

The Acute Kidney Injury Network (AKIN) Criteria Applied in Burns

Kevin K. Chung, MD,* Ian J. Stewart, MD,†‡ Christopher Gisler, MD,‡
John W. Simmons, MD,§ James K. Aden, PhD,* Molly A. Tilley, MD,†
Casey L. Cotant, MD,† Christopher E. White, MD,* Steven E. Wolf, MD,||
Evan M. Renz, MD*¶

In 2007, the Acute Kidney Injury Network (AKIN) developed a modified standard for diagnosing and classifying acute kidney injury (AKI). This classification system is a modification of the previously described risk, injury, failure, loss, and end-stage (RIFLE) criteria. Among other modifications, the AKIN staging requires an absolute serum creatinine change of 0.3 mg/dl in a 48-hour period to establish the diagnosis of AKI. The purpose of this study was to apply these new criteria in the severely burned population and to compare the prevalence, stage, and mortality impact of these criteria to the RIFLE criteria. The authors performed a retrospective analysis of consecutive patients with burns admitted to their burn center for at least 24 hours from June 2003 through December 2008. Each patient was classified by both the AKIN and RIFLE criteria by three referees. Both univariate and multivariate analyses were performed to determine the impact of the various AKI stages on mortality. A total of 1973 patients met inclusion and exclusion criteria and were included in the analysis. The average age, %TBSA, injury severity score, and percent with smoke inhalation injury were 36 ± 16 , 16 ± 18 , 10 ± 12 , and 13%, respectively. Overall, the prevalence of AKI was 33% using the AKIN criteria and 24% using the RIFLE criteria with an associated mortality of 21 and 25%, respectively. Of those meeting criteria for AKIN stage 1 ($N = 434$), 41% ($N = 180$) would have been categorized as not having AKI on the basis of the RIFLE criteria. In this cohort of patients, mortality increased by almost 8-fold when compared with those without AKI (odds ratio 7.8 [95% confidence interval (CI) 3.7–16.2], $P < .0001$). The area under the receiver operator characteristic curve for in-hospital mortality was significantly higher for the AKIN criteria at 0.877 (95% CI 0.848–0.906) when compared to the RIFLE criteria at 0.838 (95% CI 0.801–0.874; $P = .0007$). Burn patients indentified as having AKI by the AKIN criteria missed by RIFLE appear to be an important cohort. On the basis of our study, AKIN criteria may be more precise and are more predictive of death than the RIFLE criteria in this population. Prospective validation is needed. (J Burn Care Res 2012;33:483–490)

The development of acute kidney injury (AKI) in critically ill burn patients has long been recognized as an ominous sign with a reported mortality as high as 50 to 100%.^{1,2} Because of the wide variation in the definition of AKI, accurate reporting of incidence as

well as of resultant outcomes has been problematic. In a recent systematic review of AKI in burns, Brusselsaers et al³ described more than 20 different definitions of acute renal failure across a compilation of 57 studies. Depending on the definition, the prevalence

*From the *Clinical Division, United States Army Institute of Surgical Research, Fort Sam Houston, Texas; †Department of Nephrology, San Antonio Military Medical Center, Fort Sam Houston, Texas; ‡Department of Nephrology, University of Texas Health Science Center, San Antonio, Texas; §Department of Surgery, San Antonio Military Medical Center, Fort Sam Houston, Texas; ||Department of Surgery, University of Texas Southwestern, Dallas, Texas; and ¶Uniformed Services University of the Health Sciences, Bethesda, Maryland.*

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Address correspondence to Kevin K. Chung, MD, United States Army Institute of Surgical Research, 3400 Rawley E Chambers Ave, San Antonio, Texas 78234-6315.

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of AKI in patients admitted with burn injury ranged from as low as 0.9% and as high as 64%, and reported mortality ranged from a low of 28% to a high of 100%.³ These differences complicate the interpretation and comparison of reported frequency, outcomes, and the impact of therapeutic interventions.

