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## RIFLE: association with mortality and length of stay in critically ill acute kidney injury patients

*Associação do RIFLE com letalidade e tempo de internação em pacientes críticos com lesão renal aguda*

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### ABSTRACT

**Objective:** To correlate the RIFLE classification with mortality and length of stay both in the intensive care unit and hospital.

**Methods:** A prospective, observational, longitudinal cohort study, approved by the Institution's Ethics Committee. Data were collected for all patients staying longer than 24 hours in the intensive care unit of Hospital Universitário Polydoro Ernani de São Thiago - Universidade Federal de Santa Catarina from September 2007 to March 2008, followed-up either until discharge or death. Patients were divided in two groups: with or without acute kidney injury. The acute kidney injury group was additionally divided according to the RIFLE and sub-divided according to the maximal score in Risk, Injury of Failure. Loss and End-stage classes were not included in the study. APACHE II and SOFA were also evaluated. The t Student and Chi-

Square tests were used. A  $P < 0.05$  was considered statistically significant.

**Results:** The sample included 129 patients, 52 (40.3%) with acute kidney injury according to RIFLE. Patients were more severely ill in this group, with higher APACHE and SOFA scores ( $P < 0.05$ ). Compared to the without kidney injury group, the kidney injury severity caused increased intensive care unit stay (Risk 25%; Injury 37.5%; Failure 62.5%) and in-hospital (Risk 50%; Injury 37.5%; Failure 62.5%) mortality, and longer intensive care unit stay ( $P < 0.05$ ).

**Conclusion:** The RIFLE system, according to the severity class, was a marker for risk of increased intensive care unit and in-hospital mortality, and longer intensive care unit stay. No relationship with in-hospital length of stay was found.

**Keywords:** Renal insufficiency, acute; Intensive care units; Creatinine; Hospital mortality; Length of stay; APACHE

### INTRODUCTION

Acute Kidney Injury (AKI) is a common medical condition in critically ill patients, and is well recognized for its impact in the intensive care unit setting. However, even largely acknowledged, there is a lack of AKI consensus and definition, with more than 30 different concepts counted for this illness. This multitude of concepts accounts for a variable AKI frequency both in single center (1-25%)<sup>(1,2-8)</sup> and multicenter trials (39-71%),<sup>(6)</sup> and mortality (19 to 90%).<sup>(2,3,6,9-20)</sup>

To establish an uniform AKI definition and scoring, the Acute Dialysis Quality Initiative (ADQI)<sup>(21)</sup> formulated in 2002 the RIFLE (Risk, Injury, Failure, Loss and End-stage kidney disease) classification.<sup>(2)</sup> RIFLE (Table

1) defines three grades of acute kidney injury – Risk (class R), Injury (class I) and Failure (class F) based on serum creatinine and urine output changes – and two outcome classes (loss – class L - and end-stage kidney disease – class E).

This new system is fundamental, as its criteria allow confirming the correlation of each RIFLE class with mortality rate and length of stay, and allowing comparisons between different trials due using uniform AKI definitions and classification criteria.

More recently, a modified RIFLE version was proposed by the Acute Kidney Injury Network (AKIN).<sup>(22)</sup> Four changes were prompted: risk, injury and failure were replaced by stages 1, 2 and 3, respectively (Table 2); an at least 0.3 mg/dL absolute creatinine increase was added to Stage 1; patients under kidney replacement therapy were automatically in Stage 3, independent of creatinine and urine output; and the Loss and End-Stage classes were deleted.

After the RIFLE in 2004 and AKIN in 2007 publications, several investigations were published using these classifications.<sup>(1,9,10,23-34)</sup> Cruz et al.<sup>(31)</sup> in their

review article acknowledge that no classification will be perfect, and that the next step would be reconciling the existing ones, moving the medical community towards a consensus. For this, the author states that more prospective studies are warranted for displaying all established criteria ability. Thus, this study aims to prospectively correlate the RIFLE classification with mortality and length of stay both in intensive care unit (ICU) and in-hospital for a general ICU admitted patients.

## METHODS

### Study design

This was a prospective, observational and longitudinal cohort study where data from all patients admitted to the Hospital Universitário Polydoro Ernani de São Thiago of the Universidade Federal de Santa Catarina (HU-UFSC)'s ICU were collected from September 2007 to March 2008. This study was approved by the UFSC's Ethics Committee, and was developed in compliance with the Declaration of Helsinki. All

**Table 1 – Proposed classification for acute kidney injury – RIFLE**

RIFLE classification	GFR criterion	Urine output criterion
Risk	SCr increase x 1.5 or GFR reduced > 25%	diuresis < 0.5mL/Kg/h in 6h
Injury	SCr increase x 2 or TFG reduction > 50%	diuresis < 0.5mL/Kg/h in 12h
Failure	SCr increase x 3 or GFR reduction > 75% or SCr > 4mg/dL	diuresis < 0.3mL/Kg/h in 24h ou anuria for 12h
Loss	completely loss renal function > 4 weeks	
End-stage kidney disease	RRT needed > 3 months	

RIFLE - Risk Injury Failure Loss End; GFR - glomerular filtration rate; SCr – serum creatinine; RRT – renal replacement therapy.

