The Predictive Value of the Oxford Acute Disease Severity Score for Clinical Outcomes in Patients with Acute Kidney Injury: A Secondary Analysis of a Large Prospective Observational Study

Na Wang  
China Rehabilitation Research Center

Mei-Ping Wang  
Capital Medical University

Li Jiang  
Xuanwu Hospital

Bin Du  
Peking Union Medical College Hospital

Bo Zhu  
Beijing Fuxing Hospital

Xiuming Xi  
Beijing Fuxing Hospital  https://orcid.org/0000-0001-6034-5279

Research

Keywords: Oxford Acute Severity of Illness Score, Intensive care unit, AKI, Mortality

DOI: https://doi.org/10.21203/rs.3.rs-640541/v1

License: © This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Background: To compare the performance of the Oxford Acute Severity of Illness Score (OASIS), the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, the Simplified Acute Physiology Score II (SAPS II) and the Sequential Organ Failure Assessment (SOFA) score in predicting 28-day mortality in acute kidney injury (AKI) patients.

Methods: Data were extracted from the Beijing Acute Kidney Injury Trial (BAKIT). 2,954 patients with complete clinical data were included in this study. We calculated the OASIS, APACHE II, SAPS II and SOFA within the first day of ICU admission. Receiver operating characteristic (ROC) curves were used to analyse and evaluate the predictive effects of the four scoring systems on the 28-day mortality risk of AKI patients and each subgroup. The best cut-off value was identified by the highest combined sensitivity and specificity using Youden's index. The significance level was set at 5%.

Results: Among the 2,954 patients, the 28-day mortality rate was 17.0% (501 patients died). The OASIS, APACHE II, SAPS II and SOFA of nonsurviving patients were higher than those of surviving patients with AKI. The 28-day mortality of AKI patients increased accordingly with the increase in OASIS. Among the four scoring systems, the area under the curve (AUC) of OASIS was the highest. The comparison of AUC values of different scoring systems showed that there were no significant differences among OASIS, APACHE II and SAPS II, which were better than SOFA. Moreover, logistic analysis revealed that OASIS was an independent risk factor for 28-day mortality in AKI patients, whether as a continuous variable or a categorical variable. OASIS also had good performance in predicting ICU mortality and in-hospital mortality in AKI patients and had good predictive ability for the 28-day mortality of each subgroup of AKI patients.

Conclusion: OASIS, APACHE II and SAPS II all presented good discrimination and calibration in predicting the 28-day mortality risk of AKI patients. OASIS, APACHE II and SAPS II had better predictive accuracy than SOFA, but due to the complexity of APACHE II and SAPS II calculations, OASIS is a good substitute.

Trial Registration

This study was registered at www.chictr.org.cn (registration number ChiCTR-ONC-11001875). Registered on 14 December 2011.

Background

Acute kidney injury (AKI) is a common and serious complication in intensive care unit (ICU) patients, and it is an important risk factor for increased early and long-term morbidity and mortality during hospitalization [1–4]. Early identification and diagnosis, correct assessment of prognosis and active treatment are the keys to reducing the mortality rate. Many severity scores have been developed to evaluate the prognosis of the critically ill patients, including AKI patients.
The Acute Physiology and Chronic Health Evaluation II (APACHE II) score is the most commonly used disease severity scoring system in ICUs around the world [5], it includes 12 physiological and laboratory parameters and two disease-related variables [6]. The Simplified Acute Physiology Score II (SAPS II) was first described in 1984 as an alternative to the APACHE scoring system [7], and it is an effective tool for evaluating AKI patient outcomes [8, 9]. However, all of the above models require considerable effort for data collection. Although the Sequential Organ Failure Assessment (SOFA) score [10] is simple to use and accurate in predicting the mortality outcome of AKI patients [11–13], it depends on laboratory results, and some important prognostic factors were not included.

In 2013, Johnson et al performed a retrospective cohort study of 72,474 ICU patients in 68 ICUs at 49 U.S. hospitals from 2007 to 2011 and developed a new reduced severity of illness score using machine learning algorithms, the Oxford Acute Severity of Illness Score (OASIS), which contained 10 parameters without any laboratory tests and had discrimination and calibration equivalent to more complex existing models [14].

The predictive value of OASIS was validated in mixed ICU patient populations, but its performance in AKI patients remains unknown. The aim of this multicentre study was to evaluate the performance of OASIS for the assessment of mortality in AKI patients in China.

**Methods**

**Study setting and data collection**

This study used a database from the Beijing Acute Kidney Injury Trial (BAKIT) [15], a prospective, multicentre, observational study that investigated the epidemiology of acute kidney injury (AKI) in critically ill patients in 30 ICUs at 28 tertiary hospitals in Beijing, China, conducted between March 1 and August 31, 2012 (for a complete list of these hospitals and the persons responsible for the data acquisition, see Additional file 1). The study subjects included all adult patients (age ≥ 18 years) admitted consecutively to the ICU. Only the initial ICU admission was considered in this study. The following patients were excluded: patients with preexisting end-stage chronic kidney disease, patients already receiving renal replacement therapy (RRT) before admission to the ICU, and patients who had received kidney transplantation in the previous 3 months [16]. Pre-existing comorbidities were diagnosed based on the International Classification of Diseases (ICD-10) codes. The patients were followed up until death, until hospital discharge, or for 28 days.

