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Original Article

Red blood cell distribution width improves the prediction of 28-day mortality for patients with sepsis-induced acute kidney injury: A retrospective analysis from MIMIC-IV database using propensity score matching

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ABSTRACT

Background: The predictive value of red blood cell distribution width (RDW) for mortality in patients with sepsis-induced acute kidney injury (SI-AKI) remains unclear. The present study aimed to investigate the potential association between RDW at admission and outcomes in patients with SI-AKI.

Methods: The Medical Information Mart for Intensive Care (MIMIC)-IV (version 2.0) database, released in June of 2022, provides medical data of SI-AKI patients to conduct our related research. Based on propensity score matching (PSM) method, the main risk factors associated with mortality in SI-AKI were evaluated using Cox proportional hazards regression analysis to construct a predictive nomogram. The concordance index (C-index) and decision curve analysis were used to validate the predictive ability and clinical utility of this model. Patients with SI-AKI were classified into the high- and low-RDW groups according to the best cut-off value obtained by calculating the maximum value of the Youden index.

Results: A total of 7574 patients with SI-AKI were identified according to the filter criteria. Compared with the low-RDW group, the high-RDW group had higher 28-day (9.49% *vs.* 31.40%, respectively, P <0.001) and 7-day (3.96% *vs.* 13.93%, respectively, P <0.001) mortality rates. Patients in the high-RDW group were more prone to AKI progression than those in the low-RDW group (20.80% *vs.* 13.60%, respectively, P <0.001). Based on matched patients, we developed a nomogram model that included age, white blood cells, RDW, combined hypertension and presence of a malignant tumor, treatment with vasopressor, dialysis, and invasive ventilation, sequential organ failure assessment, and AKI stages. The C-index for predicting the probability of 28-day survival was 0.799. Decision curve analysis revealed that the model with RDW offered greater net benefit than that without RDW.

Conclusion: The present findings demonstrated the importance of RDW, which improved the predictive ability of the nomogram model for the probability of survival in patients with SI-AKI.

Introduction

Acute kidney injury (AKI) is a common and serious complication in critically ill patients, particularly among those with sepsis.[1] Up to 60% of patients with sepsis may develop AKI, which is associated with a longer hospital stay and a greater financial burden.[2–4] Therefore, sepsis-induced acute kidney injury (SI-AKI) remains a crucial concern in clinical treatment. Early identification of patients with SI-AKI who are at a high risk of mortality can provide clinicians with valuable information and prompt them to administer appropriate therapies.

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The red blood cell distribution width (RDW) is an objective indicator of the heterogeneity of red blood cell (RBC) volume.[5] It is vital for the early diagnosis of iron deficiency anemia.[6] Theoretically, abnormal RDW values synchronize with different types of pathological changes, such as inflammatory responses, which are the commonest.[7,8] Specifically, tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6), and other inflammatory factors prevent the stimulation of RBC maturation by erythropoietin (EPO) and reduce the sensitivity of progenitor cells to this agent.[9,10] As a result, impaired RBC production leads to the early presence of reticulocytes (immature RBCs) in blood circulation, thereby increasing the RDW.[11] Therefore, the abnormal metabolism of EPO produced by the peritubular cells of the kidney alters the RDW.

In recent years, some scholars have focused on RDW owing to its close association with the development and prognosis of multiple diseases.[12–14] A single-center retrospective analysis involving nearly 30,000 patients who underwent primary total joint arthroplasty was conducted by the Rothman Orthopedic Institute (Philadelphia, PA, USA). According to the results, the RDW exhibited better predictive performance than a traditional assessment tool, namely the Charlson comorbidity index.[15] Another community survey confirmed a strong and independent correlation between high RDW values and the risk of death from cancer, cardiovascular diseases, and respiratory diseases.[16] Thus, the RDW may contribute to the identification of high-risk individuals with related disorders.

Early evaluation of the prognosis of SI-AKI is essential to the provision of supportive care.[17] However, thus far, there are no studies that have assessed the usefulness of the RDW in predicting the prognosis of patients with SI-AKI. Hence, in this study, an SI-AKI 28-day mortality prediction model was established to evaluate the predictive performance of RDW and investigate its actual clinical effect.

Methods

Database

Medical Information Mart for Intensive Care (MIMIC) is an open-source research database of critical care medicine based on the PhysioBank Automated Teller Machine protocol.[18] This database was developed by the Massachusetts Institute of Technology (Cambridge, MA, USA), Beth Israel Deaconess Medical Center (Boston, MA, USA), and Philips Healthcare (Andover, MA, USA).[19] MIMIC-IV (version 2.0) was released in June 2022. It includes personal information of patients and medical records for 69,639 intensive care unit (ICU) or emergency admissions between 2008 and 2019. Compared with MIMIC-IV (version 1.0), information on certain elements (e.g., death and ICU details) was enriched in version 2.0.[20,21]

Research ethics and informed consent

Medical records in MIMIC-IV (version 2.0) were collected from the Beth Israel Deaconess Medical Center. Prior to accessing the MIMIC-IV clinical data, we completed the "Data or Specimens Only Research" course of Collaborative Institutional Training Initiative Program. This is a specific training program for research in human subjects (record ID: 43,500,746). The collection and creation of study information were reviewed by the Institutional Review Board, which waived the requirement for informed consent and approved the data-sharing initiative.[20] Moreover, our study did not affect the normal treatment of patients; thus, there were no ethical concerns regarding these data.

