Clinical Kidney Journal

Clinical Kidney Journal, 2022, vol. 15, no. 5, 937–941

https://doi.org/10.1093/ckj/sfab256
Advance Access Publication Date: 10 December 2021
Original Article

ORIGINAL ARTICLE

Incorrect application of the KDIGO acute kidney injury staging criteria

Izak A.R. Yasrebi-de Kom [1], Dave A. Dongelmans[2], Ameen Abu-Hanna[1], Martijn C. Schut[1], Nicolette F. de Keizer[1], John A. Kellum[3], Kitty J. Jager[1] and Joanna E. Klopotowska[1]

[1]Department of Medical Informatics, Amsterdam UMC (location AMC), Amsterdam, The Netherlands, [2]Department of Intensive Care, Amsterdam UMC (location AMC), Amsterdam, The Netherlands and [3]Department of Critical Care Medicine, Center for Critical Care Nephrology, Pittsburgh, PA, USA

Correspondence to: Izak A.R. Yasrebi-de Kom; E-mail: i.a.r.dekom@amsterdamumc.nl

ABSTRACT

Background. Recent research demonstrated substantial heterogeneity in the Kidney Disease: Improving Global Outcomes (KDIGO) acute kidney injury (AKI) diagnosis and staging criteria implementations in clinical research. Here we report an additional issue in the implementation of the criteria: the incorrect description and application of a stage 3 serum creatinine (SCr) criterion. Instead of an increase in SCr to or beyond 4.0 mg/dL, studies apparently interpreted this criterion as an increase in SCr by 4.0 mg/dL.

Methods. Using a sample of 8124 consecutive intensive care unit (ICU) admissions, we illustrate the implications of such incorrect application. The AKI stage distributions associated with the correct and incorrect stage 3 SCr criterion implementations were compared, both with and without the stage 3 renal replacement therapy (RRT) criterion. In addition, we compared chronic kidney disease presence, ICU mortality rates and hospital mortality rates associated with each of the AKI stages and the misclassified cases.

Results. Where incorrect implementation of the SCr stage 3 criterion showed a stage 3 AKI rate of 29%, correct implementation revealed a rate of 34%, mainly due to shifts from stage 1 to stage 3. Without the stage 3 RRT criterion, the stage 3 AKI rates were 9% and 19% after incorrect and correct implementation, respectively. The ICU and hospital mortality rates in cases misclassified as stage 1 or 2 were similar to those in cases correctly classified as stage 1 instead of stage 3.

Conclusions. While incorrect implementation of the SCr stage 3 criterion has significant consequences for AKI severity epidemiology, consequences for clinical decision making may be less severe. We urge researchers and clinicians to verify their implementation of the AKI staging criteria.

Keywords: acute kidney injury, clinical practice guidelines, epidemiology, KDIGO, staging error

Received: 2.9.2021; Editorial decision: 6.12.2021

INTRODUCTION

Acute kidney injury (AKI) is a frequent problem in hospitalized patients, especially in those admitted to an intensive care unit (ICU). AKI diagnosis and staging are relevant as AKI induces longer hospital stays and higher mortality [1]. The apparent incidence of AKI varies across ICUs and subpopulations due to differences in AKI definitions used, patient comorbidities and clinical practices [2, 3]. In 2012, Kidney Disease: Improving Global Outcomes (KDIGO) published a clinical practice guideline for AKI diagnosis and classification using serum creatinine (SCr), urine output (UO) and the initiation of renal replacement therapy (RRT) [4]. The KDIGO AKI definition and subsequent severity staging criteria are shown in Table 1.

Recent literature suggests that implementations of this guideline vary across studies [5]. Examples include differences in methods to calculate the SCr baseline [5] and the inclusion or exclusion of the RRT staging criterion [6, 7]. In addition, studies often refrain from using UO data, as it is frequently hampered by missing values [3, 5]. This variation has led to different and incomparable AKI rates and research results [5]. We recently identified eight publications with an additional issue: an apparently erroneous interpretation and application of a stage 3 SCr criterion (Table 2) [7–14].