Thorough follow-up of all patients included in the study was conducted in the first 10 days after ICU admission. The collected data included demographics, anthropometrics, admission diagnosis, comorbidities, daily vital signs and laboratory data (which were used to automatically calculate the APACHE II score, the SAPS II and the SOFA score), days from hospital to ICU admission, ICU length of stay (LOS), hospital LOS, use of vasoactive drugs, the occurrence of AKI, and length of mechanical ventilation (MV). RRT data were also reported.
Mortality data up to 28 days after ICU discharge were collected from hospital records, including records from hospital admissions and visits to outpatient clinics.

AKI severity was classified according to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines [17].

We calculated the OASIS within the first day of ICU admission. The parameters used to calculate the OASIS are shown in Table S1.

**Outcomes**

The primary outcome was 28-day mortality, and the secondary outcomes were ICU mortality and hospital mortality. The ICU LOS and hospital LOS were calculated only for statistical description. ICU mortality and ICU LOS were determined by the first ICU stay only.

**Statistical analysis**

Nonnormally distributed continuous variables are expressed as the medians with interquartile ranges (IQRs) and were compared using the Mann-Whitney U test or Kruskal-Wallis analysis-of-variance test with Bonferroni correction. Categorical variables are expressed as the number of cases and proportions and were compared using the Mantel-Haenszel chi-square test.

Receiver operating characteristic (ROC) curves were drawn according to the sensitivity and specificity of the four scoring systems for predicting the 28-day mortality risk of patients. The ROC curve comparison function of Medcalc software was used for pairwise comparisons of the area under the curve (AUC), the larger the AUC, the higher the predictive value. AUCs of $\geq 0.9$, 0.8 to 0.89, 0.7 to 0.79, 0.6 to 0.69 or $< 0.6$ were classified as excellent, very good, good, fair, and poor, respectively [18].

Cut-off values, sensitivities, specificities, positive predictive values and negative predictive values were calculated by ROC analysis. The best cut-off values for the prediction of 28-day mortality, ICU mortality and hospital mortality were determined by the maximum of the Youden index (i.e., sensitivity plus specificity minus one) calculated from the ROC analysis. The Hosmer- Lemeshow goodness-of-fit test was used to test the calibration of the scoring system.

We used a logistic regression model to evaluate the effect of OASIS on the 28-day mortality in AKI patients. Because OASIS was collinear with APACHE II and SAPS II scores, the variables considered for multivariable analysis included age, sex, OASIS, SOFA, use of vasoactive drugs, MV, RRT and underlying diseases. OASIS was entered as a continuous variable and a categorical variable, respectively.

To verify the predictive effect of OASIS on the 28-day mortality of patients with different AKI grades and among different populations of AKI patients, subgroup analyses were performed by ROC analysis.
All statistical analyses were performed using SPSS software (IBM Corp., Statistics for Windows, version 22.0, Armonk, NY, USA), with a two-sided P values < 0.05 considered statistically significant.

Results

Study population

During the study period, 9,079 patients were admitted consecutively. Of them, patients were excluded because of the following reasons: 5,725 patients had an ICU LOS of less than 24 hours, 110 patients were younger than 18 years old, one patient received renal transplantation during the past 3 months, 95 patients had received RRT before admission to the ICU, and 11 had insufficient clinical recordings. Thus, 3,107 patients were enrolled in the BAKIT study. Of these patients, 194 were excluded because of incomplete data for calculating OASIS, and finally, 2,954 patients were included in our study (Fig. 1).

The characteristics of the entire cohort are shown in Table 1. The median age was 64 (IQR:51–76) years, and 61.6% were men. The all-cause 28-day mortality rate was 17.0%, and the median ICU LOS was 4 (IQR:2–9) days. Among the included patients, the median OASIS was 28 (IQR:23–36), the median APACHE II score was 14 (IQR:10–20), the median SAPS II was 6 (IQR:3–8) and the median SOFA score was 6 (IQR:3–8). MV was used in 1,960 (66.4%) patients, 1,230 patients (41.6%) received vasopressors, 1,506 (51.0%) patients developed AKI as defined by the KDIGO criteria, and 252 patients (8.5%) underwent RRT.
### Table 1
Patient characteristics by 28-day mortality

| Characteristic        | All patients (n = 2954) | Survivors (n = 2453) | Nonsurvivors (n = 501) | P value |
|-----------------------|-------------------------|----------------------|------------------------|---------|
|                       | Median(IQR)             | Median(IQR)          | Median(IQR)            |         |
|                       | Number (%)              | Number (%)           | Number (%)             |         |
| Age (years)           | 64 (51–76)              | 63 (50–75)           | 72 (59–81)             | < 0.001 |
| Male sex              | 1819 (61.6)             | 1518 (61.9)          | 301 (60.1)             | 0.751   |
| **ICU course**        |                         |                      |                        |         |
| Vasoactive therapy    | 1230 (41.6)             | 1033 (42.1)          | 197 (39.3)             | 0.457   |
| MV                    | 1960 (66.4)             | 1591 (64.9)          | 369 (73.7)             | < 0.001 |
| Sepsis                | 848 (28.7)              | 540 (22.0)           | 308 (61.5)             | < 0.001 |
| AKI                   | 1506 (51.0)             | 1099 (44.8)          | 407 (81.2)             | < 0.001 |
| RRT                   | 252 (8.5)               | 127 (5.2)            | 125 (25.0)             | < 0.001 |
| **Severity of illness** |                        |                      |                        |         |
| OASIS                 | 28 (23–36)              | 27 (22–33)           | 38 (31–45)             | < 0.001 |
| APACHE II             | 14 (10–20)              | 13 (9–18)            | 22 (17–28)             | < 0.001 |
| SAPS II               | 33 (25–44)              | 31 (24–40)           | 50 (39–63)             | < 0.001 |
| SOFA                  | 6 (3–8)                 | 5 (3–7)              | 9 (6–11)               | < 0.001 |
| **Admission category** |                        |                      |                        |         |
| Urgent                | 427 (14.5)              | 367 (15.0)           | 60 (12.0)              | < 0.001 |
| Emergency             | 1068 (36.2)             | 732 (29.8)           | 336 (67.1)             |         |

