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Acute Kidney Injury (AKI) is Surprisingly Common and a Powerful Predictor of Mortality in Surgical Sepsis

Laura E. White, MD¹, Heitham T. Hassoun, MD^{1,2}, Azra Bihorac, MD³, Laura J Moore, MD^{1,4}, Matt Sailors^{1,5}, Bruce A. McKinley^{1,5}, Alicia Valdivia¹, and Frederick A. Moore, MD^{1,5}

¹Department of Surgery, The Methodist Hospital and Research Institute, Houston, TX

²The Methodist DeBakey Department of Cardiovascular Surgery, Houston, TX

³Division of Critical Care Medicine, Department of Anesthesiology, The University of Florida College of Medicine, Gainesville, FL

⁴The Department of Surgery, The University of Texas Health Science Center, Houston, TX

⁵Department of Surgery, The University of Florida College of Medicine, Gainesville, FL

Abstract

Background—Acute kidney injury (AKI) is a common and often catastrophic complication in hospitalized patients, however the impact of AKI in surgical sepsis remains unknown. We utilized RIFLE (Risk-Injury-Failure-Loss-End stage) consensus criteria to define the incidence of AKI in surgical sepsis and characterize the impact of AKI on patient morbidity and mortality.

Methods—Our prospective, Institutional Review Board-approved sepsis research database was retrospectively queried for the incidence of AKI by RIFLE criteria, excluding those with chronic kidney disease. Patients were grouped into sepsis, severe sepsis and septic shock by refined consensus criteria. Data including demographics, baseline biomarkers of organ dysfunction (BOD), and outcomes were compared by Student's *t* test and χ^2 test. Multivariable regression analysis was performed for the effect of AKI on mortality adjusting for age, gender, African-American race, elective surgery, APACHE II score, septic shock vs. severe sepsis, and sepsis source.

Results—During the 36-month study period ending December 2010, 246 patients treated for surgical sepsis were evaluated. AKI occurred in 67% of all patients and 59%, 60%, and 88% of patients with sepsis, surgical sepsis, and septic shock, respectively. AKI was associated with Hispanic ethnicity, several baseline BODs, and a greater severity of illness. Patients with AKI had fewer ventilator-free and ICU-free days and a decreased likelihood of discharge to home.

Correspondence to: Laura E. White, M.D. The Methodist Hospital Department of Surgery 6550 Fannin St. SM 1661 Houston, TX 77030 Telephone: (713) 441-5155 Fax: (713) 790-2872 LWhite@tmhs.org.

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Author Contributions

Laura E. White: Literature search, data collection, data analysis, writing, figures; Heitham T. Hassoun: Study design, data analysis, data interpretation, writing; Azra Bihorac: Study design, literature search, data analysis, data interpretation; Laura J Moore: Study design, data interpretation; Matt Sailors: Data collection, data analysis, data interpretation; Bruce A. McKinley: Study design, data collection, data analysis; Alicia Valdivia: Data collection; Frederick A. Moore MD: Study design, data interpretation, writing.

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Morbidity and mortality increased with severity of AKI, and AKI of any severity was found to be a strong predictor of hospital mortality (OR 10.59, 95% CI 1.28-87.35, $p=0.03$) in surgical sepsis.

Conclusion—AKI frequently complicates surgical sepsis, and serves as a powerful predictor of hospital mortality in severe sepsis and septic shock.

Level of Evidence—Level III

Keywords

Sepsis; Surgical Sepsis; Acute Kidney Injury; Epidemiology; Multiple Organ Failure

Introduction

Despite advancements in renal replacement therapy (RRT), acute kidney injury (AKI) is a common complication with adverse outcomes in hospitalized patients. AKI affects 25-67% of the critically ill and independently elicits a 30-60% mortality rate, even after normalization for illness severity [1-3]. Much of this increased risk of death is due to remote organ injury, as AKI occurs most often in the setting of multiple organ failure (MOF) and is independently associated with extra-renal organ dysfunction, regardless of requirement for RRT [2].

Sepsis is a notorious inciting factor for AKI, attributing to nearly half of all cases and resulting in the highest risk of death above all other etiologies [3, 4]. Surgical sepsis, defined as sepsis requiring surgical intervention for source control or sepsis occurring within 14 days of a surgical procedure, carries a mortality rate of 30-40% and occurs more frequently than other dreaded postoperative complications such as pulmonary embolism or myocardial infarction[5, 6]. Surgical trauma, induction of anesthesia, and the frequent requirement for emergent surgical source control all contribute to the formidable clinical challenge of surgical sepsis and provide a unique stimulus for AKI.

