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Rodrigo Cartin-Ceba
Eric N. Haugen
Remzi Iscimen
Cesar Trillo-Alvarez
Luis Juncos
Ognjen Gajic

Evaluation of "Loss" and "End stage renal disease" after acute kidney injury defined by the Risk, Injury, Failure, Loss and ESRD classification in critically ill patients

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R. Cartin-Ceba · E. N. Haugen ·
C. Trillo-Alvarez · O. Gajic
Multidisciplinary Epidemiology and Translational Research in Intensive Care (M.E.T.R.I.C), Mayo Clinic College of Medicine, Rochester, MN, USA

R. Iscimen
Department of Anesthesiology and Reanimation, Uludag University, Bursa, Turkey

L. Juncos
Department of Medicine,
Department of Physiology and Biophysics, University of Mississippi Medical Center, Jackson, MS, USA

R. Cartin-Ceba (✉)
Division of Pulmonary and Critical Care Medicine, Mayo Clinic College of Medicine, 200 First ST SW, Rochester, MN 55905, USA
e-mail: cartinceba.rodrigo@mayo.edu

Abstract *Purpose:* The Risk, Injury, Failure, Loss and ESRD (RIFLE) classification has been widely accepted for the definition of acute kidney injury (AKI); however, no study has described in detail the last two stages of the classification: "Loss" and "ESRD". We aim to describe and evaluate the development of "Loss" and "ESRD" in a group of critically ill patients. *Methods:* We conducted a retrospective analysis of cases prospectively collected from the Acute Physiology and Chronic Health Assessment (APACHE III) database. Subjects were consecutive critically ill patients >18 years of age admitted to three ICUs of two tertiary care academic hospitals, from January 2003 through August 2006, excluding those who denied research authorization, chronic hemodialysis therapy, kidney transplant recipients, readmissions, and admissions for less than 12 h for low risk monitoring. *Results:* 11,644 patients were included in the study. The median age was 66 (interquartile range, 52–76), 90% were Caucasians and 54% of the patients were male. Half of the patients developed AKI, and most of the patients were in the Risk and Injury stages. From the patients that developed AKI, a total of 1,065 (19%) patients required renal replacement therapy (RRT), 415 (39%) underwent continuous renal replacement therapy (CRRT) and 650 (61%) underwent intermittent hemodialysis. A total of 281 patients on RRT did not survive hospital discharge, 97 patients progressed to "Loss", and 282 patients progressed to "ESRD". After multivariable adjustment, the progression to "ESRD" was associated with higher baseline creatinine, odds ratio (OR) 1.19 per every increase in creatinine of 0.1 mg/dl (95% CI, 1.11–1.29) $P < 0.001$; and less frequent use of CRRT, OR 0.18 (95% CI, 0.11–0.29) $P < 0.001$. *Conclusion:* In this large retrospective study we found that almost 50% developed some form of AKI as defined by the RIFLE classification. Of these, 19% required RRT, and 4.9% progressed to "ESRD". "ESRD" was more likely in patients with elevated baseline creatinine and those treated with intermittent hemodialysis.

Keywords Creatinine · Acute kidney injury · Mortality · Intensive care unit

Introduction

Acute kidney injury (AKI) is a common and highly lethal problem faced in the intensive care unit (ICU) [1], with a reported incidence of 1–31% [2–4], and a mortality that ranges from 28 to 90% [3, 5–7]. This wide range in the incidence and the mortality is in part due to the near 35 different definitions of AKI [8]. To solve this problem, the RIFLE classification (acronym indicating **R**isk of renal dysfunction; **I**njury to the kidney; **F**ailure of kidney function, **L**oss of kidney function and **E**nd-stage renal disease [ESRD]) was designed in 2004 by the Acute Dialysis Quality Initiative Group (ADQIG) [9] in order to standardize the diagnosis of AKI in the ICU (Table 1). Since then, 24 studies of AKI in different populations have been reported in the literature [10–24]. However, most of the studies have relied the diagnosis of AKI based only on the creatinine (glomerular filtration rate [GFR]) criterion and not taking into account the urine output (UO) criterion which is part of the classification and increases the sensitivity of the diagnosis[9, 10]. Moreover, none of these studies reported the incidence of the two outcome-stages, "Loss" and "ESRD", after the development of AKI; consequently, there is scant information available regarding the outcome of AKI beyond the "Failure" stage utilizing the RIFLE classification. Such information is vital in order to accurately understand the impact of AKI in health costs, patient survival and quality of life, and also in providing information to patients and their families. In addition, the risk factors involved in the development of "ESRD" after an episode of acute kidney injury are important for prognostic and preventive strategies. Therefore, we carried out this retrospective cohort study of more than 10,000 patients admitted to medical and surgical ICUs in two tertiary care hospitals. Our primary objectives were to (a) describe the incidence and main outcomes of AKI in our patient cohort, as defined by the RIFLE classification utilizing both creatinine (GFR) and urine output criteria, (b) to examine the frequency with which these patients progressed to "Loss" and "ESRD", and (c) to identify risk factors that correlated with progression to "ESRD".