Data are expressed as the median (interquartile range, IQR), and number (percentage). MV, mechanical ventilation; AKI, acute kidney injury; RRT, renal replacement therapy; OASIS, the Oxford Acute Severity of Illness Score; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment; COPD, chronic obstructive pulmonary disease; LOS, length of stay.
| Characteristic                        | All patients (n = 2954) | Survivors (n = 2453) | Nonsurvivors (n = 501) | P value |
|--------------------------------------|-------------------------|----------------------|------------------------|---------|
|                                      | Median(IQR)             | Median(IQR)          | Median(IQR)            |         |
|                                      | Number (%)              | Number (%)           | Number (%)             |         |
| Elective                             | 1459(49.4)              | 1354(53.2)           | 105(20.9)              |         |
| Comorbidities                        |                         |                      |                        |         |
| Hypertension                         | 1176(39.8)              | 949(37.3)            | 227(45.3)              |         |
| Coronary heart disease               | 569(19.3)               | 427(17.4)            | 142(28.3)              |         |
| Congestive heart failure             | 188(6.4)                | 113(4.6)             | 75(15.0)               |         |
| COPD                                 | 158(5.3)                | 120(4.9)             | 38(7.6)                |         |
| Diabetes                             | 511(17.3)               | 418(17.0)            | 93(18.6)               |         |
| Chronic kidney disease               | 151(5.1)                | 108(4.4)             | 43(8.6)                |         |
| Liver disease                        | 82(2.8)                 | 63(2.6)              | 19(3.8)                |         |
| Cancer                               | 407(13.8)               | 352(14.3)            | 55(11.0)               |         |
| Hematological disease                | 24(0.8)                 | 13(0.5)              | 11(2.2)                |         |
| Category of ICU admission diagnosis  |                         |                      |                        |         |
| Cardiovascular                       | 820(27.8)               | 733(28.8)            | 87(17.4)               |         |
| Respiratory                          | 516(17.5)               | 356(14.0)            | 160(31.9)              |         |
| Neurologic                           | 436(14.8)               | 337(13.3)            | 99(19.8)               |         |
| Trauma                               | 225(7.6)                | 203(8.0)             | 22(4.4)                |         |
| Gastrointestinal                     | 578(19.6)               | 485(19.1)            | 93(18.6)               |         |
| Metabolic                            | 66(2.2)                 | 54(2.1)              | 12(2.4)                |         |
| Outcomes                             |                         |                      |                        |         |
| ICU LOS(days)                        | 4(2–9)                  | 4(2–7)               | 6(3–13)                | < 0.001 |
| Hospital LOS(days)                   | 19(12–29)               | 19(12–28)            | 21(11–34)              | 0.002   |

Data are expressed as the median (interquartile range, IQR), and number (percentage). MV, mechanical ventilation; AKI, acute kidney injury; RRT, renal replacement therapy; OASIS, the Oxford Acute Severity of Illness Score; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment; COPD, chronic obstructive pulmonary disease; LOS, length of stay.
There were statistically significant differences in age, MV, sepsis, AKI, RRT, OASIS, APACHE II, SAPS II, SOFA, admission category, ICU LOS and hospital LOS between survivors and nonsurvivors.

**Comparison of characteristics between the survival and nonsurvival groups of AKI patients**

AKI patient characteristics according to 28-day mortality are shown in Table 2. Nonsurviving AKI patients were older (P < 0.001), had higher illness severity scores and were more likely to be diagnosed with sepsis. Positive fluid balance in the first 24 hours was more common among nonsurvivors.
| Characteristic                      | AKI patients (n = 1506) | Survivors (n = 1099) | Non-survivors (n = 407) | P value |
|------------------------------------|-------------------------|----------------------|-------------------------|---------|
|                                    | Median (IQR)            | Number (%)           | Median (IQR)            | Number (%) | Median (IQR) | Number (%) |       |
| Age (years)                        | 67 (53–78)              | 64 (51–77)           | 74 (59–81)              | < 0.001  |
| Male gender                        | 918 (61.0)              | 674 (61.3)           | 244 (60.0)              | 0.886    |
| Baseline creatinine (µmol/L)       | 84.0 (71.6–97.0)        | 83.4 (71.0–97.0)     | 85.0 (75.0–97.3)        | 0.685    |
| **Severity of illness**            |                         |                      |                         |         |
| APACHE II                          | 17 (12–23)              | 15 (10–20)           | 23 (18–29)              | < 0.001  |
| SAPS II                            | 39 (30–52)              | 35 (27–45)           | 52 (41–65)              | < 0.001  |
| SOFA                               | 7 (4–10)                | 6 (4–9)              | 9 (6–12)                | < 0.001  |
| OASIS                              | 31 (24–39)              | 28 (23–35)           | 39 (32–46)              | < 0.001  |
| **ICU course**                     |                         |                      |                         |         |
| Vasoactive therapy                 | 622 (41.3)              | 451 (41.0)           | 171 (42.0)              | 0.942    |
| MV                                 | 1052 (69.9)             | 748 (68.1)           | 304 (74.7)              | 0.045    |
| sepsis                             | 603 (40.0)              | 335 (30.5)           | 268 (65.8)              | < 0.001  |
| Positive fluid balance first 24 hours | 1083 (71.9)         | 743 (67.6)           | 340 (83.5)              | < 0.001  |
| Use of diuretics on the first day of admission | 510 (33.9)        | 368 (33.5)           | 142 (34.9)              | 0.876    |
| Staging of AKI 1                   | 699 (46.4)              | 592 (53.9)           | 107 (26.3)              |         |
| 2                                  | 357 (23.7)              | 260 (23.7)           | 97 (23.8)               | < 0.001  |