Patients with AKI should be assigned stage 3 if their SCr increases to ≥4.0 mg/dL (353.6 µmol/L). However, instead of an increase in SCr to ≥4.0 mg/dL, the authors of these studies apparently interpreted this criterion as an increase in SCr of 4.0 mg/dL. As a result, patients may have been assigned an incorrect AKI stage. This suggests that the KDIGO AKI guideline criteria are not only described and applied inconsistently, but sometimes also incorrectly.

Here we demonstrate the consequences of applying the incorrect SCr stage 3 criterion on the AKI stage 3 rate in ICU admissions. In addition, we provide an implementation of the KDIGO AKI guideline SCr criteria in R code to facilitate the correct usage of the AKI and AKI staging criteria.

MATERIALS AND METHODS

We retrospectively received data from electronic hospital records of consecutive admissions to one of the ICUs in the Amsterdam University Medical Centres in the Netherlands between

Table 1. KDIGO AKI guideline: AKI diagnosis and staging criteria [4]

AKI diagnosis		
	Increase in SCr by ≥0.3 mg/dL (≥26.5 µmol/L) within 48 h or Increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days or Urine volume <0.5 mL/kg/h for 6 h	
AKI staging		
Stage	SCr	UO
1	1.5–1.9 times baseline or ≥0.3 mg/dL (≥26.5 µmol/L) increase	<0.5 mL/kg/h for 6–12 h
2	2.0–2.9 times baseline	<0.5 mL/kg/h for ≥12 h
3	3.0 times baseline or Increase in SCr to ≥4.0 mg/dL (≥353.6 µmol/L) or Initiation of renal replacement therapy or In patients <18 years, decrease in eGFR to <35 mL/min/1.73 m^2	<0.3 mL/kg/h for ≥24 h or Anuria for ≥12 h

eGFR, estimated glomerular filtration rate.

Table 2. Recent peer-reviewed publications that described the KDIGO AKI guideline stage 3 SCr criterion incorrectly

Authors	Year	Location of description	Stage 3 criterion used	Stage 3 RRT criterion used
Kang and Rovin [8]	2018	Table 1	'≥4.0 mg/dL (353.6 µmol/L) absolute increase'	Yes
Khwaja [9]	2012	Table 2	'≥4.0 mg/dL (353.6 µmol/L) increase'	Yes
Horne and Selby [10]	2015	Table 2	'Increase 354 µmol/L'	Yes
Machado *et al.* [11]	2014	Methods	Correctly described in Table 1, but incorrectly described in the methods section 'Stages of AKI based on KDIGO classification': 'Increase in SCr ≥4.0 mg/dL'	Yes
Siew and Davenport [12]	2014	Table 1	'Increase in SCr ≥4.0 mg/dL (354 µmol/L)'	Yes
Stack *et al.* [7]	2020	Materials and methods	'Increase ≥354 µmol/L'	No
Li *et al.* [13]	2020	Methods	'Absolute increase in SCr levels of ≥354 µmol/L'	Yes
Tai *et al.* [14]	2021	Supplementary data, Table S1	'Increase in serum creatinine ≥353.6 µmol/L'	Yes

Table 3. Characteristics of all included admissions, admissions correctly classified as AKI stage 1, 2 or 3, and admissions misclassified after usage of the incorrect stage 3 SCr criterion. The staging included both the SCr criteria and the stage 3 RRT criterion