In contrast to sepsis where defined consensus criteria have been used for nearly 20 years, AKI lacked a standard definition until 2004 when the Acute Dialysis Quality Initiative group published consensus RIFLE (Risk, Injury, Failure, Loss, and End-stage Kidney) criteria[7]. Recent data in surgical patients utilizing consensus criteria demonstrates that increasing severity of AKI is associated with worse outcomes after trauma, cardiac surgery or major abdominal surgery[8-10] and the effect of AKI extends well beyond discharge to impact long term mortality[11].

Extensive research describes AKI in diverse populations, however no prior studies have specifically examined the epidemiology and impact of AKI in surgical sepsis. Our surgical sepsis research team has maintained a unique prospective database of patients with surgical sepsis defined by consensus criteria[12-14]. We hypothesized that AKI is a frequent complication of surgical sepsis that serves as a harbinger for increasing patient morbidity and mortality. To address this hypothesis, we utilized the well-validated RIFLE criteria to define the incidence of AKI in surgical sepsis in a retrospective fashion and to further characterize the association of AKI with patient morbidity and mortality.

Methods

Study Site and Patients

This study was conducted at The Methodist Hospital, a 948-bed, academic tertiary referral hospital located in the Texas Medical Center in Houston, Texas. The general surgery intensive care unit (GSICU) is a 27-bed, non-cardiac unit serving a diverse group of surgical

patients including critically ill general, vascular, oncologic, transplant, thoracic, orthopedic, plastic, urologic, and head and neck surgical patients. All patients are screened for sepsis twice daily using our validated physiologic sepsis screening tool [15]. Once identified, all patients are immediately treated with an evidence-based computerized clinical decision support (CCDS) protocol including goal-directed fluid resuscitation with time-appropriate interventions based on clinical consensus and evidence-based guidelines for the management of sepsis[16, 17]. With informed consent, all GSICU patients managed with this protocol have data acquired for our surgical sepsis research database. Data collection and entry are performed prospectively by a research nurse and informaticist, respectively, and all cases are reviewed and maintained by the surgical sepsis research team. Data reports are coded and password protected to ensure patient confidentiality. The sepsis research database and current study is maintained with approval of The Methodist Hospital Research Institute Institutional Review Board.

Study Design and Data Collection

Our study population includes GSICU patients entering into the surgical sepsis database from January 1, 2008 to December 31, 2010. All study patients are entered into the database after diagnosis of sepsis, severe sepsis, or septic shock based on our modification of the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) Consensus Conference definitions[18, 19]. The database was queried for patient demographics, baseline (at time of sepsis diagnosis) biomarkers reflecting organ dysfunction (listed in Table 2), source of infection, acuity of operation, Acute Physiology and Chronic Health Evaluation (APACHE) II score, and sequential organ failure assessment (SOFA) score as previously described [19]. Outcomes included ventilator-free days, dialysis-free days, ICU-free days, secondary infections, early and late MOF, ICU mortality, hospital mortality and discharge disposition.

Methods for defining sources of infection, secondary infections, acuity of operation, APACHE-II scores, SOFA scores (renal component excluded), early and late MOF (Denver MOF score), ICU-free days, dialysis-free days and ventilator-free days were used as previously described[19]. Other outcomes included ICU mortality, hospital mortality, and discharge disposition: patients who were discharged to “other” included those transferred to a long-term acute care (LTAC) facility or a skilled nursing facility (SNF).

AKI was defined by applying RIFLE criteria on prospectively collected serum creatinine (SCr) values for all patients in the surgical sepsis database. Patients with AKI were stratified into either having AKI or no AKI according to the severity determined by comparing the highest SCr with the reference SCr. For the reference SCr we used the SCr prior to admission (if within six months of admission, n=130) when available and for all others we used the lowest measured SCr at the day of hospital admission (n=116). The RIFLE creatinine criteria were used, in which “Risk” encompasses an increase in SCr of 50%, “Injury” includes an increase in SCr of 100%, and “Failure” captures an increase in creatinine of 200% (or a SCr 4mg/dl which represents an acute change of 0.5mg/dl).