In an effort to help resolve this problem and standardize the classification of AKI, the Acute Dialysis Quality Initiative developed and reported the RIFLE (risk, injury, failure, loss of function, end-stage renal disease) criteria in 2004.⁴ Since this report, the RIFLE criteria have been applied to report the epidemiology and outcomes associated with AKI across many different patient populations including burns.⁵⁻⁹

In 2007, the Acute Kidney Injury Network (AKIN) proposed a modified version of the RIFLE system because of a number of identified limitations.¹⁰ Revised criteria were intended to simplify the definition and make it more clinically applicable. According to the AKIN criteria, AKI is defined by “[a]n abrupt (within 48 hours) reduction of kidney function currently defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dl, a percentage increase in serum creatinine of more than or equal to 50% (1.5-fold from baseline), or a reduction in urine output (documented oliguria of less than 0.5 ml/kg per hour for more than six hours).”¹⁰ The three stages of AKI are depicted in Table 1. The purpose of our study was to apply the AKIN staging criteria to burn patients to describe the incidence of AKI and its impact on outcome in this population.

METHODS

After obtaining approval from our local Institutional Review Board, we conducted a retrospective review of consecutive adult patients admitted to the burn center at the United States Army Institute of Surgical Research with burns of any size and/or inhalation injury. The study period was from June 2003 through December 2008. Patients were included in the analysis if they had a creatinine measured in the

course of their hospitalization and were more than 18 years of age. Patients were excluded from the analysis if they were less than 18 years of age, did not have a measured creatinine, had end-stage renal disease, or did not have burn injury and/or inhalation injury. If a patient was re-admitted, only the first hospitalization was considered for analysis.

Data were obtained from the COLLECTOR database and the patients’ electronic medical records. The COLLECTOR database is a prospectively collected data bank of burn admissions maintained by the United States Army Institute of Surgical Research and contains detailed demographic, laboratory, and treatment information on all patients admitted to the burn center. Demographic variables, %TBSA, presence of inhalation injury via diagnosis with fiberoptic bronchoscopy, injury severity score (ISS) as well as outcomes were extracted from the database and the electronic medical record.

AKIN stage was determined using the standard criteria, which depend on a change in serum creatinine, following the classification system outlined by Mehta et al¹⁰ in 2007 (Table 1). RIFLE stage was determined by following the classification system described by Bellomo et al.⁴ In determining changes in serum creatinine during the hospitalization, the subject’s full range of serum creatinine values were obtained from the electronic medical record. Preinjury baseline serum creatinine values were not available and were estimated by using the lowest in-hospital serum creatinine in the first 7 days of admission as previously described.¹¹ If the patient only had one serum creatinine or if the patient arrived with AKI and creatinine continued to trend upward, then we backcalculated using the modification of diet in renal disease (MDRD) equation assuming a baseline estimated glomerular filtration rate of 75. AKIN and RIFLE stages were determined by one author (C.G.) who rechecked all assignments twice. Furthermore, three referees (K.K.C., I.J.S., M.A.T.) reviewed equal portions of the data set. Resuscitation of all patients with >20% TBSA burns was performed using the

Table 1. Acute Kidney Injury Network criteria as previously published¹⁰

	Serum Creatinine Criteria	Urine Output Criteria
Stage 1	Increase in serum creatinine ≥ 0.03 mg/dl or increase to ≥ 150 –199% (1.5–1.9 fold) from baseline	<0.5 ml/kg/hr for >6 hr
Stage 2	Increase in serum creatinine to 200–299% (2.0–2.9 fold) from baseline	<0.5 ml/kg/hr for >12 hr
Stage 3	Increase in serum creatinine to $\geq 300\%$ (≥ 3 fold) from baseline or serum creatinine ≥ 4.0 mg/dl with an acute increase of at least 0.5 mg/dl or initiation of RRT	<0.3 ml/kg/hr for >24 hr or anuria for >12 hr

RRT, renal replacement therapy.

