Value of Kidney Disease Improving Global Outcomes Urine Output Criteria in Critically Ill Patients: A Secondary Analysis of a Multicenter Prospective Cohort Study

Jun-Ping Qin1,2, Xiang-You Yu1, Chuan-Yun Qian3, Shu-Sheng Li4, Tie-He Qin5, Er-Zhen Chen1, Jian-Dong Lin5, Yu-Hang Ai6, Da-Wei Wu7, De-Xin Liu8, Ren-Hua Sun9, Zhen-Jie Hu10, Xiang-Yuan Cao11, Fa-Chun Zhou12, Zhen-Yang He13, Li-Hua Zhou14, You-Zhong An15, Yan Kang16, Xiao-Chun Ma17, Ming-Yan Zhao18, Li Jiang19, Yuan Xu20, Bin Du21, for the China Critical Care Clinical Trial Group (CCCCTG)

1Medical Intensive Care Unit, Peking Union Medical College Hospital, Beijing 100730, China
2Department of Critical Care Medicine, Beijing Tongren Hospital, Capital Medical University, Beijing 100730, China
3Department of Critical Care Medicine, First Affiliated Hospital, Xuzhou Medical University, Xuzhou, Jiangsu 221000, China
4Department of Emergency Medicine and Medical Intensive Care Unit, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou, Guangdong 510006, China
5Department of Critical Care Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei 430030, China
6Department of Critical Care Medicine, Guangdong General Hospital, Guangzhou, Guangdong 510080, China
7Department of Emergency Medicine, Ruijin Hospital, Shanghai Jiao Tong University, Shanghai 200025, China
8Department of Critical Care Medicine, The First Affiliated Hospital of Fujian Medical University, Fuzhou, Fujian 350005, China
9Department of Critical Care Medicine, Xiangya Hospital, Central South University, Changsha, Hunan 410008, China
10Department of Critical Care Medicine, Qilu Hospital, Shandong University, Jinan, Shandong 250012, China
11Department of Emergency and Critical Care Medicine, The Second Hospital of Jilin University, Changchun, Jilin 130041, China
12Department of Critical Care Medicine, Zhejiang Provincial People’s Hospital, Hangzhou, Zhejiang 310014, China
13Department of Critical Care Medicine, Hebei Medical University Fourth Hospital, Shijiazhuang, Hebei 050011, China
14Department of Critical Care Medicine, Affiliated Hospital of Ningxia Medical University, Yinchuan, Ningxia 750004, China
15Department of Emergency and Intensive Care Medicine, The First Affiliated Hospital, Chongqing Medical University, Chongqing 400016, China
16Department of Critical Care Medicine, Beijing Tongren Hospital, Capital Medical University, Beijing 100730, China
17Department of Critical Care Medicine, Affiliated Hospital of Inner Mongolia Medical College, Hohhot, Inner Mongolia 010050, China
18Department of Critical Care Medicine, Peking University People’s Hospital, Beijing 100044, China
19Department of Critical Care Medicine, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China
20Department of Critical Care Medicine, The First Affiliated Hospital of China Medical University, Shenyang, Liaoning 110001, China
21Department of Critical Care Medicine, The First Affiliated Hospital, Harbin Medical University, Harbin, Heilongjiang 150001, China
22Department of Critical Care Medicine, Fuxing Hospital, Capital Medical University, Beijing 100038, China

Abstract

Background: Urine output (UO) is an essential criterion of the Kidney Disease Improving Global Outcomes (KDIGO) definition and classification system for acute kidney injury (AKI), of which the diagnostic value has not been extensively studied. We aimed to determine whether AKI based on KDIGO UO criteria (KDIGO UO) could improve the diagnostic and prognostic accuracy, compared with KDIGO serum creatinine criteria (KDIGO SCr).

Methods: We conducted a secondary analysis of the database of a previous study conducted by China Critical Care Clinical Trial Group (CCCCTG), which was a 2-month prospective cohort study (July 1, 2009 to August 31, 2009) involving 3063 patients in 22 tertiary Intensive Care Units in Mainland of China. AKI was diagnosed and classified separately based on KDIGO UO and KDIGO SCr. Hospital mortality of patients with more severe AKI classification based on KDIGO UO was compared with other patients by univariate and multivariate regression analyses.

Results: The prevalence of AKI increased from 52.4% based on KDIGO SCr to 55.4% based on KDIGO UO, combined with KDIGO UO. KDIGO UO also resulted in an upgrade of AKI classification in 7.3% of patients, representing those with more severe AKI classification based on KDIGO UO. Compared with non-AKI patients or those with...
maximum AKI classification by KDIGO, those with maximum AKI classification by KDIGO, had a significantly higher hospital mortality of 58.4% (odds ratio [OR]: 7.580, 95% confidence interval [CI]: 4.141–13.873, P < 0.001). In a multivariate logistic regression analysis, AKI based on KDIGO, (OR: 2.891, 95% CI: 1.964–4.254, P < 0.001), but not based on KDIGO, (OR: 1.322, 95% CI: 0.902–1.939, P = 0.152), was an independent risk factor for hospital mortality.

Conclusion: UO was a criterion with additional value beyond creatinine criterion for AKI diagnosis and classification, which can help identify a group of patients with high risk of death.

**Key words:** Acute Kidney Injury; Critically Ill; Mortality; Serum Creatinine; Urine Output

---

**Introduction**

Acute kidney injury (AKI) is one of the most common complications in critically ill patients. However, a wide range of prevalence and mortality rates of AKI have been reported in literature, mainly due to different diagnostic criteria of acute renal failure/AKI and the heterogeneity of patient population.[1‑4] Hence, the Acute Dialysis Quality Initiative group proposed a graded definition of AKI, the Risk, Injury, Failure, Loss, End-stage (RIFLE) criteria in 2004.[5] Three years later, a modified classification scheme from RIFLE, Acute Kidney Injury Network (AKIN) criteria, was developed by the AKIN group in order to improve the diagnostic sensitivity and specificity of AKI.[6] The latest classification system was proposed by the Kidney Disease Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group, based on the previous two classification systems, with the aim of unifying AKI definition.[7] A large body of evidence has been accumulated and suggested that the development and severity of AKI are associated with increased hospital mortality.[8‑16] Despite the difference in creatinine/glomerular filtration rate (GFR) criteria between AKIN, RIFLE, and KDIGO criteria, all use urine output (UO) for the diagnosis and classification of AKI.[5‑7] Unfortunately, hourly UO measurements are not always available even among critically ill patients in Intensive Care Unit (ICU). Furthermore, UO may be affected by volume status and diuretic use. As a result, the prognostic value of UO criteria has not been extensively studied as serum creatinine (SCr) criteria. Almost 70% of relevant studies have not employed UO criteria for AKI diagnosis and/or classification,[n‑12,17] and some studies have demonstrated that UO criteria might help to define the worst AKI stage in no more than 13% of patients with AKI.[18‑20] In addition, creatinine criteria in the consensus definition were proposed based on more solid evidence, while the consensus of UO criteria was mostly arrived through expert opinion. As a consequence, conflicting results have been reported about the role of UO criteria in AKI diagnosis and classification.

