DOI: 10.5455/msm.2023.35.304-308
Received: Nov 20 2023; Accepted: Dec 15, 2023

ORIGINAL PAPER Mater Sociomed. 2023; 35(4): 304-308

Acute Kidney Injury Classifications in the Prediction of In-hospital Mortality and Renal Function Non-recovery

Aida Hamzic-Mehmedbasic[1], Melina Mackic[2], Damir Rebic[1], Hajrudin Spahovic[3], Ajla Arnautovic-Halimic[4], Nadina Jakirlic[5]

[1]Nephrology Clinic, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina

[2]Juraklinik Scheßlitz, Scheßlitz, Deutschland

[3]Urology Clinic, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina

[4]Clinic for Nuclear Medicine and Endocrinology, Clinical Center University of Sarajevo, Nephrology Clinic, Sarajevo, Bosnia and Herzegovina

[5]Radiology Clinic, Clinical Center University of Sarajevo, Nephrology Clinic, Sarajevo, Bosnia and Herzegovina

Corresponding author: Aida Hamzic-Mehmedbasic, MD, PHD, Nephrology Clinic, Clinical Center University of Sarajevo, Bolnicka 25, 71 000, Sarajevo, Bosnia and Herzegovina, E-mail: aida.mehmedbasic@mf.unsa.ba, ORCID ID: http//www.orcid.org/0000-0002-4967-7616.

ABSTRACT

Background: In the last two decades diagnostic criteria for acute kidney injury (AKI) were developed: Risk, Injury, Failure, Loss of Kidney Function, End-Stage Kidney Disease (RIFLE), Acute Kidney Injury Network (AKIN), and Kidney Disease: Improving Global Outcomes (KDIGO) classifications. **Objective:** The study aimed to determine the incidence of AKI based on the RIFLE, AKIN, and KDIGO criteria, as well as analyze their predictive value for mortality and renal function outcome. **Methods:** This was a single-center prospective study of patients diagnosed with AKI. Acute kidney injury was defined and classified according to the RIFLE, AKIN, and KDIGO criteria. The outcomes were renal function outcome and in-hospital mortality. **Results**: The incidence rates of AKI based on the RIFLE, AKIN, and KDIGO criteria were 13.4%, 14-36%, and 14.64%, respectively. Multiple regression analysis showed that higher stages of AKI according to the KDIGO criteria were independently associated with non-recovery of renal function (p=0.011). However, the predictive ability of RIFLE, AKIN and KDIGO classifications for renal function recovery was poor (Area Under the Receiver Operating Characteristics-AUROC=0.599, AUROC=0.637, AUROC=0.659, respectively). According to the RIFLE and AKIN criteria, in-hospital mortality was statistically significantly higher in stage Failure/3 (p=0.0403 and p=0.0329, respectively) compared to stages Risk/1 and Injury/2. Receiver Operating Characteristics (ROC) analysis showed that all three classifications had poor predictive ability for in-hospital mortality (AUROC=0.675, AUROC=0.66, AUROC=0.681). **Conclusions**: KDIGO classification is an independent predictor of renal function non-recovery. However, by ROC analysis, all three classifications have poor predictive ability for renal function outcome and mortality.

Keywords: acute kidney injury, classifications, renal function non-recovery, in-hospital mortality.

1. BACKGROUND

Acute kidney injury (AKI) is a frequent and complex syndrome defined by a sudden decline in renal function or reduction in urine output (1). Acute kidney injury is a common complication in patients admitted to hospital (10-15%), with increasing incidence in recent years, especially in the intensive care unit (ICU), where it can sometimes exceed 50% (2). It is associated with adverse short- and long-term outcomes and increased mortality, placing a high cost to patients, as well as healthcare systems. There are significant variations in the reported incidence of AKI, which can be explained by population differences, differences between high-income and low-to-middle-income countries, and most importantly by the inconsistent use of diagnostic criteria for AKI (3).

