AKIN Criteria for Acute Kidney Injury in Critically Ill Cirrhotic Patients

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Abstract: Background. The Acute Dialysis Quality Initiative Group has published a consensus definition/classification system for acute kidney injury (AKI) termed the RIFLE criteria. The Acute Kidney Injury Network (AKIN) group has recently proposed modifications to this system. It is currently unknown whether there are advantages between these criteria. **Methods .**We interrogated 100 Adult critically ill cirrhotic patients for which RIFLE and AKIN criteria where done. **Aim of the work.** Comparison of RIFLE and AKIN criteria for AKI in critically ill cirrhotic Patients. **Results.** This study was performed on 100 cirrhotic patients admitted to Intensive Care Unit in the hospital of Theodore Bilharz Research Institute. According to the RIFLE classification, there were 40 Non-ARF patients, 22 RIFLE-R patients, 8 RIFLE-I patients and 30 RIFLE-F patients. According to AKIN criteria there were 38 Non-ARF patients, 24 (Stage 1) patients, 8 (Stage 2) patients and 30 (Stage 3) patients. The Non-Survivor group had a significantly longer duration of hospital stay than the Survivor group. There was insignificant correlation between RIFLE / AKIN score and the LOS (length of stay) as the R= 0.135 and *p* value = 0.179. RIFLE and AKIN classifications studied in this study were highly predictive of poor outcome in cirrhotic patients at different cut-off points as studied by ROC curve analysis. The patients' ages were ranging from 43 to 73with a mean age of 59±8.06 years. **Conclusion**. Compared to the RIFLE criteria, the AKIN criteria do not materially improve the sensitivity, robustnessand predictive ability of the definition and classification ofafter admission to ICU.

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1.Introduction

Liver cirrhosis represents the final common pathway of virtually all chronic liver disease and is characterized by anaccumulation of extracellular matrix rich in fibrillar collagen (1).

A feature of liver cirrhosis is the existence of disturbances in systemic circulation characterized by marked arterial vasodilation that occurs principally in the splanchnic circulation and generates a reduction in total peripheral vascular resistance and arterial pressure and a secondary increase in cardiac output. These abnormalities are central to the development of several major complications of cirrhosis, such as hepatorenal syndrome, ascites, spontaneous bacterial peritonitis, dilutionalhyponatremia, and hepatopulmonary syndrome. Renal failure is the most clinical relevant of these conditions as its appearance generally indicates very poor prognosis (2- 5).

Elevated serum creatinine (SCr) levels of > 1.3 or 1.5mg/dl have been identified as a predictor of poor prognosis in patients with advanced liver cirrhosis (6).

The common used scoring systems for predicting the outcome in critically ill cirrhotic patients, such as Child–Pugh score (7), Sequential Organ Failure Assessment (SOFA) (8), Model for End-stage Liver Disease (MELD) (9), and Acute Physiology, Age, Chronic Health Evaluation II (APACHE II)(10) evaluate renal function according to the serum creatinine.

The RIFLE (risk of renal failure, injury to the kidney, failure of kidney function, loss of kidney function, and end-stage renal failure) classification was first proposed by the Acute Dialysis Quality Initiative (ADQI) group at the second ADQI conference in Vicenza, Italy, in May 2002, in an attempt to standardize the study of ARF. The RIFLE criteria classify ARF into three groups (risk, injury, and failure) according to changes in SCr and urine output (UO) (Table 1). The RIFLE classification has been evaluated in a number of clinical studies of critically ill patients with AKI. In general, these criteria have been found to have clinical relevance for the diagnosis of AKI, classifying the severity of AKI and for monitoring the progression of AKI, as well as having modest predictive ability for mortality(11-14).

More recently, the Acute Kidney Injury Network (AKIN) group (Table 2), an international collaboration of nephrologists and intensivists, has proposed refinements to the RIFLE criteria. In particular, the AKIN group sought to increase the

sensitivity of the RIFLE criteria by recommending that a smaller change in serum creatinine (0.3 mg/dl) be used as a threshold to define the presence of AKI and identify patients with stage I AKI (analogous to RIFLE-Risk). It is currently unknown whether discernible advantages exist with one approach to definition and classification versus the other.