We hereby conducted a secondary analysis of a database of a multicenter prospective cohort study in order to test the hypothesis that KDIGO urine output criteria (KDIGO_UO) may help to improve the diagnostic and prognostic value of AKI, and patients who met KDIGO_UO without significant changes in SCr levels had a higher hospital mortality rate.

**Methods**

**Subject enrollment**

This study was a secondary analysis of the database of a previous study conducted by China Critical Care Clinical Trial Group (CCCCTG), which was a 2-month prospective cohort study (July 1, 2009 to August 31, 2009) involving 3063 patients in 22 tertiary ICUs in the Mainland of China.[21] The study was approved by the Institutional Review Boards of Fuxing Hospital and granted a waiver of informed consent due to the observational nature of the study. Inclusion criteria in the current study included: (1) Age ≥18 years old, (2) ICU length of stay (LOS) ≥24 h, and (3) at least two SCr measurements were available in a 7-day time window during the first 28 days in ICU. We excluded those patients who had already received chronic dialysis or renal transplantation for end-stage renal disease prior to this ICU admission and those patients with incomplete clinical data.

**Data collection and measurements**

For every enrolled patient, demographic data, underlying diseases, severity of illness, admission status, laboratory findings, complications, intervention and treatment during ICU stay, and patient outcome were extracted from the database. The severity of illness, including Acute Physiology and Chronic Health Evaluation (APACHE) II score and Sequential Organ Failure Assessment (SOFA) score, was assessed based on the worst variables recorded during the first 24 h of ICU admission.[22,23] Severe sepsis and septic shock at ICU admission or during ICU stay were defined according to the American College of Chest Physicians/Society of Critical Care Medicine consensus definitions.[24] Acute lung injury and acute respiratory distress syndrome (ARDS) were defined according to the American-European Consensus Conference criteria.[25] Chronic renal insufficiency was defined as GFR <60 ml·min⁻¹·1.73 m² according to the Kidney Disease Outcomes Quality Initiative criteria.[26]

**Diagnosis and classification of acute kidney injury**

AKI was diagnosed and staged according to KDIGO definition and classification system,[7] i.e., both SCr and UO criteria, based on clinical data during the first 28 days during ICU stay. With regards to SCr criteria, AKI was diagnosed in terms of a process of results in a 50% increase in SCr within 1 week or a 3 mg/L (26.5 μmol/L) increase within 48 h. Patient’s body weight used in UO criteria was either estimated or measured according to the routine clinical practice of individual ICU. All patients were further classified according to KDIGO SCr (KDIGO_SCr) or
KDIGO<sub>UO</sub> criteria only. In particular, AKI was staged over the entire episode, based on the maximal SCr increase during the study period. For example, if a patient developed a 50% increase in SCr in 5 days but ultimately had a three-fold increase over 3 weeks, he or she would be diagnosed with AKI and ultimately staged as stage 3. Given the objective of the current study, those patients receiving renal replacement therapy (RRT) were classified according to KDIGO<sub>SCr</sub> or KDIGO<sub>UO</sub> criteria rather than assigned to AKI stage 3 based on KDIGO criteria.\textsuperscript{[7]}

In order to examine the clinical significance of UO criteria, we classified patients with AKI into three groups according to the diagnostic consistency of KDIGO<sub>SCr</sub> and KDIGO<sub>UO</sub> i.e., those whose KDIGO<sub>SCr</sub> stage was more severe than KDIGO<sub>UO</sub> stage (Group A), those whose KDIGO<sub>SCr</sub> stage was consistent with KDIGO<sub>UO</sub> stage (Group B), and those whose KDIGO<sub>SCr</sub> stage was less severe than KDIGO<sub>UO</sub> stage (Group C).

**Outcome measures**

All enrolled patients were followed up until discharge from the current hospital admission, death during the current hospital admission, or 3 months after study entry, whichever occurred earlier. The primary outcome was all-cause hospital mortality. Patients who were still in hospital on November 30, 2009 were deemed survivors.

**Statistical analysis**

Continuous data were reported as median (Q<sub>1</sub>, Q<sub>3</sub>) and compared with Mann-Whitney U-test or Kruskal-Wallis test. Categorical variables were expressed as proportions and compared with Chi-square test or Fisher’s exact test. The predictive value of KDIGO<sub>SCr-UO</sub> for hospital mortality was examined by multivariate logistic regression analysis. Variables including demographics, comorbidities, severity of illness, admission status, and complications were added into the model using stepwise conditional forward entry, if \( P < 0.10 \) in univariate analysis. The agreement between KDIGO<sub>SCr</sub> and KDIGO<sub>UO</sub> was evaluated with Cohen’s kappa coefficient. The second multivariate logistic regression model was constructed to explore the relative influence of KDIGO<sub>SCr</sub> and KDIGO<sub>UO</sub> on hospital mortality as the dependent variable in addition to other covariates. Collinearity was analyzed by assessing the correlation between KDIGO<sub>SCr</sub> and KDIGO<sub>UO</sub>. The predictive value of KDIGO<sub>SCr</sub> and KDIGO<sub>UO</sub> was analyzed with an area under the receiver operating curve (AuROC). In order to further delineate the predictive value of KDIDG<sub>UO</sub> criteria, we also constructed the third multivariate regression model, including AKI status (i.e., non-AKI, Group A, Group B, and Group C) as an independent variable for hospital mortality. Kaplan-Meier survival analysis was used to compare 90-day mortality. The log-rank statistic was used to test the difference between the above groups. All comparisons were unpaired, and all tests of significance were two-tailed. A \( P < 0.05 \) was considered as statistically significant. All statistical analyses were performed with SPSS 20.0 (SPSS Inc., Chicago, IL, USA) or MedCalc 11.4 (MedCalc Software bvba, Oostende, Belgium).

