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ORIGINAL RESEARCH

Prognostic Implications of a Cumulative Renal Score Based on Both Serum Creatinine and Urine Output Criteria for Staging of Acute Kidney Injury: A Cohort Study

Yun Ji
Libin Li

Department of Surgical Intensive Care Unit, The Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang, 310009, People's Republic of China

Purpose: Traditionally, the Kidney Disease: Improving Global Outcomes (KDIGO) stages acute kidney injury (AKI) into three stages based on the highest severity of increase in serum creatinine (SC) or urine output (UO) criteria. Clinically, however, the two criteria do not provide equivalent information. Thus, we aimed to develop a cumulative renal score (the sum of the highest KDIGO SC and UO severity stages) for staging of AKI, expanding the original three KDIGO stages to six stages. We hypothesized that the cumulative renal score would more accurately describe AKI severity and outcomes.

Patients and Methods: Critically ill adult patients were identified from the Multiparameter Intelligent Monitoring in Intensive Care III Database. The primary outcome was hospital mortality. Logistic regression was used to explore the association between cumulative renal score and hospital mortality.

Results: A total of 17,404 critically ill adult patients were enrolled. Patients with higher cumulative renal scores had greater hospital mortality than patients with lower cumulative renal scores (score 0, 7.6%; score 1, 9.3%; score 2, 12.5%; score 3, 18.9%; score 4, 27.1%; score 5, 34.7%; score 6, 46.8%, $p < 0.001$). After adjustment for significant covariates, relative to cumulative renal score 0, cumulative renal scores 2–6 were associated with increased hospital mortality. Within the traditional KDIGO stage 2 AKI, when compared with cumulative renal score 2, cumulative renal score 4 had increased hospital mortality. Within the traditional KDIGO stage 3 AKI, when compared with cumulative renal score 3, cumulative renal score 6 had increased hospital mortality.

Conclusion: Our study demonstrates that the KDIGO SC and UO criteria have a cumulative effect on AKI severity staging. The cumulative renal score improves the traditional KDIGO AKI staging by applying the two sets of criteria sequentially and provides more insight into the relationship between AKI and outcomes.

Keywords: acute kidney injury, critical care, critically ill patients, Kidney Disease: Improving Global Outcomes, mortality

Introduction

Acute kidney injury (AKI) is a common and serious complication of critical illness.[1–4] The first consensus criteria for AKI were established to reduce heterogeneity in reporting AKI and outcomes; the Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease (RIFLE) classification, which were slightly modified into the Acute Kidney Injury Network (AKIN) classification.[5,6] The

Correspondence: Yun Ji
Department of Surgical Intensive Care Unit, The Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang, 310009, People's Republic of China
Tel +8615805817268
Email yunji@zju.edu.cn

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Kidney Disease: Improving Global Outcomes (KDIGO) criteria combine the two previous classifications and are currently recommended to assess AKI.[7]

The KDIGO stages AKI into three stages based on the highest severity of increase in serum creatinine (SC) or urine output (UO) criteria.[7] Patients are assigned the same stage of AKI regardless of which criteria (SC, UO or both) for that stage are met. Clinically, however, a rising SC is reflective of renal excretory dysfunction, whereas oliguria is indicative of impaired fluid homeostasis; thus the two criteria do not provide equivalent information. Indeed, recent studies have demonstrated that patients who meet both the SC and UO criteria have poorer outcomes.[8,9] Thus, in this study, we developed a cumulative renal score (the sum of the highest KDIGO SC and UO severity stages) for staging of AKI, expanding the original three KDIGO stages to six stages. We hypothesized that critically ill patients with higher cumulative renal scores are at increased risk for poorer outcomes.

Materials and Methods

Sources of Data

All data in this study were extracted from the Multiparameter Intelligent Monitoring in Intensive Care (MIMIC) III database version 1.4.[10] MIMIC-III is an openly available database developed by the computational physiology laboratory of Massachusetts Institute of Technology. The database contains de-identified clinical data for over 50,000 adult intensive care unit (ICU) stays at Beth Israel Deaconess Medical Center in Boston, MA, from 2001 to 2012. The institutional review boards of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center approved the establishment and use of the database.

Study Population

The primary study population consists of adult (age ≥ 18 years) ICU patients. For patients who were admitted to the ICU more than once, only the first ICU stay was considered in this study. Patients with one or more of the following conditions were excluded: 1) chronic renal failure which was defined by the Elixhauser comorbidity index; 2) discharge or death within 48 hours after ICU admission; and 3) insufficient information to determine AKI status.

