Journal of Surgery and Medicine

The relationship of KDIGO classification and incidence & mortality of acute kidney injury in sepsis patients in intensive care unit: A retrospective cohort study

Bilge Banu Taşdemir Mecit [1], Mustafa Deniz [2]

[1] Afyonkarahisar University of Health sciences Faculty of Medicine, Department of Anesthesiology and Reanimation, Afyon, Turkey
[2] Bolu Izzet Baysal State Hospital, Intensive Care Department, Bolu, Turkey

ORCID ID of the author(s)

BBTM: 0000-0002-7994-7816
MD: 0000-0002-1243-3028

Corresponding Author
Bilge Banu Taşdemir Mecit
Afyonkarahisar Health Sciences, University
Faculty of Medicine, Department of
Anesthesiology and Reanimation, 03030,
Afyonkarahisar, Turkey
E-mail: bilgebanutasdemir@hotmail.com

Abstract

Background/Aim: Acute kidney injury (AKI) is a common and serious complication associated with morbidity and mortality in patients with sepsis. This study aimed to determine the severity of AKI according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria and evaluate its relationship with mortality in patients who were followed up in the intensive care unit (ICU) due to sepsis and developed AKI.

Methods: We retrospectively analyzed patients diagnosed with sepsis and followed up in the ICU, including all patients with AKI. The severity of AKI was determined for all patients using the KDIGO criteria. The patients were divided into four groups: Stage 1, Stage 2, Stage 3, and without AKI. Patients with missing data, COVID-19 patients, patients with chronic kidney insufficiency, and kidney transplant patients were excluded.

Results: A total of 1,177 sepsis patients were included in the study, of whom 52.4% were male (n=617). The median age of the study group was 78 years (Q1-Q3: 68-85 years). It was determined that 57.9% of the patients (n=681) developed AKI at any stage. According to the KDIGO criteria, the rates of patients in Stage 1, Stage 2, and Stage 3 developing AKI were 23.9%, 16.2%, and 17.8%, respectively. The incidence of hypertension (HT) and diabetes mellitus (DM), which are comorbidities, increased as the patients' KDIGO stage increased ($P<0.001$).

Conclusion: AKI occurred in 57.9% of sepsis patients in the ICU, and 30.4% received renal replacement therapy (RRT). It was determined that mortality increased as the KDIGO stage of our patients increased.

Keywords: acute renal injury, critical care, KDIGO, mortality

Introduction

Acute kidney injury (AKI) is a common complication observed in patients undergoing intensive care unit (ICU) treatment. It is associated with adverse outcomes, including prolonged ICU and hospital stays, the development of chronic kidney disease, and an increased risk of short- and long-term mortality [1].

In the intensive care setting, AKI serves as an independent risk factor for mortality, with patients requiring renal replacement therapy (RRT) experiencing mortality rates ranging from 40% to 55%. The elevated mortality is primarily attributed to systemic effects on various organs, such as the lungs, heart, liver, brain, and immune system, rather than mere loss of clearance. Studies have demonstrated that AKI heightens susceptibility to infections, doubles the incidence of respiratory failure, and directly or indirectly compromises cardiac function [2].

Numerous risk factors have been identified in association with the development of AKI, with the most common being renal hypoperfusion, which can arise from conditions such as hypovolemia, heart failure, and arterial hypotension. Additionally, the administration of nephrotoxic drugs and contrast-related AKI are known contributors. Among these factors, sepsis-related AKI is particularly prevalent in the intensive care setting [3]. The prevention of septic AKI primarily revolves around prompt sepsis treatment and early resuscitation. In cases where sepsis resolves, most patients regain normal kidney function. However, even a single episode of septic AKI is linked to an elevated risk of subsequent chronic kidney disease [4].

The Kidney Disease: Improving Global Outcomes (KDIGO) guideline, established in 2012, defines AKI as a rapid decline in kidney function within 7 days or less [5,6].

