## RESEARCH

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# The predictive value of the serum creatinine-to-albumin ratio (sCAR) and lactate dehydrogenase-to-albumin ratio (LAR) in sepsis-related persistent severe acute kidney injury

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## Abstract

**Background/objectives** Sepsis-related acute kidney injury (SA-AKI) is a severe condition characterized by high mortality rates. The utility of the sCAR (secrum creatinine/albumin) and LAR (Lactate dehydrogenase/albumin) as diagnostic markers for persistent severe SA-AKI remains unclear.

**Methods** We acquired training set data from the MIMIC-IV database and validation set data from the First Affiliated Hospital of Harbin Medical University. Logistic regression analysis was used to identify key predictors of persistent severe SA-AKI, considering factors such as sCAR, LAR, PAR (Platelet/albumin), BAR (BUN/albumin), and LAO (Lactic/ albumin). Independent predictors, sCAR and LAR, were combined into a composite Log(sCAR)\_Log(LAR) score, denoted as the Log(sCAR)\_Log(LAR) score. Possible confounding factors were screened out by univariate logistic regression, and multivariable logistic regression was applied to evaluate the association of Log (sCAR)\_Log (LAR) score with persistent severe sepsis and other secondary clinical outcomes. The ROC curve was utilized to obtain the best cutoff value of the Log(sCAR)\_Log(LAR) score. The Kaplan–Meier curve was used to evaluate the prognosis predictive ability of the risk model.

**Results** Logistic regression analysis indicated that sCAR and LAR independently predicted persistent severe SA-AKI. This led to the creation of Log(sCAR)\_Log(LAR) score on the base of logarithms of sCAR and LAR. ROC curve analysis showed that the Log(sCAR)\_Log(LAR) score was more effective in predicting persistent severe SA-AKI (AUC = 0.71) than Log(sCAR) (AUC = 0.69), Log(LAR) (AUC = 0.65), SOFA score (AUC = 0.66) and  $\Delta$  Scr (AUC = 0.70). Multivariate regression identified that the SOFA score, PT,  $\Delta$ Scr, Tbil, chronic liver disease, and Vasopressor use as independent risk factors for persistent severe SA-AKI (P < 0.05). A basic clinical prediction model was created using these variables, and its predictive ability, recognition capability, and clinical utility improved with the inclusion of the Log(sCAR)\_Log(LAR) score. The model's predictive ability for secondary outcomes, such as renal replacement therapy (RRT), also improved with the addition of the Log(sCAR)\_Log(LAR) score. The sensitivity analysis further corroborated the stability of the Log(sCAR)\_Log(LAR) score in predicting persistent severe SA-AKI and secondary outcomes, such as RRT.

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**Conclusions** The Log(sCAR)\_Log(LAR) score effectively predicted persistent severe SA-AKI, potentially aiding intensive care physicians in risk assessment.

Keywords Sepsis, Acute kidney injury, Albumin, Creatinine, Lactate dehydrogenase

## Introduction

Acute kidney injury (AKI), a sudden decline in kidney function. Sepsis is the leading cause of AKI in critically ill patients, responsible for 40% of cases [1]. The established link between AKI duration and negative outcomes contrasts with the limited research on biomarkers predicting AKI persistence [2]. Recent studies show that about two-thirds of AKI patients regain renal function within 3-7 days, while those with persistent dysfunction have significantly lower survival rates over the following year [3]. The persistence of AKI is associated not only with long-term outcomes but also with clinicians 'decisions about whether and when patients start renal replacement therapy. Recent studies have shown that there is no benefit in starting RRT early in acute cases; therefore, it is also important to predict which AKI patients will recover quickly.

Serum albumin, a negative acute-phase protein, indicates inflammation severity. Studies show its levels are linked to AKI onset and mortality [4]. Lactate dehydrogenase (LDH), an enzyme involved in cellular energy metabolism, independently predicts outcomes in sepsis [5] and AKI [6] patients. A high LAR (lactic dehydrogenase/albumin ratio) at admission correlates with poor prognosis in critically ill AKI patients and adverse outcomes in sepsis-associated AKI (SA-AKI) patients [7].

BUN, which is filtered by the glomeruli and excreted in the urine, is useful for assessing glomerular filtration function. Creatinine, derived from creatine and phosphocreatine metabolism, is found primarily in skeletal muscle and excreted by the kidneys [8, 9]. The BAR (BUN/ albumin) is a prognostic marker for AKI and hospital mortality in ICU patients with intracerebral hemorrhage [10]. Research shows that the sCAR (creatinine/albumin ratio) can independently predict both short-term and long-term all-cause mortality in acute pancreatitis patients [11]. Studies have also shown that a high LAR upon ICU admission is an independent risk factor for short-term (30 days) and long-term (360 days) all-cause mortality in AKI patients [12].