Data extraction

Navicat Premium (Version 15.0.12; CyberTech Ltd., Kowloon, Hong Kong, China) was used for data extraction. It is a database development tool that provides Structured Query Language (SQL) service and allows editing, querying, and selecting database objects. Corresponding data were obtained from each time slice assigned by SQL, and the hospital admission ID (expressed as "hadm_id" in the database) was used to match the identified patient.

According to the Sepsis 3.0 criterion,[22] sepsis was diagnosed or infection was suspected in patients with a sequential organ failure assessment (SOFA) score ≥2. The SOFA score of each patient was calculated per hour during the hospital stay. According to the Kidney Disease Improving Global Outcomes (KDIGO) criterion, AKI is a sudden (within 48 h) decrease in renal function, decrease in urine output, or requirement for dialysis.[23] AKI is classified into three stages, and staging is based on the baseline levels of creatinine and urine output rates derived from the MIMIC-IV database. Only patients with AKI following the diagnosis of sepsis were recruited in this study.[24]

The basic information, blood test results at admission, daily urine volume, comorbidity, length of stay in the ICU, medical intervention, first-day SOFA score, AKI stage, and 28-day mortality rate of the identified patients with SI-AKI were extracted. The basic information comprised age, sex, and body mass index. The blood test results at admission covered the RDW, white blood cell (WBC) count, platelet count, lactic acid concentration, and creatinine levels. Comorbidities, including hypertension, diabetes, chronic obstructive pulmonary disease, and malignant tumor, were identified based on the International Classification of Diseases-Ninth/Tenth Revision. Medical interventions, such as the use of vasopressor, dialysis, and invasive ventilation, were noted.

The worst blood test values (i.e., highest WBC count, lowest platelet count, highest creatinine levels, highest lactic acid levels, and highest RDW) within 24 h after admission were collected. The first stage recorded in the course of SI-AKI was utilized as the stage of AKI. Prognostic information was generated by calculating the difference between the date of admission (expressed as "admittime") and that of death (expressed as "dod" and "deathtime"). In case information on death was not available, we considered that the patient did not expire during the observation period. Vasopressors used to treat the patients included dopamine, epinephrine, norepinephrine, phenylephrine, vasopressin, and milrinone.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) diagnosis of SI-AKI; (2) age ≥18 years; and (3) first admission for SI-AKI.

The exclusion criteria were as follows: (1) length of hospital stay ≤24 h; (2) pregnancy; (3) history of chronic kidney disease (CKD); (4) history of drug abuse and acquired immune de-

ficiency syndrome; and (5) incomplete data on observed variables.

Outcomes

The primary outcome was 28-day mortality, while the secondary outcomes included 7-day mortality and AKI stage progression.

Statistical analysis

Normally distributed and skewed continuous variables are presented as the mean ± standard deviation and medians (25th and 75th quartiles), respectively. Categorical variables are shown as frequency (%). Student's *t*-test, Wilcoxon rank-sum test, and chi-squared test were used, as appropriate, to compare the two groups. Receiver operating characteristic (ROC) curve analysis was used to assess the relationship between RDW at admission and 28-day mortality. Patients with SI-AKI were classified into the high- and low-RDW groups according to the best cut-off value obtained by calculating the maximum value of the Youden index. The Kaplan–Meier curve was used to describe the survival status of patients with different RDW. Cox proportional hazards regression analysis was used to identify independent risk factors for mortality. A nomogram was constructed for the prediction of prognosis. The concordance index (C-index) was used to assess the reliability of the model. Decision curve analysis was used to assess the utility of the model for clinical decision-making.

Statistical analyses were performed using R software (version 3.6.3; R Foundation for Statistical Computing, Vienna, Austria). GraphPad Prism (version 8.0.2; GraphPad Software Inc., San Diego, CA, USA) and Office Excel (version 2016; Microsoft Corporation, Redmond, WA, USA) software were used to produce figures and tables. All *P*-values <0.05 denoted statistically significant differences.

Results

Basic clinical characteristics

A total of 7574 adult patients with SI-AKI were selected. Figure 1 shows the flow diagram of the patient selection process.

The median age of patients was 68 years, and 58.95% of those selected were male. The median values of WBC, platelets, lactic acid, creatinine, and RDW were 10.0×10^9/L, 157×10^9/L, 2.3 mmol/L, 1.0 mg/dL, and 14.3%, respectively. Among the selected patients, hypertension was the most common comorbidity (57.62%), followed by diabetes (15.00%), chronic obstructive pulmonary disease (14.58%), and malignancy (14.11%). The median length of stay in the ICU was 4.1 days. Regarding treatment, only 5.95% of the selected patients with SI-AKI underwent dialysis. Approximately 5239 patients (69.17%) underwent invasive ventilation, and 1123 patients (14.83%) required vasopressor therapy. In addition, the median SOFA score was 7. More than half of the patients (54.62%) suffered from stage II AKI in the early phase of sepsis. Furthermore, the 28- and 7-day mortality rates were 20.74% and 7.91%, respectively. AKI progressed in 16.45% of the patients. The basic clinical characteristics of patients with SI-AKI are listed in Table 1.