Over the last few decades, the definition and classifications of AKI have been modified and improved significantly, starting with the Risk, Injury, Failure, Loss of Kidney Function, End-Stage Kidney Disease (RIFLE) classification in 2004, Acute Kidney Injury Network (AKIN) classification in 2007, un-

AKI criteria	n	Incidence based on the total number of patients	Incidence on 1000 patients	AKI stage	n	%	p
RIFLE	97	13.4	9.7	Risk Injury Failure	12 26 61	12.4 24.7 62.9	0.974
AKIN	104	14.36	10.4	Stage 1 Stage 2 Stage 3	13 27 64	12.5 26.0 61.5	0.887
KDIGO	106	14.64	10.6	Stage 1 Stage 2 Stage 3	13 24 69	12.3 22.6 65.1	0.777

Table 1. Incidence of AKI and distribution of patients with AKI according to the stages of RIFLE, AKIN, and KDIGO classifications. AKI-acute kidney injury; RIFLE-Risk, Injury, Failure, Loss of Kidney Function, End-Stage Kidney Disease; AKIN-Acute Kidney Injury Network; KDIGO-Kidney Disease Improving Global Outcomes.

til the recently developed Kidney Disease Improving Global Outcomes (KDIGO) classification, which had the aim of unifying the definition of AKI (4-6). Since then, some authors have compared the three classifications in their reported incidence of AKI, as well as sensitivity, accuracy, and predictive ability for various short- and long-term outcomes (3).

2. OBJECTIVE

The present study aimed to determine the incidence and severity of AKI according to the RIFLE, AKIN, and KDIGO classifications, as well as analyze the predictive value of these classifications for in-hospital mortality and renal function outcome of patients with AKI.

3. MATERIAL AND METHODS

This single-center prospective study included all patients admitted to the Nephrology Clinic, Clinical Center University of Sarajevo during one-year period. Of 724 patients admitted to the Nephrology Clinic; based on the inclusion and exclusion criteria, the final studied cohort consisted of 106 patients. Inclusion criteria were: adult patients (>18 years old), patients diagnosed with AKI, and patients with hospital stay longer than 48 hours. Exclusion criteria were: renal transplantation, end-stage kidney disease (ESKD), and chronic dialysis.

Relevant demographic data, laboratory, and clinical parameters were recorded. Clinical parameters included: measurement of 24-hour urine output, type of AKI, presence of underlying chronic kidney disease (CKD) and type of treatment (conservative or dialysis).

Acute kidney injury was defined and classified using the RIFLE, AKIN, and KDIGO criteria (4-6). When pre-admission serum creatinine (SCr) was unavailable, it was estimated as recommended by the Acute Dialysis Quality Initiative (ADQI) Work Group (7). Anuria was defined as a 24-hour urine output <100 mL and oliguria was defined as a 24-hour urine output of 100-400 mL.

The outcomes were in-hospital mortality and renal function non-recovery. Renal function recovery was defined as eGFR>60 mL/min/1.73m2, while non-recovery was defined as eGFR<60 mL/min/1.73m2 at discharge from the hospital. The estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (8). For patients with underlying CKD, recovery of renal function was defined according to the values of SCr at discharge, closest to the baseline value at admission (for AKIN and KDIGO). For the RIFLE criteria, recovery of renal function was defined according to the values of SCr at discharge closest to the previously recorded SCr or estimated pre-admission SCr.

Data were analyzed using SPSS computer program version 17. Category variables were represented by frequency as an absolute number or percentage and compared using the Chi-Square test. The specificity and sensitivity of classifications in predicting renal function non-recovery and mortality were evaluated with the Receiver Operating Characteristics (ROC) curve analysis. Logistic regression analysis was used to determine predictors of renal function outcome. A p-value of <0.05 was considered statistically significant.

4. RESULTS

The incidence of AKI among 724 hospitalized patients of the Nephrology Clinic during one-year period and the incidence of AKI calculated on 1000 patients as well as the distribution of patients with AKI according to the stages of RIFLE, AKIN, and KDIGO classifications is presented in Table 1. When comparing the severity of AKI according to the RIFLE, AKIN, and KDIGO, there was no statistically significant difference in distribution between stages of AKI.