To identify patients with chronic kidney disease (CKD), we performed review of all admission notes (LW and AB) to exclude all patients with documented history of CKD prior to admission. Among patients without history of CKD on admission we excluded those with a reference estimated glomerular filtration rate (eGFR) 60ml/min/1.72m² (calculated by applying CKD-EPI equation on reference sCr (n=26) [20]. Additional specific exclusion criteria used during review of admission notes were diagnosis of end stage renal disease (ESRD), obstructive uropathy, urosepsis, presence of only one kidney (congenital or acquired), patients with previous surgical bladder reconstruction, and patients with previous organ transplantation (n=9).

Statistical Analysis

In comparing two study groups, a two-tailed student's *t* test was used for continuous data. If the assumptions for this test were not met, the appropriate test (Mann-Whitney U test) was used. For univariate analysis of categorical variables we used Pearson χ^2 analysis or Fisher's exact test as appropriate. For categorical variables, a multiple logistic regression analysis was performed to determine an association between AKI and in-hospital mortality, adjusting for age, gender, African-American race, elective surgery, APACHE II score, septic shock vs. severe sepsis, and sepsis source (abdominal vs. respiratory vs. other). The goodness-of-fit of the logistic regression models was assessed with the Hosmer-Lemeshow test, and c-statistics evaluated the discriminatory capability of the models. For non-categorical variables, linear regression models were fitted to compare the effect of AKI on the length of ICU and ventilator-free periods after adjusting for all other variables as above. Least squares means were compared for the AKI-adjusted multiple regression models. The coefficient of determination, R^2 , was calculated as an indicator of the proportion of variability explained by each model. Diagnostic plots were examined to assess the assumptions of the regression models, and no serious departures from the assumptions were observed. All significance tests were 2-sided, with an α of 0.05, which we considered to be statistically significant. All analyses were performed using SAS (v.9.2, Cary, N.C.).

Results

During the 36-month study period, a total of 246 patients who did not meet exclusion criteria were treated for surgical sepsis. Most patients presented with severe sepsis (58%) or septic shock (24%) compared to sepsis (18%). When defined by RIFLE criteria, AKI occurred in 65% of all patients with surgical sepsis. When stratified by sepsis severity, AKI affected 59%, 59%, and 86% of patients with sepsis, surgical sepsis, and septic shock, respectively. AKI developed within the first 7 days of resuscitation in the majority (80%), and 17% had AKI at the time of sepsis diagnosis and ICU admission.

Patients who developed AKI were 59 years of age on average, mostly women (55%) and mostly caucasian (70%) (Table 1). The most common site of infection was the abdomen (70%) and most patients underwent emergency surgery (67%). There were no significant differences in patient age, gender, race, pre-existing conditions, presumed infection sites and acuity of operation amongst those who developed AKI compared to those who did not.

Patients with AKI were more likely to have a lower mean arterial pressure (MAP) at time of sepsis diagnosis compared to those without AKI (Table 2). Patients with AKI also had higher serum blood urea nitrogen (BUN), creatinine, lactate, INR, Fibrinogen, D-Dimer, and TSH levels and lower CO_2 , T_3 , T_4 and pH levels compared to those who did not develop AKI. Additionally, patients with AKI had a greater severity of illness with higher APACHE II (27 ± 1 vs 21 ± 1 , $p < 0.001$) and non-renal SOFA (6 ± 0 vs 4 ± 0 , $p < 0.001$) scores.

The overall hospital mortality rate for surgical sepsis was 17%. Patients with sepsis had the lowest mortality rate (7%) followed by severe sepsis (11%) and septic shock (37%). For all patients, AKI was associated with significantly fewer ventilator-free (18 ± 1 vs 25 ± 1 , $p < 0.001$), dialysis-free (22 ± 1 vs 28 ± 0 , $p < 0.001$), and ICU-free days (14 ± 1 vs 21 ± 1 , $p < 0.001$) (Table 3). AKI was associated with an increase in secondary infections, early MOF, ICU mortality (17% vs 1%, $p < 0.001$) and hospital mortality (24% vs 2%, $p < 0.001$), and were less likely to be discharged home (42% vs 63%, $p < 0.001$).