Methods

The Institutional Review Board of our institution approved the study protocol and waived the informed consent because this study was considered a minimal risk observational study. We performed a retrospective analysis of prospectively collected data in the Acute Physiology and Chronic Health Evaluation (APACHE) database, including consecutive critically ill patients (>18 years old of age) admitted from January of 2003 until August 2006 to three medical and surgical ICUs at the two Mayo Clinic hospitals in Rochester, MN. Patients on chronic renal replacement therapy (RRT), kidney transplant recipients, readmissions, admissions for less than 12 h for low risk monitoring, and those who denied research authorization for their medical records to be reviewed were excluded from the study. Patients (including patients that required RRT) were classified according to the maximum RIFLE class reached during their ICU stay [9, 25]. Patients who developed "Failure" or were started on RRT during the hospitalization were followed for at least 3 months to evaluate the progression to either "Loss" or "ESRD". The RIFLE class was determined based on the worst of either creatinine criterion or UO criterion (based on the hourly UO). The main outcomes measured were hospital mortality, renal recovery (defined as liberation from renal replacement therapy), and hospital and ICU length of stay (LOS).

In order to compare the characteristics between the patients that required RRT but did not progress to ESRD, we performed two different analyses: first, we excluded from the comparison all patients that did not survive hospital discharge because they did not have the possibility to progress to "ESRD" due to timing; secondly, we analyzed all RRT patients to evaluate for possible biases of not including the sickest patients that died during their hospitalization and were not able to develop ESRD. Risk factors identified in the development of "ESRD" were compared and analyzed in a multivariate analysis.

Survival analysis is initially reported for 28 days after admission for the following RIFLE categories: No AKI, Risk, Injury and Failure. Because "Loss" and "ESRD"

Table 1 Risk, Injury, Failure, Loss, and End-stage Kidney (RIFLE) classification [1]

Class	GFR criteria	Urine output criteria
Risk	Serum creatinine* × 1.5	<0.5 ml/kg/h × 6 h
Injury	Serum creatinine × 2	<0.5 ml/kg/h × 12 h
Failure	Serum creatinine × 3, or serum creatinine ≥4 mg/dl with an acute rise >0.5 mg/dl	<0.3 ml/kg/h × 24 h, or anuria × 12 h
Loss	Persistent acute renal failure = complete loss of kidney function >4 weeks	
End-stage kidney disease	End-stage kidney disease >3 months	

GFR Glomerular filtration rate
*Creatinine in mg/dl

contain only patients who at least survived 4 weeks, we also reported the long term survival (until May of 2009) for all RIFLE classes including only patients that at least survived 4 weeks after ICU admission.

Statistical analysis

All continuous data are summarized as medians (interquartile range, IQR) or means (standard deviation, SD). Categorical data are summarized as percentages. Difference in medians between groups was tested with the Wilcoxon sum rank test or the Kruskal–Wallis one-way analysis of variance where appropriate. Differences in proportions were compared utilizing the chi-squared test or the Fisher exact test. Standardized mortality ratios (SMRs) were calculated by dividing the number of observed deaths per group by the number of expected deaths per group (predicted by the APACHE III score).

The predictive accuracy of the multivariate models is reported as the area under the curve (AUC). Odds ratio (OR) and 95% confidence intervals (CI) were calculated and *P*-values of <0.05 were considered statistically significant. Survival analysis was performed with a Kaplan–Meier Curve and the log-rank test. JMP statistical software (version 8.0, SAS, Cary, NC) was used for all analyses.

Additional detailed information regarding the methodology of the study is provided in the Electronic supplementary material of the journal.

