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STUDY OF CLINICAL PROFILE OF COMMUNITY-ACOUIRED ACUTE KIDNEY INJURY DEFINED USING RIFLE CRITERIA IN IGIMS PATNA

General Medicine

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ABSTRACT

Aim: To examine the progression between stages of the classification, and to relate this classification to the length of stay and mortality in a large cohort of critically ill patients.

Material and methods: A total of 5,383 patients was evaluated. We classified patients according to the maximum RIFLE class (class R, class I or class F) reached during their hospital stay. The RIFLE class was determined based on the worst of either glomerular filtration rate criteria or urine output criteria. We used the change in serum creatinine level and urine output to classify patients according to the RIFLE criteria.

Result: Increasing severity of acute kidney injury was associated with an increasing length of ICU stay and hospital stay, and higher mortality. Patients with maximum RIFLE class R, class I and class F had hospital mortality rates of 8.6%, 11.7% and 26.8%, respectively, compared with 5.5% for patients without acute kidney injury.

Conclusion: ICU population, newly developed RIFLE classification was associated with increased hospital mortality.

KEYWORDS

Acute kidney injury, Community-acouired acute kidney injury, RIFLE, Serum creatinine

INTRODUCTION

Acute kidney injury (AKI), formerly called acute renal failure (ARF), is commonlydefined as an abrupt decline in renal function, clinically manifesting as a reversible acute increase in nitrogen waste products - measured by blood urea nitrogen(BUN) and serum creatinine levels- over the course of hours to weeks.[1]

Every year, there are about 13.3 million cases of acute kidney injury (AK). Aburden that is becoming particularly high in emerging countries.

Out of 1.7 million deaths per year caused by AKI globally, around 1.4 millionOccur in low- and middle-income countries[2]. AKI is often preventable andtreatable with few, if any, long-term health consequences. Identifying the signs andbeginning treatment early means more patients will get essential care before 1t istoo late.

Community acquired acute kidney injury is defined as the presence of AKI atadmission or developing AKI within 48 hours of admission affecting younger andpreviously healthy individuals. Specific causes include diarrheal diseases with dehydration, infectious diseases (malaria, dengue, yellow-fever, tetanus and HIV),animal venoms (snakes, bees, spiders), septic abortion, dyes and natural medicines.Most of these factors are associated with poverty and affect vulnerable populationsdue to poor sanitation and water hygiene, a lack of education and poor access tothe healthcare system.

Between 5% and 7% of all hospitalized patients develop AKI. 'A greaterprevalence of AKI is found in critically ill patients (ICU-Acquired AK).' Despiteimprovements in the medical care of individuals with AKI, mortality generallyexceeds 50%.[3]

CLASSIFICATION OF AKI Criteria used for AKI classification RIFLE: Risk,Injury, Failure, Loss of Kidney Function and End Stage Renal Disease). AKIN:Acute Kidney Injury Network, KDIGO: Kidney Disease Improving GlobalOutcome.

The Acute Dialysis Quality Initiative (ADQ) group developed a system fordiagnosis and classification of a broad range of acute impairment of kidneyfunction through a broad consensus of experts.

The acronym RIFLE stands for the increasing severity classes Risk, Injury, andFailure; and the two outcome classes, Loss and End-Stage Renal Disease (ESRD).The three severity grades are defined on the basis of the changes in SCr or urineoutput where the worst of each criterion is used. The two outcome criteria, Lossand ESRD, are defined by the duration of loss of kidney function.

AIMS AND OBJECTIVES:

1. To characterize acute kidney injury defined by the RIFLE classification.
2. To examine the progression between stages of the classification, and to relate this classification to the length of stay and mortality in a large cohort of critically ill patients.

MATERIAL AND METHODS

We performed a retrospective cohort study, in seven intensive care units in a single tertiary care academic center, on 5,383 patients admitted during a one-year period (1 July 2019–30 June 2020).