Managing AKI in the ICU presents significant challenges, necessitating appropriate volume control, careful management of nephrotoxic drugs, and strategic decision-making regarding the timing and type of renal replacement therapy. Effective management of fluid and electrolyte balance is crucial in this regard [7].

In this study, our primary objective was to examine the incidence of AKI, the requirement for RRT, and the association between AKI and mortality among sepsis patients in the ICU. Additionally, our secondary objective was to assess the relationship between the ratios of white blood cell (WBC)/lymphocyte and C-reactive protein (CRP)/albumin with mortality.

Materials and methods

This retrospective study was conducted between January 1, 2018, and December 31, 2020, following approval from the Afyon Health Sciences University Faculty of Medicine Clinical Research Ethics Committee (Decree no: 416, date: 2021). The study aimed to analyze the clinical data of patients over 18 years old who were admitted to the ICU with a diagnosis of sepsis. A total of 1,177 patients diagnosed with sepsis accompanied by organ failure due to infection were included in the analysis. Patients with missing data, COVID-19 patients, those with chronic kidney insufficiency, and kidney transplant patients were excluded from the study. The recorded parameters for all patients included age, gender, comorbidities, Acute Physiology and Chronic Health Assessment (APACHE) II score, duration of intensive care and hospital stay, WBC/lymphocyte ratios, and CRP/Albumin ratios.

In this study, AKI was defined and staged according to the KDIGO (Kidney Disease: Improving Global Outcomes) serum creatinine criteria. According to KDIGO, AKI is defined as an increase of ≥0.3 mg/dl in serum creatinine within 48 hours, or a 1.5-fold increase in serum creatinine from baseline within seven days, or urine output of <0.5 ml/kg/h in the last 6 hours [5]. The baseline creatinine value was determined as the most recent creatinine value available in the pre-hospital system within the past year. The patients were categorized into four groups: Stage 1, Stage 2, Stage 3, and without AKI. A comparison of clinical features was performed among the patients, and subgroup analysis was conducted based on the KDIGO staging criteria and the implementation of RRT.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 20. The data were presented as ratios, medians, and interquartile ranges (IQR). The normal distribution of variables was assessed through visual examination (histogram) and analytical methods (Kolmogorov-Smirnov test). The Kruskal-Wallis test was employed to compare continuous variables, while the Chi-square test was used for categorical variables. Receiver operating characteristic (ROC) curves were utilized to evaluate the predictive power of WBC/lymphocyte and CRP/albumin values for mortality. A P-value of less than 0.05 was considered statistically significant.

Results

The study enrolled a total of 1,177 patients, with 52.4% (n=617) being male. The median age of the study group was 78 years (Q1-Q3: 68-85 years). AKI was observed in 57.9% (n=681) of the patients at any stage. The characteristics of the patient groups are presented in Table 1, where Stage 1 AKI was found in 23.9% (n=281) of patients, Stage 2 AKI in 16.2% (n=190), and Stage 3 AKI in 17.8% (n=210). Among those who developed AKI, 69.6% (n=474) did not require RRT, while 23.2% (n=158) received intermittent RRT, and 7.2% (n=49) underwent continuous RRT treatments.