Results

A total of 16,009 consecutive patients were admitted during the study period. After exclusion of 4,365 patients (254 denied research authorization, 110 were readmissions, 550 were on chronic RRT, 27 were kidney transplant recipients, and 3,425 were admitted for less than 12 h for low risk monitoring), a total of 11,644 patients were included in the study. Baseline creatinine was available in 11,316 patients (97.2%). Half of the patients developed AKI, and most of the patients were in the Risk and Injury stages. A total of 326 patients (2.8% of the cohort) had a baseline creatinine $\geq$4 mg/dl. The diagnosis of acute kidney injury was based in 26% of the cases on the urine output criteria (59.3% of Risk patients, 74.8% of Injury patients and 10.3% of Failure patients). RRT was used in 9.1% of the total critically ill patients (19% of all patients that developed AKI), of whom 41 patients were in the Injury group, and the remainder (1,024 patients) were in the Failure group. Forty-one patients in the failure group did not require RRT for several reasons: patients were given comfort care only, not clinically indicated, or patients died before initiation of RRT. None of the patients in the Injury group progressed to "Loss" or "ESRD" because they either died or recovered their renal function.

The general characteristics and main outcomes of the patients according to the RIFLE classification group are described in detail in Table 2. A total of 1,065 patients required RRT, 415 (39%) underwent continuous renal replacement therapy (CRRT) and 650 (61%) underwent intermittent hemodialysis (IHD) (Fig. 1). A total of 281 patients that required RRT died before hospital discharge. From hospital survivors, 97 patients progressed to "Loss", and 282 patients progressed to "ESRD" (Fig. 1). Most of the patients that progressed to ESRD had advanced chronic kidney disease (CKD) according to their hospital admission stage of the CKD classification [26] (Fig. 2). A total of 74 patients in the Failure group did not progress and remained in the failure category because they died within 4 weeks (27 patients), their renal function improved and dialysis was withdrawn (26 patients), or because they were recipients of renal or liver transplant and their renal function subsequently improved (21 patients). A total of 453 patients were discharged on RRT which is only 7.9% of all the patients that developed AKI.

As seen in the univariate analysis (Table 3), patients in the "ESRD" group were slightly younger, presented significantly higher baseline creatinine levels and higher worst creatinine levels during their hospitalization, were less acutely ill as measured by the APACHE III predicted hospital mortality, were less likely to be treated with CRRT as opposed to IHD; and presented less oliguria upon presentation than the patients with renal recovery.

In the multivariate analysis of the risk factors for the development of "ESRD", we included the following variables in the two models: age, APACHE III ICU predicted mortality, baseline creatinine levels, CRRT actual utilization, and oliguria. We excluded worst creatinine during the hospitalization due to strong collinearity with baseline creatinine. We also excluded APS and mechanical ventilation due to strong collinearity with the predicted mortality. After adjustment, the progression to "ESRD" was associated with higher baseline creatinine, lower predicted mortality as predicted by APACHE III, and less frequent use of CRRT in both analyses. The results of the two models with their respective AUC are presented in Table 4.

The 28-day survival was significantly affected in the "Failure" group as compared to No AKI, Risk or Injury (Fig. 3). We were also able to follow the patients that survived at least 4 weeks after admission for 6 years and the survival according to the different categories of the RIFLE classification is described in Fig. 4. There was an

Table 2 General characteristics of 11,644 patients admitted to ICU from 2003 to 2006 according to the RIFLE classification