The data on the first day of ICU admission were extracted from MIMIC III database including demographic information (eg, age, gender) and clinical information from the admission notes. The following admission data were collected: ethnicity (white, black, or other), admission type (elective, emergency, or urgent), Elixhauser comorbidity index,[11] and disease severity as assessed by the Simplified Acute Physiology Score II (SAPS II).[12] We also recorded the need for mechanical ventilation, vasopressors, and renal replacement therapy.

Cumulative Renal Score

AKI stages were classified by the KDIGO defined SC and UO criteria during the first 48 hours after ICU admission. Minimum of the SC values available within the 7 days before admission was used as the baseline SC. If the baseline was unknown, it was estimated using the Chronic Kidney Disease Epidemiology Collaboration equation, assuming an glomerular filtration rate of 75 mL/min/1.73 m^2 of body surface area.[13] We developed and calculated a cumulative renal score for the included patients. The cumulative renal score is calculated by adding the highest KDIGO SC stage to the highest KDIGO UO stage within the first 48 hours of ICU admission. For example, a patient with stage 3 AKI according to the KDIGO SC criteria and stage 2 AKI according to the KDIGO UO criteria would be assigned a cumulative renal score of 5. Thus, the cumulative renal score ranges from 0 (no AKI) to 6 (stage 3 AKI meeting both SC and UO criteria).

Endpoints

The primary endpoint was the hospital mortality, which was defined as the status of patient survival at the time of hospital discharge. Secondary endpoints included recovery from AKI, early resolution of AKI, time taken for renal recovery, and length of stay (LOS) in hospital and ICU. Recovery from AKI was defined as being discharged from ICU with SC below 1.5 times the baseline value and normal UO (> 0.5 mL/kg/h for 24 hours on discharge). Early resolution of AKI was defined as AKI of less than 48 hours' duration according to the consensus report of the ADQI 16 Workgroup.[14] Time taken for renal recovery was defined as the number of days from AKI onset until the SC remained less than 1.5 times the baseline value.

Statistical Analysis

Categorical data were shown as frequency (percent), while continuous ones as mean (standard deviation [SD]) or median (interquartile range [IQR]). We did comparisons between groups by the chi-square test for categorical data and the

Kruskal–Wallis test for continuous ones. A multivariable Cox proportional hazards regression model was constructed to evaluate the association between the cumulative renal score and mortality. Covariables used in the multivariable model were age, gender, ethnicity, admission type, Elixhauser comorbidity index, SAPS II, mechanical ventilation, vasopressors, and renal replacement therapy. These covariables were selected based on clinical relevance for risk of death (age, gender) or statistical criteria (univariable $p < 0.05$ for inclusion in the analysis). The results were expressed as hazard ratios (HRs) with 95% confidence intervals (CIs). Stratified analyses of the original KDIGO AKI stages 1, 2, and 3 cohorts were performed. The area under the receiver operating characteristic curves (AUC) was used to assess the performance of cumulative renal score and original KDIGO stage for predicting mortality. A two-tailed test was performed, and $p < 0.05$ was considered statistically significant. All statistical analyses were performed using STATA V.16.0.

Results

AKI Staging and Baseline Characteristics

Data on 17,404 ICU patients were included in this study (Figure 1). KDIGO defined AKI was diagnosed in 11,711 patients (67.3%); 3907 (33.4%), 5912 (50.5%), and 1892 (16.2%) experienced KDIGO stage 1, stage 2, and stage 3 AKI, respectively. When the SC and UO criteria were applied additively to calculate the cumulative renal score, it was distributed as follows: cumulative renal score 0 (n = 5693; 32.7%), cumulative renal score 1 (n = 3372; 19.4%), cumulative renal score 2 (n = 4540; 26.1%), cumulative renal score 3 (n = 2015; 11.6%), cumulative renal score 4 (n = 819; 4.7%), cumulative renal score 5 (n = 467; 2.7%), and cumulative renal score 6 (n = 498; 2.9%). As shown in Table 1, patients with higher cumulative renal scores had higher Elixhauser comorbidity indices and SAPS II calculated at ICU admission.