Adapted from: Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P; Acute Dialysis Quality Initiative workgroup. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care. 2004;8(4):R204-12.

**Table 2 - AKIN classification**

RIFLE Classification	GFR criterion	Diuresis criterion
Stage 1	SCr increase x 1.5 or > 0.3mg/dL	diuresis < 0.5mL/Kg/h in 6h
Stage 2	SCr increase x 2	diuresis < 0.5mL/Kg/h in 12h
Stage 3	SCr increase x 3 or SCr > 4mg/dL (with acute increase > 0.5mg/dL)	diuresis < 0.3mL/Kg/h in 24h or anuria for 12h

GFR - glomerular filtration rate; SCr – serum creatinine.

Adapted from: Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, Levin A; Acute Kidney Injury Network. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care. 2007;11(2):R31.

patients consenting to participate in the study who signed the informed consent form (ICF) were included. When the patient was unable to consent, the ICF was presented to their legally accepted representatives. For patients readmitted to the ICU during the study period, only the first admission was considered.

### Exclusion criteria

Were excluded patients below 16 years old; patients with clinically diagnosed encephalic death by the ICU admission time or within 6 hours; with renal failure under dialysis before admission; transferred from other ICU where stayed longer than 24 hours; not completing 24 hours in the HU-UFSC's ICU and those not consenting.

### Procedures

The study was developed during each patient's stay, and the patient's development was just followed, the data collected from their medical charts according to a protocol, and the RIFLE classification rated during the ICU stay. Each patient was followed-up to the final outcome, either discharge or death, being recorded the respective dates for both ICU and in-hospital stay calculations.

Clinical physiological (Acute Physiology and Chronic Health Evaluation II – APACHE II<sup>(35)</sup> and Sequential Organ Failure Assessment – SOFA<sup>(36)</sup>) and laboratory (serum creatinine –  $S_{cr}$  before and during ICU admission) parameters were evaluated. Physiological parameters were collected for each patient illness severity evaluation. APACHE II was collected after the patient completed 24 hours in the ICU. SOFA score was collected by the ICU admission, and again when the patient completed 24 hours, three days, five days and seven days in the ICU. The mean SOFA score was calculated for all patients having more than one SOFA evaluation. The calculation was made by plain arithmetic mean.

The investigator classified the patients according to their maximal RIFLE class during the ICU stay. For example, if a patient had a kidney injury (class I) by the ICU admission, and during the ICU stay showed renal function failure (class F), he/she was counted as Failure (class F). Many patients with renal dysfunction identified by the ICU admission had no previously measured  $S_{cr}$  value. This would pose an issue for the RIFLE system, which takes into consideration this value proportional change. Thus, when a  $S_{cr}$  value before admission was missing, it was esti-

mated by the Modification of Diet in Renal Disease (MDRD)<sup>(37)</sup> simplified equation, as defined by the original RIFLE publication, and recommended by the ADQI.<sup>(2)</sup> To solve the MDRD equation, a glomerular filtration rate (GFR) of 75 ml/minute/1.73m<sup>2</sup> was assumed. The RIFLE classes were determined based on the worse variable, which depended on the change of laboratory-measured or MDRD-estimated serum creatinine. Thus, patients fitting to RIFLE classification had a LRA diagnosis. The LRA group was sub-divided in R (Risk), I (Injury) and F (Failure). In this study the L and E RIFLE classes were not evaluated.

### Statistical analysis

Descriptive and analytical statistics were performed by plain percentages and association measures (relative risk – RR – with a 95% confidence interval – CI). As central trend was used, as well as the mean  $\pm$  standard deviation ( $\pm$ SD) and the median for continued variables. Qualitative variables were analyzed by the non-parametrical Chi-Square test, and considered statistically significant when  $P < 0.05$ . When an anticipated value below five was found in a contingency table cell, the Fisher exact test was used. Quantitative variables were compared by the t Student parametrical test, and when having unknown population variances, the F test was used. These last two tests significance level was  $P < 0.05$ .

Multivariate analysis was performed by Cox regression for independent variables control. The variable “time” used in the regression was the in-hospital stay. Due to the colinearity between the variables sepsis and septic shock, according to the multi-colinearity principle, only the last one was used.

A Kaplan-Meier curve was built to estimate the survival versus in-hospital stay, AKI and maximal RIFLE (R, I and F). A 95% CI was built, censoring the discharged patients. For this estimation, the log-rank test was used, deemed statistically significant when  $P < 0.05$ .

## RESULTS

During the study period 198 patients were admitted to the ICU. From these, 69 were excluded: one for being below 16 years old, five for having previous dialysis renal failure before ICU admission, three for being transferred from another ICU where they stayed longer than 24 hours, 57 for not completing 24 hours ICU stay, two for not consenting, and one for escap-

ing the hospital. Thus, 129 patients constituted this study cohort.

The studied population clinical and demographical aspects are shown in Table 3 with univariate analysis. The no-AKI group consisted of 77 (59.7%) patients and the AKI group of 52 (40.3%) patients. AKI incidence, according to the maximal RIFLE class was 15.5%, 12.4% and 12.4% for R, I and F, respectively (Table 4).