Table 1: The Acute Dialysis Quality Initiative (ADQI) criteria for the definition and classification of AKI (i.e. RIFLE criteria)

RIFLE	Serum Creatinine Criteria	Urine Output Criteria
Risk	Increase in serum creatinine ≥1.5X baseline or decrease in GFR ≥25%	<0.5 mL/kg/h for ≥6 h
Injury	Increase in serum creatinine ≥2.0X baseline or decrease in GFR ≥50%	<0.5 mL/kg/h for ≥12 h
Failure	Increase in serum creatinine ≥3.0X baseline or decrease in GFR ≥75% or an absolute serum creatinine ≥354 µmol/L with an acute rise of at least 44 µmol/L	<0.3 mL/kg/h ≥24 h oranuria ≥12 h

Table 2: The proposed Acute Kidney Injury Network (AKIN) criteria for the definition and classification of AKI

AKIN	Serum Creatinine Criteria	Urine Output Criteria
Stage 1	Increase in serum creatinine ≥26.2 µmol/L or increase to ≥150–199% (1.5- to 1.9-fold) from baseline	<0.5 mL/kg/h for ≥6 h
Stage 2	Increase in serum creatinine to 200–299% (>2–2.9 fold) from baseline	<0.5 mL/kg/h for ≥12 h
Stage 2	Increase in serum creatinine to ≥300% (≥3-fold) from baseline or serumcreatinine ≥354 µmol/L with an acute rise of at least 44 µmol/L or initiation ofRRT	<0.3 mL/kg/h ≥24 h oranuria ≥12 h

Aim of study:

The aim of this study is to evaluate and compare RIFLE and AKIN criteria in evaluating AKI and predicting mortality in critically ill cirrhotic patients.

2.Patients and Methods:

This study will be performed on 100 cirrhotic patients admitted to Intensive Care Unit in the hospital of Theodore Bilharz Research Institute.

Exclusion criteria are:

* Pediatric patients ≤ 18 years of age.
* Uremic patients undergoing renal replacement therapy.
* Patients who had undergone liver transplantation.

The following data will be collected for each patient on the 1st day of admission:

→ Demographics.
→ Reason for ICU admission.
→ RIFLE classification.
→ AKIN Classification.

And finally, the duration of hospitalization and the outcome of each patient will be recorded.

Statistical Analysis

Diagnosis of cirrhosis was based on a combination of physical findings and biochemical and sonar findings. Severity of liver disease on ICU admission was graded using Child-Pugh and SOFA scoring systems.

Continuous variables were summarized using means andstandard error. The primary analysis compared hospitalsurvivors with non-survivors. All variables were testedfor normal distribution using the Kolmogorov–Smirnovtest. Student's *t*-test was employed to compare the meansof continuous variables and normally distributed data;otherwise, the Mann–Whitney *U*-test was employed.Categorical data were tested using the chi-square test. Finally, risk factors wereassessed with univariate analysis, and variables that were statistically significant (p <0.05) in the univariate analysiswere included in multivariate analysis by applyinga multiple logistic regression based on forward eliminationof data.

3.Results

The patients' ages were ranging from 43 to 73 with a mean age of 59±8.06 years. Regarding gender distribution 68% were males and 32% were females as shown in table (3):

Table 3	Number	Percent
MALE	68	68%
FEMALE	32	32%

According to the RIFLE classification, there were 40 Non-ARF patients, 22 RIFLE-R patients, 8 RIFLE-I patients and 30 RIFLE-F patients as shown in table (4):

Table 4	Survivor	Non-Survivor	Total
Non-ARF	27	13	40
Risk	7	15	22
Injury	2	6	8
Failure	2	28	30

According to the AKIN criteria, there were 38 Non-ARF patients, 24(Stage 1) patients, 8 (Stage 2) patients and 30 (Stage 3) patients as shown in table (5):

Table 5	Survivor	Non-Survivor	Total
Non-ARF	26	12	38
Stage 1	8	16	24
Stage 2	2	6	8
Stage 3	2	28	30

Morbid and Co-morbid conditions: Table (6):

Table 6		Number	Percent
Diabetes Mellitus	**No DM**	67	67%
	DM	33	33%
Hypertension	**No HTN**	84	84%
	HTN	16	16%
Hepatocellular Carcinoma	**No HCC**	80	89%
	HCC	10	11%

Laboratory values of the studied population:
The mean values of laboratory data with Standard deviation are shown in table (7):