Characteristics of patients with AKI are presented

Age (years)		73 (64-81)	-
Male n (%)		50 (47.2)	-
Underlying CKD	n (%)	47 (44)	-
Types of AKI n (%)	Prerenal	48 (45.3)	p<0.001*
	Intrinsic	45 (42.5)	
	Postrenal	13 (12.3)	
Diuresis n (%)	Anuria	8 (7.5)	p<0.001*
	Oliguria	17 (16)	
	Diuresis >400 ml	81 (74.6)	
Types of treatment n (%)	Conservative	86 (81.2)	p<0.001*
	Hemodialysis	20 (18.8)	
Renal function outcome n (%)	Recovery	65 (61.4)	p=0.002*
	Non-recovery	41 (39.6)	
In-hospital mortality n (%)	Non-survivors	13 (12.3)	p<0.001*
	Survivors	93 (87.7)	

Table 2. Characteristics of patients with AKI. Data are presented as numbers and percentages, or median and interquartile range. AKI-acute kidney injury; CKD-chronic kidney disease.* p<0.05

Classification	Stage	Renal function outcome		p
		Recovery	Non-recovery	
		n (%)	n (%)	
RIFLE	Risk & Injury	26 (72.2)	10 (27.8)	0.088
	Failure	32 (52.5)	29 (47.5)	
AKIN	Stage 1&2	31 (77.5)	9 (22.5)	0.014*
	Stage 3	33 (51.5)	31 (48.5)	
KDIGO	Stage1&2	31 (83.8)	6 (16.2)	0.001*
	Stage 3	34 (49.3)	35 (50.7)	
Classification	Stage	In-hospital mortality		p
		Survivors	Non-survivors	
		n (%)	n (%)	
RIFLE	Risk & Injury	35 (97.3)	1 (2.7)	0.04*
	Failure	49 (80.3)	12 (19.7)	
AKIN	Stage 1&2	39 (97.5)	1 (2.5)	0.032*
	Stage 3	52 (81.3)	12 (18.7)	
KDIGO	Stage1&2	36 (97.3)	1 (2.7)	0.059
	Stage 3	57 (82.6)	12 (17.4)	

Table 3. Comparison of renal function outcome and in-hospital mortality between patients in different stages of AKI. AKI-acute kidney injury; RIFLE-Risk, Injury, Failure, Loss of Kidney Function, End-Stage Kidney Disease; AKIN-Acute Kidney Injury Network; KDIGO-Kidney Disease Improving Global Outcomes; *p <0.05.

Dependent variable: Non-recovery of renal function					
Model	B	SE	OR	95% CI	p
KDIGO stage 1,2,3	0.204	0.079	0.256	0.003-0.662	0.011*

Table 4. Independent predictor of non-recovery of renal function in patients with AKI. AKI-acute kidney injury; KDIGO-Kidney Disease Improving Global Outcomes; SE-standard error; OR-odds ratio; CI-confidence interval; *p <0.05.

in Table 2. The median age of the patients with AKI was 73 years and nearly half of them were male. Underlying CKD was found in 44% patients. In comparison with other types of AKI, the postrenal type was the least prevalent type of AKI (p<0.001). Patients with AKI had statistically significantly more common diuresis >400 ml than anuria and oliguria (p<0.001). Conservative treatment was significantly more frequent option of choice for treatment in comparison to hemodialysis (p<0.001). Compared to the non-recovery of renal function, a statistically significant number of patients with AKI had recovered renal function (p=0.002). A statistically significant number of patients had survived compared to the deceased (87.% vs. 12.3%; p<0.001).