**RESULTS**

**General information**

Of the 3063 patients who were screened during the 2-month period in the original study, 2005 patients were excluded from the current study. Reasons for exclusion were ICU LOS \(< 24 \text{ h} \ (n = 1623)\), fewer than two SCr measurements during ICU stay \((n = 182)\), age \(< 18 \text{ years} \ (n = 127)\), chronic dialysis and/or renal transplant recipient \((n = 30)\), and incomplete clinical data \((n = 43)\). As a result, 1058 patients were finally included for analysis [Figure 1].

The patients in the cohort under analysis had a median age of 62 years (45 years, 74 years), and 677 (64.0%) were male. Median APACHE II score was 18 (13, 23), and median SOFA score was 6 (4, 9). A total of 729 patients (68.9%) were admitted into ICU due to medical diseases, while respiratory disorders were the most common reason for ICU admission. There were 222 nonsurvivors, among whom 183 died in ICU, and the other 39 died in general wards, corresponding to ICU mortality and hospital mortality of 17.3% and 21.0%, respectively [Table 1].

**Acute kidney injury defined by Kidney Disease Improving Global Outcomes serum creatinine criteria and urine output criteria**

Using KDIGO<sub>SCr-UO</sub> criteria within the first 28 days of ICU admission, AKI occurred in 586 patients (55.4%), with 238 (22.5%) in stage 1, 154 (14.6%) in stage 2, and 194 (18.3%) in stage 3. Compared with patients without AKI, patients with AKI were older, had a higher burden of comorbidities (such as hypertension, diabetes, and chronic renal insufficiency), and higher overall severity of illness scores (such as APACHE II score and SOFA score). Moreover, patients with AKI were more likely to develop complications (such as septic shock and ARDS) and require...
Table 1: Univariate analysis of patient’s characteristics in this study

| Variables                              | All Patients (n = 1058) | Non-AKI (n = 472) | Any AKI (n = 586) | P (non-AKI vs. AKI) | AKI (n = 586) | P       |
|----------------------------------------|-------------------------|-------------------|-------------------|---------------------|---------------|---------|
|                                        |                         |                   |                   |                     |               |         |
| Male, n (%)                            | 677 (64.0)              | 297 (62.9)        | 380 (64.8)        | 0.517               | 269 (64.7)   | 0.566   |
| Age (years), median (Q1, Q3)           | 62 (45.74)              | 59 (41.73)        | 65 (46.75)        | <0.001              | 63 (45.73)   | <0.001  |
| Body weight (kg), median (Q1, Q3)      | 65 (56.70)              | 65 (57.70)        | 65 (56.70)        | 0.722               | 65 (59.70)   | 0.129   |
| APACHE II score, median (Q1, Q3)       | 18 (13, 23)             | 14 (10, 19)       | 20 (16, 26)       | <0.001              | 19 (15, 25)  | <0.001  |
| SOFA on admission, median (Q1, Q3)     | 6 (4, 9)                | 5 (3, 7)          | 8 (5, 10)         | <0.001              | 7 (5, 10)    | <0.001  |
| Comorbidities, n (%)                   |                         |                   |                   |                     |               |         |
| None                                   | 439 (41.5)              | 227 (48.1)        | 212 (36.2)        | <0.001              | 165 (39.7)   | 0.021   |
| CHD                                    | 195 (18.4)              | 83 (17.6)         | 112 (19.1)        | 0.524               | 66 (15.9)    | 0.002   |
| Hypertension                           | 351 (33.2)              | 133 (28.2)        | 218 (37.2)        | <0.001              | 142 (34.1)   | 0.049   |
| Diabetes                               | 169 (16.0)              | 62 (13.1)         | 107 (18.3)        | 0.024               | 76 (18.3)    | 0.737   |
| COPD                                   | 111 (10.5)              | 45 (9.5)          | 66 (11.3)         | 0.362               | 36 (8.7)     | 0.002   |
| Solid tumor                            | 122 (11.5)              | 50 (10.6)         | 72 (12.3)         | 0.391               | 48 (11.5)    | 0.599   |
| CKI                                    | 51 (4.8)                | 6 (1.3)           | 45 (7.7)          | <0.001              | 25 (6.0)     | 0.060   |
| Admission status, n (%)                |                         |                   |                   |                     |               |         |
| Medical                                | 729 (68.9)              | 288 (61.0)        | 441 (75.3)        | <0.001              | 306 (73.6)   | 0.175   |
| Elective surgery                       | 192 (18.1)              | 126 (26.7)        | 66 (11.3)         | <0.001              | 46 (11.1)    | 0.873   |
| Emergency surgery                      | 137 (12.9)              | 58 (12.3)         | 79 (13.5)         | 0.566               | 64 (15.4)    | 0.066   |
| Reasons for ICU admission, n (%)       |                         |                   |                   |                     |               |         |
| Respiratory                            | 367 (34.7)              | 154 (32.6)        | 213 (36.3)        | 0.206               | 144 (34.6)   | 0.038   |
| Gastrointestinal                       | 198 (18.7)              | 101 (21.4)        | 97 (16.6)         | 0.045               | 72 (17.3)    | 0.468   |
| Neurological                           | 161 (15.2)              | 78 (16.5)         | 83 (14.2)         | 0.288               | 71 (17.1)    | 0.005   |
| Cardiovascular                         | 133 (12.6)              | 49 (10.4)         | 84 (14.3)         | 0.054               | 55 (13.2)    | 0.484   |
| Trauma                                 | 108 (10.2)              | 58 (12.3)         | 50 (8.5)          | 0.045               | 39 (9.4)     | 0.521   |
| Renal                                  | 46 (4.3)                | 4 (0.8)           | 42 (7.2)          | <0.001              | 20 (4.8)     | <0.001  |
| Other                                  | 45 (4.3)                | 28 (5.9)          | 17 (2.9)          | 0.015               | 15 (3.6)     | 0.281   |
| On ICU admission, median (Q1, Q3)      |                         |                   |                   |                     |               |         |
| Creatinine (µmol/L)                    | 77.0                    | 66.0              | 95.5              | <0.001              | 92.0         | <0.001  |
| Urine output (ml)                      | 2000                    | 2200              | 1900              | <0.001              | 2178         | <0.001  |
| Interventions during ICU stay, n (%)   |                         |                   |                   |                     |               |         |
| Mechanical ventilation                 | 798 (75.4)              | 322 (68.2)        | 476 (81.2)        | <0.001              | 328 (78.8)   | 0.069   |
| Vasopressor                            | 406 (38.4)              | 99 (21.0)         | 307 (52.4)        | <0.001              | 183 (44.0)   | <0.001  |
| RRT                                    | 135 (12.8)              | 18 (3.8)          | 117 (20.0)        | <0.001              | 43 (10.3)    | <0.001  |
| Diuretics                              | 539 (50.9)              | 173 (36.7)        | 366 (62.5)        | <0.001              | 232 (55.8)   | <0.001  |
| Complication, n (%)                    |                         |                   |                   |                     |               |         |
| ICU-acquired infection                 | 121 (11.4)              | 43 (9.1)          | 78 (13.3)         | 0.033               | 65 (15.6)    | 0.025   |
| Severe sepsis/septic shock             | 412 (38.9)              | 127 (26.9)        | 285 (48.6)        | <0.001              | 179 (43.0)   | <0.001  |
| ALI/ARDS                               | 490 (46.3)              | 159 (33.7)        | 331 (56.5)        | <0.001              | 219 (52.6)   | 0.009   |
| Clinical outcome                       |                         |                   |                   |                     |               |         |
| ICU mortality, n (%)                   | 183 (17.3)              | 32 (6.8)          | 151 (25.8)        | <0.001              | 66 (15.9)    | <0.001  |
| Hospital mortality, n (%)              | 222 (21.0)              | 44 (9.3)          | 178 (30.4)        | <0.001              | 85 (20.4)    | <0.001  |
| ICU LOS (days), median (Q1, Q3)        | 6 (3, 12)               | 4 (3, 7)          | 8 (4, 17)         | <0.001              | 9 (4, 18)    | 0.026   |
| Hospital LOS (days), median (Q1, Q3)   | 22 (12, 42)             | 22 (12, 39)       | 23 (12, 45)       | 0.036               | 24 (12, 47)  | 0.931   |