Table 7	N	Mean	±Std. Deviation
BUN	100	38.64	23.30
Na	100	130.03	7.35
K	100	4.41	.725
AST	100	70.23	57.95
ALT	100	35.90	23.95
Albumin	100	2.05	0.44
Bilirubin	100	6.70	5.88
Hb	100	8.79	1.43
WBC	100	10.43	6.15
Platelets	100	120.46	71.87
PT	100	18.54	2.70
INR	100	1.67	0.26
PH	100	7.35	0.10
PO2	100	83.06	17.75
PCO2	100	26.36	5.81
HCO3	100	16.77	4.80
Hct	100	24.90	6.65
Creatinine at baseline	100	0.96	0.27
Creatinine on follow up	100	1.89	1.23

Length of hospital stay:
The mean duration of hospital stay in the whole studied population was 11.6± 6.58 days with least of 3 days and maximum 30 days.

Mortality in the whole studied population:
There were 62% non-survival cases and 38 % survival as described for overall population in this study as shown in table (8):

Table 8	Number	Percent	
Survivor	38	38%	
Non-Survivor	62	62%	

According to RIFLE classification, the mortality rate was as follow:
32.5% in Non-ARF category
68% in RIFLE-R category
75% in RIFLE-I category
93% in RIFLE-F category
According to AKIN criteria, the mortality rate was as follow:
31.5% in Non-ARF category
66% in Stage 1 category
75% in Stage 2 category
93% in Stage 3 category

Comparative analysis between Non-Survivor group and survivor group:
There was statistically insignificant difference between both groups regarding age, gender, DM, HTN and HCC occurance as shown in table (9):

Table 9	DEATH	Mean	±Std. Deviation	*P* VALUE
Age	Survivor	59.73	5.71	0.625
	Non-Survivor	58.91	9.24	
Gender		Male	Female	0.27
	Survivor	23	15	
	Non-Survivor	45	17	
DM		No DM	DM	0.589
	Survivor	23	15	
	Non-Survivor	44	18	
HTN		No HTN	HTN	0.589
	Survivor	33	5	
	Non-Survivor	51	11	
HCC		No HCC	HCC	0.485
	Survivor	30	2	
	Non-Survivor	50	8	

- **Univariate analysis for laboratory data:**

Table 10	DEATH	Mean	±Std. Deviation	*P* VALUE
BUN	Survivor	24.50	15.34	0.0001
	Non-Survivor	47.30	23.19	
Na	Survivor	135.42	5.55	0.0001
	Non-Survivor	126.72	6.31	
K	Survivor	4.29	0.39	0.20
	Non-Survivor	4.48	0.86	
AST	Survivor	54.86	33.98	0.037
	Non-Survivor	79.64	67.18	
ALT	Survivor	36.86	28.05	0.75
	Non-Survivor	35.30	21.29	
Albumin	Survivor	2.23	0.44	0.0001
	Non-Survivor	1.93	0.40	
Bilirubin	Survivor	3.53	2.20	0.0001
	Non-Survivor	8.65	6.57	
Hb	Survivor	8.96	1.27	0.35
	Non-Survivor	8.68	1.52	
WBC	Survivor	9.23	4.78	0.12
	Non-Survivor	11.16	6.78	
Platelets	Survivor	135.71	88.93	0.09
	Non-Survivor	111.11	57.91	
PT	Survivor	16.88	1.30	0.0001
	Non-Survivor	19.56	2.83	
INR	Survivor	1.51	0.13	0.0001
	Non-Survivor	1.77	0.27	
pH	Survivor	7.41	0.07	0.0001
	Non-Survivor	7.32	0.11	
PO_2	Survivor	86.28	12.43	0.15
	Non-Survivor	81.08	20.18	
PCO_2	Survivor	27.18	6.08	0.27
	Non-Survivor	25.85	5.63	
HCO_3	Survivor	18.41	4.21	0.0001
	Non-Survivor	15.76	4.90	
Hct	Survivor	25.26	6.39	0.672
	Non-Survivor	24.67	6.85	
Creatinine at baseline	Survivor	0.77	0.22	0.0001
	Non-Survivor	1.08	0.23	
Creatinine on follow up	Survivor	1.02	0.63	0.0001
	Non-Survivor	2.42	1.21	

As described in table (10) Non-Survivor group had significantly higher serum creatinine level at baseline and during follow up, also higher BUN, serum bilirubin, PT and INR in comparison to Survivor group. The Non-Survivor group had a significantly lower serum sodium level, serum albumin, blood pH and HCO_3.