Data are expressed as the median (interquartile range, IQR), and number (percentage). AKI, acute kidney injury; OASIS, the Oxford Acute Severity of Illness Score; SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment; APACHE II, Acute Physiology and Chronic Health Evaluation II; MV, mechanical ventilation; LOS, length of stay; RRT, renal replacement therapy.
| Characteristic | AKI patients (n = 1506) | Survivors (n = 1099) | Non-survivors (n = 407) | P value |
|---------------|-------------------------|----------------------|-------------------------|---------|
|               | Median (IQR)            | Median (IQR)         | Median (IQR)            |         |
|               | Number (%)              | Number (%)           | Number (%)              |         |
| 3             | 450 (29.9)              | 247 (22.5)           | 203 (49.9)              |         |
| RRT           | 241 (16.0)              | 121 (11.0)           | 120 (29.5)              | < 0.001 |

| Outcomes      |                        |                      |                         |         |
|---------------|-------------------------|----------------------|-------------------------|---------|
| Hospital LOS (days) | 20 (11–30)              | 22 (14–34)           | 13 (6–23)               | < 0.001 |
| ICU LOS (days)  | 5 (3–11)                | 5 (3–11)             | 6 (4–12)                | 0.030   |

Data are expressed as the median (interquartile range, IQR), and number (percentage). AKI, acute kidney injury; OASIS, the Oxford Acute Severity of Illness Score; SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment; APACHE II, Acute Physiology and Chronic Health Evaluation II; MV, mechanical ventilation; LOS, length of stay; RRT, renal replacement therapy.

The 28-day Mortality Of Aki Patients According To Oasis

The distribution of OASIS in AKI patients is shown in Fig. 2. OASIS ranged from 6 to 64, and the median value was 31 (IQR: 24, 39). The distributions of the OASIS with corresponding 28-day mortality are also presented in Fig. 2. As each score increased, the 28-day mortality of AKI patients increased accordingly, indicating more serious illness and worse prognosis.

Comparison of ROC curve and AUCs of the four scoring systems in evaluating the 28-day mortality of AKI patients

In Fig. 3, OASIS had the highest discriminatory power in predicting the prognosis of AKI patients. The AUC values of OASIS, APACHE II and SAPS II in predicting 28-day mortality were 0.771 (95% CI, [0.742, 0.799]), 0.764 (95% CI, [0.735, 0.792]), and 0.767 (95% CI, [0.739, 0.796]), respectively, which were higher than that of SOFA (0.686; P < 0.001). Table 3 shows the pairwise comparison of the ROC curves, and there were no statistically significant differences between the AUC values of OASIS, APACHE II, and SAPS II in predicting 28-day mortality.
Table 3
Pairwise comparison of ROC curves for predicting 28-day mortality in AKI patients

| Variables       | Difference between areas | Standard Error | Z     | P value   |
|-----------------|--------------------------|----------------|-------|-----------|
| APACHEII~OASIS  | 0.00706                  | 0.0115         | 0.612 | 0.5408    |
| APACHEII~SAPSII | 0.00377                  | 0.0112         | 0.336 | 0.737     |
| APACHEII~SOFA   | 0.0774                   | 0.0155         | 4.995 | <0.0001   |
| OASIS~SAPSII    | 0.00329                  | 0.0125         | 0.264 | 0.7917    |
| OASIS~SOFA      | 0.0845                   | 0.0172         | 4.91  | <0.0001   |
| SAPSII~SOFA     | 0.0812                   | 0.0167         | 4.864 | <0.0001   |

OASIS, the Oxford Acute Severity of Illness Score; APACHE II, the Acute Physiology and Chronic Health Evaluation II; SOFA, the Sequential Organ Failure Assessment; SAPS II, the Simplified Acute Physiology Score II.

The predictive ability of OASIS, APACHE II, SAPS II and SOFA score for poor outcomes

The ROC curves for the prediction of 28-day mortality, ICU mortality and in-hospital mortality by each severity scale are shown in Table 4. The sensitivities, specificities, positive predictive values, and negative predictive values of the optimal cut-off values (from the Youden index) for each scale to predict the three outcomes are listed in Table 5. The cut-off value of OASIS for the prediction of 28-day mortality was 33 with a sensitivity of 87.75% and specificity of 46.26%, as calculated by the ROC curve analysis. OASIS ≥ 33 predicts poor short-term prognosis in patients with AKI.
Table 4
Area under the curve of various parameters for predicting poor outcomes in AKI patients

| Severity of illness | AUC   | Standard error | P-Value | 95% confidence interval |
|---------------------|-------|----------------|---------|------------------------|
|                     |       |                |         | Lower limit Upper limit|
| **28-day mortality**|       |                |         |                        |
| OASIS               | 0.771 | 0.015          | 0.000   | 0.742 0.799            |
| APACHEII            | 0.764 | 0.014          | 0.000   | 0.735 0.792            |
| SAPSII              | 0.767 | 0.015          | 0.000   | 0.739 0.796            |
| SOFA                | 0.686 | 0.017          | 0.000   | 0.653 0.719            |
| **ICU mortality**   |       |                |         |                        |
| OASIS               | 0.804 | 0.014          | 0.000   | 0.777 0.832            |
| APACHEII            | 0.800 | 0.014          | 0.000   | 0.773 0.827            |
| SAPSII              | 0.801 | 0.014          | 0.000   | 0.774 0.829            |
| SOFA                | 0.689 | 0.018          | 0.000   | 0.654 0.724            |
| **Hospital mortality** |     |                |         |                        |
| OASIS               | 0.783 | 0.014          | 0.000   | 0.756 0.811            |
| APACHEII            | 0.776 | 0.014          | 0.000   | 0.748 0.804            |
| SAPSII              | 0.784 | 0.014          | 0.000   | 0.757 0.811            |
| SOFA                | 0.676 | 0.017          | 0.000   | 0.643 0.709            |