Nearly half (48%) of all patients with AKI had Failure and 30% were categorized as having Risk and 22% had Injury (Table 4). Patients with the most severe AKI (Failure) had fewer ventilator-free and ICU-free days than patients with lesser AKI, as well as a higher

incidence of secondary infections. The hospital mortality rate for patients with the mildest form of AKI (Risk) was 4% but in patients with Injury and Failure, mortality rates were 25% and 36%, respectively.

On multivariable logistic regression analysis, AKI was found to be a strong predictor of hospital mortality (OR 7.12, 95% CI 1.35-37.58, $p=0.03$) in patients with severe sepsis and septic shock (Table 5). Other independent predictors were age (OR 1.04, 95% CI 1.01-1.07, $p=0.02$) and APACHE II score (OR 1.13, 95% CI 1.06-1.20, $p<0.0001$). On multivariable linear regression analysis, AKI was also found to be a significant independent predictor of fewer ventilator-free (Difference between means = 3.8 days; 95% CI 0.9-6.6, $p=0.0097$) and ICU-free (3.0 days; 95% CI 0.6-5.4, $p=0.0162$) days (Table 6).

Discussion

AKI remains one of the most challenging public health problems in modern medicine, affecting 7% of all hospitalized patients and up to two-thirds of the critically ill[1, 21]. Despite improvements in RRT and advances in supportive care, the significant morbidity and mortality associated with AKI has remained unchanged over the past several decades[4]. This is likely due to the fact that AKI rarely occurs in isolation and emerging evidence suggests that altered homeostasis during AKI leads to an activated immune response and distant organ dysfunction[22].

Across the spectrum of medical and surgical admissions, AKI most commonly occurs as a consequence of shock, sepsis, major surgery, or hypovolemia[3, 23]. Sepsis is a well-established leading risk factor for AKI[23-25], and mortality rates in patients with both AKI and sepsis are much greater than in patients with either AKI or sepsis alone, particularly in the setting of MOF[26]. Surgical trauma, induction of anesthesia, and the frequent requirement for emergent surgical source control all contribute to the formidable clinical challenge of surgical sepsis and provide a unique stimulus for AKI.

We hypothesized that AKI is a frequent complication of surgical sepsis that predicts increasing patient morbidity and mortality. To address this hypothesis, we utilized the well-validated RIFLE criteria to identify the incidence of AKI in surgical sepsis and define the impact of AKI on hospital mortality. In the current manuscript, we identify that in surgical sepsis, 1) AKI occurs in **67%** of all patients, 2) patients who develop AKI have a significantly higher morbidity and mortality, 3) patients with AKI who survive are less likely to be discharged home, 4) patients with renal failure have a higher morbidity and mortality than patients with less severe AKI, and 5) AKI serves as a powerful predictor of hospital mortality in patients with severe sepsis and septic shock.

With the recent introduction of the RIFLE classification for AKI, the adverse effects of small changes in SCr have begun to be recognized and systematically studied. Hence, the term AKI has been proposed to replace “acute renal failure” and encompass the entire spectrum of the syndrome, from minor changes in renal function to the requirement for RRT[27]. Initial studies using established definitions of AKI demonstrate that among medical patients with sepsis, progression from severe sepsis to septic shock correlates with a stepwise increase in severity of AKI, increasing RIFLE stages of AKI correlate linearly with hospital mortality, and AKI of any severity is an independent predictor of mortality[28, 29]. We found that in surgical sepsis, progression to renal failure was associated with significantly higher morbidity and mortality compared to milder AKI and no AKI at all, which parallels data after trauma, cardiac surgery, or major abdominal surgery[8-10].

While we used RIFLE criteria to identify AKI, the Acute Kidney Injury Network (AKIN) criteria, introduced by the Acute Dialysis Quality Initiative (ADQI) in 2007 [30] have several key refinements of the RIFLE definition. AKIN criteria include an increase in the absolute value of SCr of $\geq 0.3\text{mg/dl}$ for Stage 1 AKI (RIFLE “Risk” category) as well as a 48-hour time window for detection of changes in kidney function (compared to 7 days for RIFLE criteria). In large epidemiological studies, AKIN and RIFLE criteria are found to have strikingly similar efficacy in clinical application, including diagnosis of AKI, severity classification and association with mortality [31]. We chose RIFLE criteria due to the 7 day period which would recognize patients who have a slower rise in creatinine (>48 hours) during surgical sepsis who would otherwise be missed with the AKIN classification. Furthermore, to address potential limitations, we compared the RIFLE criteria to the new expanded RIFLE consensus criteria[32] which include an increase in SCr of $\geq 0.3\text{mg/dl}$ and queried our surgical sepsis database for the incidence of AKI. We found the sensitivity, specificity, and accuracy of both the RIFLE and expanded RIFLE criteria to be roughly equivalent predictors of mortality (data not shown).