There were statistically insignificant differences between both groups regarding values of ALT, Hb, Hct, WBCs, PLT, PO_2 and PCO_2. Table (10)

Length of hospital stay:

Table 11	Survival	Mean	±Std. Deviation	*P* VALUE
LOS	Survivor	9.18	5.99	0.004
	Non-Survivor	13.08	6.53	

The Non-Survivor group had a significantly longer duration of hospital stay than the Survivor group as shown above in table (11).

Cut-off points for prediction of mortality by different scoring systems:

All scoring systems studied in this study were highly predictive of poor outcome in cirrhotic patients at different cut-off points as studied by ROC curve analysis as shown in table (12):

Table 12	Area under the curve	Mean of Cut off point	*P* value	PPV	NPV	Sensitivity	Specificity	
RIFLE	0.798	Non ARF	0.0001	80%	78%	79%	72%	
AKIN	0.801	Non ARF	0.0001	80%	78%	79%	72%	

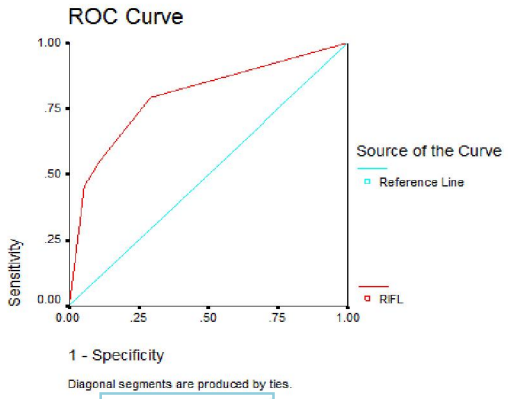
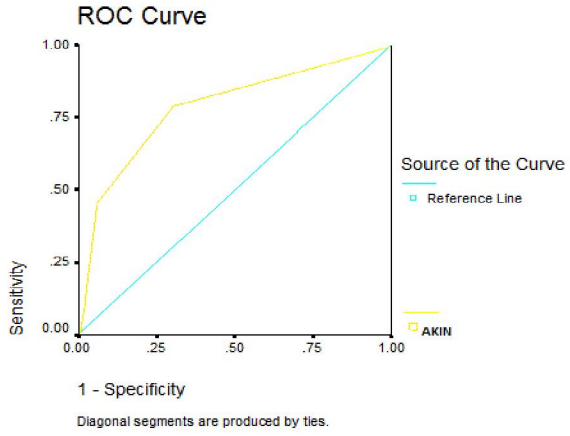


Figure 27



The predictive death rates for RIFLE stage of renal failure as compared to other stages as shown in table (13) was significantly higher
90 % at 17th day in group renal failure (RIFLE-F)
51% at 11th day in group of renal injury (RIFLE-I)
50% at 14th day of at risk group (RIFLE-R)
30 % at 17th day for (non-ARF) and the *p* value was

Table 13	Predictive mortality	Descriptive mortality
Non-ARF	30%	32,5%
Risk	50%	68%
Injury	51%	75%
Failure	90%	93%

The predictive death rates for AKIN stage of renal failure as compared to other stages as shown in table (14) was significantly higher
90 % at 17th day in group renal failure (Stage 3)
51% at 11th day in group of renal injury (Stage 2)
50% at 14th day of at risk group (Stage 1)
30 % at 17th day for (Non-ARF) and the p value was 0.016

Table 14	Predictive mortality	Descriptive mortality
Non-ARF	30%	31,5%
Stage 1	50%	66%
Stage 2	51%	75%
Stage 3	90%	93%

4.Discussion

This study was performed on 100 cirrhotic patients admitted to Intensive Care Unit in the hospital of Theodore Bilharz Research Institute. The objective of this study is to evaluate and compare RIFLE and AKIN criteria in evaluating AKI and predicting mortality in critically ill cirrhotic patients. The studied population was classified according to the primary outcome of this study (Hospital Mortality) into two main groups; Survivors and Non-Survivors.