Table 1: Characteristics of patients and comparison by groups

Characteristic	Total (n=1177)	No AKI (n=496)	Stage 1 (n=281)	Stage 2 (n=190)	Stage 3 (n=210)	P-value
Age (years)	78 (68-85)	76 (66-84)	80 (72-86)	78 (69-84)	75 (67-83)	0.004
Male, %-n	52.4-617	53.2-264	49.8-140	48.9-93	57.1-120	0.297
DM, %-n	20.4-240	14.1-70	21.4-60	25.8-49	29-61	<0.001
HT, %-n	16.6-195	11.3-56	15.3-43	21.1-40	26.7-56	<0.001
COPD, %-n	20.6-243	23-114	19.2-54	19.5-37	18.1-38	0.392
Malignancy, %-n	16.7-197	12.9-64	18.1-51	20-38	21-44	0.021
CHF, %-n	13-153	11.3-56	13.9-39	14.7-28	14.3-30	0.515
RRT, %-n	17.6-207	0	15.7-44	15.8-30	63.3-133	<0.001
Dead, %-n	51.1-602	35.5-176	56.9-160	57.9-110	74.3-156	<0.001
WBC/Lymphocyte	15 (9-22)	12 (8-20)	15 (10-24)	16 (11-25)	18 (12-30)	<0.001
CRP/Albumin	38 (18-51)	31 (12-44)	38 (20-53)	40 (18-57)	49 (34-62)	<0.001
APACHE II	23 (18-30)	20 (16-26)	24 (19-30)	27 (20-32)	30 (24-35)	<0.001

DM: diabetes mellitus, HT: Hypertension, COPD: Chronic obstructive pulmonary disease, CHF: Congestive heart failure, RRT: Renal replacement therapy, APACHE: Acute Physiology and Chronic Health Assessment

The overall survival rates were as follows: 64.5% in the group without AKI, 43.1% in the KDIGO 1 group, 42.1% in the KDIGO 2 group, and 25.7% in the KDIGO 3 group (log-rank

P<0.001). The survival chart of these groups is illustrated in Figure 1. The average duration of ICU stay was 8.4 days (Q1-Q3: 4-11 days).
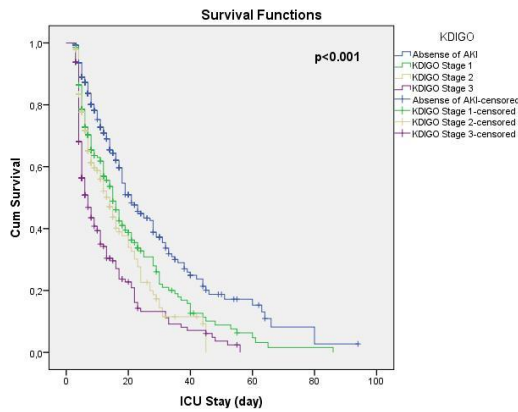
Figure 1: Survival chart of the groups

Figure 2 displays the ROC curve depicting the predictive value for mortality of WBC/lymphocyte and CRP/albumin values, along with the corresponding *P*-values at the 95% confidence interval. The area under the curve (AUC) for WBC/lymphocyte was 0.670 (95% CI: 0.640-0.701, [*P*<0.001]), and for CRP/albumin, it was 0.696 (95% CI 0.666-0.726, [*P*<0.001]).

Figure 2: The ROC curve for predicting mortality of WBC/lymphocyte and CRP/alb values
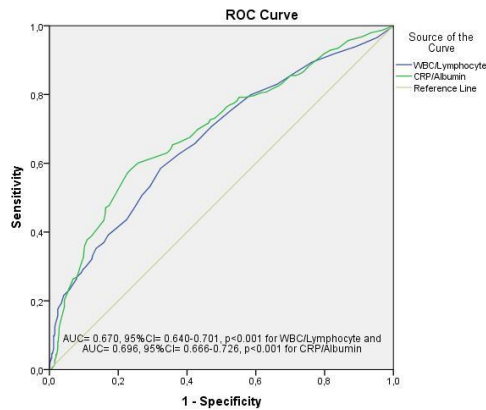
The optimal cutoff value determined by the Youden index was 15.5 for WBC/lymphocyte, with a sensitivity of 58.6% and specificity of 67.7%. For CRP/albumin, a value of 41.5 predicted mortality with a sensitivity of 58.2% and specificity of 76.3%.

Discussion

Sepsis-related AKI is defined as the development of AKI within seven days following the onset of sepsis [8]. The prognosis for sepsis-associated AKI is worse compared to sepsis or AKI alone. Prolonged stays in the ICU and hospital are linked to increased mortality rates and a diminished quality of life [1,9].