We did not see an increase in early or late MOF in patients with AKI during surgical sepsis, however recent data suggests that the late peak in MOF has largely disappeared, primarily due to the implementation of evidence based guidelines [33]. We believe that a new phenotype of MOF has emerged: the persistent inflammatory/immunosuppression catabolism syndrome (PICS)[34]. PICS is characterized by prolonged ICU stays, manageable organ dysfunctions, and recurrent infections with mild the systemic inflammatory response syndrome (SIRS) that rarely induces septic shock. Despite adequate nutritional support, patients remain persistently catabolic, display signs of poor wound healing and muscle wasting, and are ultimately discharged to LTACs where they suffer indolent death. We hypothesize that AKI predisposes patients to develop PICS, as these patients had prolonged hospital stays, increased morbidity, and were less likely to be discharged home. Clinical data also indicates that even small changes in SCr can portend dramatic increases in patient morbidity and mortality and the effect of AKI extends well beyond initial hospitalization to impact long term mortality, extending over a decade beyond hospital discharge[11].

The relationship between AKI and PICS remains undefined, however data suggest that immune dysregulation may play a key role. Patients with PICS have a persistent acute phase response (characterized by elevated CRP and undetectable pre-albumin levels) with elevated white blood cell counts but with a very low percentage of lymphocytes[35]. Recent laboratory studies demonstrate the long-term emergence of myeloid derived suppressor cells (MDSCs) during sepsis: immature innate immune cells that suppress lymphocytes but simultaneously cause persistent inflammation. We believe they play central role in PICS and this is a current focus of our ongoing research related to MOF pathogenesis[35]. Similarly, emerging evidence suggests that altered homeostasis during AKI leads to an activated innate and adaptive immune response and distant organ dysfunction [22, 36-40]. These data challenge traditional concepts of the role of the T lymphocyte in innate and adaptive immune responses and suggest that AKI should not be regarded as a treatable component of MOF but as an independent contributor to immune dysregulation and mortality.

Limitations of our study include its retrospective nature and relatively small sample size, however the well-defined selection criteria for both surgical sepsis and AKI and combined with a rigorous method for prospective data collection ensure a high quality of data to characterize AKI in surgical sepsis. In our patients, it can also be clinically challenging to distinguish pre-renal azotemia from true AKI, however the RIFLE criteria allow for the development of AKI over a 7-day period, thus capturing AKI occurring after adequate volume resuscitation, a clinical outcome target which has been validated by our CCDS

system in our patients with surgical sepsis[5]. Our patients averaged 59 years of age and were mostly Caucasian; a demographic which may not mirror all other surgical ICUs. Additionally, the clinical diagnosis of severe sepsis and septic shock includes evidence of acute organ decompensation such as renal dysfunction, however the RIFLE classification is more inclusive. The ACCP/SCCM SCr criteria for renal dysfunction in severe sepsis/septic shock specifies an increase in SCr 0.5mg/dl from baseline measured within 24 hours of sepsis resuscitation as opposed to the 1.5x increase for RIFLE[18, 19]. Therefore RIFLE criteria captures more patients with AKI who had reference creatinines <1.0mg/dL, commonly found in elderly patients and women. Accordingly, RIFLE criteria identified a high incidence of AKI (59%) in patients with surgical sepsis who lacked evidence of baseline organ dysfunction per the ACCP/SCCM definitions.

In conclusion, AKI frequently complicates surgical sepsis and serves as a powerful predictor of patient morbidity and mortality. Using defined consensus criteria to identify early AKI may facilitate goal-directed therapy and reduce morbidity and mortality in patients with surgical sepsis.