AUC, area under the receiver operating characteristic curve; OASIS, the Oxford Acute Severity of Illness Score; APACHE II, the Acute Physiology and Chronic Health Evaluation II; SOFA, the Sequential Organ Failure Assessment; SAPS II, the Simplified Acute Physiology Score II.
Table 5
Performance of multivariable models for predicting poor outcomes in AKI patients

| Severity of illness | YI     | Cutoff | Sen%  | Spe%  | +LR   | -LR   | PPV  | NPV  |
|---------------------|--------|--------|-------|-------|-------|-------|------|------|
| **28-day mortality**|        |        |       |       |       |       |      |      |
| APACHEII            | 0.3976 | 17     | 63.02 | 76.73 | 2.71  | 0.48  | 87.2 | 45.3 |
| SAPSII              | 0.4142 | 39     | 61.37 | 80.06 | 3.08  | 0.48  | 88.5 | 45.2 |
| SOFA                | 0.2885 | 7      | 60.15 | 68.70 | 1.92  | 0.58  | 82.8 | 40.7 |
| OASIS               | 0.4305 | 33     | 87.75 | 46.26 | 2.55  | 0.40  | 86.5 | 49.6 |
| **ICU mortality**   |        |        |       |       |       |       |      |      |
| APACHEII            | 0.4562 | 16     | 57.95 | 87.67 | 4.70  | 0.48  | 94.0 | 38.4 |
| SAPSII              | 0.4794 | 39     | 60.62 | 87.33 | 4.78  | 0.45  | 94.1 | 39.9 |
| SOFA                | 0.2877 | 7      | 58.56 | 70.21 | 1.97  | 0.59  | 86.8 | 33.7 |
| OASIS               | 0.4930 | 33     | 69.85 | 79.45 | 3.40  | 0.38  | 91.9 | 44.1 |
| **Hospital mortality**|      |        |       |       |       |       |      |      |
| APACHEII            | 0.4200 | 16     | 59.53 | 82.47 | 3.40  | 0.49  | 89.4 | 45.2 |
| SAPSII              | 0.4499 | 39     | 62.53 | 82.47 | 3.57  | 0.45  | 89.8 | 47.1 |
| SOFA                | 0.2677 | 7      | 59.65 | 67.12 | 1.81  | 0.6   | 81.8 | 40.2 |
| OASIS               | 0.4636 | 33     | 71.84 | 74.52 | 2.82  | 0.38  | 87.4 | 51.7 |

YI, Youden's index; Sen, sensitivity; Spe, specificity; LR+, positive likelihood ratio; LR−, negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; OASIS, the Oxford Acute Severity of Illness Score; APACHE II, the Acute Physiology and Chronic Health Evaluation II; SOFA, the Sequential Organ Failure Assessment; SAPS II, the Simplified Acute Physiology Score II.

Logistic Regression Analyses Of 28-day Mortality In Aki Patients

Logistic regression model was used to test the efficacy of OASIS in predicting 28-day mortality in patients with AKI (Table 6). Because OASIS is collinear with APACHE II and SAPS II, variables considered for multivariable analysis included age, sex, OASIS, SOFA, use of vasoactive drugs, MV, RRT and underlying diseases. OASIS was entered as a continuous variable and a categorical variable (the cut-off value of OASIS was 33), respectively. Multivariable analysis showed that 28-day mortality increased by 8.5% (95% CI, 1.065–1.106) for every point increase in the OASIS, and the 28-day mortality of patients with high OASIS was 3.826 times higher than that of patients with low OASIS. In addition to OASIS, sepsis (OR, 1.823; 95% CI, 1.339–2.481), RRT (OR, 1.802; 95% CI, 1.263–2.570), old age (OR, 1.012; 95% CI, 1.003–
1.021), higher SOFA score (OR, 1.091; 95% CI, 1.042–1.141) and MV (OR, 2.016; 95% CI, 1.416–2.871) were significantly associated with a higher risk of death in multivariable analysis.

Table 6
Logistic regression analyses of 28-day mortality in AKI patients

| variable | P-value | OR (95CI%) | variable | P-value | OR (95CI%) |
|----------|---------|------------|----------|---------|------------|
| Sepsis   | 0.000   | 1.823(1.339–2.481) | Sepsis   | 0.000   | 2.002(1.479–2.711) |
| RRT      | 0.000   | 1.802(1.263–2.570) | RRT      | 0.002   | 1.755(1.232–2.500) |
| Age      | 0.013   | 1.012(1.003–1.021) | Age      | 0.001   | 1.016(1.007–1.025) |
| OASIS\(^a\) | 0.000 | 1.085(1.065–1.106) | OASIS\(^b\) | 0.000 | 3.826(2.724–5.326) |
| SOFA     | 0.000   | 1.091(1.042–1.141) | SOFA     | 0.000   | 1.123(1.075–1.173) |
| MV       | 0.000   | 2.016(1.416–2.871) | MV       | 0.001   | 1.779(1.251–2.529) |

Multivariable logistic regression to assess the association of OASIS with 28-day mortality.

a. OASIS was entered as a continuous variable.

b. OASIS was entered as a categorical variable, the cut-off value of OASIS was 33.