The PAR (Platelets/albumin ratio) is a sophisticated and reliable marker of systemic inflammation and immunonutritional status [13]. PAR offers a comprehensive measure of inflammatory and nutritional states [14]. Recent research indicates that the PAR is a superior marker for evaluating the incidence and outcomes of acute kidney injury (AKI) in patients with cardiogenic shock (CS) [15]. The findings suggest that LAO, LAR, sCAR, BAR, and PAR could indicate kidney damage during sepsis, though their link to ongoing renal dysfunction is unclear. This study evaluates whether plasma levels of these markers within 24 h of ICU admission can predict persistent severe acute kidney injury and the necessity for renal replacement therapy. It also explores the potential use of these markers alongside standard clinical information.

## **Materials and methods**

## Data source

Data was sourced from the MIMIC-IV database (version 2.2) and the First Affiliated Hospital of Harbin Medical University. The MIMIC-IV, an open-access ICU database, contains records of severely ill patients admitted to the ICU at Beth Israel Deaconess Medical Center from 2008 to 2019 [16]. Access was granted to researchers after completing an online course and passing the Protection of Human Research Participants exam (number 62332160). The validation cohort was obtained from the electronic records of the First Affiliated Hospital of Harbin Medical University, with approval from the institution's Ethics Committee (哈医一科研/文章 伦审 2024181). Informed consent was waived due to the retrospective nature of the study.

### Study population and definitions

This study examined adult ICU patients using the MIMIC-IV database, with measurements of lactate, lactate dehydrogenase, serum creatinine, BUN, PLT, and albumin taken within 24 h of admission. Ratios calculated included the sCAR (creatinine/albumin), LAR (Lactic dehydrogenase/albumin), PAR (Platelets/albumin), BAR (BUN/albumin), and LAO (Lactate/albumin) ratios. Logarithmic transformations were applied due to non-normal distribution. Sepsis patients met the Sepsis-3 criteria (Singer et al., 2016). AKI diagnosis followed the KDIGO criteria, indicating a Scr increase over 26.5  $\mu$ mol/L (0.3 mg/dl) within 48 h or a 50% rise from baseline within 7 days [17]. Urine output criteria were excluded due to data unavailability. Exclusion criteria included ICU stays under 48 h, CKD patients, kidney transplant recipients, and patients with known HIV infection. The primary endpoint was persistent AKI, defined as stage 3 AKI during an ICU stays over 72 h, including those who died or received RRT before 72 h [18]. Secondary

outcomes included in-hospital mortality, ICU mortality, and RRT incidence.

### Data extraction and preprocessing

Data from the MIMIC-IV database and the First Affiliated Hospital of Harbin Medical University's electronic health records included patient characteristics, physiological metrics, clinical history, lab results, assessment Log(sCAR)\_Log(LAR) scores, and treatment outcomes. Comorbidities in the MIMIC-IV database were classified using ICD-9 and ICD-10 codes. Laboratory tests such as lactate, lactate dehydrogenase, serum creatinine, BUN, PLT, and albumin were performed within the first 24 h of ICU admission, with only initial results considered. We supplemented all missing data in the training and validation sets using the method of Multivariate Imputation by Chained Equations. The variables supplemented in the training set and their missing rates were  $\Delta$ Scr(9.88%), MAP(43.82%), Heart rate(0.13%), SBP(0.20%), DBP(0.20%), RR(0.13%), bicarbonate(0.13%), calcium(0.87%), FIB(48.86%), INR(3.16%), PT(3.09%), APTT(4.17%), HB(0.07%), RBC(0.07%), ALT(1.14%), ALP(0.81%), AST(0.87%), TBIL(1.01%), NEUT(68.75%), NEUT%(32.53%), lymphocyte(68.75%), Mg(0.27%), race(23.12%), and infection(7.47%). The variables supplemented in the validation set and their missing rates were heart rate (0.37%), SBP (5.22%), DBP (5.22%), RR (5.22%), MAP (2.61%), APACHEII (50.75%), ΔScr (16.05%), NEUT (2.24%), NEUT% (2.61%), lymphocyte (2.24%), FIB (0.75%), INR (0.75%), PT (0.37%), APTT (1.87%), DBIL (0.37%), HCO3-(0.75%), and AG(1.49%)

## Statistical methods

Continuous data are presented as mean  $\pm$  SD or median with quartiles, while categorical data are presented as frequencies (percentages). Student's *t* test and Mann–Whitney *U* test were used to compare normally and non-normally distributed continuous data, respectively. Chi-square tests were used to assess differences in categorical data frequencies, with P < 0.05 indicating statistical significance.