Progression of AKI during the ICU stay to the maximal RIFLE class is shown in Figure 1. By the first

ICU day, 25 patients (19.4%) had already RIFLE-defined AKI. From these, 4 (3.1%) were already in class F. During the entire ICU stay, from the admission day, 52 patients (40.3%) had an AKI episode, and are in the AKI group. Seven class R patients (5.4%) progressed to RIFLE class I (1.5%) or F (3.9%). From patients admitted in class I, only one (0.8%) developed renal failure. There were patients who after entering class R (6.2%) or class I (3.9%) remained there until the outcome, either discharge or death. From the 104 patients (80.6%) with preserved function by the ad-

**Table 3 – Univariate analysis of clinical and demographic characteristics – with and without kidney injury patients**

Characteristics	No AKI		AKI		Relative risk (95%CI)	P value
	N	%	N	%		
N	77	59.7	52	40.3	-	-
Age (years)						
Mean + SD	46.8 + 16.5		56.4 + 18.8		-	0.0028*
Gender						NS
Female	36	46.8	24	46.2	1.01 (0.67-1.55)	
Male	41	53.2	28	53.8		
Race						NS
White	68	88.3	46	88.5	0.99 (0.51-1.92)	
Black	9	11.7	6	11.5		
Patient's origin <sup>†</sup>						
Emergency	35	45.5	17	32.7	-	NS
Ward	6	7.8	11	21.2	-	0.02
Surgery	21	27.2	14	26.9	-	NS
Other ICU	0	0	2	3.8	-	NS
Other hospital	15	19.5	8	15.4	-	NS
Admission cause						NS
Clinical	49	63.6	33	63.5	1.00 (0.65-1.55)	
Surgical	28	36.4	19	36.5		
Sepsis						0.012‡
Yes	3	3.9	9	17.3	2.04 (1.36-3.06)	
No	74	96.1	43	82.7	-	
Septic shock						<0.05§
Yes	5	6.5	10	19.2	1.81 (1.18-2.78)	
No	72	93.5	42	80.8	-	
Mechanic ventilation						NS
Yes	51	66.2	41	78.8	1.50 (0.87-2.59)	
No	26	33.8	11	21.2	-	
Vasoactive drug						< 0.0001§
Yes	22	28.6	35	67.3	2.60 (1.64-4.13)	
No	55	71.4	17	32.7		

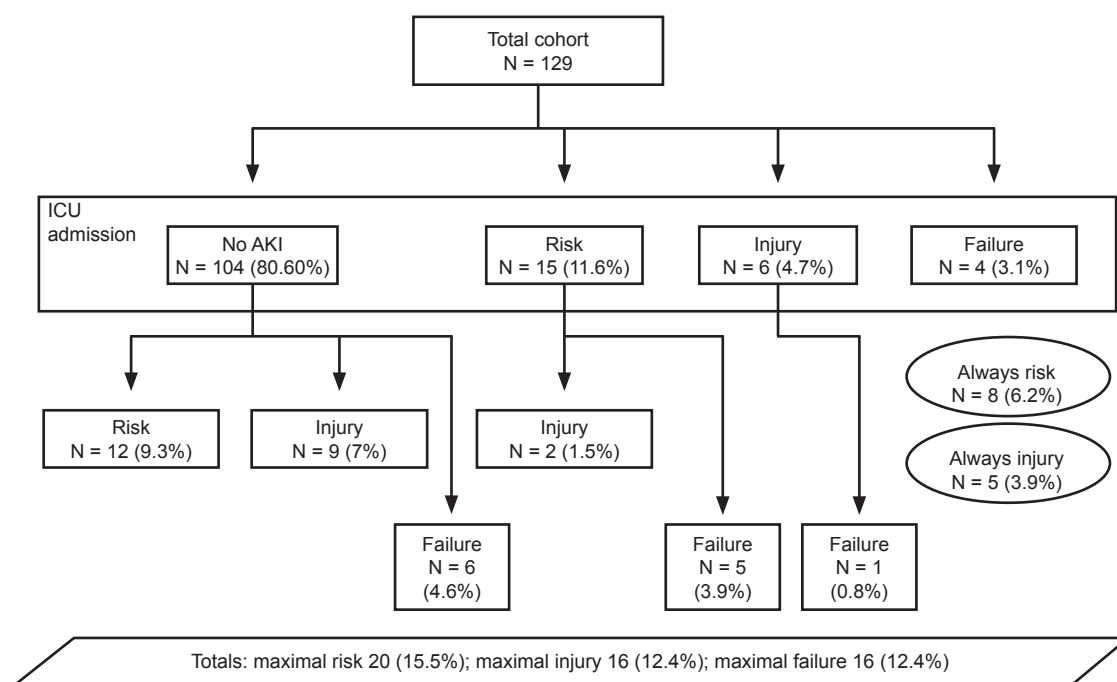
AKI – acute kidney injury; NS - non-significant; SD - Standard deviation; CI - Confidence interval.