A total of 5,383 patients was evaluated. The baseline characteristics of the patient cohort are presented according to the maximum RIFLE class. The four groups differed in age, race, pre-existing chronic kidney insufficiency, admission type, severity of illness on admission and at the time of maximum RIFLE class, APACHE III score, SOFA score and the nonrenal SOFA score, and the proportion of patients already admitted inhospital to another non-ICU ward.

We classified patients according to the maximum RIFLE class (class R, class I or class F) reached during their hospital stay. The RIFLE class was determined based on the worst of either glomerular filtration rate criteria or urine output criteria. We used the change in serum creatinine level and urine output to classify patients according to the RIFLE criteria.

STATISTICAL ANALYSIS:

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Data had been summarized as meanand standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. One-way analysis of variance (one-way ANOVA) was a technique used to compare means of three or more samples for numerical data (using the F distribution). A chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate.

The Mann–Whitney U test is a nonparametric test of the null hypothesis that it is equally likely that a randomly selected value from one sample is less than or greater than a randomly selected value from a second sample. This test can be used to determine whether two independent samples were selected from populations having the same

distribution; a similar nonparametric test used on dependent samples is the Wilcoxon signed-rank test.

Z-test (Standard Normal Deviate) was used to test the significant difference of proportions. Correlation was calculated by Pearson correlation analysis. The Pearson product-moment correlation coefficient was a measure of the linear dependence between two variables X and Y. Multivariate analysis was performed by logistic regression method for calculation of risk factors. The Kaplan–Meier estimator (Kaplan-Meier survival analysis) was a non-parametricstatistic used to estimate the survival function from time data.

Explicit expressions that can be used to carry out various *t*-tests are given below. In each case, the formula for a test statistic that either exactly follows or closely approximates a *t*-distribution under the null hypothesis is given. Also, the appropriate degrees of freedom are given in each case. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test.

Once a *t* value is determined, a *p*-value can be found using a table of values from Student's t-distribution. If the calculated *p*-value is below the threshold chosen for statistical significance (usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis is rejected in favour of the alternative hypothesis.

p-value ≤ 0.05 was considered for statistically significant.

RESULTS

On the first day of ICU admission, 1,182 patients (22.7%) already had acute kidney injury, defined by the RIFLE criteria. During the entire ICU stay, 3,617 patients (68.3%) had an episode of acute kidney injury defined by RIFLE criteria. One-half of the patients reached the maximum RIFLE class within 2 days after ICU admission.

Most of the patients with RIFLE class R progressed to RIFLE class I or class F, and more than one-third of the patients with RIFLE class I progressed to class F. The time to progress to class I was 1 (0.5–3.6) days and the time to progress to class F was 4 (1.4–9.5) days. Patients who progressed to a higher RIFLE class during the ICU stay were older compared to patients whose renal function did not deteriorate, (63.3 ± 18.7 years versus 57.7 ± 18.9 years, P < 0.001) and were already more severely ill on admission.

Less than 1% of patients with maximum RIFLE class I and 14.3% of patients with maximum RIFLE class F received renal replacement therapy. Increasing severity of acute kidney injury was associated with an increasing length of ICU stay and hospital stay, and higher mortality. Patients with maximum RIFLE class R, class I and class F had hospital mortality rates of 8.6%, 11.7% and 26.8%, respectively, compared with 5.5% for patients without acute kidney injury. Patients with maximum RIFLE class F based on glomerular filtration rate criteria had a somewhat higher inhospital mortality compared with patients who had a maximum RIFLE class F on urine output criteria (28.7% versus 22.3%, P = 0.020). The unadjusted hazard ratios (95% confidence interval) for hospital mortality for acute kidney injury and RIFLE class R, class I and class F were, respectively, 2.3 (1.66–2.68, P < 0.001), 1.4 (0.81–1.94, P = 0.144), 1.7 (1.46–2.58, P < 0.001) and 3.5 (2.54–4.37, P < 0.001). After adjustment for covariates, acute kidney injury was still associated with an almost twofold increased hazard for hospital mortality. Maximum RIFLE class I and class F were both associated with mortality in the covariate-adjusted Cox regression model.