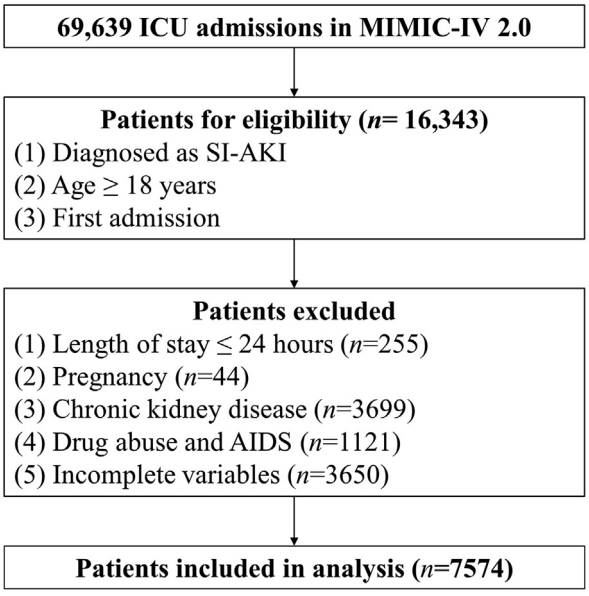

Figure 1. Flow diagram showing the exclusion and inclusion criteria of this study.
AIDS: Acquired immune deficiency syndrome; ICU: Intensive care unit; MIMIC: Medical Information Mart for Intensive Care; SI-AKI: Sepsis-induced acute kidney injury.

Table 1
Basic clinical characteristics of S-AKI patients ($n = 7574$).

Variable	Data
Basic information	
Age (years)	68 (58, 78)
Male	4465 (58.95)
BMI (kg/m^2)	27.5 (24.1, 31.7)
Blood test	
WBC ($\times 10^9$/L)	10.0 (7.0, 13.7)
Plt ($\times 10^9$/L)	157 (109, 220)
Lac (mmol/L)	2.3 (1.6, 3.5)
Cr (mg/dL)	1.0 (0.8, 1.3)
RDW (%)	14.3 (13.3, 15.8)
Urine volume (mL/24 h)	1300 (720, 2000)
Comorbidity	
Hypertension	4364 (57.62)
Diabetes	1136 (15.00)
COPD	1104 (14.58)
Malignancy	1069 (14.11)
Length of stay in ICU (days)	4.1 (2.0, 8.7)
Intervention	
Vasopressor	1123 (14.83)
Dialysis	451 (5.95)
Invasive ventilation	5239 (69.17)
SOFA (points)	7 (4, 10)
AKI stage	
Stage I	2249 (29.70)
Stage II	4137 (54.62)
Stage III	1188 (15.69)
Stage progression	1246 (16.45)
Mortality	
28-day mortality	1571 (20.74)
7-day mortality	599 (7.91)

Data are expressed as median (IQR) and *n* (%).
AKI: Acute kidney injury; BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; Cr: Creatinine; ICU: Intensive care unit; IQR: Inter-quartile range; Lac: Lactic acid; Plt: Platelets; RDW: Red blood cell distribution width; S-AKI: Sepsis-induced acute kidney injury; SOFA: Sequential organ failure assessment; WBC: White blood cell.

Comparison of RDW values between groups

According to the results of the ROC analysis, for the prediction of 28-day mortality, the best cut-off value of RDW was 14.75%; the sensitivity was 93.2%; the Youden index was 0.353; and the area under the ROC curve (AUC) was 0.730 (95% confidence interval [95%CI]: 0.716–0.745). For the prediction of 7-day mortality, the AUC of RDW was 0.713 (95%CI: 0.693–0.733) (Figure 2).

Differences in variables between the high- and low-RDW groups were observed (P <0.05) (Table 2), excluding the WBC count, platelet count, lactic acid levels, diabetes, and invasive ventilation. Compared with the low-RDW group, the high-RDW group had higher 28-day (9.49% *vs.* 31.40%, respectively, P <0.001, Figure 3) and 7-day (3.96% *vs.* 13.93%, respectively, P <0.001) mortality rates. Patients in the high-RDW group were more prone to AKI progression than those in the low-RDW group (20.80% *vs.* 13.60%, respectively, P <0.001).

Propensity score matching (PSM) was used to balance the confounders between the high- and low-RDW groups; the caliper width was set to 0.05. Ultimately, 4816 patients with SI-AKI were matched using a 1:1 ratio and included in the matching cohort; the matching percentage was 63.59%. After matching, the standardized mean difference values of all variables were <0.1 (Table 2 and Figure 4).