AKI, acute kidney injury; RRT, renal replacement therapy; OASIS, the Oxford Acute Severity of Illness Score; SOFA, Sequential Organ Failure Assessment; MV, mechanical ventilation; OR, odds ratio; CI, confidence interval.

Subgroup Analyses

According to the KDIGO criteria, AKI patients were divided into stage 1, stage 2 and stage 3. Patient characteristics by AKI stage are shown in Table S2. The ROC curves of OASIS, APACHE II, SAPS II and SOFA score for predicting of 28-day mortality in each subgroup are shown in Table 7. OASIS had a good predictive effect in each subgroup. Table 7 shows the calibration of the risk scores. OASIS had good calibration in each subgroup, except the stage 3 subgroup. To verify the predictive effect of OASIS on the 28-day mortality among different populations of AKI patients, we divided the AKI patients into elective surgery, nonelective surgery, MV, non-MV, Sepsis, nonsepsis, RRT, non-RRT, over 65 years and up to 65 years groups, as shown in Table S3. OASIS had a good prediction effect in most subgroups.
Table 7
Receiver operating characteristic curves of risk scores for predicting of 28-day mortality of each subgroup according to KDIGO criteria in AKI patients. * Denotes P > 0.05 for Hosmer-Lemeshow test, reflecting good calibration. The risk score column in bold has the highest AUC value for each group.

| Group   | APACHEII | SAPSII | SOFA | OASIS |
|---------|----------|--------|------|-------|
| Stage1  | 0.780*   | 0.803* | 0.657* | 0.767* |
| Stage2  | 0.728*   | 0.707* | 0.619* | 0.765* |
| Stage3  | 0.675*   | 0.709  | 0.649* | 0.730  |

AKI, acute kidney injury; AUC, area under the receiver operating characteristic curve; APACHE II, the Acute Physiology and Chronic Health Evaluation II; SAPS II, the Simplified Acute Physiology Score II; SOFA, the Sequential Organ Failure Assessment; OASIS, the Oxford Acute Severity of Illness Score.

Discussion

In this large, multicentre prospective study, we evaluated the ability of the OASIS, APACHE II, SAPS II and SOFA score to predict the 28-day mortality in AKI patients, and we found that the performance of OASIS was the best, followed by APACHE II and SAPS II, but there were no significant differences among the three scoring systems. The predictive value of the SOFA score was the worst, and the difference was statistically significant compared with the other three scores. OASIS was significantly associated with a higher risk of death in the logistic regression model, whether as a continuous variable or a categorical variable, which further indicated that OASIS had good value in judging the severity of AKI patients. OASIS has been studied in the mixed ICU [19], in the cardiac ICU [20–22], in patients with sepsis [23–27], and in patients admitted to the surgical intensive care unit (SICU) [28], but to date, there has been no study on OASIS in AKI patients.

Deliberato et al performed a secondary analysis of the electronic health records of patients included in the eICU Collaborative Research Database (eICU-CRD), 108,402 patients in 189 different ICUs across the USA were included in the analysis [19]. In this study, underweight patients had higher OASIS scores, the median value was 31 (IQR:25, 38), and OASIS demonstrated good discrimination (AUC = 0.79 (0.78 ~ 0.80)) in predicting in-hospital mortality in all body mass index (BMI) subgroups. Our study showed similar results, the median value was 31(IQR: 21, 39), and the performance of OASIS in predicting in-hospital mortality was good (AUC = 0.783 (0.756 ~ 0.811)).

Recently, Hu et al collected the data of 2,470 sepsis patients recorded in the Medical Information Mart for Intensive Care III (MIMIC-III) database [29] from 2001 to 2012 and retrieved the SOFA, SAPSII, OASIS and Logistic Organ Dysfunction System (LODS) scores [30] of the patients within the first day admission to the ICU and compared the predictive value of the four scoring systems for ICU mortality of the patients [25]. The AUC values of SAPSII and OASIS were 0.768 (0.745 ~ 0.791) and 0.762 (0.738 ~ 0.785), respectively, which were significantly higher than those of the other two scoring systems. In our study, the AUC values of OASIS, APACHE II and SAPS II in predicting the 28-day mortality of AKI patients were 0.771 (0.742 ~ 0.799), 0.764 (0.735 ~ 0.792) and 0.767 (0.739 ~ 0.796), respectively, which were higher than
that of the SOFA score (0.686; P < 0.001) (Fig. 3). Although the subjects of the two studies were different, we both found that OASIS had good predictive value for mortality in ICU patients. In contrast, another study found that SAPS II (AUC = 0.741 (0.703 ~ 0.778)) and SOFA score (AUC = 0.687 (0.645 ~ 0.728)) showed significantly and slightly better discrimination than OASIS (AUC = 0.684 (0.643 ~ 0.725)) [27]. More clinical studies are needed to investigate the validity of OASIS.