Primary Analysis: Strong Association of Cumulative Renal Score with Hospital Mortality

Patients with higher cumulative renal scores had higher hospital mortality than patients with lower cumulative renal scores (score 0, 7.6%; score 1, 9.3%; score 2, 12.5%; score 3, 18.9%; score 4, 27.1%; score 5, 34.7%; score 6, 46.8%, $p < 0.001$) (Table 2 and Figure 2). Unadjusted Cox proportional hazards regression modeling showed that patients with cumulative renal score 1 or greater were at increased odds for hospital mortality compared with those with cumulative renal score 0 (Figure 3A). After multivariable risk adjustment for age, gender, ethnicity, admission type, Elixhauser comorbidity index, SAPS II, mechanical ventilation, vasopressors, and renal replacement therapy, cumulative renal score 2 or higher remained independently associated with hospital mortality (Figure 3B). The AUC for predicting hospital mortality of cumulative renal scores (AUC, 0.663; 95% CI 0.651–0.675) was statistically higher than that of original KDIGO stages (AUC, 0.649; 95% CI 0.637–0.661) ($p < 0.001$) (Figure 4).

Primary Analysis Stratified by the Original KDIGO AKI Stages

In order to better clarify the impact of the expanded staging provided by the cumulative renal score, we conducted our primary analysis of hospital mortality separately for each of the three original KDIGO stages. In unadjusted analyses, hospital mortality still increased significantly in patients with higher cumulative renal scores across original KDIGO stages (Figure 3A). In adjusted analyses,

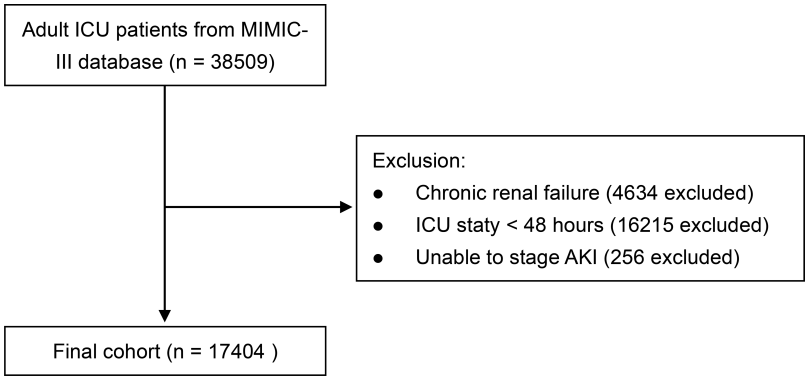

Figure 1 Flow chart of patient selection.

Table 1 Characteristics of the Study Cohort Stratified by the Cumulative Renal Score

	Cumulative Renal Score 0	Cumulative Renal Score 1	Cumulative Renal Score 2	Cumulative Renal Score 3	Cumulative Renal Score 4	Cumulative Renal Score 5	Cumulative Renal Score 6	*p* value
Number of patients, n (%)	5693 (32.7)	3372 (19.4)	4540 (26.1)	2015 (11.6)	819 (4.7)	467 (2.7)	498 (2.9)	NA
Age, years	59 (46–72)	68 (56–78)	68 (56–79)	73 (59–82)	75 (63–83)	71 (57–82)	64 (52–75)	< 0.001
Gender, n (%)								< 0.001
Male	3122 (54.8)	1943 (57.6)	2541 (56.0)	1043 (51.8)	407 (49.7)	233 (49.9)	285 (57.2)	
Female	2571 (45.2)	1429 (42.4)	1999 (44.0)	972 (48.2)	412 (50.3)	234 (50.1)	213 (42.8)	
Ethnicity, n (%)								< 0.001
White	3905 (68.6)	2392 (70.9)	3299 (72.7)	1437 (71.3)	594 (72.5)	334 (71.5)	337 (67.7)	
Black	384 (6.8)	198 (5.9)	290 (6.4)	152 (7.5)	53 (6.5)	44 (9.4)	27 (5.4)	
Other	1404 (24.7)	782 (23.2)	951 (21.0)	426 (21.1)	172 (21.0)	89 (19.1)	134 (26.9)	
Admission type, n (%)								< 0.001
Elective	813 (14.3)	625 (18.5)	708 (15.6)	288 (14.3)	95 (11.6)	37 (7.9)	37 (7.4)	
Emergency	4716 (82.8)	2637 (78.2)	3692 (81.3)	1651 (81.9)	695 (84.9)	413 (88.4)	445 (89.4)	
Urgent	164 (2.9)	110 (3.3)	140 (3.1)	76 (3.8)	29 (3.5)	17 (3.6)	16 (3.2)	
Elixhauser comorbidity index	8 (0–17)	10 (3–19)	11 (3–20)	16 (7–24)	18 (9–27)	19 (10–29)	21 (12–30)	< 0.001
SAPS II	30 (23–38)	34 (27–42)	35 (27–44)	40 (32–50)	47 (39–56)	51 (41–59)	57 (48–67)	< 0.001
Mechanical ventilation, n (%)	3153 (55.4)	2071 (61.4)	2840 (62.6)	1204 (60.0)	530 (64.7)	286 (61.2)	341 (68.5)	< 0.001
Vasopressors, n (%)	1603 (28.2)	1341 (39.8)	1666 (36.7)	833 (41.3)	426 (52.0)	234 (50.1)	299 (60.0)	< 0.001
Renal replacement therapy, n (%)	0 (0)	0 (0)	0 (0)	35 (1.7)	8 (1.0)	38 (8.1)	137 (27.5)	< 0.001