Factors associated with 28-day mortality

The univariate and multivariate Cox proportional hazards regression analyses revealed that age, WBC count, RDW, hypertension combined with the presence of malignancy, use of vasopressor, dialysis, invasive ventilation, SOFA score, and stage III AKI were independent predictors of 28-day mortality (Table 3).

In addition, patients in the high-RDW group were more likely to have poor prognosis than those in the low-RDW group (hazard ratio [HR]=2.36; 95%CI: 2.07–2.71, P <0.001). However, the levels of creatinine and urine were not linked to 28-day mortality (HR=0.97, 95%CI: 0.91–1.04, P=0.376 and HR=1.00, 95%CI: 1.00–1.00, P=0.451). Risk factors also included advanced age, high WBC count, high SOFA score, comorbidity of malignant tumor, requirement for interventions (i.e., vasopressor, dialysis, and invasive ventilation), and stage III AKI (all HR >1, P <0.05). In contrast, hypertension was independently associated with better prognosis of SI-AKI (HR = 0.80, 95%CI: 0.70–0.91, P=0.001).

The nomogram model constructed using the above-mentioned variables for the prediction of 28-day and 7-day mortality rates in patients with SI-AKI is shown in Figure 5.

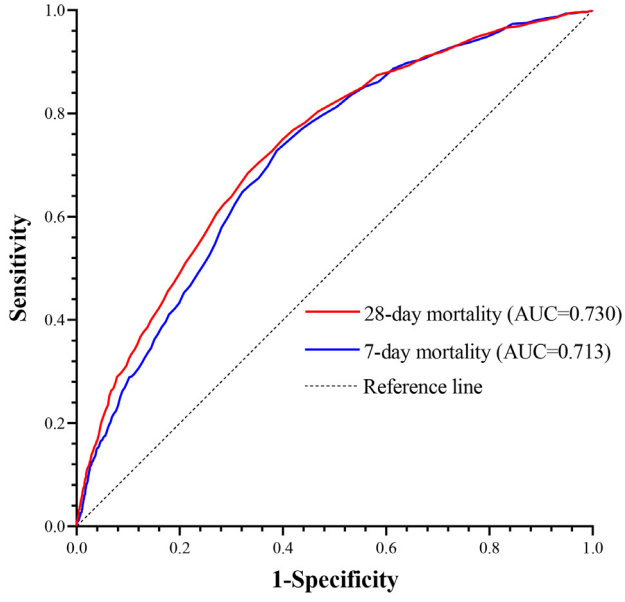

Figure 2. ROC analysis of RDW for the prediction of 28-day mortality.
AUC: Area under the ROC; RDW: Red blood cell distribution width; ROC: Receiver operating curve.

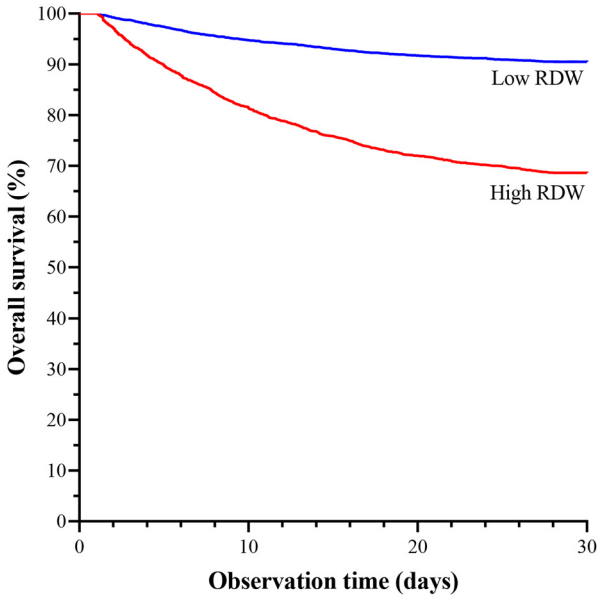

Figure 3. Kaplan–Meier curves for the description of survival between groups with different RDW values (cut-off value: 14.75%) during the follow-up.
RDW: Red blood cell distribution width.

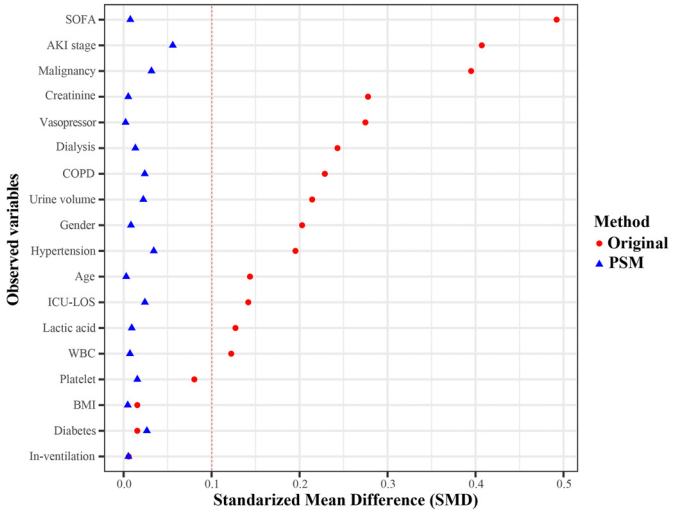

Figure 4. SMD between the original and matched cohorts.
AKI: Acute kidney injury; BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; ICU-LOS: Intensive care unit-length of stay; PSM: Propensity score matching; SMD: Standardized mean difference; SOFA: Sequential organ failure assessment; WBC: White blood cell.