In studies examining AKI, it has been reported that AKI classifications can serve as predictors of mortality, with mortality rates rising as the stage of AKI increases [10-12]. Our study found a similar trend, where mortality increased in correlation with the severity of AKI among sepsis patients in the ICU.

In a multicenter study encompassing 15,132 patients in general intensive care, the incidence of AKI development was reported to be 32% [13]. Another study focused on ICU patients and employed the KDIGO criteria to assess AKI, revealing an occurrence rate of 57.3% among 1802 patients [1]. Similarly, our study found that the frequency of AKI among sepsis patients was 57.9%.

In a study investigating the epidemiology of acute kidney injury in intensive care sepsis patients, KDIGO guidelines were utilized for AKI staging and were found to be a reliable measure when compared to Acute Kidney Injury Network (AKIN) criteria. The incidence of AKI was determined to be 47.9%, with a corresponding 28-day mortality rate of 32.7% [14]. In our own study, we similarly employed the KDIGO staging for sepsis patients and observed a 28-day mortality rate of 62%. It is worth noting that our higher mortality rate could be attributed to a significant number of deaths caused by factors other than sepsis.

In a prospective study conducted on sepsis patients in the ICU, it was observed that mortality rates were elevated among patients who experienced recurrent AKI during their stay. Specifically, AKI recurred in 20% of the patients [15]. One limitation of our own study is that we did not investigate or document episodes of recurrent AKI.

Studies have reported AKI-related mortality rates ranging from 30% to 60% among patients with sepsis [16-18]. In our study, the mortality rate among sepsis patients was 51.1%. However, it is important to note that mortality is influenced by various factors beyond AKI. One limitation of our study is that we did not investigate other contributing factors to mortality.

The international AKI-EPI study, which examined the prevalence of AKI in the ICU, revealed a high incidence of AKI among patients with diabetes mellitus (DM) and hypertension (HT) [1], consistent with our findings.

In a multicenter intensive care study conducted in China, focusing on the association between AKI and mortality among general intensive care patients, it was observed that KDIGO Stage-1 patients did not exhibit an elevated 30-day mortality rate [19]. However, in our study, we found a 30-day mortality rate of 72% among our Stage-1 patients. It is important to note that this finding cannot be solely attributed to AKI, as our sample predominantly consisted of sepsis patients, which may contribute to the higher mortality rate observed.

In a study examining AKI in a cohort of 1689 ICU patients, sepsis was identified as the primary cause of acute kidney injury necessitating dialysis [20].

In the study conducted by Hoste et al. [1] in the ICU, RRT was administered to 23.5% of patients with AKI. Similarly, in a study focused on AKI among sepsis patients in the ICU, the rate of RRT utilization was 15%. In our cohort of AKI patients, the rate of RRT utilization was notably higher at 30.4%. This increase may be attributed to the timing of RRT initiation. While we did not have a specific strategy for early or late initiation of RRT, we speculate that RRT might have been initiated early due to the presence of sepsis or septic shock.

The kidneys are among the organs most vulnerable to early injury during sepsis. Approximately two-thirds of patients with septic shock develop AKI [1], with half of them experiencing AKI before even being admitted to the emergency department [21]. Hence, it is appropriate to regard AKI as an early indicator of sepsis. In our study, the mortality rate among patients who developed AKI was 51.1%, whereas the mortality

rate among sepsis patients who did not develop AKI was 62%. Notably, the mortality rates of sepsis patients with and without AKI were comparable [22].

Irrespective of whether sepsis occurs prior to, concurrently with, or after AKI, it is evident that it contributes to additional mortality in AKI cases. A study examining the mortality of ICU patients with AKI compared individuals with and without sepsis, revealing that septic shock resulted in higher mortality rates than sepsis alone [23]. Moreover, other studies have reported significantly elevated rates of AKI among patients with septic shock, ranging from 60% to 70% [24]. One limitation of our study was its retrospective nature, which prevented us from examining the rates of AKI in patients who developed septic shock.