Abbreviations: NA, not applicable; SAPS II, Simplified Acute Physiology Score II.

Table 2 Association Between Cumulative Renal Score and Clinical Outcomes in Critically Ill Patients

		Cumulative Renal Score 0	Cumulative Renal Score 1	Cumulative Renal Score 2	Cumulative Renal Score 3	Cumulative Renal Score 4	Cumulative Renal Score 5	Cumulative Renal Score 6	*p* value
Primary outcome									
Hospital mortality, n (%)		432 (7.6)	315 (9.3)	567 (12.5)	380 (18.9)	222 (27.1)	162 (34.7)	233 (46.8)	< 0.001
Secondary outcomes									
Recovery from AKI, n (%)		NA	2770 (88.0)	3138 (76.2)	974 (56.1)	268 (41.2)	88 (26.0)	49 (16.7)	< 0.001
Early resolution of AKI, n (%)		NA	1995 (59.2)	2353 (51.8)	685 (34.0)	129 (15.8)	27 (5.6)	3 (0.6)	< 0.001
Time taken for renal recovery, days		NA	2.5 (2.3–2.7)	2.5 (2.2–2.7)	2.5 (2.3–3.0)	3.3 (2.4–5.5)	5.8 (3.5–14.1)	9.7 (5.0–21.3)	< 0.001
ICU LOS, days		3.5 (2.6–6.1)	3.8 (2.7–6.3)	4.0 (2.8–7.3)	4.3 (2.9–8.2)	5.0 (3.2–9.2)	5.5 (3.2–10.2)	7.3 (3.7–13.7)	< 0.001
Hospital LOS, days		8.8 (5.7–14.7)	9.0 (6.0–14.6)	9.5 (6.3–15.5)	10.3 (6.6–17.0)	11.3 (6.9–19.3)	12.2 (7.1–22.5)	14.6 (7.0–27.0)	< 0.001

Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; LOS, length of stay; NA, not applicable.

however, this finding was attenuated (Figure 3B). Within KDIGO stage 1 AKI, patients with cumulative renal score 2 did not have higher adjusted odds of hospital mortality compared with those with cumulative renal score 1. Within KDIGO stage 2 AKI, only patients with cumulative renal score 4 had higher adjusted odds of hospital mortality compared with those with cumulative renal score 2. Within KDIGO stage 3 AKI, only patients with cumulative renal score 6 had higher adjusted odds of hospital mortality compared with those with cumulative renal score 3.

Secondary Analyses

We found that increasing cumulative renal score was associated with a decreased chance of recovery from AKI (score 1, 88.0%; score 2, 76.2%; score 3, 56.1%; score 4, 41.2%; score 5, 26.0%; score 6, 16.7%, $p < 0.001$) and early resolution of AKI (score 1, 59.2%; score 2, 51.8%; score 3, 34.0%; score 4, 15.8%; score 5, 5.8%; score 6, 0.6%, $p < 0.001$) (Table 2 and Figures 5–6). Furthermore, we found that increasing cumulative renal score was associated with a longer time taken for renal recovery ($p < 0.001$) (Table 2). We also found that increasing cumulative renal score was associated with longer LOS in ICU and hospital; the lowest LOS was seen in patients with cumulative renal score 0 (ICU LOS: 3.5 days, IQR, 2.6–6.1 days; hospital LOS: 8.8 days, IQR, 5.7–14.7 days), and the longest LOS was seen in patients with cumulative renal score 6 (ICU LOS: 7.3 days, IQR, 3.7–13.7 days; hospital LOS: 14.6 days, IQR, 7.0–27.0 days) (Table 2).

