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Original article

Predictive Value of Rifle Criteria on Renal Function Recovery of Patients with Septic and Non-Septic Acute Kidney Injury

Aida Hamzic-Mehmedbasic[1], Senija Rasic[1], Sukrija Zvizdic[2], Alma Muslimovic[1], Damir Rebic[1] and Amila Mehmedovic[3]

[1]Clinical Centre University of Sarajevo, Nephrology Clinic, [2]Medical Faculty University of Sarajevo, Institute of Microbiology, [3]Clinical Centre University of Sarajevo, Gastroenterohepatology Clinic, Sarajevo, Bosnia and Herzegovina

Abstract

Introduction. Recently proposed RIFLE criteria appear to have prognostic ability and to stimulate advances in therapy of patients with acute kidney injury (AKI). It is yet unknown whether this classification has predictive value on tubular function recovery or impact in the presence or absence of urinary protein in AKI patients. The aim of this study was to identify three classes of AKI severity defined by RIFLE classification, and to assess whether these RIFLE criteria have any impact on renal function outcome.
Methods. Retrospective-prospective study was performed on Clinical Centre University of Sarajevo, Nephrology Clinic and Clinic for Infectious Diseases during 5-year period. One hundred patients with presence of AKI (according to RIFLE criteria) were enrolled in the study. Patients were divided in two groups: patients with septic AKI and patients non-septic AKI. Microbiological tests, relevant clinical and laboratory parameters were determined. Patients were followed up until discharge or death. Outcome of renal function was defined by creatinine clearance, urine to serum creatinine ratio (U/Scr) and urinary protein levels.
Results. The results of the study showed the RIFLE class Risk represents an independent predictor of recovered tubular function and lack of proteinuria in all AKI patients. On the contrary, class Failure represents an independent predictor of lack of recovery of renal function, in the group of patients with septic AKI.
Conclusion. RIFLE classification has very good predictive value for prognosis of renal function recovery in AKI patients.

Key words: acute kidney injury, outcome, RIFLE classification, predictors, renal function outcome, mortality

Introduction

Acute kidney injury is a complex clinical syndrome, which can be observed in a wide variety of clinical settings. The etiology of AKI is often multifactoral. Sepsis has constantly been found to be a leading contributing factor to AKI. Discriminating between AKI of septic and non-septic origin may have clinical relevance [1]. Introducing RIFLE criteria [2], a consensus definition of AKI, in practice of nephrology, has enabled better determination of AKI in the diagnostic, therapeutic and prognostic terms [3]. However, it is still unknown whether this classification has predictive value on tubular function recovery or impact in the presence or absence of proteinuria in AKI patients. It is also unknown whether these RIFLE criteria have any influence on renal function outcome if we define outcome by the values of creatinine clearance.
The aim of this study was to identify three classes of AKI severity defined by RIFLE classification, and to assess whether these RIFLE criteria have any impact on renal function outcome in patients with AKI of septic and non-septic origin.

Material and methods

This combined retrospective-prospective study was performed by Nephrology Clinic and Clinic for Infectious Diseases in Clinical Centre University of Sarajevo during the period between 2006 and 2010. One hundred patients with presence of AKI according to the RIFLE criteria were enrolled in the study. Patients were divided in two groups: patients with septic AKI and patients with non-septic AKI.
Vital clinical parameters were collected for the first 24 hours of hospital admission. During hospitalization microbiological tests were performed and relevant laboratory parameters were determined.
AKI was defined and categorized according to RIFLE classification, based on creatinine criteria. Class R (Risk) was considered if there was an increase of baseline serum creatinine x1.5; Class I (Injury) was considered if there was an increase of baseline serum creatinine ×2; and Class F (Failure) was considered if there was an increase of baseline serum creatinine ×3, or if there was an acute rise in serum creatinine of at least 44 µmol/L in patients with baseline serum creatinine >354 µmol/L. When pre-admission