General characteristics	No AKI *N* (%) 5906 (50.7)	Risk *N* (%) 3347 (28.8)	Injury *N* (%) 1326 (11.4)	Failure *N* (%) 686 (5.9)	Loss *N* (%) 97 (0.8)	ESRD *N* (%) 282 (2.4)	Total 11644
Age (years) Median (IQR)	65 (50–75)	68 (55–78)	69 (55–79)	63 (51–74)	64 (52–74)	60 (48–73)	66 (52–76)
APS Median (IQR) $N = 11{,}568$	34 (24–47)	41 (29–57)	39 (29–53)	65 (46–89)	53 (43–72)	48 (37–65)	38 (27–53)
APACHE III Median (IQR) $N = 11{,}568$	47 (34–62)	56 (41–74)	55 (40–70)	81 (60–105)	70 (53–87)	62 (49–80)	53 (38–69)
Predicted hospital Mortality Mean (SD) $N = 11{,}568$	11.7 (1.6)	19 (2.2)	10.1 (1.8)	39 (2.9)	26 (2.3)	20 (2)	16.4 (2)
Actual Hospital Mortality, *N* (%)	330 (5.6)	491 (14.7)	119 (9)	281 (41)	N/A	N/A	1,218 (10.5)
Standardized mortality ratio (95% CI)	0.47 (0.44–0.49)	0.77 (0.73–0.80)	0.89 (0.8–0.97)	1.05 (0.98–1.11)	N/A	N/A	0.64 (0.62–0.66)
ICU LOS (days) Median (IQR)	0.5 (0.3–0.9)	0.8 (0.5–1.7)	0.9 (0.6–1.7)	1.5 (0.6–3.7)	1 (0.7–2.1)	0.9 (0.4–1.4)	0.7 (0.4–1.3)
Hospital LOS (days) Median (IQR)	2.9 (1.7–4.8)	3.4 (2–6)	3.6 (2.2–6)	5.9 (2.7–11)	5.7 (2.9–17)	4 (2.3–7.1)	3.22 (1.9–5.7)
Baseline creatinine $N = 11{,}316$ Median (IQR)	1 (0.9–1.3)	1.1 (0.9–1.3)	1.1 (0.9–1.3)	1.7 (1.2–2.8)	2 (1.3–3.6)	2.9 (1.7–3.8)	1.1 (0.9–1.4)
Worst creatinine (mg/dl) Median (IQR)	1 (0.8–1.1)	1.1 (0.9–1.4)	1.1 (0.9–1.6)	2.9 (1.9–4.3)	3.4 (1.8–5)	3.7 (2–5.3)	1.1 (0.8–1.6)
Body mass index (Kg/m^2) Median (IQR)	26 (23–30)	28 (24–34)	29 (25–35)	28 (24–33)	28 (24–33)	27 (24–32)	27 (24–32)
Male gender *N* (%)	3,207 (54)	1,790 (53)	732 (55)	410 (60)	60 (62)	162 (57)	6,361 (54)
Caucasians *N* (%)	5,295 (90)	3,068 (92)	1,217 (92)	609 (89)	83 (86)	248 (88)	1,0520 (90)
Post surgical status, *N* (%)	2,451 (41)	1,282 (38)	529 (39)	107 (16)	25 (26)	62 (22)	4,447 (38)
Mechanical ventilation *N* (%)	2,269 (38)	1,468 (44)	583 (44)	364 (53)	36 (37)	81 (29)	4,801 (41)
Days on mechanical ventilation, Median (IQR)	0.5 (0.4–1)	0.7 (0.8–1.2)	1 (0.9–1.5)	2 (1–3)	1.5 (1.2–2)	1.6 (0.8–2)	0.8 (0–1.1)
Renal replacement therapy, *N* (%)	0	0	41 (3.8)	645 (60.5)	97 (9.2)	282 (26.5)	1065 (9.1)
Renal replacement therapy days, Median (IQR)	0	0	3 (1–5)	4 (2–11)	43 (33–64)	374 (122–1045)	10 (2–72)
Initial therapy CRRT, *N* (%)	0	0	41 (10)	318 (76.5)	30 (7.3)	26 (6.2)	415 (3.6)

ICU intensive care unit, *IQR* interquartile range, *SD* Standard deviation, *APS* acute physiologic score, *APACHE* acute physiologic and chronic health evaluation, *LOS* length of stay, *CRRT* continuous renal replacement therapy, *AKI* acute kidney injury, *N/A* Not applicable, *CI* confidence interval, *ESRD* end stage renal disease