In our study, with the increase in OASIS, the mortality rate of patients increased (Fig. 2). In AKI patients, OASIS of the nonsurvivors was higher than that of the survivors (39 vs 28, P < 0.001), which is consistent with the finding of another study (38 vs 33, P < 0.001) [23], indicating that OASIS has a good predictive value for the 28-day mortality. Moreover, it has a good predictive value for both the ICU mortality and the in-hospital mortality, which is similar to the findings of the original study, hospital and ICU mortality increased exponentially as OASIS increased [14]. In contrast to that in the original study, the AUC value of OASIS in our study (AUC = 0.771) was significantly lower than that of the former (AUC = 0.902), but significantly higher than that of Chen et al (AUC = 0.652) [23]. The reasons are as follows: first, the original research was performed in a mixed ICU, and the other study was conducted in septic patients, while our subjects were AKI patients. Second, the original research admitted 72,474 ICU patients in 68 ICUs at 49 U.S hospitals, the other study was conducted using data from a public database and a total of 10,305 septic patients were included. The large sample size of the studies reduced selection bias and made the results more convincing. Third, the above two studies were retrospective cohort studies, while ours was a prospective observational study. Retrospective studies are prone to confusion and bias.

ROC curve analysis showed that the cut-off value of OASIS for predicting 28-day mortality in AKI patients was 33, OASIS had the highest sensitivity (87.75 %) for predicting 28-day mortality, but a lower specificity (46.26%). In another study, the best threshold of OASIS was 34.5, with a specificity of 55.80% and a sensitivity of 64.93% [23]. We divided AKI patients into 3 subgroups according to the KDIGO criteria, OASIS increased with the increase of the AKI classification (Table S2), Table 7 shows that OASIS had a good predictive value in each subgroup. We also divided AKI patients into groups based on their characteristics. Other studies also grouped subjects to determine the predictive value of OASIS, for example, septic patients were grouped according to age [24], cardiac intensive care unit (CICU) populations were grouped by admission diagnosis [20], and ICU patients were grouped by BMI [19]. Subgroup analysis may be more predictive of patient outcomes. In addition, OASIS includes elective surgery, which is not included in other scores. There were 1,459 (49.4%) elective surgery patients in our study, so it may be more meaningful to use OASIS to evaluate their prognosis.

There were some limitations in the present study. First, we did not consider factors such as the aetiology, duration, and whether RRT was used for AKI, which might affect the predictive power of OASIS. Second, although this was a prospective study, OASIS was not included in the study design, resulting in incomplete OASIS data for some patients. Third, all AUC values were less than 0.8, indicating that the four risk scores may be inaccurate for AKI patients, which prompt further prospective studies and the development of new scales in this population. OASIS is not widely used at present, probably because it is simpler than APACHE II and SAPS II, but more complex than the SOFA score. Moreover, the values used
are all the worst ones selected from the daily minimum and maximum values. If the data records of patients are incomplete, the application of OASIS will be limited. At present, most studies on OASIS are retrospective studies [14, 19, 21, 22, 24–28], therefore, large-scale prospective studies are needed to further verify the predictive value of OASIS.

**Conclusion**

Because of the simplicity and effectiveness of OASIS, this study recommends the use of OASIS to evaluate 28-day mortality in patients with AKI admitted to the ICU. OASIS ≥ 33 should be considered an indicator of a negative short-term outcome.

**Abbreviations**

AKI
acute kidney injury
ICU
intensive care unit
OASIS
the Oxford Acute Severity of Illness Score
APACHE II
Acute Physiology and Chronic Health Evaluation II
SAPS II
Simplified Acute Physiology Score II
SOFA
Sequential Organ Failure Assessment
BAKIT
the Beijing Acute Kidney Injury Trial
MV
mechanical ventilation
RRT
renal replacement therapy
KDIGO
Kidney Disease Improving Global Outcomes
COPD
chronic obstructive pulmonary disease
LOS
length of stay
ROC
receiver operating characteristic
AUC
area under curve
IQR
interquartile range
HR
hazard ratio

Declarations

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Acknowledgments

The authors thank all members of the Beijing Acute Kidney Injury Trial (BAKIT) work group (see Additional file 1) for participating in database management.

Funding

The study was supported by a grant from the Beijing Municipal Science & Technology Commission, a government fund used to improve health-care quality (No. D101100050010058). It offered financial support for data collection.

Author information

Affiliations

Emergency department of China rehabilitation research center, Capital Medical University, no.10 Jiaomen north Street, Fengtai District, Beijing 100068, China

Na Wang

Department of Epidemiology and Health Statistics, School of Public Health, Capital Medical University, NO.10 Xitoutiao, Youanmen, Fengtai District, Beijing, China

Mei-Ping Wang

Department of Critical Care Medicine, Xuan Wu Hospital, Capital Medical University, no. 45 Changchun Street, Xicheng District, Beijing 100053, China

Li Jiang

Medical intensive care unit, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, NO.1 Shuaifuyuan, Dongcheng District, Beijing, China
Contributions

NW and MPW contributed equally to the designed and implementation of the study, NW conducted the primary data search, performed the statistical analysis, and drafted the manuscript. LJ and BD were responsible for the conception, study execution, oversight of data management, and manuscript reviewing and editing. BZ was involved in the design and the statistical analysis. The Beijing Acute Kidney Injury Trial (BAKIT) Workgroup participated in acquisition and interpretation of data. XX designed the study and helped to revise manuscript. All authors read and approved the final manuscript.

Corresponding author

Correspondence to Xiuming Xi

Ethics declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained. This project was approved by the institutional review board of the ethics committee of the lead study center (Fu Xing Hospital, Capital Medical University, Beijing China) and all other participating hospitals (see Additional file 2).

Consent for publication

Not applicable.

Conflict of interests

The authors declare that they have no conflict of interest.