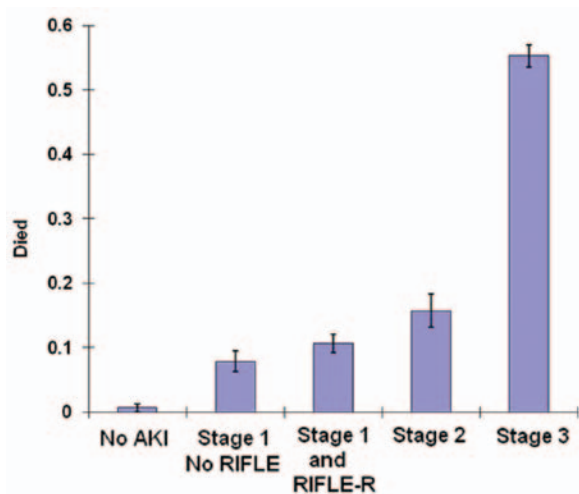


Figure 1. Mortality rate of various Acute Kidney Injury Network (AKIN) stages.

modified Brooke formula¹² to determine the initial intravenous fluid rate with subsequent titration of intravenous fluid to sustain a 30-ml to 50-ml hourly urine output. In addition to AKI staging, various outcome measures to include hospital days, intensive care unit (ICU) days, ventilator days, and in-hospital mortality were collected.

Continuous variables were compared with a Kruskal-Wallis test, and categorical variables were compared with χ^2 analysis. Multivariate logistic regression was used to determine the influence of independent variables on various outcome measures to include mortality. Variables were included in the model when $P \leq .2$ on univariate analysis, whereas they were removed if significant collinearity was determined by Spearman's correlation coefficient. Statistical analysis was performed with SAS 9.1 (Cary, NC) with statistical significance defined as $P < .05$.

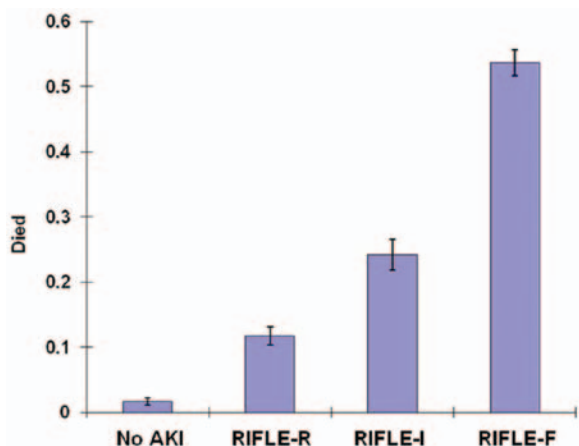


Figure 2. Mortality rate of various risk, injury, failure, loss, and end (RIFLE) stages.

Table 2. A comparison of select demographics and outcomes between those without AKI and those with AKI

	No AKI (N = 1317)	AKI* (N = 656)	P
Age†	30 (22–44)	33 (24–50)	<.0001
Male (%)	86	86	NS
Military (%)	35	36	NS
% TBSA†	6 (3–11)	25 (13–42)	<.0001
Inhalation (%)	5%	30%	<.0001
ISS†	4 (1–9)	18 (9–26)	<.0001
ICU length of stay†	0 (0–2)	9 (3–28)	<.0001
Ventilator days†	0 (0–0)	3 (0–12)	<.0001
Hospital length of stay†	4 (2–11)	24 (11–58)	<.0001
In-hospital mortality	1%	21%	<.0001

ISS, Injury Severity Scale score; AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; ICU, intensive care unit; NS, nonsignificant.

*By AKIN criteria.

†Median (Interquartile range 1–3).

RESULTS

During the study period, 1973 patients met the inclusion and exclusion criteria. The average age, %TBSA, ISS, and percent with smoke inhalation injury were 36 ± 16 , 16 ± 18 , 10 ± 12 , and 13%, respectively. Overall, the prevalence of AKI was 33% using the AKIN criteria and 24% using the RIFLE criteria, with an associated mortality of 21 and 25%, respectively. Among those with >20% TBSA burns, the prevalence of AKI was 77% using the AKIN criteria and 62% using the RIFLE criteria with an associated mortality of 29 and 32%, respectively. For both criteria, mortality increased with each increase in stage (Figures 1 and 2). Among those with AKIN stage 3, 81 underwent some form of renal replacement therapy. Of these who underwent renal replacement therapy, the mortality was 62%.