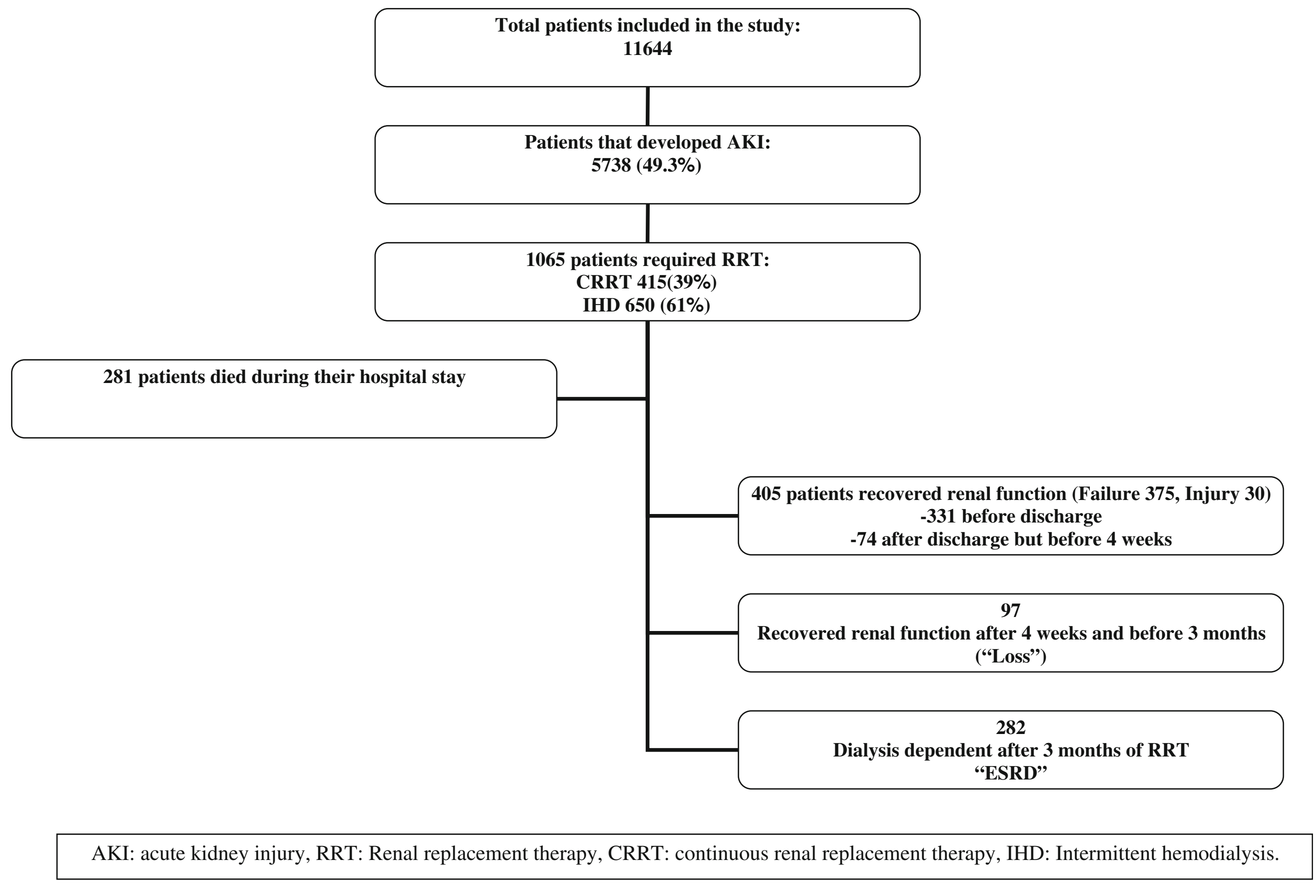

Fig. 1 Renal outcomes according to the RIFLE classification in 11,644 critically ill patients admitted to three ICUs from January 2003 through August 2006

early and sustained drop in survival in both the "Failure" and "Loss" groups during the long term follow-up period.

Discussion

Our study reports that AKI defined by the RIFLE classification complicated almost 50% of 11,644 consecutive critically ill patients admitted during a 4 year period to three different ICUs in the two Mayo Clinic hospitals in Rochester, MN. In this large cohort of ICU patients, we provide significant new information regarding the progression of AKI to "Loss" and "ESRD". Among all patients that developed AKI and after excluding 281 patients that died before hospital discharge, we found that nearly 8% of the survivors required prolonged RRT or permanent hemodialysis. This information is novel and represents an important outcome beyond survival, given the significant burden that this represents for the healthcare system, and the quality of life of the patients and their families. In addition, our study is one of the largest studies