Characteristics	All admissions (*N* = 8124)	AKI stage 1 (*n* = 683)	AKI stage 2 (*n* = 121)	AKI stage 3 (*n* = 421)	Misclassified (*n* = 64)
Age (years), median (Q1–Q3)	64.0 (52.0–72.0)	67.0 (56.0–74.0)	66.0 (56.0–73.0)	63.0 (54.0–72.0)	65.5 (55.0–72.0)
Male sex, *n* (%)	5165 (63.6)	465 (68.1)	76 (62.8)	253 (60.1)	47 (73.4)
Chronic kidney disease, *n* (%)	446 (5.5)	56 (8.2)	4 (3.3)	93 (22.1)	35 (54.7)
SCr baseline (mg/dL), median (Q1–Q3)	0.9 (0.7–1.2)	1.2 (0.9–1.5)	1.0 (0.8–1.2)	1.9 (1.2–3.5)	3.7 (2.8–4.6)
Planned admission, *n* (%)	2690 (33.1)	181 (26.5)	26 (21.5)	54 (12.8)	10 (15.6)
Admission type					
Medical, *n* (%)	4376 (53.9)	367 (53.7)	73 (60.3)	301 (71.5)	52 (81.2)
Emergency surgical, *n* (%)	992 (12.2)	121 (17.7)	20 (16.5)	67 (15.9)	4 (6.2)
Elective surgical, *n* (%)	2740 (33.7)	195 (28.6)	27 (22.3)	53 (12.6)	8 (12.5)
APACHE IV score, median (Q1–Q3)	43.0 (30.0–64.0)	58.0 (42.5–80.0)	62.0 (45.8–94.0)	67.0 (53.0–92.0)	64.0 (51.0–85.8)
APACHE IV admission diagnosis category, *n* (%)					
Cardiovascular	4186 (51.7)	386 (56.6)	67 (55.8)	251 (60.2)	39 (61.9)
Gastrointestinal	613 (7.6)	67 (9.8)	10 (8.3)	40 (9.6)	6 (9.5)
Genitourinary	92 (1.1)	3 (0.4)	2 (1.7)	21 (5.0)	0 (0.0)
Haematology	117 (1.4)	6 (0.9)	0 (0.0)	12 (2.9)	1 (1.6)
Metabolic/endocrine	123 (1.5)	3 (0.4)	0 (0.0)	2 (0.5)	1 (1.6)
Musculoskeletal/skin	44 (0.5)	7 (1.0)	1 (0.8)	3 (0.7)	1 (1.6)
Neurologic	1480 (18.3)	84 (12.3)	13 (10.8)	23 (5.5)	4 (6.3)
Respiratory	969 (12.0)	92 (13.5)	22 (18.3)	56 (13.4)	11 (17.5)
Transplant	9 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Trauma	469 (5.8)	33 (4.8)	5 (4.2)	9 (2.2)	0 (0.0)

November 2015 and December 2019. We linked these data to the minimal dataset (MDS) of the Dutch National Intensive Care Evaluation (NICE) quality registry [15]. The linked data included encoded admission identification numbers, admission and discharge timestamps, patient demographics, admission type specifications, Acute Physiology and Chronic Health Evaluation IV (APACHE IV) admission diagnoses and scores [16], SCr measurements with timestamps, chronic dialysis at admission (yes/no), chronic kidney disease (CKD) at admission (yes/no), RRT initiation during admission (yes/no), ICU survival (yes/no) and hospital survival (yes/no). We excluded admissions with chronic dialysis at admission. The SCr baseline was defined as the first SCr value within the first 24 h of ICU admission. We compared the AKI stage distribution after applying the correct and incorrect SCr criteria, both with and without the stage 3 RRT criterion. In addition, we compared the presence of CKD and the ICU and hospital mortality rates associated with each stage and in the misclassified cases. Lastly, we compared the AKI stage distributions after AKI staging with and without the 4.0 mg/dL SCr stage 3 threshold criterion while applying the stage 3 RRT criterion. All data analyses were performed in R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

This study was exempted from formal approval by the Medical Ethics Committee of the Amsterdam University Medical Centres (waiver W19_433 # 19.499), as it did not fall within the scope of the Dutch Medical Research Involving Human Subjects Act (WMO). The Dutch legal framework for research with care data (i.e. non-WMO) allows working with encoded routinely collected data without informed consent under specific conditions, e.g. when datasets consist of a very large number of patients.

RESULTS

We received encoded data for 8124 ICU admissions. The median patient age was 64 years, and the majority of patients were men (63.6%). The median SCr baseline was 0.9 mg/dL, 5.5% of the admissions had CKD at admission and the minority of the admissions were planned (33.1%; Table 3). In 1225 admissions {15%, [95% confidence interval (CI) 14–16]}, we identified AKI based solely on the KDIGO AKI SCr criteria (Table 4a).