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Table 1

Characteristics of Study Cohort

	All Patients	
	No AKI (n=85)	AKI (n=161)
Age (years)	58±2	59±1
Male gender n(%)	31 (36)	72 (45)
Race n(%)		
Caucasian	67 (79)	113 (70)
African-American	12 (14)	34 (21)
Asian	3 (4)	6 (4)
Other	3 (4)	8 (5)
Ethnicity n(%)		
Hispanic	7 (8)	17 (11)
Non-hispanic	78 (92)	144 (89)
Pre-existing Conditions n(%)		
Smoker	10(12)	33(20)
ETOH User	3(4)	11(7)
CNS	18(21)	36(22)
Pulmonary	20(24)	60(37)
Cardiac	29(34)	68(42)
Diabetes	22(26)	38(24)
Vascular	4(5)	10(6)
Liver	1(1)	0(0)
GI	7(8)	15(9)
Immunocompromised	18(21)	46(29)
Coagulopathy	5(6)	17(11)
Any of above	54(64)	127(79)
Presumed Infection Site		
Abdomen	64 (75)	113 (70)
Pulmonary/thoracic	5 (6)	15 (9)
Wound/soft tissue	10 (12)	13 (8)
Line infection	4 (5)	10 (6)
Other	2 (2)	10 (6)
Elective Surgery n(%)	27 (32)	53 (33)
Emergency Surgery n(%)	58 (68)	108 (67)

*p<0.05 for AKI vs. No AKI, all continuous variables expressed as mean ± SEM (standard error of the mean)

Table 2**Baseline Evidence of Organ Dysfunction**

	No AKI n=85	AKI n=161
Vital Signs (mean±SEM)		
Temp (°C)	37.5±0.2	37.5±0.1
Heart Rate (bpm)	112±2	113±2
Resp Rate (bpm)	23±1	23±1
MAP (mmHg)	86±2	80±1 *
BOD		
WBC (k/μL)	17.54±1	14.7±1
Hemoglobin (g/dL)	10.2±0.2	10±0.2
Sodium (mEq/L)	136±1	136±1
Potassium (mEq/L)	4.7±0.9	4.1±0.1
Chloride (mEq/L)	103±1	107±2
CO ₂ (mEq/L)	25±1	22±0 †
BUN (mg/dL)	17±1	32±2 †
Creatinine (mg/dL)	0.8±0	1.5±0.1 †
Lactate(Mean)(mg/dL)	1.6±0.1	3.5±0.3 †
Ph	7.39±0.01	7.34±0.01 †
PaO ₂ /FIO ₂	251±22	223±17
T. Bilirubin (mg/dL)	1.1±0.1	2.7±1
Alk Phos (U/L)	132±13	157±13
AST (U/L)	35±6	59±12
ALT (U/L)	49±8	98±25
BNP (pg/mL)	112±17.8	181.9±52.9
INR	1.5±0	1.7±0.1 *
Platlet Count (k/μL)	269±17	233±11
Fibinogen (mg/dL)	180±33	282±27 *
D-Dimer (μg/L)	4.6±0.4	6.85±0.53 *
T3 (ng/dL)	74±3	65±3 *
T4 (μg/dL)	6±0.2	5±0 *
TSH (mIU/L)	2.95±1.1	3.15±0.7 *
SIRS Severity	4±0	4±0
APACHE II (at 24 hrs)	21±1	27±1 †
SOFA_{non-renal} (at 24 hrs)	4±0	6±0 †

SEM=standard error of the mean, MAP=mean arterial pressure, BOD= biomarkers of organ dysfunction at time of sepsis diagnosis, BUN=blood urea nitrogen, SIRS=systemic inflammatory response syndrome, SOFA_{non-renal}=sequential organ failure assessment with renal score excluded; all continuous variables expressed as mean ± SEM (standard error of the mean)

†
p<0.001

*
p<0.05

Table 3

Patient Outcomes and Occurrence of RIFLE AKI

	No AKI (n=85)	AKI (n=161)
Ventilator-Free Days	25±1	18±1 [†]
Dialysis-Free Days	28±0	22±1 [†]
ICU-Free Days	21±1	14±1 [†]
Secondary Infections (%)	7	17 [*]
Early MOF (%)	1	19 [*]
Late MOF (%)	1	6
ICU Mortality (%)	1	17 [†]
Hospital Mortality (%)	2	24 [†]
Discharged Home (%) [†]	63	42 [*]
Discharged Other (%) [†]	37	58 [*]

all continuous variables expressed as mean ± SEM (standard error of the mean)