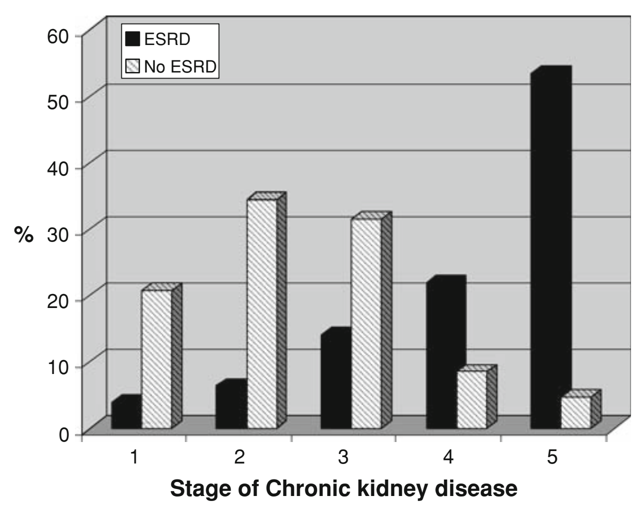

Fig. 2 Percentage of patients that progressed to end stage renal disease (ESRD) according to their hospital admission stage of chronic kidney disease

reporting the incidence of AKI in the ICU utilizing both the creatinine criterion (GFR) and the UO criterion of the RIFLE classification; moreover, the measured

Table 3 Comparison of "Renal Recovery", "ESRD" and "Death" patients among 1065 patients who required renal replacement during hospital stay

Variable	Renal recovery 502 (47.1) (Injury = 30, Failure = 375, Loss = 97) Median (IQR)	"ESRD" 282 (26.5) Median (IQR)	Hospital deaths 281 (26.4) Median (IQR)	*P* value
Age (years)	63 (51–74)	60 (48–73)	63 (51–73)	0.10
Baseline creatinine (mg/dl)	1.7 (1.2–3)	2.9 (1.8–4.6)	1.7 (1.2–2.6)	<0.001
Worst creatinine (mg/dl)	3.1 (1.7–4.6)	3.7 (2.1–5.3)	2.9 (2.1–3.9)	<0.001
Body mass index (kg/m^2)	28 (25–34)	27 (24–32)	27 (23–31)	0.11
APS	57 (42–77)	48 (37–64)	78 (56–105)	<0.001
APACHE III score	71 (55–93)	62 (49–80)	96 (72–123)	<0.001
Predicted APACHE III hospital mortality score %	10.7 (4–29)	5.3 (2.5–16)	39 (14–67)	<0.001
Mechanical ventilation days	2 (0–2.6)	1.6 (0.8–2)	2 (0–4)	<0.001
Hospital LOS (days)	6 (3.1–11.5)	4 (2.3–7)	5 (1.8–10.4)	<0.001
Variable	**Renal recovery *N* (%)**	**"ESRD" *N* (%)**	**Hospital deaths**	***P* value**
Caucasians	449 (89.4)	248 (88)	243 (86.5)	0.45
Male gender	289 (57)	162 (57)	181 (64)	0.23
Mechanical ventilation	224 (45)	81 (29)	176 (62.6)	<0.001
CRRT	203 (40.4)	26 (9.2)	186 (66)	<0.001
Postoperative status	98 (19.6)	62 (22.3)	34 (12)	0.40
Oliguria at diagnosis of AKI	299 (59)	142 (50.4)	240 (85)	<0.001

ICU intensive care unit, *IQR* interquartile range, *APS* acute physiologic score, *APACHE* acute physiologic and chronic health evaluation, *CRRT* continuous renal replacement therapy, *AKI* acute kidney injury, *ESRD* end stage renal disease

Table 4 Multivariate analysis of risk factors for the development of "ESRD" in patients that required Renal Replacement Therapy

Risk factor	Odds ratio and 95% CI (784 patients that survived hospital discharge)	AUC (95% CI)	*P* value	Odds ratio and 95% CI (all patients)	*P* value	AUC (95% CI)
Baseline creatinine (mg/dl)[a]	1.19 (1.11–1.29)	0.74 (0.71–0.82)	<0.001	1.2 (1.14–1.3)	<0.001	0.80 (0.78–0.83)
Predicted APACHE III ICU mortality	0.31 (0.10–0.89)		0.01	0.1 (0.03–0.2)	<0.001	
CRRT	0.18 (0.11–0.29)		<0.001	0.15 (0.1–2.4)	<0.001	
Age (years)[b]	0.98 (0.96–1.2)		0.1	0.98 (0.97–1.1)	0.13	
Oliguria	0.98 (0.69–1.39)		0.94	0.89 (0.63–1.24)	0.49	

CRRT continuous renal replacement therapy, *CI* confidence interval, *AUC* area under the curve

[a] Per 0.1 mg/dl increment

[b] Per year increment

baseline creatinine was available in >97% of the patients.