After AKI staging using both the SCr criteria and the RRT stage 3 criterion, stage 3 AKI occurred in 421 cases [34% (95% CI 32–37)] when SCr criteria were applied correctly versus 357 cases [29% (95% CI 27–32)] when SCr criteria were applied incorrectly, mainly due to a shift to cases misclassified as AKI stage 1 (Tables 3 and 4a).

AKI staging without the stage 3 RRT criterion showed a more pronounced impact of the incorrect SCr stage 3 criterion: stage 3 AKI occurred in 237 cases [19% (95% CI 17–22)] versus 113 cases [9% (95% CI 8–11)] after correct and incorrect application, respectively (Table 4b).

The ICU and hospital mortality rates in cases misclassified as stage 1 or 2 were most similar to those in correctly classified AKI stage 1 cases, irrespective of the use of the RRT stage 3 criterion. Furthermore, 55% (95% CI 42–67) of the misclassified cases using the RRT stage 3 criterion and 43% (95% CI 34–51) without use of this criterion concerned cases with CKD at admission (Tables 4a and 4b). A comparison of characteristics of the CKD and non-CKD patients is provided in the Supplementary data, Table S3.

Lastly, omitting the 4.0 mg/dL SCr stage 3 threshold criterion showed an impact similar to that of the incorrect application of this criterion (Supplementary data, Table S4).

DISCUSSION

We found that the KDIGO AKI guideline is described and—most probably—applied not only inconsistently, but also incorrectly. We detected this problem in eight studies and cannot exclude that it occurs more often, both in research and in clinical practice. We illustrated that application of the incorrect stage 3 SCr

Table 4a. AKI staging using both SCr criteria and the stage 3 RRT criterion

	Incorrect stage 3 criterion			Correct stage 3 criterion			
Characteristics	Stage 1	Stage 2	Stage 3	Stage 1	Stage 2	Stage 3	Misclassified
Cases, *n*	738	130	357	683	121	421	64
% [95% CI]	60 [57–63]	11 [9–12]	29 [27–32]	56 [53–59]	10 [8–12]	34 [32–37]	5 [4–6]
ICU mortality, *n*	163	51	161	154	48	173	12
% [95% CI]	22 [19–25]	39 [31–48]	45 [40–50]	23 [19–26]	40 [31–48]	41 [36–46]	19 [9–29]
Post-ICU hospital mortality, *n*	47	5	23	42	5	28	5
% [95% CI][a]	8 [6–10]	6 [1–12]	12 [7–16]	8 [6–10]	7 [1–13]	11 [7–15]	10 [1–18]
Hospital mortality, *n*	210	56	184	196	53	201	17
% [95% CI]	28 [25–32]	43 [34–52]	52 [46–57]	29 [25–32]	44 [35–53]	48 [43–53]	27 [16–37]
RRT, *n*	NA	NA	305	NA	NA	305	0
% [95% CI]			85 [82–89]			72 [68–77]	0 [0–0]
CKD, *n*	91	4	58	56	4	93	35
% [95% CI]	12 [10–15]	3 [0–6]	16 [12–20]	8 [6–10]	3 [0–6]	22 [18–26]	55 [42–67]

Total admissions = 8124, admissions with AKI = 1225 [15% (95% CI 14-16)].