Table 2
Comparison of the variables between the original cohort and matched cohort.

Variable	Original cohort (*n*=7574)				Matched cohort (*n*=5056)			
	Low RDW (*n*=4574)	High RDW (*n*=3000)	*P*-value	SMD	Low RDW (*n*=2408)	High RDW (*n*=2408)	*P*-value	SMD
Basic information								
Age (years)	67 (57, 77)	69 (58, 80)	<0.001	0.144	69 (59, 79)	68 (58, 79)	0.397	0.003
Male	2877 (62.90)	1588 (52.93)	<0.001	0.203	1323 (54.94)	1333 (55.36)	0.794	0.008
BMI (kg/m^2)	27.7 (24.3, 31.6)	27.2 (23.8, 32.0)	0.031	0.016	27.5 (23.9, 31.6)	27.2 (23.8, 32.0)	0.614	0.005
Blood test								
WBC (× 10^9/L)	10.0 (7.2, 13.3)	13.5 (6.7, 14.7)	0.291	0.122	10.2 (7.2, 14.0)	9.9 (6.7, 14.1)	0.802	0.007
Plt (× 10^9/L)	158 (117, 211)	157 (96, 238)	0.065	0.080	163 (116, 223)	158 (100, 233)	0.589	0.016
Lac (mmol/L)	2.3 (1.6, 3.3)	2.2 (1.5, 3.8)	0.749	0.127	2.4 (1.6, 3.6)	2.2 (1.5, 3.7)	0.749	0.009
Cr (mg/dL)	0.9 (0.8, 1.2)	1.1 (0.8, 1.6)	<0.001	0.278	1.0 (0.8, 1.4)	1.1 (0.8, 1.5)	0.136	0.005
Urine volume (mL/24 h)	1400 (830, 2100)	1100 (590, 1800)	<0.001	0.214	1200 (740, 1900)	1200 (680, 1900)	0.176	0.022
Length of stay in ICU (days)	3.6 (1.9, 7.8)	5.0 (2.6, 9.7)	<0.001	0.142	4.4 (2.2, 9.6)	4.8 (2.5, 9.0)	0.073	0.024
Comorbidity								
Hypertension	2810 (61.43)	1588 (52.93)	<0.001	0.195	1351 (56.10)	1310 (54.40)	0.246	0.034
Diabetes	676 (14.78)	460 (15.33)	0.530	0.015	360 (14.95)	383 (15.91)	0.380	0.026
COPD	518 (11.32)	586 (19.53)	<0.001	0.229	434 (18.02)	412 (17.11)	0.426	0.024
Malignancy	391 (8.55)	678 (22.60)	<0.001	0.395	373 (15.49)	401 (16.65)	0.289	0.032
Intervention								
Vasopressor	498 (10.89)	625 (20.83)	<0.001	0.275	401 (16.65)	403 (16.74)	0.969	0.002
Dialysis	164 (3.59)	287 (9.57)	<0.001	0.243	155 (6.44)	163 (6.77)	0.685	0.013
Invasive ventilation	3159 (69.06)	2080 (69.33)	0.824	0.006	1670 (69.35)	1664 (69.10)	0.876	0.005
SOFA	6 (4, 8)	8 (5, 11)	<0.001	0.492	7 (5, 10)	7 (5, 10)	0.493	0.008
AKI stage			<0.001	0.407			0.153	0.056
Stage I	1569 (34.30)	680 (22.67)			597 (24.79)	623 (25.87)		
Stage II	2537 (55.47)	1600 (53.33)			1409 (58.51)	1345 (55.86)		
Stage III	468 (10.23)	720 (24.00)			402 (16.69)	440 (18.27)		
Outcome								
28-day mortality	434 (9.49)	942 (31.40)	<0.001	0.565	318 (13.20)	644 (26.74)	<0.001	0.344
7-day mortality	181 (3.96)	418 (13.93)	<0.001	0.355	133 (5.52)	279 (11.59)	<0.001	0.218
Stage progression	622 (13.60)	624 (20.80)	<0.001	0.192	379 (15.74)	520 (21.59)	<0.001	0.151

Data are expressed as median (IQR) and *n* (%).
AKI: Acute kidney injury; BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; Cr: Creatinine; ICU: Intensive care unit; IQR: Inter-quartile range; Lac: Lactic acid; Plt: Platelets; RDW: Red blood cell distribution width; SMD: Standardized mean difference; SOFA: Sequential organ failure assessment; WBC: White blood cell.

Table 3
Univariate and Multivariate Cox proportional hazards regression analysis for risk factors of 28-day mortality.