A comparison of renal function outcome and in-hospital mortality between patients in different stages of AKI is presented in Table 3. Regarding renal function outcome, stage 3 of AKIN and KDIGO classifications showed a significantly higher percentage of non-recovery of renal function, compared to stages 1 and 2 (p=0.014 and p=0.001, respectively). Based on the RIFLE and AKIN criteria, the number of in-hospital mortalities was significantly higher in stage Failure/3 compared to stages Risk/1 and Injury/2 (p=0.04 and p=0.032 respectively).

Using a logistic regression model, KDIGO classification was confirmed as a significant independent predictor of non-recovery of renal function in patients with AKI (OR 0.256, 95% CI 0.003-0.662, p=0.011). With each increase in the stage of AKI according to the KDIGO criteria, the probability of renal function non-recovery is rising (Table 4).

The predictive value of AKI classifications (RIFLE, AKIN, and KDIGO) for renal function non-recovery and in-hospital mortality is presented in Table 5. RIFLE, AKIN, and KDIGO classifications had poor accuracy in the prediction of non-recovery of renal function (AUROC=0.599, AUROC=0.637, AUROC=0.659, respectively) and in-hospital mortality (AUROC=0.675, AUROC=0.681, AUROC=0.66, respectively) with rather higher sensitivities but low specificities for detection of renal function outcome and in-hospital mortality.

5. DISCUSSION

In the present study, the incidence of AKI among hospitalized patients during a one-year period did not significantly differ according to the three contemporary AKI classifications (RIFLE, AKIN, and KDIGO). By logistic regression analysis, KDIGO classification proved to be an independent predictor of renal function non-recovery. However, by ROC analysis, all three classifications have poor predictive ability for renal function outcome and in-hospital mortality.

The incidence of AKI defined by the KDIGO classification was very similar but slightly higher (14.6%) than that defined by RIFLE and AKIN classifications (13.4% and 14.4%, respectively) in this study. In accordance with our results, in the study of hospitalized patients, the KDIGO classification had a slightly higher incidence (18.3%) compared to the AKIN and RIFLE classifications (16.6% and 16.1%, respectively) (9). In a large retrospective study conducted on critically ill patients, the incidence was the highest according to the KDIGO criteria (51%), followed by RIFLE (46.9%) and AKIN criteria (38.4%) (10). An increased incidence of AKI according to the KDIGO criteria compared to the AKIN criteria could be explained by a longer timeframe of seven days for AKI diagnosis, compared to the timeframe of only 48 hours used to diagnose AKI according to the AKIN criteria. Variations in the incidence of AKI in different studies are probably a result of different patient populations and a higher bur-

Non-recovery of renal function					
	AUROC	Sensitivity	Specificity	95% CI	p
RIFLE	0.599	74.36	44.83	0.494 – 0.697	0.0448*
AKIN	0.637	92.31	41.67	0.537 – 0.729	0.0029*
KDIGO	0.659	85.37	47.69	0.561 – 0.748	0.0003*
In-hospital mortality					
	AUROC	Sensitivity	Specificity	95% CI	p
RIFLE	0.675	92.31	41.67	0.573 – 0.767	<0.0001*
AKIN	0.681	92.31	42.86	0.583 – 0.769	<0.0001*
KDIGO	0.66	92.31	38.71	0.562 – 0.750	0.0001*

Table 5. Sensitivity and specificity of RIFLE, AKIN, and KDIGO classification for detecting renal function non-recovery and in-hospital mortality. RIFLE-Risk, Injury, Failure, Loss of Kidney Function, End-Stage Kidney Disease; AKIN-Acute Kidney Injury Network; KDIGO-Kidney Disease Improving Global Outcomes, AUROC-Area Under the Receiver Operating Characteristic; CI-confidence interval; *p <0.05.

den of illness in critically ill patients compared to other hospitalized patients.

In the present study, the prerenal type of AKI was the most frequently diagnosed (45.3%), followed by the intrinsic type diagnosed in 42.5% of patients, and the postrenal type in 12.3% of patients. Similar results were found by other authors with the most prevalent prerenal and intrinsic type of AKI (11). Underlying CKD was found in 44% of patients with AKI in this study which was higher prevalence of CKD compared to reported prevalence by other authors. Increased CKD prevalence in the present study could be explained with the higher median age of patients included in the study when compared to the patients in the other studies (12).