Table 4b. AKI staging using only SCr criteria

	Incorrect stage 3 criterion			Correct stage 3 criterion			
Characteristics	Stage 1	Stage 2	Stage 3	Stage 1	Stage 2	Stage 3	Misclassified
Cases, *n*	924	188	113	823	165	237	124
% [95% CI]	75 [73–78]	15 [13–17]	9 [8–11]	67 [64–70]	13 [11–15]	19 [17–22]	10 [8–12]
ICU mortality, *n*	243	86	46	223	77	75	29
% [95% CI]	26 [23–29]	46 [38–53]	41 [31–50]	27 [24–30]	47 [39–54]	32 [25–38]	23 [16–31]
Post-ICU hospital mortality, *n*	58	10	7	49	8	18	11
% [95% CI][a]	9 [6–11]	10 [4–16]	10 [3–18]	8 [6–10]	9 [3–15]	11 [6–16]	12 [5–18]
Hospital mortality, *n*	301	96	53	272	85	93	40
% [95% CI]	33 [29–36]	51 [44–58]	47 [38–56]	33 [30–36]	52 [44–59]	39 [33–46]	32 [24–41]
RRT, *n*	186	58	61	140	44	121	60
% [95% CI]	20 [17–23]	31 [24–37]	54 [44–64]	17 [14–20]	27 [20–34]	51 [44–58]	48 [39–58]
CKD, *n*	135	8	10	83	7	63	53
% [95% CI]	15 [12–17]	4 [1–7]	9 [4–14]	10 [8–12]	4 [1–7]	27 [21–32]	43 [34–51]

NA, not applicable

[a]Percentage represents the percentage of ICU survivors that subsequently died in the hospital.

criterion—an increase in SCr of 4.0 mg/dL—leads to underreporting of stage 3 AKI and overreporting of stage 1 and stage 2 AKI. This underreporting was most pronounced when the stage 3 RRT criterion was not used.

Therefore, incorrect application of the stage 3 SCr criterion has significant consequences for AKI severity epidemiology and the interpretation of results across studies, especially when the AKI stage is solely based on the SCr criteria. However, as the ICU and hospital mortality rates in cases misclassified as stage 1 or 2 were similar to those in correctly classified AKI stage 1 cases, the clinical decision making for misclassified cases may still have been accurate despite their misclassification. Therefore, the incorrect staging may be less of a problem in clinical practice.

A potential explanation for this phenomenon may lie in the presence of CKD at ICU admission. About half of the misclassified cases had CKD at admission. While use of an incorrect stage 3 SCr criterion identifies cases with a 4.0 mg/dL increase in SCr—and may therefore only identify those with a major and rapid decrease in renal function during ICU admission—the correct criterion identifies cases with AKI with an SCr value that exceeds 4.0 mg/dL. This threshold will be reached sooner in AKI cases with a high SCr baseline or CKD at admission, also without a major decrease in renal function. Correct implementation of the stage 3 SCr criterion may therefore result in staging a subgroup of cases as stage 3 who have a lower mortality rate compared with the stage 3 cases who were identified with the ≥3 times baseline stage 3 SCr criterion or with the incorrect stage 3 SCr criterion that reflect major renal function loss during ICU admission. In line with our results, the phenomenon of lower in-hospital mortality among ICU patients with CKD experiencing AKI compared with those without CKD experiencing AKI has been described previously [17]. However, the former patients may have higher long-term mortality compared with the latter patients [18]. We wonder if the presence of CKD in an ICU patient should be taken into consideration during KDIGO AKI staging, as it may improve alignment between AKI staging and short-term mortality. This is to be addressed in future research together with investigating effects on other relevant outcomes, such as renal function recovery or post-discharge RRT dependency [19].

In conclusion, given the epidemiological implications of the incorrect application of stage 3 AKI SCr criteria, we urge researchers and clinicians to verify their AKI staging implementation. In addition, we suggest the KDIGO leadership address the apparent ambiguity in the AKI staging criteria to prevent further implementation errors. To assist, we provide an

implementation of the KDIGO SCr AKI and AKI staging criteria in R (https://github.com/IYdK/RESCUE, descriptions in Supplementary data, S1 and S2).

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

ACKNOWLEDGEMENTS

We would like to thank the NICE registry for their support in the data acquisition.

FUNDING

This work was supported by the Amsterdam UMC Innovation Fund (round 2018). The funder had no role in the design of the study or writing the manuscript. The funding was received by the Department of Medical Informatics of the Amsterdam UMC.