Discussion

Summary of Key Findings

In this study, we developed a cumulative renal score, expanding AKI staging from three to six stages. Critically ill patients with higher cumulative renal scores had greater hospital mortality than patients with lower cumulative renal scores. After adjustment for potential covariates using logistic regression, cumulative renal score 2 or higher remained significantly associated with hospital mortality. Then, we applied the cumulative renal score within each of the three original KDIGO stages. Within KDIGO stage 2 and 3 AKI, we found significantly greater hospital mortality in patients in the highest cumulative renal score. Furthermore, increasing cumulative renal score was associated with an increased risk for non-recovery from AKI, longer time to renal recovery, and greater need for ICU and hospital stay.

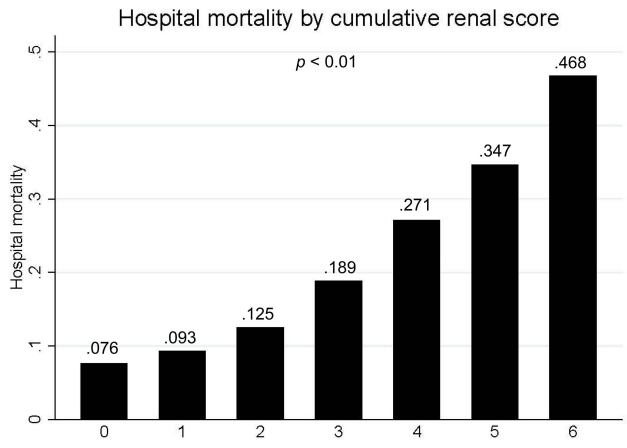

Figure 2 Hospital mortality rate by cumulative renal score.

Context with Prior Literature

KDIGO adjudicates AKI diagnosis when patients meet either the SC or the UO criteria and ultimately confers a severity stage (1 to 3) based upon the more severe of the two. It is well established that increases in the severity stage of AKI by KDIGO criteria have a progressively larger negative impact on patient outcomes.[15–20] Several reports have implied that the current staging of AKI by KDIGO criteria has a room for improvement in the detection of high-risk patients. A recent study by Kellum et al[8] in adult ICU patients found that the risk of death or renal replacement therapy was greater in patients who fulfilled both criteria for SC and UO than in patients with either criteria. Another recent study by Kaddourah et al[9] in pediatric ICU patients showed that when compared with those meeting either the highest SC or UO stage, children who met the highest stage for both criteria were more likely to require dialysis and experienced higher 28-day mortality. A further study by Sutherland et al[21] in pediatric ICU patients demonstrated that cumulative application of SC and UO staging optimizes the KDIGO