No AKI vs AKI

Demographic and select outcome variables between those subjects with and without AKI (by AKIN criteria) were compared for the entire study population (Table 2) as well as those with >20% TBSA (Table 3). Subjects with AKI also had longer hospital and ICU stays, and required longer ventilator support. On multiple logistic regression analysis, increasing age, TBSA, ISS, and various AKIN stages were all independently associated with death (Table 4). In a separate model, the same is true except for RIFLE-Risk (Table 5). The area under the receiver

Table 3. Demographics and outcomes comparison for those with burns >20% TBSA

	No AKI (N = 115)	AKI* (N = 380)	P
Age†	30 (22–45)	31 (23–46)	<.01
Male	82%	88%	.09
Military (%)	38%	42%	.49
% TBSA†	26 (23–37)	39 (30–57)	.20
Inhalation (%)	15%	40%	<.0001
ISS†	16 (9–25)	25 (19–34)	.49
ICU length of stay†	3 (1–6)	16 (7–41)	<.0001
Ventilator days†	1 (0–2)	7 (3–19)	<.0001
Hospital length of stay†	14 (5–27)	44 (17–76)	<.0001
In-hospital mortality (%)	4%	29%	<.0001

AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; ISS, Injury Severity Score; ICU, intensive care unit.

*By AKIN criteria.

†Median (Interquartile range 1–3).

operator characteristic curve for in-hospital mortality was significantly higher for the AKIN criteria at 0.877 (95% confidence interval [CI] 0.848–0.906) when compared with the RIFLE criteria at 0.838 (95% CI 0.801–0.874; $P = .0007$; Figure 3).

Stage 1 AKI Without RIFLE

Of those meeting criteria for AKIN stage 1 ($n = 434$), 41% ($n = 180$) would have been categorized as not having AKI based on the RIFLE criteria (Figure 4). In this cohort of patients, mortality increased by almost 8-fold when compared to those without AKI (odds ratio 7.8 [95% CI 3.7–16.2], $P < .0001$) in univariate analysis. Additionally, both ICU length of stay (LOS; 1.7 vs 8.4, $P = .0001$) and hospital LOS (9.4 vs 23.9, $P < .0001$) were significantly higher in this cohort when compared to those without

Table 4. Logistic regression model with various AKIN stages: risk factors for death

	Odds Ratio	95% CI	P
Age	1.09	1.07–1.10	<.0001
% TBSA	1.05	1.03–1.07	<.0001
ISS	1.07	1.04–1.10	<.0001
AKIN Stage 1	3.80	1.46–9.87	.0062
AKIN Stage 2	6.87	2.16–21.87	.0011
AKIN Stage 3	29.55	11.14–78.39	<.0001

CI, confidence interval; ISS, Injury Severity Score; AKIN, Acute Kidney Injury Network.

Table 5. Logistic regression model with various RIFLE stages: risk factors for death

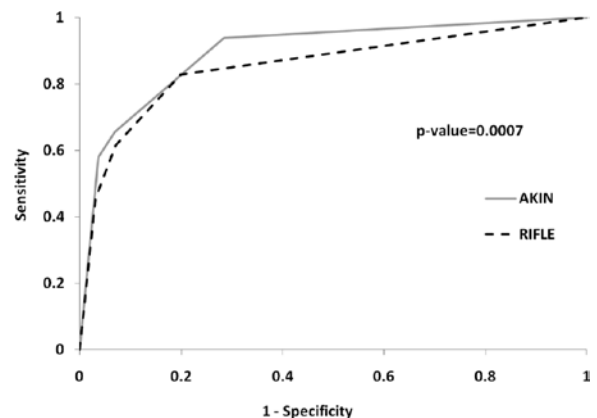
	Odds Ratio	95% CI	P
Age	1.09	1.07–1.10	<.0001
% TBSA	1.05	1.03–1.07	.0067
ISS	1.08	1.03–1.07	<.0001
RIFLE-Risk	1.58	0.63–3.96	.3266
RIFLE-Injury	2.98	1.12–7.90	.0284
RIFLE-Failure	6.73	2.79–16.25	<.0001