Correspondence to: Aida Hamzic-Mehmedbasic, Nephrology Clinic, Clinical Center University of Sarajevo, Bolnicka 25, Sarajevo, Bosnia and Herzegovina; Phone: 00 387 33 297 401; Fax: 00 387 33 297 816; E-mail: aida_mehmedbasic@yahoo.com

serum creatinine was unavailable it was estimated as recommended by the ADQI working group [4] using the following Modification of Diet in Renal Disease (MDRD) equation: Serum creatinine=(75/[186×(age$^{-0.203}$)×(0.742 if female)×(1.21 if black)])$^{-0.887}$

Septic origin of AKI was diagnosed in those patients who had recognized source of infection, regardless of whether the blood culture was positive or not, and if they had verified increased blood urea nitrogen and serum creatinine. Criteria for the diagnosis of sepsis and septic shock were defined according to ACCP / SCCM consensus [5].

Patients were followed up until hospital discharge or death. Outcome of AKI was defined according to the values of creatinine clearance as recovered (creatinine clearance >60 mL/min) and unrecovered (creatinine clearance <60 mL/min) with impaired renal function. The outcome of the tubular function was defined by the value of urine to serum createnine ratio (U/Scr) as favorable (U/Scr >60) and adverse (U/Scr <60). This ratio is commonly used to distinguish acute tubular necrosis from prerenal azotemia [6]. Urinary protein levels were classified as normal (<0.20 g/day) and abnormal (>0.20 g.day).

Statistical analysis

We used descriptive statistics, Student's t-test (for variables with normal distribution) and Mann Whitney U test (for variables without normal distribution) to compare mean values between groups. Analysis of associations between death and categorized risk factors was done with chi-square test. A multivariate logistic regression was performed to evaluate the impact of the variables on mortality and renal outcome. *P* values <0.05 were considered significant.

Results

Patients with AKI and RIFLE criteria

One hundred patients with AKI were divided in two groups according to the etiology of AKI. There were 66 patients in the group of AKI of non-septic etiology and 34 patients in the group of AKI of septic etiology (34 patients). The incidence of the certain grade of AKI according to RIFLE classification did not significantly differ between these two groups of patients. The first grade of AKI (Risk) was present in 8.8% of septic AKI patients and 7.6% of non-septic AKI patients. The second class of AKI (Injury) was observed in 17.6% of patients with septic and 12.1% of patients with non-septic AKI. Finally, Failure was present in 73.5% of patients with septic and 80.3% of patients with non-septic AKI (Figure 1).

In order to estimate outcome of AKI, defined by the values of creatinine clearance, we measured creatinine clearance values in all three RIFLE classes of AKI patients at the end of treatment. It was confirmed that Risk group of patients had statistically significantly higher mean createnine clearance values (97.19±5.93 mL/min) in comparison to the Injury group (71.42±4.61 mL/min) and Failure group of patients (66.31±4.08 mL/min) (p<0.001). The mean values of creatinine clearance did not significantly differ between the groups of patients with Injury and Failure (Table 1). However, when related to the etiology of AKI, there was a statistically significant difference in mean values of the creatinine clearance in Injure and Failure groups of patients. In comparison to the non-septic AKI patients, patients with septic AKI had significantly lower average values of creatinine clearance in Injury group (60.9±6.6 vs. 79.3±5.0 mL/min; p=0.042) and Failure group (38.3±4.1 vs. 76.7±4.5 mL/min; p<0.001) (Figure 2).