\*t Student test. † Chi-Square test, using as reference: Emergency, Ward, Surgery, other ICU, other hospital, respectively; ‡ Chi-Square test with exact Fisher correction. § Statistical analysis using only Chi-Square.

**Table 4 – Association of the patient's severity scores (APACHE II, admission SOFA and mean SOFA) and outcomes (mortality and length of stay) with the no-kidney injury and the different RIFLE subgroups**

	No AKI N = 77	Risk N = 20	Injury N = 16	Failure N = 16	P value
%	59.7	15.5	12.4	12.4	
APACHE II					< 0.0000*
Mean ± SD	14.5 ± 4.9	18.5 ± 5.8	19.0 ± 5.8	23.0 ± 5.2	
Median	14	18.5	17.5	23.5	
SOFA (admission)					< 0.0000*
Mean ± SD	2.4 ± 2.3	2.9 ± 1.8	3.9 ± 2.1	7.0 ± 3.0	
Median	2	3	3.5	7	
SOFA (mean)					< 0.0000*
Mean ± SD	3.5 ± 2.3	5.5 ± 3.0	5.7 ± 3.2	8.5 ± 2.5	
Median	3	5	5.3	8.8	
ICU mortality					< 0.00001†
%	7.8	25	37.5	62.5	
RR (95% CI)	0.19 (0.10-0.35)	1.24 (1.14-1.34)	2.07 (1.58-2.71)	4.16 (2.45-7.04)	
In-hospital mortality					< 0.00001†
%	10.4	50	37.5	62.5	
RR ( 95% IC)	0.20 (0.11-0.36)	2.27 (1.67-3.07)	1.51 (1.29-1.75)	2.97 (1.98-4.44)	
ICU length of stay hours (mean ± SD)	127.7 ± 133.05	186.8 ± 177.66	244.5 ± 180.71	312.7 ± 386.30	
In-hospital stay hours (mean ±SD)	572.8 ± 650.09	655.2 ± 716.67	826.5 ± 882.03	603.0 ± 599.64	

AKI – acute kidney injury; ICU – intensive care unit; SD – standard deviation; NS – non-significant; RR – relative risk; CI – confidence interval; APACHE – Acute Physiologic Chronic Health Evaluation; SOFA - Sequential Organ Failure Assessment; RIFLE - Risk Injury Failure Loss End. \*Single association for each score with t Student test (significance level < 5% or  $P < 0.05$ ). †RIFLE subgroups association with ICU mortality rate, using the Chi-Square test ( $p < 0.05$ ; statistically significant).‡ Association using the F test ( $p < 0.05$ , statistically significant).



Data express the number of patients identified in each level and the percent of the total study number. "Always risk" and "Always injury" were those patients who were rated so in the admission and did not show progression to the next class.

ICU – intensive care unit; AKI - acute kidney injury.

**Figure 1 – Flow-chart of the patients course until maximal RIFLE class.**



mission, 12 (9.3%) progressed to class R, 9 (7%) to class I and 6 (4.6%) to class F.

The Table 4 shows that APACHE II means were higher in the RIFLE AKI subgroups ( $P<0.0000$ ). Similarly, this was observed for the mean admission SOFA, highly statistically significant ( $P<0.0000$ ). In addition, the medians were also higher in the AKI subgroups.

The progressive AKI severity, according to RIFLE for the subgroups R, I and F, was associated with increased ICU mortality (Table 4) as well as with longer ICU lengths of stay (Table 4). It was also identified that, the higher RIFLE classification reached, the higher relative ICU mortality risk (Table 4). Regarding the in-hospital mortality rate (Table 4), it was found that subgroup I, although representing a higher severity class compared to R, had a lower mortality rate. The class F continued showing the higher in-hospital mortality rate, as with the ICU mortality rate. The class F had higher in-hospital mortality RR (2.97;  $P<0.00001$ ), as found for ICU mortality. However, the less severe classes, R and I, didn't keep the same standard of increased RR with the AKI severity (RR=2.27 for R and RR=1.51 for I).

The AKI group patients stayed in average longer in the ICU (Table 4). The comparison between the in-hospital length of stay (Table 4) for each AKI subgroup was not statistically significant.

In the multivariate analysis (Table 5) the factors independently associated to in-hospital mortality were use of vasoactive drug (VAD) and APACHE II.

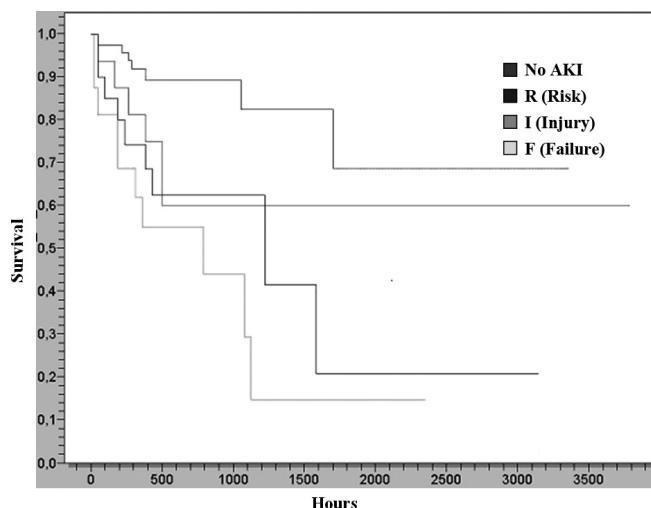
**Table 5 – In-hospital mortality-associated factors multivariate analysis**

