbidity indexes to capture comorbid disease in the inpatient rehabilitation burn injury population. *Am J Phys Med Rehabil.* 2015; 94:373–384. [PubMed: 25171665]

Table 1
Demographics, Characteristics, and Incidence of AKI Among All Burn Patients

Variable	No AKI (n = 17,313)	AKI (n = 842)	P
Age, yrs	46.7 (18.2)	60.3 (16.7)	<0.001
Male, %	65.22%	65.91%	0.678
Race, %			<0.001
Caucasian	60.78%	60.92%	
African American	14.21%	19.90%	
Hispanic	13.50%	7.84%	
Other	11.50%	11.34%	
Burn severity, %			<0.001
First degree	6.83%	4.99%	
Second degree	53.05%	24.47%	
Third degree	40.13%	70.55%	
Elixhauser comorbidities (n)	1.34 (1.32)	3.19 (3.05)	<0.001

Results are given as mean + standard deviation or percent, as appropriate.
 Burn severity reflects the highest degree of burn attained in each individual.

Table 2
Demographics, Characteristics, and Incidence of AKI Among Patients With >20% TBSA Burn

Variable	No AKI (n = 1170)	AKI (n = 306)	P
Age, yrs	47.2 (19.2)	54.5 (17.2)	<0.001
Male, %	70.77%	67.75%	0.288
Race, %			0.169
Caucasian	62.19%	64.41%	
African American	14.73%	12.54%	
Hispanic	12.66%	9.49%	
Other	10.42%	13.56%	
Burn severity, %			<0.001
First degree	1.03%	0.98%	
Second degree	26.75%	7.84%	
Third degree	72.22%	91.18%	
Elixhauser comorbidities (n)	1.86 (1.76)	2.72 (2.51)	<0.001

Results are given as mean + standard deviation or percent, as appropriate.

Burn severity reflects the highest degree of burn attained in each individual.

Table 3
Differences in Outcomes During Initial Hospitalization Between AKI and Non-AKI Burn Patients

AKI Development:	All Burn Patients			TBSA >20%		
	No (n = 17,313)	Yes (n = 842)	P	No (n = 1170)	Yes (n = 306)	P
Pulmonary failure	1.40%	15.80%	<0.001	8.97%	20.59%	<0.001
Mechanical ventilation	1.69%	18.17%	<0.001	12.05%	27.45%	<0.001
Pneumonia	2.21%	22.57%	<0.001	14.27%	35.29%	<0.001
Wound infection	0.61%	2.38%	<0.001	*	*	
MI	0.16%	3.92%	<0.001	0.94%	3.59%	0.001
DVT	0.29%	2.85%	<0.001	1.97%	5.23%	0.002
Mortality	1.89%	32.54%	<0.001	19.91%	62.42%	<0.001
Discharged home	86.29%	36.58%	<0.001	54.27%	11.11%	<0.001
Length of stay, d (SD)	8.9 (13.6)	31.9 (40.3)	<0.001	25.1 (31.6)	42.1 (48.1)	<0.001
Estimated cost \$ (SD)	\$22,293 (\$44,630)	\$107,953 (\$155,628)	<0.001	\$76,674 (\$103,463)	\$169,696 (\$194,280)	<0.001

* As per HCUP guidelines, groups containing 10 patients or less cannot be reported.

Table 4
Association of AKI Development With Clinical Outcomes (Initial Hospitalization)

	Odds Ratio	95% Confidence Interval	P
Pulmonary failure	2.497	1.896–3.289	<0.001
Mechanical ventilation	2.406	1.858–3.115	<0.001
Pneumonia	2.386	1.864–3.054	<0.001
Wound infection	1.480	0.836–2.619	0.178
MI	10.110	5.434–18.812	<0.001
DVT	1.587	0.888–2.836	0.119
Mortality	7.092	5.447–9.235	<0.001
Discharged home	0.340	0.284–0.407	<0.001
Lengthy stay (top quartile)	1.543	1.287–1.850	<0.001
Expensive stay (top quartile)	1.898	1.580–2.279	<0.001

Data reflect multivariate logistic regression models controlling for patient age, sex, burn size, burn severity, and presence of 29 comorbidities.

Table 5
Differences in Outcomes 1 Year After Injury Between AKI and Non-AKI Burn Patients

	All Burn Patients		TBSA >20%	
	No (n = 16,985)	Yes (n = 568)	No (n = 937)	Yes (n = 115)
AKI Development:				
Severe CKD	0.71%	5.81%	<0.001	*
Chronic dialysis	0.33%	4.58%	<0.001	*
Pneumonia	2.54%	4.75%	0.001	*
Readmission (30 d)	11.51%	29.93%	<0.001	<0.001
Readmission (1 yr)	25.34%	51.94%	<0.001	<0.001
Postdischarge mortality	1.29%	5.28%	<0.001	*
Total mortality [†]	3.16%	36.10%	<0.001	<0.001

Patient population for 1-year outcomes includes only those patients who survived initial hospitalization.

* As per HCUP guidelines, groups containing 10 patients or less cannot be reported.

[†]Total mortality rate includes those patients that died during initial hospitalization.

Table 6
Association of AKI Development With Clinical Outcomes (1 Year After Injury)

	Odds Ratio	95% Confidence Interval	P
Severe CKD	2.473	1.525–4.011	<0.001
Chronic dialysis	2.660	1.448–4.885	0.002
Pneumonia	0.675	0.432–1.056	0.085
Readmission (30 d)	1.556	1.264–1.915	<0.001
Readmission (1 yr)	1.272	1.048–1.544	0.015
Postdischarge mortality	1.518	0.960–2.402	0.074
Total mortality *	4.604	3.687–5.748	<0.001

Data reflect multivariate logistic regression models controlling for patient age, sex, burn size, burn severity, and presence of 29 comorbidities.

* Total mortality rate includes those patients that died during initial hospitalization.