CI, confidence interval; ISS, Injury Severity Score; RIFLE, risk, injury, failure, loss, and end-stage.

AKI. There was a trend toward increased ventilator days (0.7 vs 3.3, $P = .09$). Approximately half of this cohort was classified as “early AKI,” defined as meeting AKIN stage 1 criteria within 48 hours of admission. Of those with early AKI ($N = 92$), 73% were those that were deemed to have AKI based on their initial serum creatinine that corrected to their “baseline” within the first 48 hours (Figure 5). No difference in mortality was identified between this cohort and those who were classified on the basis of an increase of serum creatinine either within the first 48 hours or later in the hospital course.

DISCUSSION

To our knowledge this is the first study to date that describes AKI incidence and associated outcomes in an adult burn population using the AKIN staging criteria. Overall, the prevalence of AKI was 33% among those admitted to our burn center with a mortality of 21%. This is in line with the prevalence reported in a recent systematic review by Brusselsaers et al³ who

**Figure 3.** The receiver operating characteristic curves of both the Acute Kidney Injury Network (AKIN) and risk, injury, failure, loss, and end-stage (RIFLE) criteria against mortality.

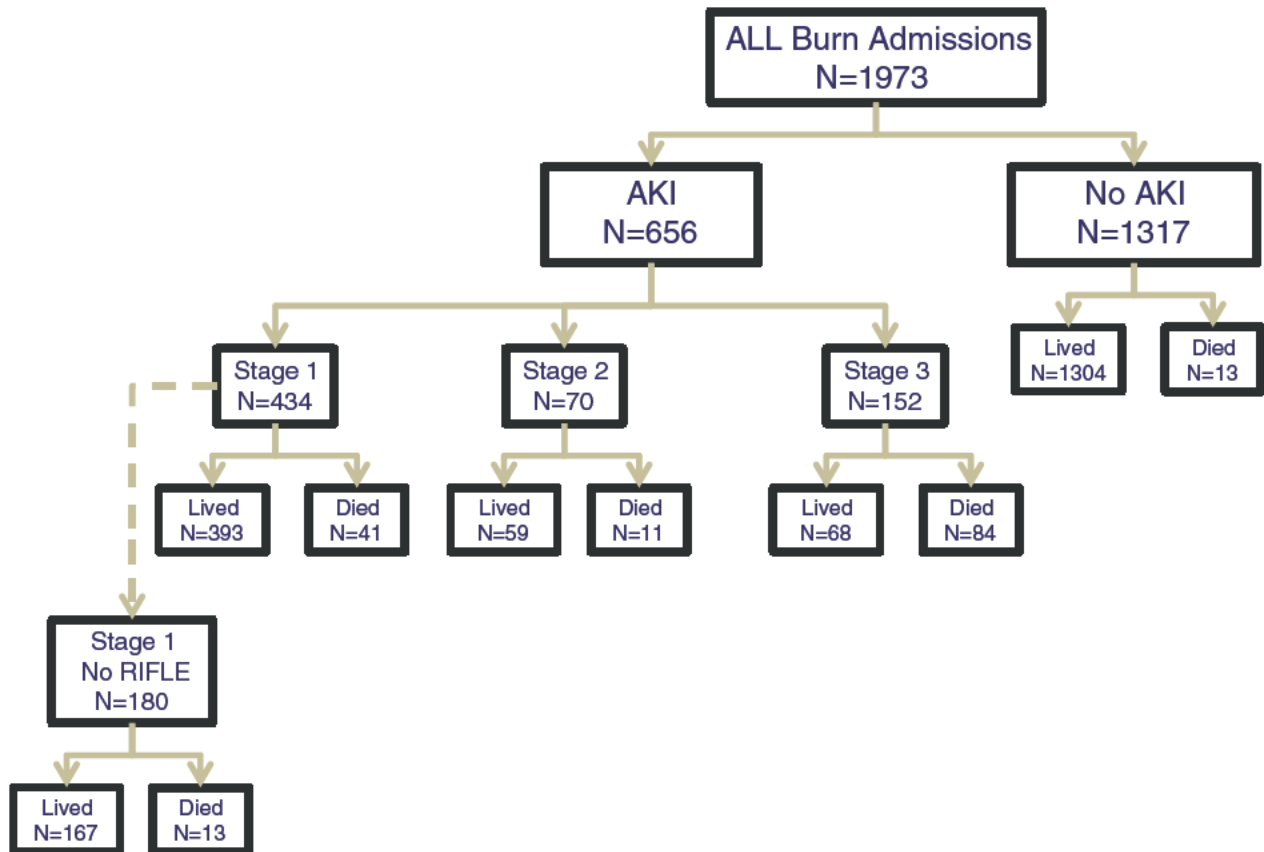


Figure 4. Consort diagram of entire study population.

reported a prevalence of 25% and a median mortality of 34.9% across 30 published studies in the burn population using various definitions.

Among those with severe burns (>20% TBSA involvement) in our study population, the prevalence of AKI was 77% with an associated mortality of 29% by the AKIN criteria. When the RIFLE criteria were applied in our same data set, the prevalence was 62% with an associated mortality of 32%. Palmieri et al⁸ applied the RIFLE criteria and reported AKI in 53% among 60 patients with an associated mortality of 