The incidence of AKI utilizing the RIFLE classification varies in the literature depending on the population studied. In ICU patients, our cohort reports similar incidence (49.3%) as compared to the incidence reported in a study of 85 critically ill patients by Herget-Rosenthal et al. [27]. However, the incidence found in our study differs from the 67% AKI incidence found by Hoste et al. [12] in one of the largest studies on AKI in ICU patients. Similar to our study, the latter study utilized both the UO and the GFR criteria; however, our lower incidence could be explained by the fact that we included only three ICUs with fewer surgical patients (38%), whereas the study by Hoste et al. included a more diverse ICU population with close to 60% of surgical patients. The higher risk of AKI in the surgical population is well known [18, 28], which was also found in the same study [12]. Recently, in a large cohort study by Ostermann and colleagues in more than 40,000 critically ill patients, the reported incidence of AKI was 36% [15]. This lower incidence is likely an underestimation explained by the fact that the UO criteria were not used in the determination of AKI in the aforementioned study.

The hospital mortality follows an escalating pattern when patients develop AKI and advance from Risk to Failure in most of the studies reported in the literature [12, 13, 19, 21]. Our study followed a similar pattern for all-cause hospital mortality with the exemption of Injury that presented a lower actual mortality than Risk. Bell and colleagues found a similar response for 30 day mortality

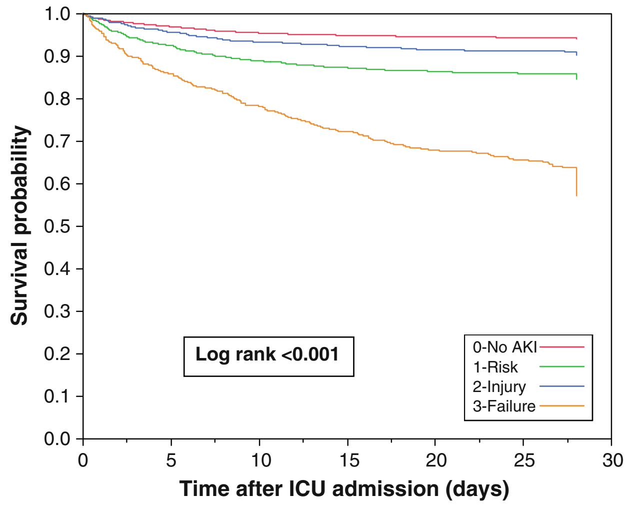

Fig. 3 Survival probability by RIFLE classification after 28 days of follow up

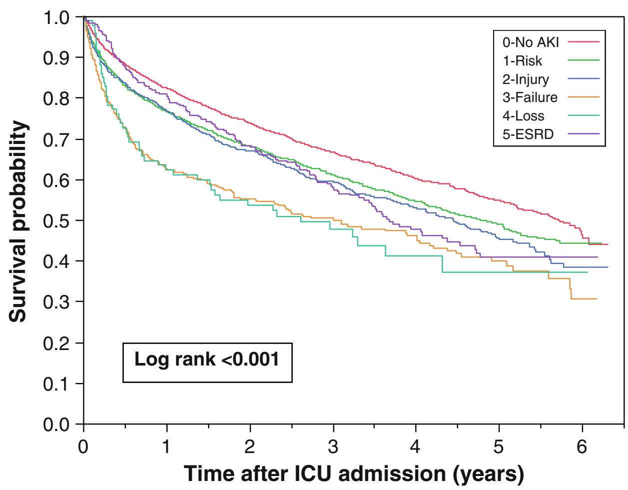

Fig. 4 Survival probability by RIFLE classification after 6 years of follow up

[14]. This discrepancy found in our study is likely explained by a lower severity of disease in this group as we can see from the lower predicted mortality calculated by their APACHE III scores. Furthermore, the diagnosis of AKI was based on the urine UO in 74.8% of Injury patients, and it has been shown that mortality rates of AKI stages defined by worst UO are consistently lower than for worst serum creatinine [10, 24, 29]. The actual mortality follows the predicted mortality in all groups of AKI defined by the RIFLE classification but does not match it very well. This is understandable because one would not expect that a measure of one organ system will provide accurate information on mortality, and the RIFLE classification was never intended to be a scoring system such as APACHE or SAPS [30, 31]. When comparing the SMRs, there is almost a linear increment in the different RIFLE stages in a similar trend as recently reported by Joannidis and collegues [29].