Group A: KDIGO Cr stage more severe than KDIGO stage; Group B: KDIGO stage consistent with KDIGO stage; Group C: KDIGO stage less severe than KDIGO stage; AKI: Acute kidney injury; APACHE II: Acute Physiology and Chronic Health Evaluation II; ARDS: Acute respiratory distress syndrome; CHD: Coronary heart disease; CKI: Chronic kidney insufficiency; COPD: Chronic obstructive pulmonary disease; ICU: Intensive Care Unit; IQR: Interquartile range; KDIGO: Kidney Disease Improving Global Outcomes; KDIGO Cr: KDIGO serum creatinine criteria; KDIGO stage: KDIGO urine output criteria; LOS: Length of stay; RRT: Renal replacement therapy; SOFA: Sequential Organ Failure Assessment.
Interventions including vasopressors, mechanical ventilation, diuretics, and RRT [Table 1]. Compared with patients without AKI, patients with AKI had a higher ICU mortality (25.8% vs. 6.8%, \( P < 0.001 \)) and hospital mortality (30.4% vs. 9.3%, \( P < 0.001 \)). In multivariate logistic regression, AKI was an independent risk factor for hospital mortality (odds ratio [OR]: 2.326, 95% confidence interval [CI]: 1.574–3.437, \( P < 0.001 \)).

**Acute kidney injury diagnosis and classification by Kidney Disease Improving Global Outcomes urine output criteria versus Kidney Disease Improving Global Outcomes serum creatinine criteria**

Among the 1058 enrolled patients, 554 patients with AKI (52.4%) could be diagnosed by KDIGO\(_{\text{SO}}\) alone, whereas the other 32 AKI patients (3.0%) were identified only by KDIGO\(_{\text{UO}}\). Agreement between KDIGO\(_{\text{SCr}}\) and KDIGO\(_{\text{UO}}\) in the diagnosis of AKI versus non-AKI was poor as suggested by Cohen’s kappa coefficient of 0.255 (95% CI: 0.211–0.300).

KDIGO\(_{\text{SO}}\) also exerted a significant impact on AKI classification. According to KDIGO\(_{\text{SCr}}\), alone, 504 (47.6%), 257 (24.3%), 148 (14.0%), and 149 (14.1%) patients were classified as non-AKI, AKI stages 1, 2, and 3, respectively [Table 2]. However, the use of UO criteria would result in upgrade of AKI classification in 77 patients (7.3%), including 32 patients upgraded from KDIGO\(_{\text{SO}}\) non-AKI to KDIGO\(_{\text{UO}}\), AKI stage 1 (\( n = 12 \)), stage 2 (\( n = 8 \)), and stage 3 (\( n = 12 \)), 31 patients upgraded from KDIGO\(_{\text{SCr}}\) stage 1 to KDIGO\(_{\text{UO}}\) stage 2 (\( n = 12 \)) and stage 3 (\( n = 19 \)), and 14 patients upgraded from KDIGO\(_{\text{SCr}}\) stage 2 to KDIGO\(_{\text{UO}}\) stage 3. Agreement between KDIGO\(_{\text{SCr}}\) and KDIGO\(_{\text{UO}}\) for AKI classification was also poor (Cohen’s kappa coefficient of 0.312, 95% CI: 0.265–0.359).

**Acute kidney injury prognosis by Kidney Disease Improving Global Outcomes urine output criteria versus Kidney Disease Improving Global Outcomes serum creatinine criteria**

As expected, hospital mortality significantly increased with increasing severity of AKI, regardless of criteria for AKI staging (i.e., KDIGO\(_{\text{SO}}\); KDIGO\(_{\text{SCr}}\); KDIGO\(_{\text{UO}}\); or KDIGO\(_{\text{SO}}\)) [Table 3]. However, the predictive values of KDIGO\(_{\text{SCr}}\) and KDIGO\(_{\text{UO}}\) classification were comparable, with AuROC of 0.666 (95% CI: 0.637–0.694) and 0.678 (95% CI: 0.649–0.706), respectively (\( P = 0.579 \)).

