Incorrect application of the KDIGO acute kidney injury staging criteria

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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
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 \( \geq 4.0 \text{ mg/dL} \) (353.6 \( \mu \text{mol/L} \)). However, instead of an increase in SCr to \( \geq 4.0 \text{ mg/dL} \), 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 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 | Male sex, 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 53.

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 54).

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

| Characteristics | Incorrect stage 3 criterion | Correct stage 3 criterion | Misclassified |
|-----------------|----------------------------|---------------------------|---------------|
| Cases, n        |                            |                           |               |
| % [95% CI]      |                            |                           |               |
| ICU mortality, n|                            |                           |               |
| % [95% CI]      |                            |                           |               |
| Post-ICU hospital mortality, n |          |                           |               |
| % [95% CI]a    |                            |                           |               |
| Hospital mortality, n |              |                           |               |
| % [95% CI]      |                            |                           |               |
| RRT, n         |                            |                           |               |
| % [95% CI]      |                            |                           |               |
| CKD, n         |                            |                           |               |
| % [95% CI]      |                            |                           |               |

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

Table 4b. AKI staging using only SCr criterion

| Characteristics | Incorrect stage 3 criterion | Correct stage 3 criterion | Misclassified |
|-----------------|----------------------------|---------------------------|---------------|
| Cases, n        |                            |                           |               |
| % [95% CI]      |                            |                           |               |
| ICU mortality, n|                            |                           |               |
| % [95% CI]      |                            |                           |               |
| Post-ICU hospital mortality, n |          |                           |               |
| % [95% CI]a    |                            |                           |               |
| Hospital mortality, n |              |                           |               |
| % [95% CI]      |                            |                           |               |
| RRT, n         |                            |                           |               |
| % [95% CI]      |                            |                           |               |
| CKD, n         |                            |                           |               |
| % [95% CI]      |                            |                           |               |

NA, not applicable

aPercentage 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
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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.

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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.

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