First, we performed univariate and multivariate logistic regression to assess the diagnostic value of LAO, LAR, PAR, SAR, LAR, Log (LAO), Log (LAR), Log (PAR), Log (SAR), Log (LAR) for persistent severe SA-AKI. The results of multivariate logistic regression analysis showed that Log (SAR) and Log (LAR) were independent risk factors for persistent severe SA-AKI, and we obtained Log (SAR) \_ Log (LAR) score from the results of multivariate logistic regression [Log (SAR) \_ Log (LAR) score = 1.19 Xlog (SAR) +0.41 Xlog (LAR)]. We also performed ROC curve analysis for Log (SAR) \_ Log (LAR) score, Log (SAR), Log (LAR), SOFA score,  $\Delta$ Scr. To assess the diagnostic ability of Log(SAR)\_Log(LAR) score, we used DeLong test to compare the area under the curve (AUC) of Log(SAR)\_Log(LAR) score  $\land \Delta$ Scr  $\land Sofa_$  score  $\land SAR$  and LAR. We also tested the optimal threshold, Joden index, sensitivity, and specificity of the Log (SAR) \_ Log (LAR) score. And got from it Log (SAR) \_ Log (LAR) score's sensitivity, specification, cutoff point, and Youden's index.

Then, the variables with P < 0.05 were screened out through univariate logistic regression, and then the selected variables were included in multivariate logistic regression after collinearity analysis. Finally, influencing factors independently related to persistent severe SA-AKI were identified. We used these independently related influencing factors to form a basic clinical prediction model. The ROC curve, net reclassification index (NRI), comprehensive discriminant improvement index (IDI), and decision curve analysis (DCA) were used to determine whether the addition of the Log (SAR) \_ Log (LAR) score can improve the predictive power and clinical utility of the underlying prediction model. We also used the same method to screen out independent risk factors for predicting RRT and tested whether the addition of the Log (SAR) Log (LAR) score can improve the ability of the basic prediction model to predict RRT.

Next, we perform a sensitivity analysis of the log (SAR) \_ Log (LAR) score. We first performed univariate and multivariate logistic regression or Cox regression to determine whether the Log (SAR) \_ Log (LAR) score can predict persistent severe SA-AKI and other secondary clinical outcomes. In this process, we adjusted for the potential confounding factors. The confounding variables with P value < 0.05 in univariate logistic regression analysis and removing the variables related to Log (SAR) \_ Log (LAR) score are the confounding factors we adjusted. Through visual subgroup analysis of the forest graph, we also calculated the P interaction value of each subgroup in this process and analyzed the interactive factors in the hierarchy again. We also used the Kaplan-Meier method to compare survival between the high Log (SAR) \_ Log (LAR) score group and the low Log (SAR) \_ Log (LAR) score group. All statistical analyses were performed using R version 4.2. 3, and Python version 3.11. 4.

## Results

## **Baseline table**

This study examined 1488 sepsis-related acute kidney injury (SA-AKI) patients from the MIMIC-IV database and 268 from the First Affiliated Hospital of Harbin Medical University. In the training set, 391 (26.3%) patients developed persistent severe SA-AKI, while 100 (37.3%) did in the validation set developed persistent severe SA-AKI (Fig. 1). In the training set,



Fig. 1 Study flow chart. ICU, intensive care unit; LDH, lactate dehydrogenase; plt, platelet; bun, blood–urea–nitrogen; alb, albumin; crea, creatintine; CKD, chronic kidney disease; KRT, kidney replacement therapy; SA-AKI, sepsis-associated acute kidney injury

Patients with persistent severe SA-AKI were generally younger than those with non-persistent severe SA-AKI. Hypertension, diabetes, and cancer were more frequent in non-persistent severe SA-AKI patients, whereas chronic liver disease was more common in persistent cases. Patients with persistent severe SA-AKI were more likely to need mechanical ventilation and vasopressors, had higher heart and respiratory rates, lower mean arterial pressure (MAP), and elevated Sequential Organ Failure Assessment (SOFA) scores compared to non-persistent cases. These patients also had higher dialysis treatment rates, in-hospital and ICU mortality rates, with extended hospital and ICU stays. Laboratory results showed lower levels of chloride, sodium, bicarbonate, calcium, fibrinogen, red blood cells, platelets, and albumin , higher levels of INR, PT, aPTT,  $\Delta$ Scr, potassium, ALT, AST, total bilirubin, magnesium, BUN, creatinine, the anion gap, lactate, and lactate dehydrogenase (all p<0.05) (Table 1). In the validation cohort, persistent severe SA-AKI patients had higher chronic liver disease rates, higher rates of dialysis treatment, in-hospital and ICU mortality, and longer hospital and ICU stays. Laboratory tests revealed lower lactate, red blood cells, and hemoglobin, but higher LDH, blood urea nitrogen, blood creatinine,  $\Delta$ Scr, potassium, and INR levels (all p<0.05) (Table 2).