In this study, 39% of patients with AKI had non-recovered renal function. Stage 3 of AKIN and KDIGO classifications showed a significantly higher percentage of non-recovery of renal function, compared to stages 1 and 2. Logistic regression analysis proved that only AKI progressing according to the KDIGO classification can be used as a predictor of renal function non-recovery. Such results are to be expected, given that as AKI progresses to the higher stages, renal function significantly deteriorates, and the chance of recovery decreases. However, when analyzed with ROC analysis, all three AKI classifications (RIFLE, AKIN, and KDIGO) had poor predictive ability (AUROC=0.599, AUROC=0.637, AUROC=0.659, respectively) in the prediction of non-recovery of renal function. Higher stages of AKI according to the KDIGO were also independently associated with ESKD and mortality in the study of patients with AKI and lupus nephritis. However, it is difficult to compare these results with ours, because the patient population included lupus nephritis as the cause of AKI, and the outcome was defined differently (13).

In the present study, the in-hospital mortality of patients with AKI was 12%. The number of in-hospital mortalities was significantly higher in stage Failure/3, compared to stages Risk/1 and Injury/2 of RIFLE and AKIN classification. However, the KDIGO classification did not show any statistically significant difference in in-hospital mortality between stages of AKI. Similarly, Fujii and colleagues have found that in-hospital mortality increased in accordance with staging, for all classifications (14). When analyzed by ROC analysis, all three classifications (RIFLE, AKIN, KDIGO) in the present study have similar but poor predictive ability (AUROC=0.675, AUROC=0.66, AUROC=0.681, respectively) for in-hospital mortality. These results are similar to the results of a study conducted by Pereira and colleagues on the population of septic patients which revealed that all three classifications (RIFLE, AKIN, KDIGO) have similar prognostic abilities for predicting mortality (AUROC=0.652, AUROC=0.686, AUROC=0.658, respectively) (2). However, in critically ill patients the RIFLE, AKIN, and KDIGO criteria were rather good tools for predicting mortality with no significant difference between them (AUROC=0.735, AUROC=0.74, AUROC=0.733 for RIFLE, AKIN and KDIGO, respectively) (15). In the study of cardiac surgery patients, there were differences between the predictive ability of classifications and the AKIN classification correlated better with in-hospital mortality than the RIFLE classification (AUROC=0.86 for AKIN and AUROC=0.78 for RIFLE classification) (16). Finally, in patients on extracorporeal membrane oxygenation support, all three classifications had excellent predictive ability (AUROC=0.826, AUROC=0.836, AUROC=0.840 for RIFLE, AKIN. and KDIGO, respectively) (17.) These differences between the results of the present study and some others could be explained by a rather small sample size in the present study, and lower in-hospital mortality rate in our Nephrology Clinic, compared to the higher mortality rates in critically ill patients.

6. CONCLUSION

The incidence of AKI in patients hospitalized at the Nephrology Clinic during a one-year period according to the RIFLE, AKIN, and KDIGO criteria was 13.40%, 14.36%, and 14.64%, respectively. Renal function non-recovery was registered in 39.6% of patients with AKI, and in-hospital mortality in 12.3% of patients. When using logistic regression analysis, only KDIGO classification was an independent predictor of renal function non-recovery in patients with AKI. In-hospital mortality was significantly higher in stage Failure/3, compared to stages Risk/1 and Injury/2 of RIFLE, and AKIN classification. However, by ROC analysis, RIFLE, AKIN, and KDIGO classifications showed similar, but poor predictive ability for renal function non-recovery and in-hospital mortality.

- **Author's contribution:** All authors were involved in the preparation of this article. Final proofreading was made by the first author.
- **Conflict of interest:** The authors do not have any conflicts of interest to disclose.
- **Financial support and sponsorship:** None.