There was statistically insignificant difference between both groups regarding age, gender distribution, DM, HTN and HCC occurance on both groups. The Non-Survivor group had

significantly higher serum creatinine level at baseline and during follow up, also higher BUN, serum bilirubin, PT and INR in comparison to Survivor group. The Non-Survivor group had a significantly lower serum sodium level, serum albumin, blood PH and HCO3. There were also statistically insignificant differences between both groups regarding values of ALT, Hb, Hct, WBCs, PLT, PO_2 and PCO_2(*Tables 9, 10).*

In this study, 60% of the ICU patients developed AKI; as defined by RIFLE classification; which was associated withincreased mortality, compared with those who did notdevelop AKI. There were 40 Non-ARF patients, 22 RIFLE-R patients, 8 RIFLE-I patients and 30 RIFLE-F patients (*Table 4).*As defined by AKIN criteria, 62% of the ICU patients developed AKI which was associated withincreased mortality, compared with those who did notdevelop AKI. There were 38 Non-ARF patients, 24 (Stage 1) patients, 8 (Stage 2) patients and 30 (Stage 3) patients (*Table 5).*

The overall mortality rate in thisstudy was 62%,and is in agreement with previous reports indicating thatcirrhotic patients admitted to an ICU have a very poorprognosis (11, 15, 16, 17, 18, and 19).This study identified that RIFLE classification and AKIN criteria on the first day of ICU admission was prognostically significantvariables for critically ill cirrhotic patients. Importantly, even a mild degree of kidney dysfunction,RIFLE class risk or injury or AKIN Stage 1 or 2, were associated with elevatedmortality rate, compared with patients who maintainednormal function. In the present study, the hospitalmortality rate of ICU patients wassignificantly higher for AKI patients (Risk, Injury, Failure) or (stages 1, 2, 3) versus non-AKI (Non-ARF) patients. We also found that there is stepwise increase in the mortality rate among RIFLE classes (32.5% in Non-ARF group, 68% in RIFLE-R group, 75% in RIFLE-I group and 93% in RIFLE-F group). Also there was a stepwise increase in mortality rate among AKIN classes (31.5% in Non-ARF group, 66% in Stage 1 group, 75% in Stage 2 group and 93% in Stage 3).

This study concluded that the predictive and descriptive mortality of RIFLE classification / AKIN classes are almost the same for Non-ARF and RIFLE-F/ Stage 3 categories while there was a little difference between predictive and descriptive mortality in the Risk / Stage 1 and Injury / Stage 2 categories of RIFLE / AKIN scores owing to the small number of patients in these groups and thus we recommend that this study be done on a larger number of patients.

We comparedthe overall incidence and severity classification of theRIFLE and AKIN criteria in this study and found no significantdifferences. We also compared the clinical outcomes,specifically hospital mortality and duration of stay in ICU, and found no material differences.

These findings are relevant as they suggest that the proposedmodifications to an already recognized and establisheddefinition/classification system (i.e. RIFLE criteria) fail to bring about material advantages. Moreover, our resultssuggest that future effort should focus more on the successfulapplication and extend use of the RIFLE criteria tothe randomization of patients in clinical trials or on its use asa surrogate marker of a clinically important outcome in clinicaltrials aimed as prevention or attenuation of renal injury.

From the previous studies and the current study, it is clear that RIFLE classification is a very important tool that can be used simply to stratify mortality in critically ill patients either medically (Cirrhosis, Sepsis, Respiratory failure, etc.) or surgically (patients whom admitted to ICU after major surgeries) and thus it is recommended to use it with other scoring systems to predict mortality among these patients.

Despite the encouraging results, this study has severallimitations. First, this study was conducted at just oneinstitution; consequently, the results may not be directlyextrapolated to other patient populations. Second, the predictive accuracy oflogistic regression models has its own limitations. Finally, the prognostic instruments weretested on patients already admitted to ICUs, rather thanapplied as a preadmission screening tool; this may haveskewed the measured results.

Conclusion

In conclusion, this study demonstrated that theprognosis for cirrhotic patients admitted to ICU is poor. Compared to the RIFLE criteria, the newlyproposed AKIN criteria do not materially improve the sensitivity, robustness or predictive ability of the definitionand classification of AKI in the first 24 h after admission to ICU. There would appear to be no justification at present for the introduction of a modified definition and classificationsystem for AKI. Any future refinements to the RIFLE criteria (i.e. time constraint or urine output) should ideallyoccur only after prospective evaluation in clinical studies. Considering the economy and ease of implementation, we suggest that RIFLE classification can increase the accuracy of short-term prognosis in this homogeneoussubset of patients.

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