Variable	Univariate analysis			Multivariate analysis		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Basic information						
Age (years)	1.01	1.01–1.02	<0.001	1.02	1.02–1.03	<0.001
Male*	1.04	0.91–1.18	0.595			
BMI (kg/m^2)	0.99	0.98–1.00	0.080			
Blood test						
WBC (× 10^9/L)	1.03	1.02–1.03	<0.001	1.02	1.02–1.03	<0.001
Plt (× 10^9/L)	1.00	0.99–1.00	0.439			
Lac (mmol/L)	1.12	1.10–1.14	<0.001	1.01	0.99–1.03	0.383
Cr (mg/dL)	1.19	1.14–1.24	<0.001	0.97	0.91–1.04	0.376
High RDW group†	2.20	1.93–2.52	<0.001	2.36	2.07–2.71	<0.001
Urine volume (mL/24 h)	0.99	0.99–0.99	<0.001	1.00	1.00–1.00	0.451
Length of stay in ICU (days)	0.99	0.99–1.00	0.080			
Comorbidity						
Hypertension	0.82	0.72–0.93	0.002	0.80	0.70–0.91	0.001
Diabetes	0.79	0.66–0.96	0.017	0.87	0.72–1.05	0.148
COPD	1.04	0.88–1.23	0.620			
Malignancy	1.58	1.35–1.83	<0.001	1.87	1.60–2.19	<0.001
Intervention						
Vasopressor	3.33	2.92–3.81	<0.001	1.97	1.68–2.31	<0.001
Dialysis	3.02	2.53–3.60	<0.001	1.24	1.00–1.53	0.048
Invasive ventilation	1.86	1.59–2.18	<0.001	1.26	1.06–1.51	0.009
SOFA (points)	1.15	1.13–1.17	<0.001	1.09	1.07–1.12	<0.001
AKI stage‡						
Stage II	1.06	0.89–1.25	0.532			
Stage III	2.82	2.35–3.37	<0.001	1.98	1.60–2.44	<0.001

AKI: Acute kidney injury; BMI: Body mass index; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease; Cr: Creatinine; HR: Hazard ratio; ICU: Intensive care unit; Lac: Lactic acid; Plt: Platelets; RDW: Red blood cell distribution width; SOFA: Sequential organ failure assessment; WBC: White blood cell.

* Compared with the female.
† Compared with the low RDW group (RDW value ≤14.75).
‡ Compared with the Stage I.