In multivariate logistic regression analysis, AKI based on KDIGO\(_{\text{SO}}\) (KDIGO\(_{\text{UO}}\); KDIGO; OR: 2.891, 95% CI: 1.964–4.254, \( P < 0.001 \)), but not based on KDIGO\(_{\text{SCr}}\) (KDIGO\(_{\text{SCr}}\); AKI; OR: 1.322, 95% CI: 0.902–1.939, \( P = 0.152 \)), was an independent risk factor for hospital mortality, after adjusting for other potential confounders [Table 4]. No collinearity had been found with either KDIGO\(_{\text{SO}}\); AKI or KDIGO\(_{\text{SO}}\); AKI, with variance inflation factor of 1.306 and 1.408, respectively. We did not find any interaction between KDIGO\(_{\text{SO}}\); AKI and KDIGO\(_{\text{SO}}\); AKI (\( P = 0.125 \)).

Among the 586 patients with AKI, there were 416 patients (71.0%) in Group A (i.e., KDIGO\(_{\text{SCr}}\) stage was more severe than KDIGO\(_{\text{UO}}\) stage), 93 patients (15.9%) in Group B (i.e., KDIGO\(_{\text{SO}}\) stage was consistent with KDIGO\(_{\text{UO}}\) stage), and 77 patients (13.1%) in Group C (i.e., KDIGO\(_{\text{SCr}}\) stage was less severe than KDIGO\(_{\text{UO}}\) stage). These patients differed significantly with regards to age, comorbidities, severity of illness, renal function on ICU admission, and hospital mortality [Table 1]. Multivariate logistic regression analysis showed that compared with non-AKI, patients in group B (OR: 3.916, 95% CI: 2.201–6.968, \( P < 0.001 \)) and group C (OR: 7.580, 95% CI: 4.141–13.873, \( P < 0.001 \)) had a significantly higher risk of hospital mortality, whereas patients in group A had a similar hospital mortality [Table 4]. These findings were also confirmed by Kaplan-Meier survival curve [Figure 2].

**Discussion**

The current study showed that AKI as defined by KDIGO definition and classification system was common (55.4%) among critically ill patients, with a hospital mortality of 30.4%. In addition to KDIGO\(_{\text{SO}}\), alone, use of KDIGO\(_{\text{UO}}\) could identify an additional 3.0% of patients as having AKI and result in a change of AKI stage in 7.3% patients. Furthermore, KDIGO\(_{\text{SO}}\) had a better predictive value for hospital mortality than KDIGO\(_{\text{SCr}}\).

There were wide variations in the reported prevalence of AKI (5.7–74.5%) in different studies, possibly due to different study designs, heterogeneity of patient population, different diagnostic criteria, and determination of baseline creatinine levels.\[4,8,12,15,19,27,32\] In a recent cohort study involving 32,045 ICU patients, Kellum et al.\[13\] reported an AKI prevalence of 74.5% based on KDIGO criteria. However, in a retrospective analysis of prospectively collected data by Bagshaw et al.\[19\] AKI occurred in 36.1% of 120,123 ICU patients. Likewise, Joannidis et al.\[15\] reported an AKI prevalence of 35.5% among 16,784 patients from 303 ICUs in a cohort analysis of SAPS 3 database. The latter two large studies, based on SCr and UO data within the first 24 or 48 h after ICU admission, reported the prevalence of AKI that was much lower than that of our study.

In the 1058 critically ill patients in our study, 32 (3.0%) patients without significant SCr change were diagnosed as AKI based on KDIGO\(_{\text{UO}}\), similar to 4.8% as reported in a recent cohort study involving 32,045 ICU patients. Kellum et al.\[13\] reported an AKI prevalence of 74.5% based on KDIGO criteria. However, in a retrospective analysis of prospectively collected data by Bagshaw et al.\[19\] AKI occurred in 36.1% of 120,123 ICU patients. Likewise, Joannidis et al.\[15\] reported an AKI prevalence of 35.5% among 16,784 patients from 303 ICUs in a cohort analysis of SAPS 3 database. The latter two large studies, based on SCr and UO data within the first 24 or 48 h after ICU admission, reported the prevalence of AKI that was much lower than that of our study.

In the 1058 critically ill patients in our study, 32 (3.0%) patients without significant SCr change were diagnosed as AKI based on KDIGO\(_{\text{UO}}\), similar to 3.0% as reported in a recent cohort study involving 32,045 ICU patients. Kellum et al.\[13\] reported an AKI prevalence of 74.5% based on KDIGO criteria. However, in a retrospective analysis of prospectively collected data by Bagshaw et al.\[19\] AKI occurred in 36.1% of 120,123 ICU patients. Likewise, Joannidis et al.\[15\] reported an AKI prevalence of 35.5% among 16,784 patients from 303 ICUs in a cohort analysis of SAPS 3 database. The latter two large studies, based on SCr and UO data within the first 24 or 48 h after ICU admission, reported the prevalence of AKI that was much lower than that of our study.

### Table 2: Cross tabulation of patients classified by KDIGO\(_{\text{SCr}}\) criteria versus KDIGO\(_{\text{UO}}\) criteria

| KDIGO\(_{\text{SO}}\) | No AKI | AKI stage 1 | AKI stage 2 | AKI stage 3 | Total |
|-------------------|--------|------------|------------|------------|-------|
| KDIGO\(_{\text{SCr}}\) | 472    | 12         | 8          | 12         | 504   |
| KDIGO\(_{\text{UO}}\) | 208    | 18         | 12         | 19         | 257   |
| KDIGO\(_{\text{SCr}}\) | 106    | 17         | 11         | 14         | 148   |
| KDIGO\(_{\text{UO}}\) | 59     | 13         | 13         | 64         | 149   |