A high CRP/Albumin ratio serves as an indicator of severe inflammation. In a study involving sepsis patients in the ICU, it was observed that the CRP/Albumin ratio yielded more consistent prognostic information than CRP levels alone, and it was also correlated with mortality [25]. Furthermore, the association between CRP/Albumin ratios and hospital mortality has been reported in studies conducted both in general ICUs and among ICU patients with AKI [26,27].

Upon analyzing the WBC/lymphocyte and CRP/albumin values of our patients as predictors of mortality, we observed that the sensitivity and specificity were relatively low. Given the multitude of factors influencing patient mortality, we believe it would be inappropriate to draw conclusions regarding mortality based solely on these indices.

Limitations

This study has several limitations, including the absence of data regarding urine output, fluid administration, and nutritional management. Due to the retrospective nature of our study, we were unable to analyze the occurrence of septic shock, which directly impacts both mortality and the development of AKI. Furthermore, another limitation is our failure to investigate organ failures other than AKI among sepsis patients in the ICU. Future research must address these limitations by conducting prospective and multicenter studies focused on sepsis patients in the ICU.

Conclusion

In this study, we observed the development of AKI in 57.9% of sepsis patients admitted to the ICU. By categorizing patients with AKI according to KDIGO staging, we investigated their respective mortality rates. Our findings demonstrated a correlation between the severity of AKI and mortality, as indicated by the KDIGO criteria. Early identification and appropriate management of sepsis in the ICU can potentially decrease mortality rates and the occurrence of AKI, ultimately leading to improved outcomes for patients with sepsis admitted to the ICU.