[†] p<0.001 for AKI vs. No AKI

^{*} p<0.05 for AKI vs. No AKI

[†] Data available for 205/246 patients

Table 4

Severity of AKI and Outcomes in Surgical Sepsis

	No AKI 85 (35%)	Risk 48 (30%)	Injury 35 (22%)	Failure 78 (48%)
Ventilator-Free Days	25 ± 1	21 ± 1 ^a	21 ± 2 ^a	15 ± 1 ^{a,b,c}
Dialysis-Free Days	28 ± 0	27 ± 1	25 ± 2 ^a	19 ± 1 ^{a,b,c}
ICU-Free Days	21 ± 1	17 ± 1 ^a	17 ± 2	12 ± 1 ^{a,b,c}
Secondary Infections n(%)	6 (7)	5 (10)	4 (11)	18 (23) ^a
Early MOF n(%)	1 (1)	5 (10) ^a	5 (14) ^a	21 (27) ^{a,b}
Late MOF n(%)	1 (1)	2 (4)	1 (3)	7 (9) ^a
ICU Mortality (%)	1	4	11 ^a	28 ^{a,b,c}
Hospital Mortality n(%)	2	4	26 ^{a,b}	36 ^{a,b}
Discharged Home n (%)	52 (63)	18 (39) ^a	14 (54)	19 (38) ^a

* $p=5.0 \times 10^{-7}$ by χ^2 test; all continuous variables expressed as mean ± SEM (standard error of the mean)

^a $p<0.05$ vs. No AKI

^b $p<0.05$ vs. Risk

^c $p<0.05$ vs. Injury by t-test

Table 5Multivariable Regression Analysis for Hospital Mortality, Ventilator-Free Days and ICU-Free Days^{*}

Predictors	Hospital Mortality <i>c-statistic</i> =0.894, <i>Hosmer-Lemeshow GOF</i> 0.812		Ventilator-Free Days <i>R</i> ² =34.5%		ICU-Free Days <i>R</i> ² =39.9%	
	OR (CI for OR)	p-value	Estimate (SE)	p-value	Estimate (SE)	p-value
Age (years)	1.04 (1.01, 1.07)	0.0208	−0.05 (0.04)	0.2368	0.003 (0.03)	0.9369
Male Gender (vs. Female)	1.38 (0.56, 3.42)	0.4910	0.14 (1.29)	0.9114	−0.44 (1.11)	0.6922
African-American Race (vs. Other)	0.86 (0.27, 2.75)	0.7983	−0.55 (1.58)	0.7270	−1.1 (1.38)	0.4282
Elective (vs. Emergent)	1.48 (0.54, 4.07)	0.4508	−0.81 (1.38)	0.5579	−1.44 (1.18)	0.2233
APACHE II	1.13 (1.06, 1.20)	<.0001	−0.53 (0.08)	<.0001	−0.57 (0.07)	<.0001
Septic Shock (vs. Severe Sepsis)	1.53 (0.60, 3.92)	0.3732	−0.71 (1.49)	0.6352	−0.97 (1.31)	0.4618
Sepsis Source						
(Abdominal vs. Other [*])	0.74 (0.25, 2.19)	0.5819	0.97 (1.57)	0.5384	0.79 (1.36)	0.5610
(Respiratory vs. Other [*])	1.08 (0.20, 5.78)	0.9280	−0.61 (2.59)	0.8154	−2.09 (2.27)	0.3593
RIFLE AKI (Yes vs. No)	7.12 (1.35, 37.58)	0.0208	−3.76 (1.44)	0.0097	−2.97 (1.22)	0.0162

OR= Odds ratio, CI=Confidence interval, GOF=goodness-of-fit

^{*} Other: UTI, central line infections, soft tissue, other

Table 6

Comparison of Adjusted Mean Ventilator-Free and ICU-Free Days Stratified by the Occurrence of RIFLE AKI^{*}

	RIFLE AKI Adjusted Mean (95% CL)	No RIFLE AKI Adjusted Mean (95% CL)	Difference Between Means (95% CL)	p-value[†]
Ventilator-Free Days	18.6 (17.1, 20.1)	22.3 (20.1, 24.6)	3.8 (0.9, 6.6)	0.0097
ICU-Free Days	14.9 (13.6, 16.2)	17.9 (16.0, 19.8)	3.0 (0.6, 5.4)	0.0162

CL=Confidence limit

^{*} Adjusted for all other variables (age, race, gender, elective vs. emergent surgery, severity of sepsis and sepsis source)

[†] p value for difference between means