Total: 845, 60, 44, 109, 1058

Numbers of patients classified into the respective stages of AKI by KDIGO\(_{\text{SO}}\) or KDIGO\(_{\text{SCr}}\) are cross-tabulated against each other. AKI: Acute kidney injury; KDIGO: Kidney Disease Improving Global Outcomes; KDIGO\(_{\text{SCr}}\): KDIGO serum creatinine criteria; KDIGO\(_{\text{UO}}\): KDIGO urine output criteria.
by Joannidis et al.\textsuperscript{[13]} Moreover, in 77 out of 586 AKI patients (13.1\%) in the current study, it was the KDIGO\textsubscript{UO} stage that led to a worse AKI class, which was also consistent with the findings (13\%) of Cruz et al.\textsuperscript{[18]} In contrast, in a prospective observational study, the prevalence of AKI increased from 24%, based solely on SCr, to 52\% by adding UO as a diagnostic criterion.\textsuperscript{[32]} This might be explained by the difference in patient population. Compared with our study, patients in the above study were less severely ill, as suggested by younger age, fewer patients with severe sepsis (12.6\% vs. 38.9\%) and mechanical ventilation (45.4\% vs. 75.4\%), as well as lower hospital mortality (5.7\% vs. 21.0\%).\textsuperscript{[32]} However, patient characteristics in studies by Joannidis et al.\textsuperscript{[13]} and Cruz et al.\textsuperscript{[18]} were comparable to our study, with regards to age (63.0 years vs. 64.3 years vs. 62.0 years), male (59.2\% vs. 62.2\% vs. 64.0\%), medical admissions (76.0\% vs. 72.2\% vs. 68.9\%), and mortality rate of AKI patients (36.4\% vs. 36.3\% vs. 30.4\%). It was intuitive that severely ill patients were more likely to have decreased GFR and increased SCr level, which might compromise the diagnostic value of UO criteria. All these might indicate that UO criteria might help improve diagnostic sensitivity in mild-to-moderately ill patients. Poor agreement either between KDIGO\textsubscript{SCr} and KDIGO\textsubscript{UO} with regards to the diagnosis and classification of AKI further suggested less validity of SCr monitoring in this cohort and the complexity of UO in different clinical settings.

Our study also suggested that KDIGO\textsubscript{UO} might exert a better prognostic value than KDIGO\textsubscript{SCr}. In a retrospective analysis of a high-resolution database of 14,524 patients admitted to 7 ICUs between 2001 and 2007, UO outperformed creatinine as a better mortality predictor than creatinine alone or the combination of both in patients who developed AKI.\textsuperscript{[34]} In clinical practice, UO monitoring might exhibit some advantages over SCr measurements as an early warning sign of deteriorating renal function without the need for blood sampling.\textsuperscript{[34,35]} Nevertheless, conflicting results had also been reported. For example, with the use of multivariate logistic regression analysis, RIFLE classification based on both SCr and UO criteria was the strongest predictor of ICU mortality, while diuresis was not significantly associated with mortality (\textit{P} = 0.058).\textsuperscript{[19]} In a prospective study of 282 cardiac surgery patients, creatinine-based RIFLE or AKIN classes were the strongest predictors of hospital mortality, whereas the UO criteria showed the lowest predictive value.\textsuperscript{[36]} Ricci et al.\textsuperscript{[36]} in a systematic review in 2008, found that the relative risk for death appeared to be higher when only the creatinine criteria were used. The exact reason for the conflicting results remained unclear. UO was neither sensitive nor specific marker of renal function.\textsuperscript{[37,38]} For example, a decrease of GFR might be associated with impaired ability to concentrate urine; therefore without significant decrease of UO, on the other hand, a nonsustained decrease of UO could simply represent a physiological renal adaptation to maintain the body volume and/or electrolytes homeostasis.\textsuperscript{[38]} Therefore, the better prognostic value of KDIGO\textsubscript{UO} observed in our study might be explained by the fact that decreased UO not only reflected the deterioration of renal function but also suggested tissue hypoperfusion. In fact, studies demonstrated that increase in SCr was more common in patients with oliguria accompanied by hemodynamic compromise (hypotension, tachycardia, or increasing vasopressor and/or inotrope dose).\textsuperscript{[27]}

### Table 3: Hospital mortality of AKI stages according to KDIGO criteria by univariate analysis

| KDIGO stage | KDIGOSCr + UO | KDIGOUO alone | KDIGOSCr alone |
|-------------|--------------|---------------|----------------|
| No AKI      | Total, n     | Mortality, n (%) | OR (95% CI) | P     | Total, n     | Mortality, n (%) | OR (95% CI) | P     | Total, n     | Mortality, n (%) | OR (95% CI) | P     |
|             | Reference    | (9.3)         |              |       | Reference    | (11.9)         |              |       | Reference    | (11.9)         |              |       |
| AKI stage 1 | 238          | 43            | 2.145        | 0.001 | 60           | 18             | 2.640        | 0.001 | 257           | 56             | 2.062        | <0.001 |
|             | (18.1)       | (1.363–3.375) |              |       | (30.0)       | (1.470–4.742)  |              |       | (21.8)       | (1.381–3.077)  |              |       |
| AKI stage 2 | 154          | 42            | 3.648        | <0.001| 44           | 18             | 4.265        | <0.001| 148           | 44             | 3.131        | <0.001 |
|             | (27.3)       | (2.277–5.843) |              |       | (40.9)       | (2.268–8.022)  |              |       | (29.7)       | (2.009–4.879)  |              |       |
| AKI stage 3 | 194          | 93            | 8.957        | <0.001| 109          | 68             | 10.218       | <0.001| 149           | 62             | 5.274        | <0.001 |
|             | (47.9)       | (5.890–13.619)|              |       | (62.4)       | (6.623–15.765) |              |       | (41.6)       | (3.455–8.049)  |              |       |

AKI: Acute kidney injury; KDIGO: Kidney Disease Improving Global Outcomes; KDIGOSCr: KDIGO serum creatinine criteria; KDIGOEUO, KDIGO urine output criteria; KDIGOSCr + UO: KDIGO serum creatinine criteria and urine output criteria; OR: Odds ratio; CI: Confidence interval.