34% in a retrospective study. In the only prospective observational multicenter study done to date in a similar population, Mosier et al¹³ representing the “Inflammation and the Host Response to Injury” study, reported a combined prevalence of both early and late AKI via RIFLE criteria of 49% with an associated mortality of 35%. When compared to these two studies (Palmieri et al [$P = .2$] and Mosier et al [$P = .002$]), our prevalence is close but still higher for this cohort. It is interesting to note that the reported mortalities based on the RIFLE criteria were no different (32% vs 34 and 35%).

The AKIN and RIFLE criteria were both developed to standardize the diagnosis of AKI.

However, a number of issues have surfaced when applying these criteria that complicate our efforts of standardization. One such issue is the determination of the baseline creatinine when a measured value prior to the hospitalization is not known. Prior work has used the lowest creatinine in the first 5 days,⁵ the earliest creatinine available,¹⁴ and a creatinine derived by solving the MDRD study equation^{8,13} for this value. For the majority of our study population (99%), we used the lowest creatinine in the first 7 days as the baseline. Although this method has been shown to be more accurate in defining AKI than by estimating a baseline by solving the MDRD study equation for creatinine, it may overestimate AKIN stage 1.¹¹ The higher rates of AKI by both criteria seen in the present study should be placed in this context.

Evidently, the AKIN criteria were more sensitive at determining patients as having AKI. The main question that arises is whether capturing those additional patients and categorizing them as having AKI is clinically relevant in this population. Among the few subtle differences between the AKIN and the RIFLE is the application of a small absolute increase in serum creatinine (0.3 mg/dl) in a 48-hour period