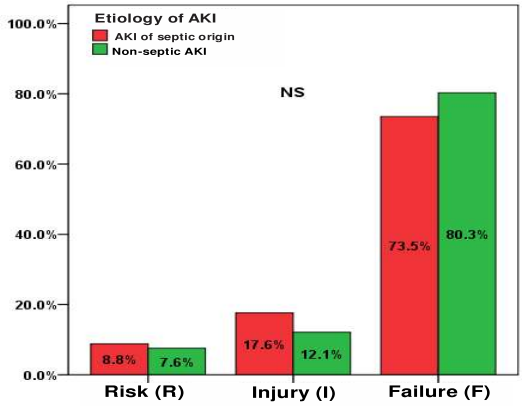

Fig. 1. Distribution of patients according to the class of AKI

Table 1. Average values of the creatinine clearance at the end of treatment comparing to the class of AKI

	Risk (R)	Injury (I)	Failure (F)
Creatinine clearance (mL/min)	97.19±5.93*╪	71.42±4.61	66.31±4.08

*- significant difference between Risk (R) and Injure (I) groups (p<0.001)

╪- significant difference between Risk (R) and Failure (F) groups (p<0,001)

Predictors of outcome according to RIFLE classification

Using a stepwise logistic regression model, it was found that the third grade of RIFLE classification nominated as Failure was an independent predictor of creatinine clearance values <60 mL/min, but only in the group of septic AKI patients (β coefficient 0.150, 95% confidence interval 0.026 to 0.868, p=0.034), which means that class Failure was an independent predictor of lack of recovery of renal function at the end of treatment. In the group of non-septic AKI patients, none of the RIFLE classes proved to be predictor of lack of recovery of renal function.

By using logistic regression model, it was found that the first RIFLE class Risk was an independent predictor of the U/Scr >60 in all monitored patients (β coefficient 7.224, 95% confidence interval 1.189 to 43.908, p=0.032). It was also found that the Risk was an independent negative predictor of presence of abnormal urinary protein levels, also in all monitored septic and non-septic AKI patients (β coefficient 0.061, 95% confidence interval 0.009 to 0.432, p<0.005) (Table 2).

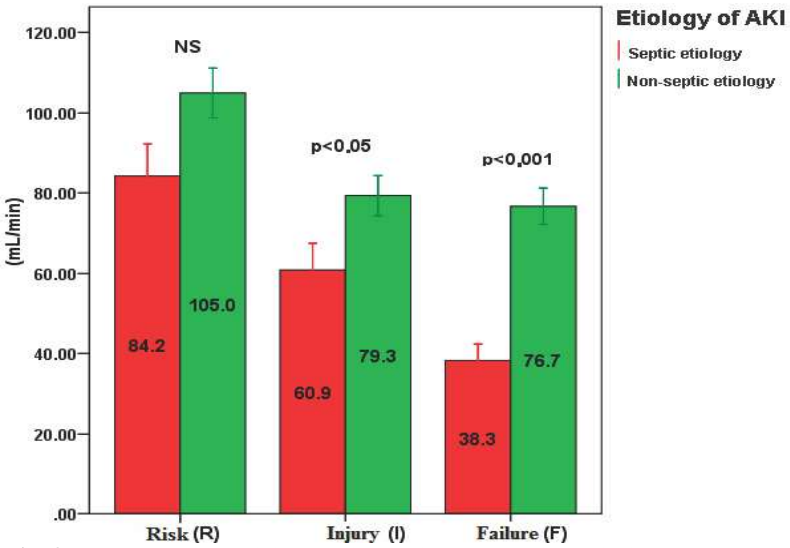

Fig. 2. Average values of the creatinine clearance at the end of treatment of patients with various grade of AKI related to the etiology of AKI

Table 2. Independent predictors of renal function outcome in AKI patients

Outcome	Predictor	β coefficient	p-value
Creatinine clearance values <60 mL/min in septic AKI patients	Failure (F)	0.150	0.034
Urine to serum creatinine ratio >60 in all AKI patients	Risk (R)	7.224	0.032
Abnormal urinary protein levels in AKI patients	Risk (R)	0.061	0.005

Mortality according to RIFLE classification

Total mortality in the studied population of AKI patients was 7%. When mortality analyzed according to the grade of AKI defined by RIFLE criteria, there was no mortality in the Risk group of patients. However, mortality rate was 7.1% in the Injury group and 7.9% in Failure group of patients (Figure 3).