Figure 2: Kaplan-Meier survival curves from ICU admission to 90 days. Group A: KDIGO\textsubscript{SCr} stage more severe than KDIGO\textsubscript{UO} stage; Group B: KDIGO\textsubscript{SCr} stage consistent with KDIGO\textsubscript{UO} stage; Group C: KDIGO\textsubscript{SCr} stage less severe than KDIGO\textsubscript{UO} stage. AKI: Acute kidney injury; ICU: Intensive Care Unit; KDIGO: Kidney Disease Improving Global Outcomes; KDIGO\textsubscript{SCr}: KDIGO serum creatinine criteria; KDIGO\textsubscript{UO}: KDIGO urine output criteria.
Acute renal failure in the ICU: Risk factors

1.107 (1.081–1.135) 1.591 (1.045–2.421) 3.916 (2.201–6.968) P 0.001
1.322 (0.902–1.939) 1.849 (1.299–2.631) 0.001

Model 1
1.109 (1.082–1.136) 1.821 (1.282–2.587) 2.891 (1.964–4.254) <0.001

Model 2
2.302 (1.424–3.721) 0.030 <0.001

UO 7.580 (4.141–13.873) <0.001

Table 4: Risk factors for hospital mortality by multivariate logistic regression analysis

| Variables | Model 1 | | Model 2 |
|-----------|---------|---|---------|
| OR (95% CI) | P | OR (95% CI) | P |
| APACHE II score | 1.107 (1.081–1.135) | <0.001 | 1.109 (1.082–1.136) | <0.001 |
| Comorbidity | | | |
| Solid tumor | 2.367 (1.473–3.806) | <0.001 | 2.302 (1.424–3.721) | 0.001 |
| Complications | | | |
| Severe sepsis/septic shock | 1.821 (1.282–2.587) | 0.001 | 1.849 (1.299–2.631) | 0.001 |
| AKI diagnosis | | | |
| Non‑AKI | Reference | | Reference |
| KDIGO<sub>SCR</sub> AKI | 1.322 (0.902–1.939) | 0.152 | |
| KDIGO<sub>Cr</sub> AKI | 2.891 (1.964–4.254) | <0.001 | |
| AKI classification | | | |
| AKI Group A | 1.591 (1.045–2.421) | 0.030 | |
| AKI Group B | 3.916 (2.201–6.968) | <0.001 | |
| AKI Group C | 7.580 (4.141–13.873) | <0.001 | |

*Covariates included in multivariate logistic regression model included AKI diagnosis based on KDIGO<sub>SCR</sub> or KDIGO<sub>Cr</sub> and all variables with P<0.1 in univariate analysis, such as gender, age, APACHE II score, SOFA score, comorbidities (no comorbidities, hypertension, chronic obstructive pulmonary disease, solid tumor, chronic kidney insufficiency), admission status (medical, elective surgery, emergency surgery), reasons of ICU admission (respiratory, gastrointestinal, trauma, and other diseases), renal function on ICU admission (serum creatinine level on ICU admission, urine output during first 24 h after ICU admission), complications (severe sepsis/septic shock, and acute lung injury/acute respiratory distress syndrome);
†Covariates included in multivariate logistic regression model included AKI classifications (non‑AKI, AKI Group A, B, and C), and all variables with P<0.1 in univariate analysis. Group A: KDIGO<sub>SCR</sub> stage more severe than KDIGO<sub>Cr</sub> stage; Group B: KDIGO<sub>SCR</sub> stage consistent with KDIGO<sub>Cr</sub> stage; Group C: KDIGO<sub>SCR</sub> stage less severe than KDIGO<sub>Cr</sub> stage.

Our study had several limitations. First, this was a secondary analysis of prospectively collected data and should be regarded as hypothesis generating rather than hypothesis validating. Second, AKI diagnosis and classification were based on clinical data within the first 28 days of ICU admission, which might underestimate the prevalence and severity of late AKI. However, Mandelbaum et al. found that for observation periods longer than 2 days, mortality risk was independent of observation period but related to the severity of SCR increase or oliguria. This might indicate that observation periods exerted little impact, if any, on the prognostic value of creatinine and/or UO in AKI patients. Third, we did not investigate the potential influence of fluid balance, vasopressors, and diuretics on UO. In addition, volume status before AKI diagnosis and classification was not assessed. Last, we did not examine the association between duration of oliguria and a subsequent elevated SCR level.

In conclusion, we demonstrated that in adult patients with ICU LOS more than 24 h, UO provided a criterion with additional value beyond creatinine criterion for AKI diagnosis and classification. Compared with creatinine criterion alone, the application of both UO and creatinine criteria may help identify a group of patients who were oliguric but without significant SCR change. This group of patients, despite only representing 7.3% of the cohort (or 13.1% of patients with AKI), had a similar hospital mortality to patients who were oliguric and with significant SCR change, which was markedly higher than that of non‑AKI patients or nonoliguric patients with significant SCR change. Based on the above findings, we believed that UO criteria represent an important element of the KDIGO definition and classification system.

Financial support and sponsorship
The study was supported by a grant from the Capital Clinical Application Research of the Beijing Municipal Science and Technology Commission (No. Z131107002213112).

Conflicts of interest
There are no conflicts of interest.

References
1. Chertow GM, Levy EM, Hammermeister KE, Grover F, Daley J. Independent association between acute renal failure and mortality following cardiac surgery. Am J Med 1998;104:343‑8. doi: 10.1016/S0002‑9343(98)00058‑8.
2. de Mendonça A, Vincent JL, Suter PM, Moreno R, Dearden NM, Antonelli M, et al. Acute renal failure in the ICU: Risk factors and outcome evaluated by the SOFA score. Intensive Care Med 2000;26:915‑21. doi: 10.1007/s001340051281.
3. Nash K, Hafeez A, Hou S. Hospital‑acquired renal insufficiency. Am J Kidney Dis 2002;39:930‑6. doi: 10.1053/ajkd.2002.32766.
4. Uchino S, Kellum JA, Bellomo R, Doig GS, Morimatsu H, Morgera S, et al. Acute renal failure in critically ill patients: A multinational, multicenter study. JAMA 2005;294:813‑8. doi: 10.1001/jama.294.7.813.
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. Crit Care 2004;8:R204‑12. doi: 10.1186/cc2872.
6. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, et al. Acute Kidney Injury Network: Report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11:R31. doi: 10.1186/cc5713.
7. Section 2: AKI definition. Kidney Int Suppl 2012;2:19‑36. doi: 10.1038/issup.2011.32.
et al. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: A cohort analysis. Crit Care 2006;10:R73. doi: 10.1186/cc4915.

9. Uchino S, Bellomo R, Goldsmith D, Bates S, Ronco C. An assessment of the RIFLE criteria for acute renal failure in hospitalized patients. Crit Care Med 2006;34:1913-7. doi: 10.1097/01.ccm.0000224227.70642.4f.

10. Ali T, Khan I, Simpson W, Prescott G, Townend J, Smith W, et al. Incidence and outcomes in acute kidney injury: A comprehensive population-based study. J Am Soc Nephrol 2007;18:1292-8. doi: 10.1681/asn.2006070756.