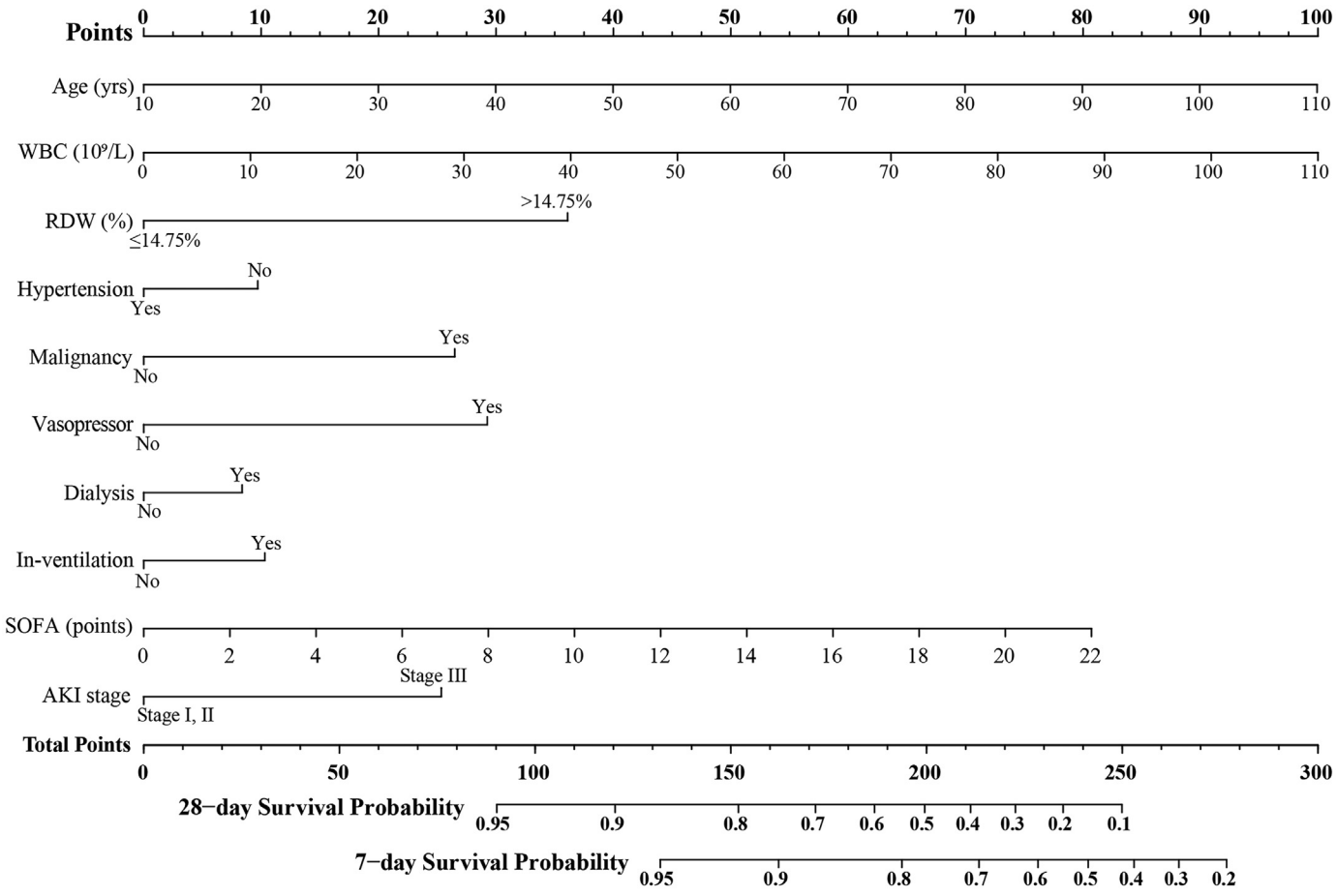

Figure 5. Nomogram model for estimating 28- and 7-day OS.
AKI: Acute kidney injury; OS: Overall survival; RDW: Red blood cell distribution width; SOFA: Sequential organ failure assessment; WBC: White blood cell.

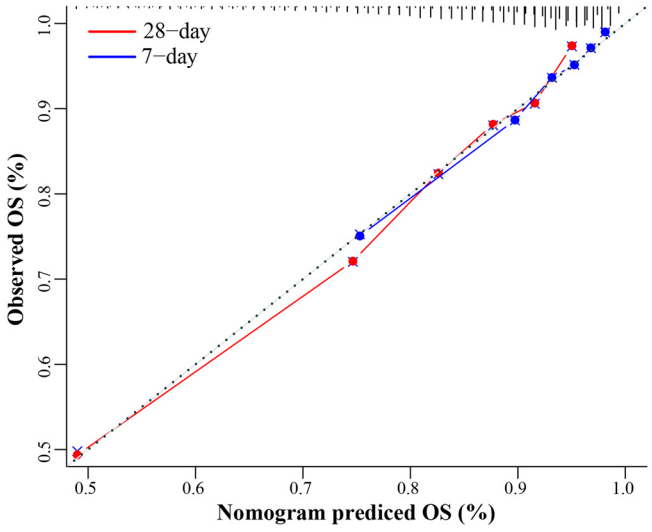

Figure 6. Calibration curves of the predictive model for 28- and 7-day mortality in the matched cohort. OS: Overall survival.

According to the bootstrapping technique (1000 random bootstraps were sampled), which was used to assess the performance of the model, the C-index for 28-day survival was 0.799. As shown in Figure 6, the 28-day and 7-day calibration curves indicated that values predicted by the nomogram model were in agreement with the observed values.

RDW value and overall survival

As a significant prognostic factor of SI-AKI, the RDW was an essential part of the nomogram model. Removal of the RDW from the model reduced the C-index to 0.727 (reduction of 0.072). The clinical decision curve analysis for predicting 28-day mortality demonstrated that the model with RDW resulted in a higher net benefit for most of the predicted survival probabilities than the model without RDW (Figure 7). The full model could accurately predict 28-day mortality, with more merits.

Discussion

In this study, a highly efficient model was constructed for the prediction of 28-day mortality in patients with SI-AKI. Inclusion of the RDW improved the performance of the model. Moreover, the RDW offered clinical benefits regarding short-term prediction. In addition, the PSM method was adopted in this analysis to adjust for other factors that may affect the RDW of patients with SI-AKI. A model constructed based on the matched cohort effectively addressed the endogeneity problems caused by the descriptive variables. Furthermore, a sufficient number of patients with SI-AKI were selected from the MIMIC-IV database.

The RDW is rarely used in clinical practice, besides in the management of anemia. Nevertheless, some previous studies have investigated the role of RDW in the diagnosis and risk

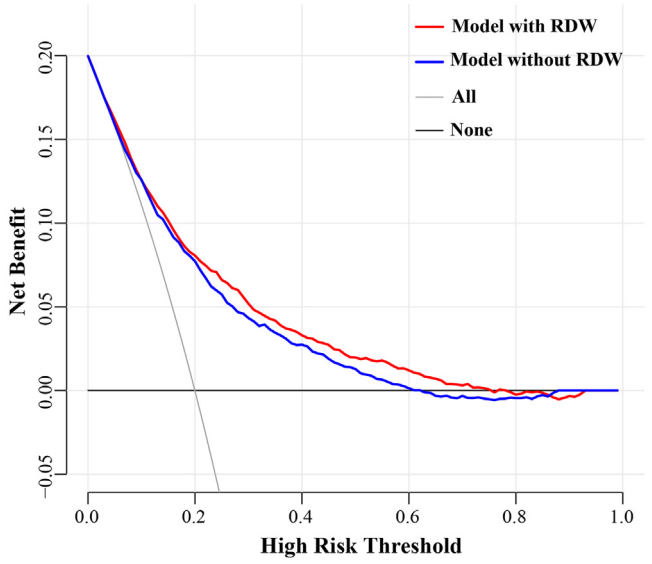

Figure 7. Decision curve analysis for the prediction of 28-day OS by the models with and without RDW. OS: Overall survival; RDW: Red blood cell distribution width.