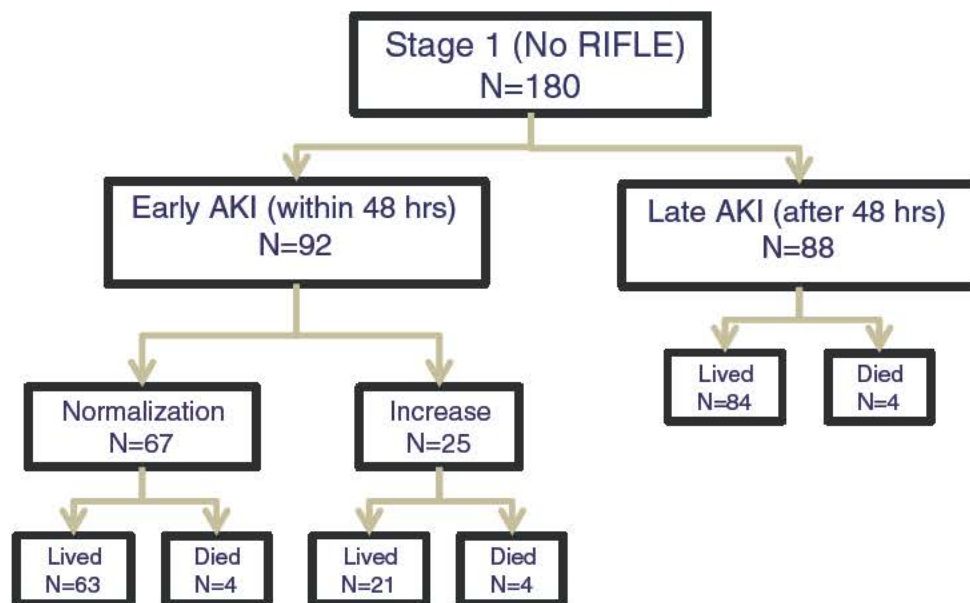


Figure 5. Consort diagram of cohort with acute kidney injury (AKI) based on the Acute Kidney Injury Network (AKIN) classification but not the risk, injury, failure, loss, and end-stage criteria (RIFLE).

compared to a relative increase in serum creatinine (50% increase from baseline) required by the RIFLE criteria. Lopes et al¹⁵ recently reported in a general ICU population that the AKIN criteria, although more sensitive, did not improve the ability of the RIFLE criteria in predicting in-hospital mortality.

On the contrary, our analysis demonstrates that the predictive value of the AKIN criteria for mortality is significantly higher than the RIFLE (Figure 3).

Furthermore, what the report by Lopes et al lacks is an analysis of the cohort that received the diagnosis of AKI by the AKIN criteria who were missed by

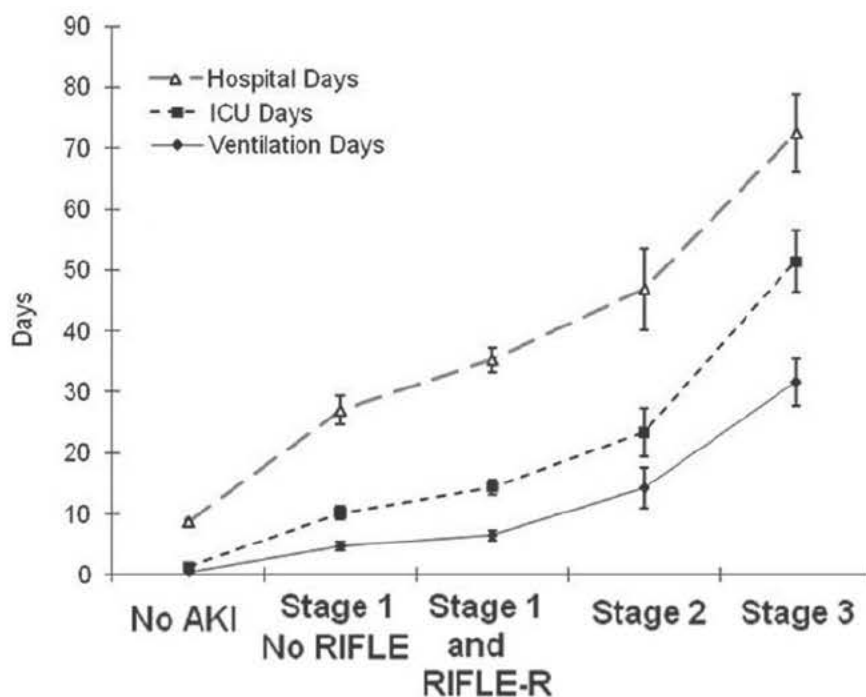


Figure 6. Ventilator days, intensive care unit (ICU) length of stay, and hospital length of stay by Acute Kidney Injury Network (AKIN) stages.