References

1. Hoste EA, Bagshaw SM, Bellomo R, Cely CM, Colman R, Cruz DN, et al. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. Intensive Care Med. 2015;41(8):1411-23.
2. Griffin BR, Liu KD, Teixeira JP. Critical Care Nephrology: Core Curriculum 2020. Am J Kidney Dis. 2020;75(3):435-52.
3. Mas-Font S, Ros-Martinez J, Pérez-Calvo C, Villa-Díaz P, Aldunate-Calvo S, Moreno-Clari E; on belhaf of the Workgroup on Nephrology Intensive Care of the SEMICYUC. Prevention of acute kidney injury in Intensive Care Units. Med Intensiva. 2017;41(2):116-26.
4. Bellomo R, Kellum JA, Ronco C, Wald R, Martensson J, Maiden M, et al. Acute kidney injury in sepsis. Intensive Care Med. 2017;43(6):816-28.
5. Ostermann M, Bellomo R, Burdmann EA, Doi K, Endre ZH, Goldstein SL, et al. Controversies in acute kidney injury: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Conference. Kidney Int. 2020;98(2):294-309.
6. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney İnjury Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int. 2012;2:1-138.
7. Kellum JA, Romagnani P, Ashuntantang G, Ronco C, Zarbock A, Anders HJ. Acute kidney injury. Nat Rev Dis Primers. 2021;7(1):52.
8. Zarbock A, Nadim MK, Pickkers P, Gomez H, Bell S, Joannidis M, et al. Sepsis-associated acute kidney injury: consensus report of the 28th Acute Disease Quality Initiative workgroup. Nat Rev Nephrol. 2023;19(6):401-17.
9. Peerapornratana S, Manrique-Caballero CL, Gomez H, Kellum JA. Acute kidney injury from sepsis: current concepts, epidemiology, pathophysiology, prevention and treatment. Kidney Int. 2019;96:1083-99.
10. Fonseca Ruiz NJ, Castro DP, Guerra AM, Saldarriaga FM, Hernández JD. Renal injury study in critical ill patients in accordance with the new definition given by the Acute Kidney Injury Network. J Crit Care. 2011;26(2):206-12.
11. 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):144.
12. Bayrakçı N, Ersan S, Çelik A, Çavdar C, Çamsarı T, Bodur HA, et al. The Role of RIFLE, AKIN and KDIGO Criteria in Determining the Relationship Between Acute Kidney Injury and Mortality in Intensive Care Patients. Namik Kemal Med J. 2022;10:37-42.
13. Srisawat N, Sileanu FE, Murugan R, Bellomod R, Calzavacca P, Cartin-Ceba R, et al; Acute Kidney Injury-6 Study Group. Variation in risk and mortality of acute kidney injury in critically ill patients: a multicenter study. Am J Nephrol. 2015;41(1):81-8.
14. Peng Q, Zhang L, Ai Y, Zhang L. Epidemiology of acute kidney injury in intensive care septic patients based on the KDIGO guidelines. Chin Med J (Engl). 2014;127(10):1820-6.
15. Rodrigo E, Suberviola B, Santibáñez M, Belmar L, Castellanos Á, Heras M, et al. Association between recurrence of acute kidney injury and mortality in intensive care unit patients with severe sepsis. J Intensive Care. 2017;5:28.
16. Martensson J, Bellomo R. Sepsis-induced acute kidney injury. Crit Care Clin. 2015;31(4):649-60.
17. Poukkanen M, Vaara ST, Pettila V, Kaukonen KM, Korhonen AM, Hovilehto S, et al; FINNAKI study group. Acute kidney injury in patients with severe sepsis in Finnish intensive care units. Acta Anaesthesiol Scand. 2013;57(7):863-72.
18. Patel S, Puri N, Dellinger RP. Sepsis Management for the Nephrologist. Clin J Am Soc Nephrol. 2022;17(6):880-9.
19. Jiang YJ, Xi XM, Jia HM, Zheng X, Wang MP, Li WX. The attributable mortality of new-onset acute kidney injury among critically ill patients: a propensity-matched analysis based on a multicentre prospective cohort study. Int Urol Nephrol. 2022;54(8):1987-94.
20. Bozkurt FT, Doganci M, Kayar Calili D, Akdag A, Izdes S. Clinical characteristics and short-term outcome of dialysis-requiring acute kidney injury in critically ill patients. J Surg Med. 2020;4(7):558-61.
21. Kellum JA, Chawla LS, Keener C, Singbartl K, Palevsky PM, Pike FL, et al. ProCESS and ProGReSS-AKI Investigators. The Effects of Alternative Resuscitation Strategies on Acute Kidney Injury in Patients with Septic Shock. Am J Respir Crit Care Med. 2016;193(3):281-7.
22. Manrique-Caballero CL, Del Rio-Pertuz G, Gomez H. Sepsis-Associated Acute Kidney Injury. Crit Care Clin. 2021;37(2):279-301.
23. Jia HM, Jiang YJ, Zheng X, Li W, Wang MP, Xi XM, et al. The attributable mortality of sepsis for acute kidney injury: a propensity-matched analysis based on multicenter prospective cohort study. Ren Fail. 2023;45(1):2162415.
24. 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):332-40.
25. Ranzani OT, Zampieri FG, Forte DN, Azevedo LC, Park M. C-reactive protein/albumin ratio predicts 90-day mortality of septic patients. PLoS One. 2013;8(3):e59321.
26. Park JE, Chung KS, Song JH, Kim SY, Kim EY, Jung JY, et al. The C-Reactive Protein/Albumin Ratio as a Predictor of Mortality in Critically Ill Patients. J Clin Med. 2018;7(10):333.
27. Wang J, Zhao K, Mao X, Zhang Y, Shao J, Fan W, et al. Relationship between CRP Albumin Ratio and the Mortality in Critically Ill Patients with AKI: A Retrospective Observational Study. Biomed Res Int. 2021;2021:9957563.