REFERENCES

1. Nateghi Haredasht F, Viaene L, Pottel H, De Corte W, Vens C. Predicting outcomes of acute kidney injury in critically ill patients using machine learning. Sci Rep. 2023; 13(1): 9864.
2. Pereira M, Rodrigues N, Godinho I, Gameiro J, Neves M, Gouveia J, et al. Acute kidney injury in patients with severe sepsis or septic shock: a comparison between the 'Risk, Injury, Failure, Loss of kidney function, End-stage kidney disease' (RIFLE), Acute Kidney Injury Network (AKIN) and Kidney Disease: Improving Global Outcomes (KDIGO) classifications. Clin Kidney J. 2017; 10(3): 332-340.
3. Hoste EAJ, Kellum JA, Selby NM, Zarbock A, Palevsky PM, Bagshaw SM, et al. Global epidemiology and outcomes of acute kidney injury. Nat Rev Nephrol. 2018; 14(10): 607-625.
4. 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.
5. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C,

Warnock DG, et al; 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.
6. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract. 2012; 120(4): c179-84.
7. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, et al; Chronic Kidney Disease Epidemiology Collaboration. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med. 2006; 145(4): 247-454.
8. Al Nasser MS, Ali AS, Sattar MAA, Abdulfattah EH, Khan LM, Al Alsheikh KA. Therapeutic drug monitoring of tacrolimus in Saudi kidney transplant patients. J Nephrol Ther. 2016; 06: 264.
9. Zeng X, McMahon GM, Brunelli SM, Bates DW, Waikar SS. Incidence, outcomes, and comparisons across definitions of AKI in hospitalized individuals. Clin J Am Soc Nephrol. 2014; 9(1): 12-20.
10. Luo X, Jiang L, Du B, Wen Y, Wang M, Xi X; Beijing Acute Kidney Injury Trial (BAKIT) workgroup. A comparison of different diagnostic criteria of acute kidney injury in critically ill patients. Crit Care. 2014; 18(4): R144.
11. Teo SH, Lee KG, Koniman R, Tng ARK, Liew ZH, Naing TT, et al. A prospective study of clinical characteristics and outcomes of acute kidney injury in a tertiary care Centre. BMC Nephrol. 2019; 20(1): 282.
12. Cheng X, Wu B, Liu Y, Mao H, Xing C. Incidence and diagnosis of Acute kidney injury in hospitalized adult patients: a retrospective observational study in a tertiary teaching Hospital in Southeast China. BMC Nephrol. 2017; 18(1): 203.
13. Chen T, Zhou Y, Zhang J, Chen C, Pan J. Long-term predictive value of acute kidney injury classification in diffuse proliferative lupus nephritis with acute kidney injury. BMC Nephrol. 2020; 21(1): 13.
14. Fujii T, Uchino S, Takinami M, Bellomo R. Validation of the Kidney Disease Improving Global Outcomes criteria for AKI and comparison of three criteria in hospitalized patients. Clin J Am Soc Nephrol. 2014; 9(5): 848-854.
15. Levi TM, de Souza SP, de Magalhães JG, de Carvalho MS, Cunha AL, Dantas JG, et al. Comparison of the RIFLE, AKIN and KDIGO criteria to predict mortality in critically ill patients. Rev Bras Ter Intensiva. 2013; 25(4): 290-296.
16. Bastin AJ, Ostermann M, Slack AJ, Diller GP, Finney SJ, Evans TW. Acute kidney injury after cardiac surgery according to Risk/Injury/Failure/Loss/End-stage, Acute Kidney Injury Network, and Kidney Disease: Improving Global Outcomes classifications. J Crit Care. 2013; 28(4): 389-396.
17. Tsai TY, Chien H, Tsai FC, Pan HC, Yang HY, Lee SY, et al. Comparison of RIFLE, AKIN, and KDIGO classifications for assessing prognosis of patients on extracorporeal membrane oxygenation. J Formos Med Assoc. 2017; 116(11): 844-851.