DISCUSSION

We found that acute kidney injury, defined by the RIFLE classification, had a high incidence and was associated with an increased risk for hospital mortality compared with those who never developed acute kidney injury. The incidence of almost 70% may appear at odds with the existing literature [4]. Even when limiting cases to those with RIFLE class F (29%) we found a higher rate for ICU patients than typically reported. Fourteen percent of class F patients received renal replacement therapy, however, leading to a rate of 4–5% among ICU patients, consistent with previous reports [5,6]. Importantly, even milder degrees of kidney dysfunction, RIFLE class R or class I, were still associated with excess mortality compared with patients who maintained normal function.

The finding that moderate degrees of kidney dysfunction pose a significant risk of death is particularly notable given that we know very little of why this should be. Acute kidney injury may simply be colinear with unmeasured elements of comorbidity, or it may be causally related to the increased mortality. Future studies should consider exploring whether alternative management of patients with mild degrees of kidney dysfunction could change the outcome. If the problem is actually the kidney, then possible mechanisms underlying the excess mortality associated with acute kidney injury are likely to be found in the pathophysiologic changes resulting from kidney insufficiency and adverse effects of renal replacement therapy [7,8].

Our study has certain limitations. First, we did not attempt to compare RIFLE with other classification systems; nor did we compare urine output and creatinine criteria, but rather used the criteria as proposed by the Acute Dialysis Quality Initiative workgroup, as the worst classification by each criterion. It is possible that urine output and creatinine criteria provide complementary information, which is lost when these criteria are combined.

We also acknowledge that some members of our research group have contributed to the consensus process by which RIFLE was developed and by which MDRD recommendations were made. In addition, patient follow-up in our study was limited to hospital discharge information.

Some patients may have died shortly after hospital discharge. Longer follow-up would also be required to examine the RIFLE endpoints 'loss' and 'end-stage disease'. Early renal replacement therapy may theoretically influence the criteria, and patients that would have reached class F could be classified in our study as class R or class I. Only four class I patients were treated with renal replacement therapy, however, and reclassification of these patients to class F does not influence our results.

Although our study is relatively large and included seven ICUs, it was conducted at a single medical center whose case mix and referral patterns may not be representative of other centers. The case mix of this study cohort could have hindered the detection of specific conditions that influence the development of acute kidney injury. Finally, our retrospective study design, using existing medical records, limited our ability to look outside the ICU and to collect information on potential mechanisms of injury. Our design also prohibited the use of more sophisticated measures of kidney function. Indeed, our assessment of time to progression of acute kidney injury may have been artificially lengthened due to daily measurement of creatinine – some patients appeared to skip class R or class I because of this limitation.

Table: Risk, Injury, Failure, Loss, and End-stage Kidney (RIFLE) classification

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

Table: Outcomes for all patients and for patients classified according to the maximum Risk, Injury, Failure, Loss, and End-stage Kidney (RIFLE) class

	No acute kidney injury (n = 1,766)	Risk (n = 670)	Injury (n = 1,436)	Failure (n = 1,511)	All injury (n = 5,383)	p-value
Renal replacement therapy*	1 (0.1%)	0 (0%)	4 (0.3%)	214 14.2%)	219 (4.1%)	0.001

Hospital LOS after reaching maximum RIFLE class (days)*	5(3–10)	5(3–10)	7(4–14)	11 (5–23)	7 (3–14)	0.001
ICU LOS (days)*	3 (2–4)	3 (2–6)	5 (3–10)	9 (4–21)	4 (2–9)	0.001
Hospital LOS (days)*	6 (4–10)	8 (5–14)	10 (6–19)	16 (9–31)	9 (5–19)	0.001
Hospital mortality*	97(5.5%)	59(8.8%)	163(11.4%)	398(26.3%)	717(13.3%)	0.001

CONCLUSION

In summary, ICU population, newly developed RIFLE classification was associated with increased hospital mortality. Patients of RIFLE class R are indeed at high risk of progression to class I or class F. Patients with RIFLE class I or class F significantly increased length of stay and an increased risk of inhospital mortality.

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