## Table 1 Baseline table of the training cohort

Variables	Category	All ( <i>n</i> = 1488)	pSA_AKI 0 ( <i>n</i> = 1097)	pSA_AKI 1 ( <i>n</i> =391)	р	
Gender, n(%)	Female	605(40.66)	445(40.57)	160(40.92)	0.902	
	Male	883(59.34)	652(59.43)	231(59.08)		
Hypertension, n(%)	No	694(46.64)	488(44.48)	206(52.69)	0.005	
	Yes	794(53.36)	609(55.52)	185(47.31)		
Coronary_heart_disease, n(%)	No	1141(76.68)	833(75.93)	308(78.77)	0.255	
	Yes	347(23.32)	264(24.07)	83(21.23)		
Chronic_heart_failure, n(%)	No	1054(70.83)	770(70.19)	284(72.63)	0.362	
	Yes	434(29.17)	327(29.81)	107(27.37)		
Chronic_liver_disease, n(%)	No	922(61.96)	738(67.27)	184(47.06)	< 0.001	
	Yes	566(38.04)	359(32.73)	207(52.94)		
Diabetes, n(%)	No	1101(73.99)	796(72.56)	305(78.01)	0.035	
	Yes	387(26.01)	301(27.44)	86(21.99)		
Chronic pulmonary disease n(%)	No	1140(76.61)	835(76.12)	305(78.01)	0.449	
	Yes	348(23 39)	262(23.88)	86(21.99)		
Cerebrovascular disease $n(\%)$	No	1304(87.63)	956(87.15)	348(89.00)	0 338	
	Yes	184(12 37)	141(12.85)	43(11.00)	0.550	
Malignant cancer $n(%)$	No	127(82.46)	801(81.22)	336(85.93)	0.035	
Malighant_cancel, n(x)	Voc	261(1754)	206(18.78)	55(14.07)	0.055	
Vacaprossor usa p(%)	No	1200(90.65)	200(10.70)	270/71 26)	< 0.001	
vasopressor_use, //(%)	No	1200(80.03)	921(03.90) 176(16.04)	2/9(/1.30)	< 0.001	
Machanical ventilation n(04)	No	200(19.33)	170(10.04)	12(20.04)	0.022	
Mechanical_ventilation, n(%)	NO	577(38.78)	443(40.38)	134(34.27)	0.033	
	Yes	911(61.22)	654(59.62)	257(65.73)	.0.001	
Deatn_in_icu, <i>n</i> (%)	NO Xa a	1110(74.60)	892(81.31)	218(55.75)	< 0.001	
	Yes	378(25.40)	205(18.69)	1/3(44.25)		
Death_in_hospital, n(%)	No	984(66.13)	/99(/2.84)	185(47.31)	< 0.001	
	Yes	504(33.87)	298(27.16)	206(52.69)		
RR1, n(%)	No	1132(/6.08)	1020(92.98)	112(28.64)	< 0.001	
	Yes	356(23.92)	77(7.02)	279(71.36)		
Infection_Sites, n(%)	Abdominal_infection	137(9.21)	92(8.39)	45(11.51)	0.227	
	Other	950(63.84)	714(65.09)	236(60.36)		
	Pneumonia	218(14.65)	158(14.40)	60(15.35)		
	Urinary_tract_infection	183(12.30)	133(12.12)	50(12.79)		
Race, n(%)	Asian	54(3.63)	37(3.37)	17(4.35)	0.891	
	Black	115(7.73)	86(7.84)	29(7.42)		
	Hispanic	48(3.23)	37(3.37)	11(2.81)		
	Other	63(4.23)	46(4.19)	17(4.35)		
	White	1208(81.18)	891(81.22)	317(81.07)		
Age, median[IQR], (years)		62.82[51.68,73.17]	63.88[52.83,74.83]	59.67[48.17,69.35]	< 0.001	
SOFA score, median[IQR]		4.00[3.00,6.00]	4.00[2.00,6.00]	6.00[3.00,8.00]	< 0.001	
Length_of_hospital_stay, median[IQR], (d)		16.03[8.62,27.22]	14.95[8.20,24.52]	19.77[9.96,32.13]	< 0.001	
Length_of_ICU_stay, median[IQR], (d)		6.84[3.71,12.52]	5.93[3.23,10.95]	10.06[5.27,15.98]	< 0.001	
Creatinine, median[IQR], (mg/dL)		1.20[0.90,1.90]	1.10[0.80,1.60]	1.80[1.10,3.00]	< 0.001	
BUN, median[IQR], (mg/dL)		25.00[17.00,40.00]	24.00[16.00,37.00]	30.00[19.00,52.00]	< 0.001	
Albumin, median[IQR], (g/dl)		2.90[2.40,3.40]	2.90[2.40,3.40]	2.80[2.40,3.30]	0.012	
Aniongap, median[IQR], (mmol/L), (mEq/L)		16.00[13.00,20.00]	15.00[13.00,19.00]	18.00[15.00,22.00]	< 0.001	
Chloride,median[IQR],(mEq/L)		103.00[99.00,108.00]	104.00[99.00,108.00]	102.00[97.00,107.00]	< 0.001	
Sodium,median[IQR],(mEq/L)		138.00[134.00,142.00]	139.00[135.00,142.00]	138.00[133.00,141.00]	0.011	
Potassium, median [IQR], (mEq/L)		4.20[3.70,4.80]	4.20[3.70,4.70]	4.30[3.80,4.90]	0.034	
Platelets,median[IQR],(k/uL)		166.00[102.00,252.00]	182.00[109.00,262.00]	133.00[82.00,215.00]	< 0.001	