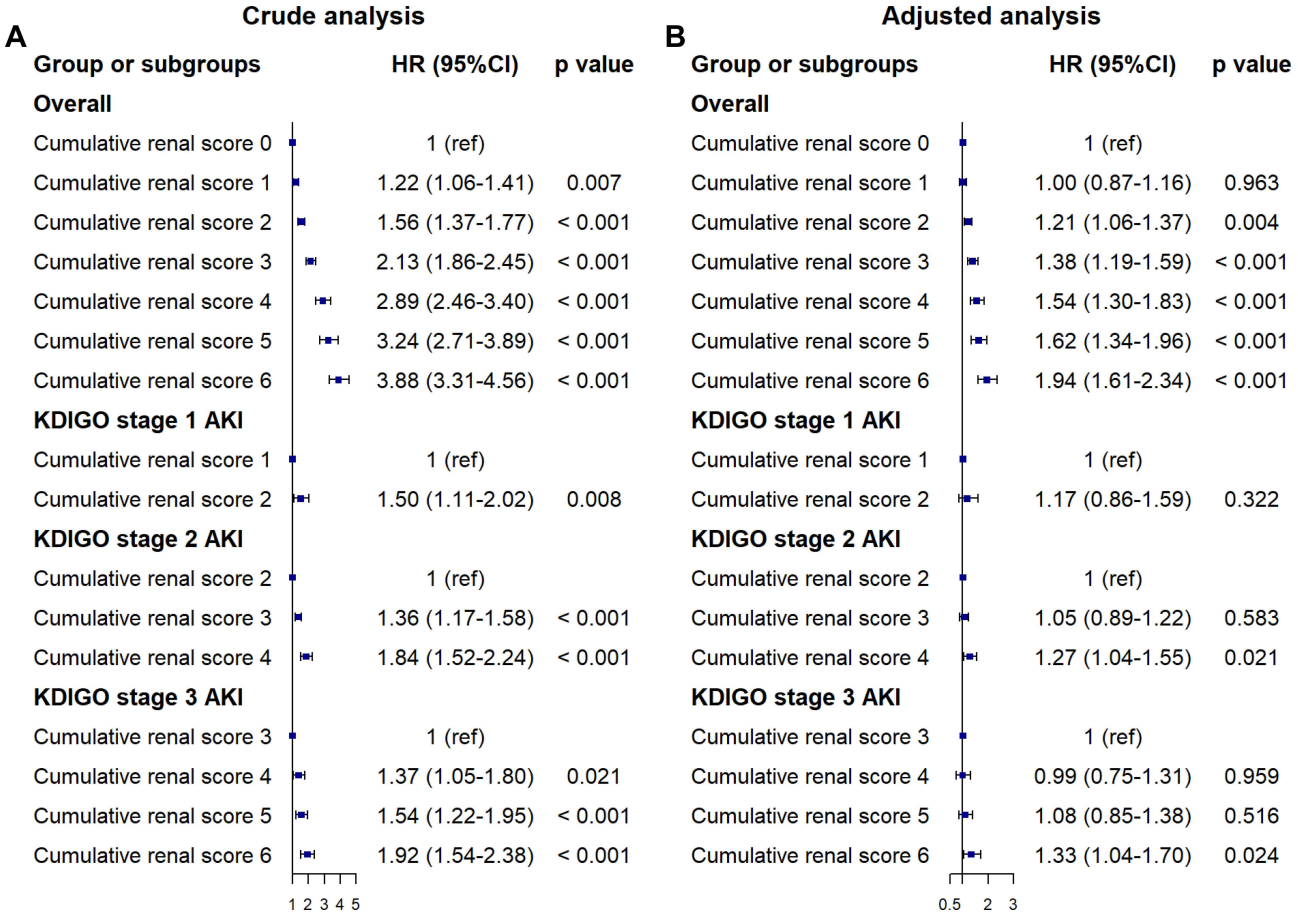

Figure 3 Forest plot showing the association between cumulative renal score and outcomes in overall population and subgroups. Univariable (**A**) and multivariable (**B**) Cox proportional hazards regression analyses were performed, yielding hazard ratios with 95% confidence intervals. The confounders included age, gender, ethnicity, admission type, Elixhauser comorbidity index, Simplified Acute Physiology Score II, mechanical ventilation, vasopressors, and renal replacement therapy.
Abbreviations: AKI, acute kidney injury; KDIGO, Kidney Disease: Improving Global Outcomes; HR, hazard ratio; CI, confidence interval.

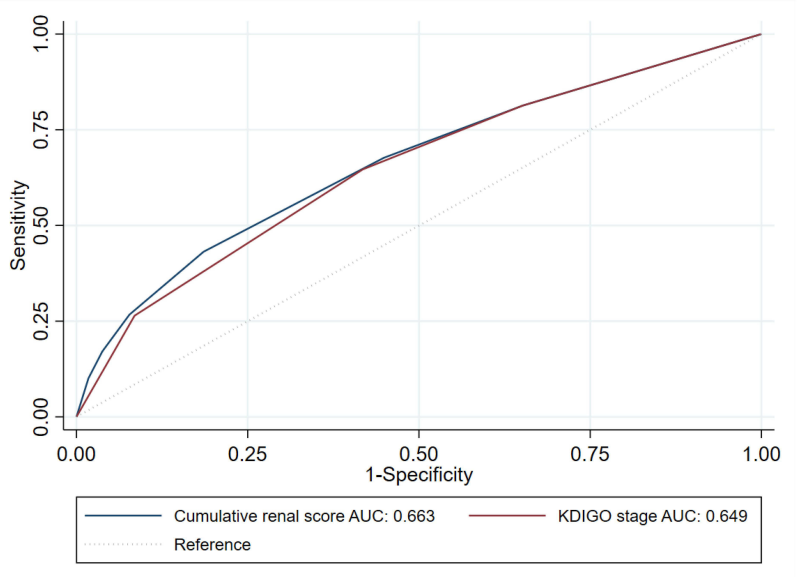

Figure 4 Comparison of the receiver operating characteristic curves of cumulative renal score and original KDIGO stage to predict hospital mortality.