assessment of diseases.[25–27] High RDW values may indicate changes in the lifespan of RBCs, which typically occur due to the lack of serum EPO and the impairment of renal function.[8,9,28] Conversely, renal function plays a critical role in iron balance in organisms, which is also reflected in the variation of the RDW.[29] The evaluation of disease occurrence and development using RDW may influence clinical decision-making with regard to treatment. Since the conditions of patients in the ICU change continuously,[30] minimizing confusion that arises from other factors may assist in gaining the benefit offered by the RDW. Therefore, numerous new attempts have been made to extract patient data. In this study, patients with SI-AKI were selected according to stricter inclusion criteria. For example, in this study, only patients with AKI following the diagnosis of sepsis were selected.[3]

Sepsis 3.0 criterion is the third international consensus for the definition of sepsis and septic shock.[22] The diagnosis of AKI is based on increased creatinine levels or decreased urine output. Hence, AKI generally occurs after the diagnosis of sepsis in patients with SI-AKI; this is consistent with the extraction method utilized in this study. At present, sepsis is the leading cause of AKI in ICU patients.[31] Nevertheless, sepsis and AKI are independently diagnosed.[32] Currently, there is a lack of specific indicators for the prognosis of SI-AKI.[33,34] However, a corrected model was proposed in the present study for the evaluation of prognosis in patients with SI-AKI. In this model, the addition of RDW may increase the net benefit.

Undoubtedly, patients with sepsis are inclined to develop AKI, as confirmed by clinical practice and pathology. Ramires et al.[26] reported that the RDW was an independent risk factor for AKI in patients with sepsis. SI-AKI and sepsis differ in terms of characteristics and prognoses because the kidney is a target organ with metabolic functions. As revealed by a multicenter prospective cohort study, the incidence rate of AKI and associated mortality rate in 1177 patients with sepsis were 51% and 41%, respectively.[35] The presence of AKI worsens the survival outcomes of patients with sepsis.

Falk and Fahey[36] reported that sepsis suppressed the functions of the hematopoietic system and increased erythrocyte heterogeneity. In particular, AKI caused by sepsis can inevitably give rise to abnormal metabolism of RBCs and related inflammatory responses. The above findings revealed a specific correlation between the RDW and the prognosis of infection and renal injury. In addition, oxidative stress plays an indispensable role in the regulation of hematopoietic cell homeostasis.[37] In particular, RBCs and hematopoietic stem cells are susceptible to the uncontrolled accumulation of reactive oxygen species. An increasing amount of reactive oxygen species results in the destruction of RBCs.[38] Furthermore, a high oxidative stress status induces the release of reticulocytes into the peripheral blood, thereby elevating the RDW.

At the early stage of SI-AKI, common markers (e.g., creatinine levels and urine output) do not reflect patient survival.[39] This may be attributed to the ability of the kidney to compensate for renal function damage. Thus, clinicians should attach importance to the incidence of AKI in patients with sepsis, even if early indicators of renal function are normal.[40] Additionally, the relationship between interventions and SI-AKI prognosis should be emphasized. Interestingly, hypertension was associated with improvement in the prognosis of SI-AKI. It is well established that patients with renal artery or parenchyma damage caused by hypertension are prone to CKD.[41] Hence, it is speculated that patients with CKD were excluded from the research, and the remaining patients with hypertension adopted blood pressure management in their daily life. Following the development of SI-AKI in patients with hypertension, previous self-disciplined measures for the control of hypertension partly prevent the damage caused by AKI. Moreover, high blood pressure may counteract the hypotension caused by sepsis.[42] However, further investigation is warranted to verify these two conjectures.

Limitations

This study has some limitations. First, suspected infection and SOFA scores are core diagnostic factors for sepsis in the Sepsis 3.0 criterion; however, the source of infection is unspecified. However, in recent years, the criterion has been utilized for the diagnosis of sepsis since it is consistent with earlier identification.[43,44] For this reason, this criterion was also adopted in this study. Second, the test method (or test machine) used to determine the RDW at Beth Israel Deaconess Medical Center is unknown. Thus, the results of this study may differ slightly from those of other clinical studies on the RDW. More updated data should be acquired from the MIMIC-IV database. Finally, evaluation of the SI-AKI prognostic model only through internal validation is insufficient. Therefore, external validation tests are being planned and more clinical data will be collected from other medical institutions. This approach may improve the reliability of the model and increase the predictive value of the RDW.

Conclusions

The RDW value is a predictor of the prognosis of patients with SI-AKI. High RDW values at admission are associated with an increased risk of 28-day mortality. The present nomogram

model with the RDW matched the patients with SI-AKI through PSM and verified the importance of RDW.

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Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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