Variables	PR	HR	95%CI	P value
	Gross	Adjusted		
Age > 30 years	3.12	1.02	1.01-1.05	0.015
Septic shock	2.03	1.84	0.62-5.51	0.2728
Mechanic ventilation	4.06	2.89	0.64-14.03	0.1635
Vasoactive drug	7.04	5.35	1.70-16.83	0.004
APACHE				
18-24	2.92	2.96	1.15-7.64	0.0241
> 25	5.56	3.11	1.02-9.48	0.0452
SOFA		0.92	0.78-1.09	0.3286
RIFLE	1.81	1.5	0.58-3.92	0.4056

PR- gross prevalence rate; HR – adjusted hazard ratio; CI - confidence interval; APACHE – Acute Physiologic Chronic Health Evaluation; SOFA - Sequential Organ Failure Assessment; RIFLE - Risk Injury Failure Loss End.

Patients using VAD had a five-fold risk (HRaj=5.35) compared to those without VAD. Those with APACHE II above 25 had more than three-fold deaths compared to those below 18.

In the Kaplan-Meier curve (Figure 2), patients in the no-AKI group had an increased survival rate ( $P=0.0002$ ), mainly when compared with the class F. In the 4 curves comparison, the log-rank test showed a  $P=0.0002$ , statistically significant.



Patients were censored by discharge. Log-Rank test;  $P=0.0002$ .

AKI - acute kidney injury. Hours = in-hospital length of stay.

**Figure 2 – Kaplan-Meier curve for (in-hospital) survival versus AKI, versus maximal RIFLE R, I e F.**

## DISCUSSION

The AKI frequency, according to the RIFLE criteria, was 40.3% in this study. Maccariello et al.,<sup>(23)</sup> Bell et al.<sup>(24)</sup> and Abosaif et al.<sup>(25)</sup> didn't identify their studies AKI frequency, as they only used AKI patients. Hoste et al.<sup>(9)</sup> found a 67.2% frequency. Ostermann and Chang<sup>(10)</sup> showed that 35.8% of their patients had AKI. There are several possible explanations for the range of frequencies. First, some mentioned studies are retrospective, relying on medical files which, frequently, lack data and may bias the disease determination. Second, Host et al.<sup>(9)</sup> and Ostermann and Chang<sup>(10)</sup> used 2000 to 2001 and 1989 to 1999 data, respectively. It is possible that with the years the AKI frequency has actually changed. Other explanations would be the different ICU patients studied; e.g., septic, burned, AKI dialysis patients. According to Uchino et al.<sup>(6)</sup> there was a significantly higher AKI frequency in specific ICUs versus general ICUs, as

well as in large ICUs versus small ones.

It was identified that patients whose presentation class was I, had little class F progression. Conversely, for patients with class R admission, about 50% progressed to class I or F. This may be explained for patients in class I, compared to class R, not only have laboratory AKI features, but also clinical. Thus, as this last condition was more evident, the therapy may have started early, preventing the illness progression. According to Hoste et al.<sup>(9)</sup>, above 50% of patients at risk (R), in their study, progressed to class I or F. These findings agree with our findings. However, the same author reported that more than one third of class I patients progressed to class F, differently of our trial where this progression occurred in one sixth of the patients.

It was also anticipated that the high scores both in SOFA and APACHE II would correlate with the AKI incidence. According to the anticipated, the single association of each score with AKI showed that the higher means and medians belonged to the AKI group. It was then realized that patients classified in the RIFLE, with AKI, had a higher illness severity, both regarding APACHE II, in the first 24 hours, and SOFA (admission and mean). This association was also shown by Abosaif et al.<sup>(25)</sup> and Hoste et al.<sup>(9)</sup> In addition, high APACHE II scores were directly correlated with an increased in-hospital death risk.

In an attempt to validate RIFLE as a predictor for ICU patients prognosis, the association of each class (R, I and F) with ICU and in-hospital mortality and in-hospital length of stay were analyzed. It was shown that the most severe was the RIFLE class, the higher was ICU mortality. When comparing the AKI-group with the no-AKI group, this last showed an even lower mortality rate. In-hospital mortality didn't show the same standard of increased mortality, however the class F remained with the lower rate. Bell et al.<sup>(24)</sup> showed that 57.9% of the class F patients died within 30 days, compared with 23.5% in the class R and 22% in class I. Abosaif et al.<sup>(25)</sup> showed an ICU mortality of 16.7% for the control group patients, and 38.3%, 50% and 74.% for patients in the groups Risk, Injury and Failure, respectively. Hoste et al.<sup>(9)</sup> found in his trial in-hospital mortality rates of 8.8%, 11.4% and 26.3% for the same groups, compared with 5.5% for preserved renal function patients.