DATA AVAILABILITY STATEMENT

We provide an implementation of the KDIGO SCr AKI and AKI staging criteria in R (https://github.com/IYdK/RESCUE, Supplementary data, S1 and S2). The data underlying this article cannot be shared publicly due to ethical and privacy reasons. The data can only be shared upon request after the explicit consent of the Amsterdam University Medical Centres.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Hoste EA, Schurgers M. Epidemiology of acute kidney injury: how big is the problem? *Crit Care Med* 2008; 36(4 Suppl): S146–S151
2. Bouchard J, Mehta RL. Acute kidney injury in Western countries. *Kidney Dis (Basel)* 2016; 2: 103–110
3. Koeze J, Keus F, Dieperink W *et al*. Incidence, timing and outcome of AKI in critically ill patients varies with the definition used and the addition of urine output criteria. *BMC Nephrol* 2017; 18: 70
4. Kellum JA, Lameire N, Aspelin P *et al*. Kidney Disease: Improving Global Outcomes Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl* 2012; 2: 1–138
5. Wiersema R, Jukarainen S, Eck RJ *et al*. Different applications of the KDIGO criteria for AKI lead to different incidences in critically ill patients: a post hoc analysis from the prospective observational SICS-II study. *Crit Care* 2020; 24: 164
6. Cheng Y, Luo R, Wang X *et al*. The incidence, risk factors, and prognosis of acute kidney injury in adult patients with coronavirus disease 2019. *Clin J Am Soc Nephrol* 2020; 15: 1394–1402
7. Stack AG, Li X, Kaballo MA *et al*. Temporal trends in acute kidney injury across health care settings in the Irish health system: a cohort study. *Nephrol Dial Transplant* 2020; 35: 447–457
8. Kang R, Rovin B. Advances and challenges on new therapies and clinical targets of acute kidney injury. *Toxicol Pathol* 2018; 46: 925–929
9. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract* 2012; 120: c179–c184
10. Horne K, Selby N. Chronic kidney disease after acute kidney injury: identifying risk factors. *J Renal Nurs* 2015; 7: 124–129
11. Machado MN, Nakazone MA, Maia LN. Acute kidney injury based on KDIGO (Kidney Disease Improving Global Outcomes) criteria in patients with elevated baseline serum creatinine undergoing cardiac surgery. *Rev Bras Cir Cardiovasc* 2014; 29: 299–307
12. Siew ED, Davenport A. The growth of acute kidney injury: a rising tide or just closer attention to detail? *Kidney Int* 2015; 87: 46–61
13. Li LJ, Zhou JJ, Hao XC *et al*. The incidence, risk factors and in-hospital mortality of acute kidney injury in patients after surgery for acute type a aortic dissection: a single-center retrospective analysis of 335 patients. *Front Med (Lausanne)* 2020; 7: 557044
14. Tai CW, Gibbons K, Schibler A *et al*. Acute kidney injury: epidemiology and course in critically ill children. *J Nephrol* 2021; doi: 10.1007/s40620-021-01071-5
15. van de Klundert N, Holman R, Dongelmans DA *et al*. Data resource profile: the Dutch National Intensive care Evaluation (NICE) registry of admissions to adult intensive care units. *Int J Epidemiol* 2015; 44: 1850–1850h
16. Zimmerman JE, Kramer AA, McNair DS *et al*. Acute Physiology and Chronic Health Evaluation (APACHE) IV: hospital mortality assessment for today's critically ill patients. *Crit Care Med* 2006; 34: 1297–1310
17. Khosla N, Soroko SB, Chertow GM *et al*. Preexisting chronic kidney disease: a potential for improved outcomes from acute kidney injury. *Clin J Am Soc Nephrol* 2009; 4: 1914–1919
18. Wu VC, Huang TM, Lai CF *et al*. Acute-on-chronic kidney injury at hospital discharge is associated with long-term dialysis and mortality. *Kidney Int* 2011; 80: 1222–1230
19. Ostermann M, Bellomo R, Burdmann EA *et al*. Controversies in acute kidney injury: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) conference. *Kidney Int* 2020; 98: 294–309