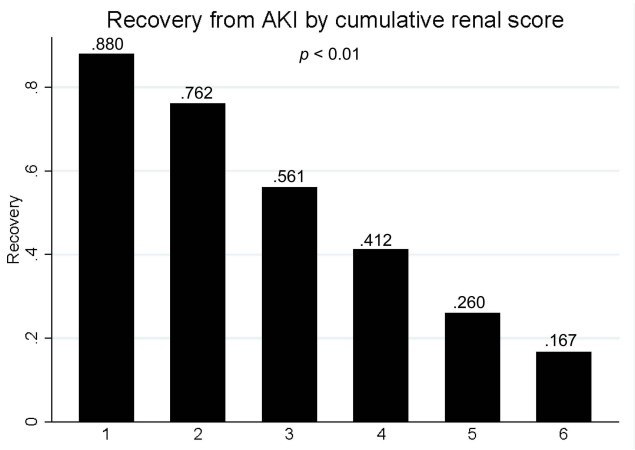

Figure 5 Rate of recovery of renal function following acute kidney injury (AKI) by cumulative renal score.

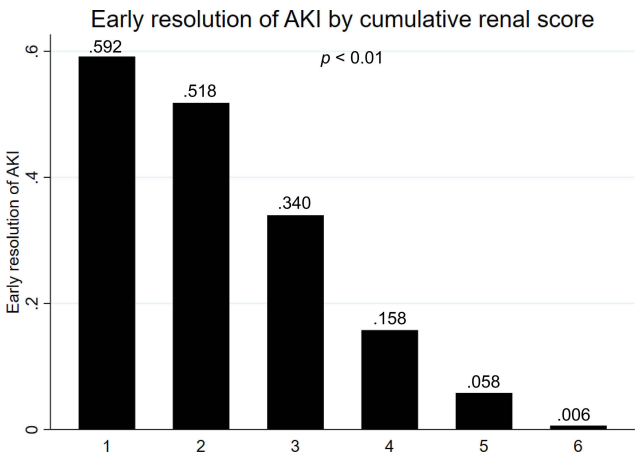

Figure 6 Rate of early resolution of acute kidney injury (AKI) by cumulative renal score.

definition and more comprehensively describes the outcome implications of severe AKI than traditional staging methods. The calculation of the cumulative renal score, as described in this study, builds on these findings. We investigated whether adult ICU patients with higher cumulative renal scores are at increased risk for poorer outcomes.

Interpretation and Implications for Clinicians and Future Research

As cumulative renal score increased, adult ICU patients experienced higher hospital mortality; this relationship remained even after adjusting for potential confounders, suggesting an independent effect. A possible explanation for this relationship is that the SC and UO are reflective of two different types of renal dysfunction. Indeed, an increasing SC is considered as a marker of renal excretory dysfunction and a decreasing UO is consistent with impaired fluid homeostasis. Patients with more substantial renal excretory dysfunction, more impaired fluid homeostasis, and more types of renal dysfunction are likely to have experienced greater injury and are at increased risk for worse outcomes.

This study demonstrates that not all traditionally staged AKI is equivalent. For example, when compared with adult who met stage 3 criteria for only SC or UO, patients

with cumulative renal score of 6 were more likely to die, had greater need for ICU care with longer hospital stays, and were less likely to recover from AKI. This study suggests that a modified 6-stage version of the KDIGO AKI classification (cumulative renal score 1, 2, 3, 4, 5, and 6) may provide additional prognostic information. Future studies are needed to validate this modification of scoring.

Limitations

The major strength of this study is the large number of ICU patients; however, there are also several limitations to this study. First, the study was limited by its retrospective nature. Second, because this was a single-center study, we did not perform a model validation. The results need to be validated by multicenter studies. Third, although we did our best to use a multivariable model to control bias, there remain the possibility of residual confounding that was not examined in our multivariable model. Fourth, although we had a relatively large number of patients in this study, the exclusion of 55% patients may have led to selection bias. Fifth since the MIMIC III database used in the present study only contains the data of ICU patients admitted between 2001 and 2012, the data may not accurately reflect the current situation. Despite these limitations, this study provides evidence that cumulative renal score may represent important evolution in staging AKI.

Conclusion

In conclusion, this study shows that increased cumulative renal score in critically ill patients is associated with worse outcomes. This finding highlights that the SC and UO criteria have a cumulative effect on AKI severity staging. The calculation of cumulative renal score improves the original KDIGO AKI staging by applying the two sets of criteria sequentially. The cumulative renal score provides more insight into the relationship between AKI and outcomes.