Uchino et al.<sup>(1)</sup> found 4.4% rats for no-AKI patients, and 15.1%, 29.2% and 41.1% for patients in classes R, I and F, respectively. Lopes et al.<sup>(27)</sup> used the

RIFLE criteria for burned patients, and found mortality rates of 11.1%, 63.6% and 75% according to the AKI severity versus 6% for no-AKI patients. Ostermann and Chang<sup>(10)</sup> showed a 27.9% mortality rate for no-AKI patients, and 19%, 26.6% and 22.98% for patients with R, I and F, respectively. For these classes, Maccariello et al.<sup>(23)</sup> established 72%, 79% and 76% rates, but not statistically significant for the association. In 2007, Lopes et al. used the RIFLE for HIV patients<sup>(28)</sup> showing mortality rates of 23.5% for R, 66.6% for I and 72% for F, and 23.5% for no-AKI patients. In the same year, however in sepsis patients, Lopes et al.<sup>(29)</sup> found 27.3% \*, 28.6% (I) and 55% (F) rates, and 9.6% (no-AKI). Although the percentages ranged in the different studies and among them and this study, the mortality rates can be noticed to have the same trend, the higher ones corresponding to more severe RIFLE.

Yet regarding ICU and in-hospital mortality, it was found that AKI exposure, according to the RIFLE, represented a mortality risk in these sites, and that the higher the class reached, the higher inherent risk. Other studies<sup>(1,9,10,27)</sup> found this same association. Bell et al.<sup>(24)</sup> only identified association for the class F. Lopes et al.<sup>(28)</sup> similarly showed association for one single class, I. There where those who couldn't associate RIFLE with mortality. For instance, Maccariello et al.<sup>(23)</sup>, who even with 1.47 and 1.19 odds ratio for class I and F, respectively, couldn't confirm by the CI, in addition to not finding statistical significance. The reason for this disagreement is supposed to be in the study populations chosen, as Bell et al.<sup>(24)</sup> and Maccariello et al.<sup>(23)</sup> used patients who already had dialysis AKI patients, and Lopes et al.<sup>(28)</sup> only had in their sample HIV positive patients. On the other hand, reviewing the multivariate analysis, RIFLE was not independently associated with in-hospital mortality.

Analyzing the mean ICU length of stay it was noticed that, as mortality, these were longer in the most severe AKI classes, and that when the class was the lowest, R, this was also higher compared to preserved renal function patients. Thus, an association of RIFLE with longer ICU stay was found. Hoste et al.<sup>(9)</sup> and Ostermann and Chang<sup>(10)</sup> found the same relationship. Other already mentioned studies do not mention this association. Similarly it was tried to associate the RIFLE class with the in-hospital length of stay, however no statistically significant difference was found, although the mean time was longer in all AKI classes compared to no-AKI patients.

This study has obvious limitations. The main issue is its time span, as a longer follow-up could provide a larger sample and possibly more robust analysis. Another not less important limitation was the use of one single study site. This has somehow limited the results generalization, giving the study little external validity. It is also known that not using the patients urine output for comparison with the creatinine criterion has compromised the study. It is possible that urine output and creatinine taken together could provide complementary information. Attempting to cover this gap, creatinine was used according to the ADQI proposal.

ADQI has as well recommended using the MDRD equation as an alternative for missing  $S_{cr}$  values. However, this has partially compromised the study, because as this equation is a creatinine estimate, AKI incidence and severity may have been overestimated. Although the MDRD equation was developed and validated in a large number of patients, conflicting results were published. It is acknowledged that calculated  $S_{cr}$  does not fully replace actual creatinine, but a MDRD validation, or developing an alternative, was far from this study aim.

Additionally, this study may had biases, mainly for the heterogeneous distribution of some RIFLE characteristics (as age, comorbidities, sepsis, VAD and mechanic ventilation use). So the multivariate analysis was used to adjust for the variables regarding in-hospital mortality.

On the other hand, we underline that, being a prospective study, this trial had additional reliability and accuracy for the associations. In addition, all results were actual observations, based on daily patients follow-up. Additionally, this study is among the few Brazilian prospective studies in a general ICUs, which makes it a reasonably actual Intensive Care Unit daily life evaluation.

## CONCLUSION

RIFLE was a risk marker for increased ICU and in-hospital mortality proportional to the AKI severity. For length of stay, RIFLE was equally a marker of longer ICU stay proportional to the progressive AKI severity. The same was not true for in-hospital length of stay.

From a scientific point of view, the author suggests the study to be continued for a longer data collection time. It is proposed that, in the future, clinical trials are conducted aiming the complete RIFLE validation. At the same time, AKI prevention is in place, mainly targeting those patients in the class R. Even that it has not brought considerable risk of death as the classes I

and F, it was identified that almost 50% of these patients progressed to most severe RIFLE classes.

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## RESUMO

**Objetivo:** Correlacionar a classificação do RIFLE com a letalidade e tempo de internação na unidade de terapia intensiva e no hospital.