the RIFLE criteria. Figure 1 depicts that this cohort (AKIN stage 1, no RIFLE) has a similar mortality rate as those with RIFLE-Risk and AKIN stage 1. However, on univariate analysis, this cohort has an 8-fold higher likelihood of death when compared to those who do not have AKI by either classification. Additionally, both ICU LOS and hospital LOS are significantly higher (Figure 6). Evidently, this is a clinically relevant cohort of patients. An even closer look at this cohort does not reveal any differences between those who were diagnosed “early” (within 48 hours of admission) and later in the hospital course (Figure 5). There is also no significant difference in mortality between those admitted with a slightly increased levels of serum creatinine and “normalize” and those who have an increase during the course of the first 48 hours ($P = .13$). These findings stand in contrast to work performed in patients admitted to a general medicine ward in which patients with an increased level of creatinine that fell by 0.3 mg/dl in the first 48 hours had a lower mortality than patients who had sustained, fully reversible or partially reversible AKI.¹⁶ Our findings suggest that even a slightly increased level of creatinine that rapidly returns to normal may have prognostic significance in the burn population.

Overall, mortality associated with AKI is much higher than those without AKI (21 vs 1%, $P < .0001$) and increases drastically with each increase in AKIN stage as demonstrated by Figure 1. These results are consistent with recent published reports in the burn population where mortality among those with AKI based on RIFLE has been reported between 14 and 34%.^{5,7,8,13,14} In addition, each AKIN stage was found to be an independent predictor of mortality on multivariate analysis, suggesting that despite being covariate with age, %TBSA, and ISS, AKIN staging provides additional prognostic information not contained within these parameters. This is not entirely true for the RIFLE criteria. Comparing the odds ratios from two separate regression models (Tables 4 and 5) emphasizes the difference between the two classification systems.

As a retrospective review, this study has its inherent limitations. The most important limitation, AKIN staging, which was designed to be applied prospectively, had to be determined retrospectively from available medical records. The various issues with applying these criteria retrospectively has been previously reported.¹⁷ One such issue, discussed previously, deals with how the baseline serum creatinine is determined for each patient. The standard is to use the patient’s preinjury serum creatinine as the baseline, but given that we are a referral center, these were not available. Instead, the baseline creatinine

was estimated based on the lowest measured serum creatinine in the first 7 days of hospitalization whenever possible. This is a departure from previous reports where the baseline creatinine was determined through backcalculation with the MDRD equation.^{8,13} We chose against routinely using backcalculated serum creatinine based on a recent report that demonstrated that this method may overestimate baseline creatinine and thus result in underreporting of disease prevalence.¹¹ An alternative method would be to use the lowest measured creatinine during the entire hospital stay. However, burn patients are known to lose significant muscle mass and thus using their lowest hospitalized creatinine would likely overestimate the prevalence of AKI.¹⁸

Another limitation of this study was that the urine output component of the AKIN and RIFLE criteria was not applied because the charting was incomplete in the data set. It is unclear how many more patients would have met the urine output criteria without meeting the serum creatinine criteria. Furthermore, our study involved a large percentage of military personnel ($N = 696$) who were burned in support of combat operations in Iraq and Afghanistan. This population may not be generalizable to the burn population as a whole. Despite these limitations, our data indicate that using the AKIN criteria to classify those with AKI identifies an important cohort of patients.

CONCLUSION

AKI is common in burn patients. The AKIN staging criteria are more sensitive in identifying a cohort of patients with mild AKI that is more at risk for morbidity and mortality when compared to the RIFLE criteria. Evidently, prospective studies validating the AKIN criteria are warranted. A prospectively validated staging system will be useful in helping to characterize severity of disease while allowing easier interpretation of the effects of interventions in future prospective clinical trials.

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