Statement of Ethics

The establishment of MIMIC III database was approved by the Massachusetts Institute of Technology (Cambridge, MA) and Beth Israel Deaconess Medical Center (Boston, MA) and consent was obtained for the original data collection. Therefore, the ethical approval statement and the need for informed consent were waived for this manuscript.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Kaddourah A, Basu RK, Bagshaw SM, Goldstein SL. Epidemiology of acute kidney injury in critically ill children and young adults. *N Engl J Med*. 2017;376(1):11–20. doi:10.1056/NEJMoa1611391
2. Hoste EAJ, Kellum JA, Selby NM, et al. Global epidemiology and outcomes of acute kidney injury. *Nat Rev Nephrol*. 2018;14(10):607–625. doi:10.1038/s41581-018-0052-0
3. Hoste EA, Bagshaw SM, Bellomo R et al. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. *Intensive Care Med*. 2015;41(8)1411–1423.
4. Ronco C, Bellomo R, Kellum JA. Acute kidney injury. *Lancet*. 2019;394(10212):1949–1964. doi:10.1016/S0140-6736(19)32563-2
5. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. 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. *Critical Care*. 2004;8(4):R204–R212. doi:10.1186/cc2872
6. Mehta RL, Kellum JA, Shah SV, et al. Acute kidney injury network: report of an initiative to improve outcomes in acute kidney injury. *Critical Care*. 2007;11(2):R31. doi:10.1186/cc5713
7. Kellum JA, Lameire N. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). *Critical Care*. 2013;17(1):204. doi:10.1186/cc11454
8. Kellum JA, Sileanu FE, Murugan R, Lucko N, Shaw AD, Clermont G. Classifying AKI by urine output versus serum creatinine level. *J Am Soc Nephrol*. 2015;26(9):2231–2238. doi:10.1681/ASN.2014070724
9. Kaddourah A, Basu RK, Goldstein SL, Sutherland SM. Oliguria and acute kidney injury in critically ill children: implications for diagnosis and outcomes. *Pediatr Crit Care Med*. 2019;20(4):332–339. doi:10.1097/PCC.0000000000001866
10. Johnson AE, Pollard TJ, Shen L, et al. MIMIC-III, a freely accessible critical care database. *Sci Data*. 2016;3:160035. doi:10.1038/sdata.2016.35
11. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care*. 1998;36(1):8–27. doi:10.1097/00005650-199801000-00004
12. Le Gall JR, Lemeshow S, Saulnier F. A new simplified acute physiology score (SAPS II) based on a European/North American multicenter study. *JAMA*. 1993;270(24):2957–2963. doi:10.1001/jama.1993.03510240069035
13. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604–612. doi:10.7326/0003-4819-150-9-200905050-00006
14. Chawla LS, Bellomo R, Bihorac A, et al. Acute kidney disease and renal recovery: consensus report of the Acute Disease Quality Initiative (ADQI) 16 Workgroup. *Nat Rev Nephrol*. 2017;13(4):241–257. doi:10.1038/nrneph.2017.2
15. Kang E, Park M, Park PG, et al. Acute kidney injury predicts all-cause mortality in patients with cancer. *Cancer Med*. 2019;8(6):2740–2750. doi:10.1002/cam4.2140
16. Selewski DT, Cornell TT, Heung M, et al. Validation of the KDIGO acute kidney injury criteria in a pediatric critical care population. *Intensive Care Med*. 2014;40(10):1481–1488. doi:10.1007/s00134-014-3391-8

17. Machado MN, Nakazone MA, Maia LN. Prognostic value of acute kidney injury after cardiac surgery according to kidney disease: improving global outcomes definition and staging (KDIGO) criteria. *PLoS One*. 2014;9(5):e98028. doi:10.1371/journal.pone.0098028
18. Pan HC, Chien YS, Jenq CC, et al. Acute kidney injury classification for critically ill cirrhotic patients: a comparison of the KDIGO, AKIN, and RIFLE classifications. *Sci Rep*. 2016;6:23022. doi:10.1038/srep23022
19. Luo X, Jiang L, Du B, Wen Y, Wang M, Xi X. A comparison of different diagnostic criteria of acute kidney injury in critically ill patients. *Critical Care*. 2014;18(4):R144. doi:10.1186/cc13977
20. Jentzer JC, Breen T, Sidhu M, Barsness GW, Kashani K. Epidemiology and outcomes of acute kidney injury in cardiac intensive care unit patients. *J Crit Care*. 2020;60:127–134. doi:10.1016/j.jcrc.2020.07.031
21. Sutherland SM, Kaddourah A, Gillespie SE, et al. Cumulative application of creatinine and urine output staging optimizes the kidney disease: improving global outcomes definition and identifies increased mortality risk in hospitalized patients with acute kidney injury. *Crit Care Med*. 2021;49(11):1912–1922. doi:10.1097/CCM.0000000000005073