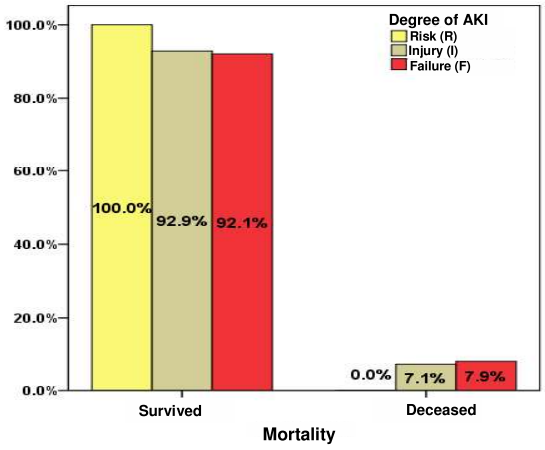

Fig. 3. Mortality of patients with AKI according to the class of RIFLE classification

Discussion

Outcome of AKI is influenced by numerous clinical and laboratory prognostic factors and among them very important predictive value seems to have classification and etiology of AKI [1,3].

The distribution of certain grade of AKI, defined in our study according to RIFLE classification as Risk, Injury and Failure, did not significantly differ between groups of patients with septic and non-septic AKI. Patients with septic AKI had a slightly higher incidence of Injury, but this difference was not statistically significant, which is in accordance with the results of Bagshaw *et al.* [7,8]. However, in our study, Failure was more frequent in the group of patients with non-septic AKI, which is not consistent with the results of mentioned studies. In the first study by Bagshaw *et al.* [7] the incidence of Failure was the same in the group of septic and non-septic AKI patients. The second and more recent study by the same authors [8] showed an association of septic AKI with class Failure when compared to non-septic AKI, but again with no statistically significant difference. Class Risk was equally represented in both monitored groups of AKI patients in our study, as well as reported in other studies. It is very important to emphasize that neither our study, nor other studies found statistical difference in distribution of any RIFLE classes between groups of patients with septic and non-septic AKI.

In this study significant differences were observed in the outcome of renal function in certain RIFLE grades of AKI. Risk group of patients had significantly higher creatinine clearance values at the end of hospitalization compared to the patients in Injury and Failure group, indicating a better outcome of renal function at this level of AKI. Etiology seemed to have influence on renal function outcome too. We found significantly lower values of creatinine clearance at the end of hospitalization among patients with Injury and Failure who had septic AKI, in comparison to the patients with Injury and Failure of non-septic etiology, which confirms a negative impact of septic etiology on renal function outcome. It was found that the Failure, as a third class of AKI, was independent predictor of the unrecovered renal function, but only in a group of septic AKI patients. On a contrary, class Risk was independent predictor of recovered tubular function and negative independent predictor of the presence of abnormal urinary protein levels in all AKI patients. That means that only Risk group of patients had low probability to have abnormal urinary protein levels at the end of hospitalization.

We analyzed hospital mortality of patients in all three classes of AKI and found that class Risk is associated with better survival. While mortality in the Injury group of patients was 7.1% and in the Failure group of patients 7.9%, patients classified as Risk had no mortality at all. In certain number of studies RIFLE classification proved to be independent predictor for mortality. Almost linear increase in mortality with each further class of AKI was verified by Bagshaw *et al.* [3], Chen *et al.* [9] and Ostermann and Chang [10]. Although in our study patients in the Injury and Failure groups proved to have higher mortality, RIFLE classification had no predictive value for mortality. This could be explained by lower hospital mortality which was only 7% in our study, while other authors reported mortality rate ranging between 45 and 70% [11]. A possible reason for this may be the illness severity, number of comorbidities, dependence on mechanical ventilation, etc.

Conclusions

RIFLE classification has very good predictive value on prognosis of renal function recovery in AKI patients. RIFLE class Risk is independent predictor of recovered tubular function and the absence of abnormal urinary protein levels in all AKI patients. On the contrary, class Failure is an independent predictor of lack of recovery of renal function, but only in a group of patients with septic AKI.

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Conflict of interest statement. None declared.

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