11. Perez-Valdivieso JR, Bes-Rastrollo M, Monedero P, de Irala J, Lavilla FJ. Prognosis and serum creatinine levels in acute renal failure at the time of nephrology consultation: An observational cohort study. BMC Nephrol 2007;8:14. doi: 10.1186/1471-2369-8-14.

12. Ostermann M, Chang RW. Acute kidney injury in the intensive care unit according to RIFLE. Crit Care Med 2007;35:1837-43. doi: 10.1097/01.ccm.0000277041.13090.0a.

13. Lopes JA, Fernandes P, Jorge S, Goncalves S, Alvarez A, Costa e Silva Z, et al. Acute kidney injury in intensive care unit patients: A comparison between the RIFLE and the Acute Kidney Injury Network classifications. Crit Care 2008;12:R110. doi: 10.1186/cc6997.

14. Bagshaw SM, George C, Bellomo R; ANZICS Database Management Committee. A comparison of the RIFLE and AKIN criteria for acute kidney injury in critically ill patients. Nephrol Dial Transplant 2008;23:1569-74. doi: 10.1093/ndt/gfn009.

15. Joannidis M, Metnitz B, Bauer P, Schuchertshitz N, Moreno R, Druml W, et al. Acute kidney injury in critically ill patients classified by AKIN versus RIFLE using the SAPS 3 database. Intensive Care Med 2009;35:1692-702. doi: 10.1007/s00134-009-1530-4.

16. Ricci Z, Cruz D, Ronco C. The RIFLE criteria and mortality in acute kidney injury: A systematic review. Kidney Int 2010;77:538-46. doi: 10.1038/sj.ki.5002242-27.70642.4f.

17. Endre ZH, Pickering JW. Outcome definitions in non-dialysis intervention and prevention trials in acute kidney injury (AKI). Nephrol Dial Transplant 2010;25:107-18. doi: 10.1093/ndt/gfp501.

18. Cruz DN, Bolgan I, Perazella MA, Bonello M, de Cal M, Corradi V, et al. North East Italian Prospective Hospital Renal Outcome Survey on Acute Kidney Injury (NEiPHROS-AKI): Targeting the problem and renal replacement therapy in the critically ill. Kidney Int 2011;79:2418-25. doi: 10.2215/cjn.03361006.

19. Bagshaw SM, George C, Dinu I, Bellomo R. A multi-centre evaluation of the RIFLE criteria for early acute kidney injury in critically ill patients. Nephrol Dial Transplant 2008;23:1203-10. doi: 10.1093/ndt/gfn744.

20. Bagshaw SM, George C, Gibney RT, Bellomo R. A multi-center evaluation of early acute kidney injury in critically ill trauma patients. Ren Fail 2008;30:581-9. doi: 10.1080/08860220802134649.

21. Du B, An Y, Kang Y, Yu X, Zhao M, Ma X, et al. Characteristics of critically ill patients in ICUs in Mainland China. Crit Care Med 2013;41:84-92. doi: 10.1097/CCM.0b013e31826a4082.

22. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: A severity of disease classification system. Crit Care Med 1985;13:818-29. doi: 10.1097/00003246-198510000-00009.

23. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonca A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the working group on sepsis-related problems of the European society of intensive care medicine. Intensive Care Med 1996;22:707-10. doi: 10.1007/BF01709751.

24. Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. Chest 1992;101:1644-55. doi: 10.1378/chest.101.6.1644.

25. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. Am J Respir Crit Care Med 1994;149(3 Pt 1):818-24. doi: 10.1164/ajrccm.149.3.7509706.

26. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Am J Kidney Dis 2002;39:2 Suppl 1:S1-266.

27. Kellum JA, Chawla LS, Keener C, Singhart K, Palevsky PM, Pike FL, et al. The effects of alternative resuscitation strategies on acute kidney injury in patients with septic shock. Am J Respir Crit Care Med 2016;193:281-7. doi: 10.1164/rcrm.201505-0995OC.

28. Lagny MG, Jouret F, Koch JN, Blaffart F, Donneau AF, Albert A, et al. Incidence and outcomes of acute kidney injury after cardiac surgery using either criteria of the RIFLE classification. BMC Nephrol 2016;15:76. doi: 10.1186/s12882-015-0066-9.

29. Gameiro J, Neves JB, Rodrigues N, Bekerman C, Melo MJ, Pereira M, et al. Acute kidney injury, long-term renal function and mortality in patients undergoing major abdominal surgery: A cohort analysis. Clin Kidney J 2016;9:192-200. doi: 10.1093/ckj/sfv144.

30. 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;41:1411-23. doi: 10.1007/s00134-015-3934-7.

31. 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;26:2231-8. doi: 10.1681/asn.2014070724.

32. 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 2014;127:1820-6. doi: 10.3760/ cmsa.j.issn.0366-6999.20140387.

33. Macedo E, Malhotra R, Bouchard J, Wynn SK, Mehta RL. Oliguria is an early predictor of higher mortality in critically ill patients. Kidney Int 2011;80:760-7. doi: 10.1038/ki.2011.150.

34. Mandelbaum T, Scott DJ, Lee J, Mark RG, Malhotra A, Waikar SS, et al. Outcome of critically ill patients with acute kidney injury using the Acute Kidney Injury Network criteria. Crit Care Med 2011;39:2659-64. doi: 10.1097/CCM.0b013e3182281f11b.

35. Mandelbaum T, Lee J, Scott DJ, Mark RG, Malhotra A, Howell MD, et al. Empirical relationships among oliguria, creatinine, mortality, and renal replacement therapy in the critically ill. Intensive Care Med 2013;39:414-9. doi: 10.1007/s00134-012-2767-x.

36. Haase M, Bellomo R, Matalanis G, Calzavacca P, Dranog D, Haase-Fielitz A. A comparison of the RIFLE and Acute Kidney Injury Network classifications for cardiac surgery-associated acute kidney injury: A prospective cohort study. J Thorac Cardiovasc Surg 2009;138:1370-6. doi: 10.1016/j.jtcvs.2009.07.007.

37. Proseur JR, Liu YL, Licari E, Bagshaw SM, Egi M, Haase M, et al. Oliguria as predictive biomarker of acute kidney injury in critically ill patients. Crit Care 2011;15:R172. doi: 10.1186/cc10318.

38. Legrand M, Payen D. Understanding urine output in critically ill patients. Ann Intensive Care 2011;1:13. doi: 10.1186/2110-5820-1-13.