Our report of the incidence of Loss and ESRD after the development of AKI in the ICU is novel and significant. Bell et al. reported preexistent "Loss" and "ESRD" on ICU admission [14] and then compared their outcomes with patients that underwent RRT after the development of AKI. To the best of our knowledge, however, no prior study has reported the incidence of these two outcome stages of the RIFLE classification after the development of AKI in the ICU. In our study, 97 hospital survivors that required RRT remained on dialysis for at least 4 weeks and 282 patients became dialysis-dependent (progressed to "ESRD"). Variable results regarding renal recovery have been reported, but these studies are difficult to directly compare because different definitions of AKI and different definitions of renal recovery have been used [32]. Most of the studies have reported results similar to ours; that approximately 85–90% of surviving AKI patients are dialysis-independent upon hospital discharge [28, 32–36]. It is interesting to note that one of these studies, Bagshaw et al. [34], not only found renal recovery rates similar to those we found in our study, but they also found that pre-RRT creatinine levels were higher in the patients that remained dialysis-dependent after 90 days, similar to our findings of significantly higher baseline creatinine in the group of patients that progressed to ESRD. Similar results were also found by Ali et al., where renal recovery was more frequent in patients without underlying renal dysfunction as evidenced by normal baseline creatinine levels [23]. Together these studies suggest that the degree of preexisting renal impairment is a strong predictor of renal recovery.

There is an ongoing controversy as to which RRT modality is better suited for patients with AKI in the ICU. Historically, most of these patients were treated with IHD. However, IHD has various limitations which include a higher risk of hemodynamic instability and the possibility that this may induce further renal injury [37, 38]. Indeed, Ronco et al. [39] performed direct measurements of blood volume during IHD showing significant drops in circulatory blood volume and perfusion, which is known to be deleterious to the recovering kidney. To circumvent these limitations, many ICUs have adopted CRRT, which provides for a gentle yet effective "clearance" of solute and excess fluid. Despite the physiologic advantages of CRRT over IHD, it has been difficult to demonstrate that CRRT improves outcomes (survival or renal recovery). A large systematic review of 15 randomized clinical trials comparing these two methods of RRT reported no differences in hospital mortality, ICU mortality, hypotension or hemodynamic instability [40]. Our study, like previous ones (as described in a meta-analysis by Kellum et al. [41]) found that our sickest patients were usually started on CRRT. Even after including in the multivariate analysis all patients who died during their hospital stays, the patients who progressed to "ESRD" were less likely to have been treated with CRRT. While we can not prove a possible advantage of CRRT on renal recovery [28, 42–45], our observations suggest different case mix and different etiologies of AKI as a more likely explanation. Further prospective studies that address this important issue are necessary. In addition, our study also showed that the patients who were treated with IHD in general had higher serum creatinine at baseline; consequently, the difference in renal recovery may have been simply due to the possibility that renal regeneration is less likely in patients with CKD. In addition, there might be significant selection bias in these studies. If the clinician sees a patient with CKD and feels that the injury has now transitioned them to stage 5 CKD, they may be treated differently. Recent published data from a small cohort of patients with AKI in the ICU of our institution revealed that patients who underwent CRRT were younger, had greater APACHE II and were less likely to have chronic renal insufficiency; results that are mirrored in our study [46]. Our study also provided a 28-day survival follow up showing an early and sustained drop in survival in the "Failure group". In addition, we also presented a long term survival follow up where it was interesting to observe a sustained drop in survival in both the Loss and Failure groups.

We acknowledge several limitations. First, our study has a retrospective observational design with its inherent biases; however, our prospectively collected APACHE III database and our electronic medical records provide accurate information with urine output validated by the bedside nurse, and we have included a large sample size. Also, our study is limited by the predominantly Caucasian population seen at our institution. The study was performed in a tertiary referral center; therefore the results are difficult to generalize; moreover, our institution's practices may differ from other institutions. Finally, we included only baseline characteristics of the patients and we understand that other variables not collected during the ICU stay might have influenced the final outcomes.

In conclusion, in this retrospective study of 11,644 consecutive critically ill patients, we found that almost 50% developed some form of AKI as defined by the RIFLE classification. Of these, 19% required RRT, and 4.9% progressed to end-stage renal disease. "ESRD" was more likely in patients with elevated baseline creatinine and those treated with IHD.

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