**Métodos:** Estudo de coorte prospectivo, observacional e longitudinal aprovado pelo Comitê de Ética da Instituição. Foram coletados os dados de todos os pacientes internados por mais de 24 horas na unidade de terapia intensiva do Hospital Universitário Polydoro Ernani de São Thiago da Universidade Federal de Santa Catarina de setembro de 2007 a março de 2008 e com seguimento até a alta ou óbito. Os pacientes foram divididos em dois grupos: com lesão renal aguda e sem lesão renal aguda. O grupo com lesão renal aguda foi classificado conforme o RIFLE e subdividido de acordo com a classe máxima alcançada: risco, injúria ou falência. Não foram incluídas as classes *loss* e *end-stage* no estudo. Analisou-se também APACHE II e SOFA. Utilizaram-se os testes *t Student* e Qui-Quadrado, principalmente. Um  $p < 0,05$  foi estatisticamente significativo.

**Resultados:** A amostra foi composta por 129 pacientes. Desses, 52 (40,3%) apresentaram lesão renal aguda segundo o RIFLE. Nesse grupo, os doentes foram considerados mais graves obtendo médias maiores de APACHE II e SOFA ( $p < 0,05$ ). Em comparação ao grupo sem dano renal, a gravidade da lesão renal aguda proporcionou maior letalidade na unidade de terapia intensiva (risco-25%; injúria-37,5%; falência-62,5%) e hospitalar (risco-50%; injúria-37,5%; falência-62,5%) e maior tempo de internação na unidade de terapia intensiva ( $p < 0,05$ ).

**Conclusão:** O sistema RIFLE, conforme a classe de gravidade, foi marcador de risco para maior letalidade na unidade de terapia intensiva e no hospital e maior tempo de internação na unidade de terapia intensiva. Não se encontrou relação para o tempo de internação hospitalar.

**Descritores:** Insuficiência renal aguda; Unidades de terapia intensiva; Creatinina; Mortalidade hospitalar; Tempo de internação; APACHE



## REFERENCES

- Uchino S, Bellomo R, Goldsmith D, Bates S, Ronco C. An assessment of the RIFLE criteria for acute renal failure in hospitalized patients. *Crit Care Med*. 2006;34(7):1913-7.
- Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P, Acute Dialysis Quality Initiative workgroup. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care*. 2004;8(4):R204-12.
- Metnitz PG, Krenn CG, Steltzer H, Lang T, Ploder J, Lenz K, et al. Effect of acute renal failure requiring renal replacement therapy on outcome in critically ill patients. *Crit Care Med*. 2002;30(9):2051-8.
- Chertow GM, Levy EM, Hammermeister KE, Grover F, Daley J. Independent association between acute renal failure and mortality following cardiac surgery. *Am J Med*. 1998;104(4):343-8.
- De Mendonça A, Vincent JL, Suter MP, Moreno R, Dearden NM, Antonelli M, et al. Acute renal failure in the ICU: risk factors and outcome evaluated by the SOFA score. *Intensive Care Med*. 2000;26(7):915-21.
- Uchino S, Kellum JA, Bellomo R, Doig GS, Morimatsu H, Morgera S, Schetz M, Tan I, Bouman C, Macedo E, Gibney N, Tolwani A, Ronco C; Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) Investigators. Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA*. 2005;294(7):813-8.
- Bellomo R, Kellum JA, Ronco C. Defining and classifying acute renal failure: from advocacy to consensus and validation of the RIFLE criteria. *Intensive Care Med*. 2007;33(3):409-13.
- Bellomo R, Kellum JA, Ronco C. Acute renal failure: time for consensus. *Intensive Care Med*. 2001;27(11):1685-8.
- Hoste EA, Clermont G, Kersten A, Venkataraman R, Angus DC, De Bacquer D, Kellum JA. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. *Crit Care*. 2006;10(3):R73.
- Ostermann M, Chang RW. Acute kidney injury in the intensive care unit according to RIFLE. *Crit Care Med*. 2007;35(8):1837-43; quiz 1852.
- Kellum JA, Levin N, Bouman C, Lameire N. Developing a consensus classification system for acute renal failure. *Curr Opin Crit Care*. 2002;8(6):509-14.
- Vivino G, Antonelli M, Moro ML, Cottini F, Conti G, Bufi M, et al. Risk factors for acute renal failure in trauma patients. *Intensive Care Med*. 1998;24(8):808-14.
- Mangano CM, Diamondstone LS, Ramsay JG, Aggarwal A, Herskowitz A, Mangano DT. Renal dysfunction after myocardial revascularization: risk factors, adverse outcomes, and hospital resource utilization. The Multicenter Study of Perioperative Ischemia Research Group. *Ann Intern Med*. 1998;128(3):194-203.
- Guerin C, Girard R, Selli JM, Perdrix JP, Ayzac L. Initial versus delayed acute renal failure in the intensive care unit. A multicenter prospective epidemiological study. Rhône-Alpes Area Study Group on Acute Renal Failure. *Am J Respir Crit Care Med*. 2000;161(3 Pt 1):872-9. Erratum in: *Am J Respir Crit Care Med* 2001 Mar;163(3 Pt 1):793-4.
- Liaño F, Junco E, Pascual J, Madero R, Verde E. The spectrum of acute renal failure in the intensive care unit compared with that seen in other settings. The Madrid Acute Renal Failure Study Group. *Kidney Int Suppl*. 1998;66:S16-24.
- Cosentino F, Chaff C, Piedmonte M. Risk factors influencing survival in ICU acute renal failure. *Nephrol Dial Transplant*. 1994;9 Suppl 4:179-82.
- Chertow GM, Christiansen CL, Cleary PD, Munro C, Lazarus JM. Prognostic stratification in critically ill patients with acute renal failure requiring dialysis. *Arch Intern Med*. 1995;155(14):1505-11.
- Neveu H, Kleinknecht D, Brivet F, Loreit P, Landais P. Prognostic factors in acute renal failure due to sepsis. Results of a prospective multicenter study. The French Study Group on Acute Renal Failure. *Nephrol Dial Transplant*. 1996;11(2):293-9.
- Mehta RL, Pascual MT, Soroko S, Savage BR, Himmel-farb J, Ikizler TA, Paganini EP, Chertow GM; Program to Improve Care in Acute Renal Disease. Spectrum of acute renal failure in the intensive care unit: the PICARD experience. *Kidney Int*. 2004;66(4):1613-21.
- Schaefer JH, Jochimsen F, Keller F, Wegscheider K, Distler A. Outcome prediction of acute renal failure in medical intensive care. *Intensive Care Med*. 1991;17(1):19-24.
- Ronco C, Kellum JA, Mehta R. Acute dialysis quality initiative (ADQI). *Nephrol Dial Transplant*. 2001;16(8):1555-8.
- Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, Levin A; Acute Kidney Injury Network. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care*. 2007;11(2):R31.
- Maccariello E, Soares M, Valente C, Nogueira L, Valença RV, Machado JE, Rocha E. RIFLE classification in patients with acute kidney injury in need of renal replacement therapy. *Intensive Care Med*. 2007;33(4):597-605.
- Bell M, Liljestam E, Granath F, Fryckstedt J, Ekblom A, Martling CR. Optimal follow-up time after continuous renal replacement therapy in actual renal failure patients stratified with the RIFLE criteria. *Nephrol Dial Transplant*. 2005;20(2):354-60.
- Abosaif NY, Tolba YA, Heap M, Russell J, El Nahas AM. The outcome of acute renal failure in the intensive care