References

1. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int. 2020 May;97(5):829–38.
2. Silver SA, Harel Z, McArthur E, Nash DM, Acedillo R, Kitchlu A, et al. Causes of death after a hospitalization with AKI. J Am Soc Nephrol. 2018;29(3):1001 – 1010.
3. Kim J, Kim YJ, Ryoo S, et al. One-year progression and risk factors for the development of chronic kidney disease in septic shock patients with acute kidney injury: a single-centre retrospective cohort
study. J Clin Med. 2018;7:554.
4. Schiffl H, Lang SM, Fischer R. Long-term outcomes of survivors of ICU acute kidney injury requiring renal replacement therapy: a 10-year prospective cohort study. Clin Kidney J. 2012;5:297–302.
5. Salluh JI, Soares M. ICU severity of illness scores: APACHE, SAPS and MPM. Curr Opin Crit Care. 2014;20(5):557–65.
6. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med. 1985;13(10):818–29.
7. 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):2957–63.
8. Legrand M, Dupuis C, Simon C, et al. Association between systemic hemodynamics and septic acute kidney injury in critically ill patients: a retrospective observational study. Crit Care. 2013 Nov;29(6):R278. 17.
9. Medve L, Antek C, Paloczi B, et al. Epidemiology of acute kidney injury in Hungarian intensive care units: a multicenter, prospective, observational study. BMC Nephrol. 2011 Sep;13:12:43.
10. Vincent JL, de Mendonca A, Cantraine F, Moreno R, Takala J, Suter PM, Sprung CL, Colardyn F, Blecher S. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: Results of a multicenter, prospective study. Crit Care Med. 1998;26(11):1793–800.
11. Cui XY, Yu X, Wu XJ, et al. Acute Kidney Injury in Patients with the Coronavirus Disease 2019: A Multicenter Study. Kidney Blood Press Res. 2020;45(4):612–22.
12. Antal O, Ștefănescu E, Mleșnițe M, et al. Hemodynamic Predictors for Sepsis-Induced Acute Kidney Injury: A Preliminary Study. J Clin Med. 2020;9(1):151.
13. Wang H, Kang X, Shi Y. SOFA score is superior to APACHE-II score in predicting the prognosis of critically ill patients with acute kidney injury undergoing continuous renal replacement therapy. Ren Fail. 2020 Nov;42(1):638–45.
14. Johnson AE, Kramer AA, Clifford GD. A new severity of illness scale using a subset of Acute Physiology And Chronic Health Evaluation data elements shows comparable predictive accuracy. Crit Care Med. 2013;41:1711–8.
15. Luo X, Jiang L, Du B, Wen Y, Wang M, Xi X, et al. A comparison of different diagnostic criteria of acute kidney injury in critically ill patients. Crit Care. 2014;18:R144.
16. Piccinni P, Cruz DN, Gramaticopolo S, et al. Prospective multicenter study on epidemiology of acute kidney injury in the ICU: a critical care nephrology Italian collaborative effort (NEFROINT). Minerva Anestesiol. 2011;77(11):1072–83.
17. KDIGO AKI Work. Group.KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl. 2012;17:1–138.
18. Vincent JL, Moreno R, Takala J, 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.
19. Deliberato RO, Neto AS, Komorowski M, et al. An evaluation of the influence of body mass index on severity scoring. Crit Care Med. 2019;47(2):247–53.

20. Jentzer JC, Diepen SV, Murphree DH, et al. Admission diagnosis and mortality risk prediction in a contemporary cardiac intensive care unit population. Am Heart J. 2020;224:57–64.

21. Bennett CE, Wright RS, Jentzer J, et al. Severity of illness assessment with application of the APACHE IV predicted mortality and outcome trends analysis in an academic cardiac intensive care unit. J Crit Care. 2019;50:242–6.

22. Chen F, Li YM, Liu Q, et al. Clinical characteristics and in-hospital outcomes of patients receiving contemporary intensive cardiac care: retrospective study from a large centre in China. J Geriatr Cardiol. 2021;28(2):94–103.

23. Chen Q, Zhang L, Ge S, et al. Prognosis predictive value of the Oxford Acute Severity of Illness Score for sepsis: a retrospective cohort study. Peer J. 2019;10:7:e7083.

24. Jia L, Hao L, Li X, et al. Comparing the predictive values of five scales for 4-year all-cause mortality in critically ill elderly patients with sepsis. Ann Palliat Med. 2021;10(3):2387–97.

25. Hu C, Hu B, Li Z, et al. Comparison of four scoring systems for predicting ICU mortality in patients with sepsis. Nan Fang Yi Ke Da Xue Xue Bao. 2020 30;40(4):513–518.

26. Chen QG, Xie RJ, Chen YZ, et al. Clinical value of Oxford acute severity of illness score in identifying quick sequential organ failure assessment-negative patients with sepsis. Zhonghua Jie He He Hu Xi Za Zhi. 2018;12(9):701–8.

27. Zhang ZH, Hong YC. Development of a novel score for the prediction of hospital mortality in patients with severe sepsis: the use of electronic healthcare records with LASSO regression. Oncotarget. 2017 Jul;25(30):49637–45.

28. Parreco J, Hidalgo A, Kozol R, et al. Predicting Mortality in the Surgical Intensive Care Unit Using Artificial Intelligence and Natural Language Processing of Physician Documentation. Am Surg. 2018 1;84(7):1190–1194.

29. Johnson AE, Pollard TJ, Shen L, et al. MIMIC-III, a freely accessible critical care database. Scientific Data. 2016;3:160035.

30. Le Gall JR, Klar J, Lemeshow S, et al. The logistic organ dysfunction system. A new way to assess organ dysfunction in the intensive care unit. ICU Scoring Group. JAMA. 1996;276:802–10.

**Supplementary Files**

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryMaterial.docx
- TableS1.docx
- tableS2.docx
- TableS3.docx