- unit according to RIFLE: model application, sensitivity, and predictability. *Am J Kidney Dis.* 2005;46(6):1038-48.
26. Kuitunen A, Vento A, Suojäranta-Ylinen R, Pettilä V. Acute renal failure after cardiac surgery: evaluation of the RIFLE classification. *Ann Thorac Surg.* 2006;81(2):542-6.
  27. Lopes JA, Jorge S, Neves FC, Caneira M, da Costa AG, Ferreira AC, Prata MM. An assessment of the RIFLE criteria for acute renal failure in severely burned patients. *Nephrol Dial Transplant.* 2007;22(1):285.
  28. Lopes JA, Fernandes J, Jorge S, Neves J, Antunes F, Prata MM. An assessment of the RIFLE criteria for acute renal failure in critically ill HIV-infected patients. *Crit Care.* 2007;11(1):401.
  29. Lopes JA, Jorge S, Resina C, Santos C, Pereira A, Neves J, et al. Acute renal failure in patients with sepsis. *Crit Care.* 2007;11(2):411.
  30. Barrantes F, Tian J, Vazquez R, Amoaeng-Adjepong Y, Manthous CA. Acute kidney injury criteria predict outcomes of critically ill patients. *Crit Care Med.* 2008;36(5):1397-403.
  31. Cruz DN, Bolgan I, Perazella MA, Bonello M, de Cal M, Corradi V, Polanco N, Ocampo C, Nalesso F, Piccinni P, Ronco C; North East Italian Prospective Hospital Renal Outcome Survey on Acute Kidney Injury (NEIPHROS-AKI) Investigators. North East Italian Prospective Hospital Renal Outcome Survey on Acute Kidney Injury (NEIPHROS-AKI): targeting the problem with the RIFLE Criteria. *Clin J Am Soc Nephrol.* 2007;2(3):418-25.
  32. Li WX, Chen HD, Wang XW, Zhao S, Chen XK, Zheng Y, Song Y. Predictive value of RIFLE classification on prognosis of critically ill patients with acute kidney injury treated with continuous renal replacement therapy. *Chin Med J (Engl).* 2009;122(9):1020-5.
  33. Bagshaw SM, George C, Bellomo R; ANZICS Database Management Committee. A comparison of the RIFLE and AKIN criteria for acute kidney injury in critically ill patients. *Nephrol Dial Transplant.* 2008;23(5):1569-74.
  34. Joannidis M, Metnitz B, Bauer P, Schusterschitz N, Moreno R, Druml W, Metnitz PG. Acute kidney injury in critically ill patients classified by AKIN versus RIFLE using the SAPS 3 database. *Intensive Care Med.* 2009;35(10):1692-702.
  35. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med.* 1985;13(10):818-29.
  36. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med.* 1996;22(7):707-10.
  37. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med.* 1999;130(6):461-70.