## Table 1 (continued)

Variables	Category	All (n = 1488)	pSA_AKI 0 ( <i>n</i> = 1097)	pSA_AKI 1 ( <i>n</i> =391)	р
WBC,median[IQR],(k/uL)		12.80[8.50,19.00]	12.70[8.40,19.20]	13.20[8.70,18.60]	0.440
Lactate,median[IQR],(mmol/L)		2.20[1.40,3.70]	2.10[1.40,3.50]	2.50[1.70,4.60]	< 0.001
Lactic_dehydrogenase,median[IQR],(mm ol/L)		364.00[246.00,653.00]	335.00[236.00,546.00]	517.00[303.00,1052.00]	< 0.001
PT,median[IQR],(s)		15.80[13.40,21.60]	15.40[13.20,19.80]	18.50[14.30,25.90]	< 0.001
INR,median[IQR]		1.40[1.20,2.00]	1.40[1.20,1.80]	1.70[1.30,2.40]	< 0.001
∆Scr,median[IQR],(mg/dL)		0.30[0.20,0.60]	0.30[0.20,0.50]	0.60[0.30,1.00]	< 0.001
MAP,median[IQR],(mmHg)		75.00[61.00,89.00]	76.00[61.00,89.00]	73.00[60.00,89.00]	0.355
Heart_rate,median[IQR],(beats/min)		97.00[81.00,112.00]	96.00[81.00,111.00]	98.00[83.00,115.00]	0.019
SBP,median[IQR],(mmHg)		118.00[101.00,134.00]	118.00[100.00,136.00]	116.00[102.00,133.00]	0.440
DBP,median[IQR],(mmHg)		65.00[55.00,79.00]	65.00[55.00,78.00]	67.00[55.00,79.00]	0.615
RR,median[IQR],(times/min)		21.00[17.00,26.00]	20.00[17.00,25.00]	22.00[18.00,27.00]	0.008
Bicarbonate,median[IQR],(mEq/L)		21.00[18.00,24.00]	22.00[18.00,25.00]	20.00[16.00,23.00]	< 0.001
Calciuml,median[IQR],(mEq/L)		8.10[7.40,8.70]	8.10[7.50,8.60]	7.90[7.20,8.70]	0.016
FIB,median[IQR],(mg/dL)		256.00[159.00,421.00]	268.00[171.00,440.00]	219.00[142.00,380.00]	0.001
APTT,median[IQR],(s)		34.90[28.80,48.20]	33.40[28.30,45.90]	38.70[31.10,53.60]	< 0.001
Hemoglobin,median[IQR],(g/uL)		10.40[8.60,12.20]	10.40[8.70,12.20]	10.30[8.20,12.00]	0.077
RBC,median[IQR],(k/uL)		3.42[2.81,4.05]	3.46[2.89,4.06]	3.31[2.63,4.01]	0.012
Alt,median[IQR],(U/L)		42.00[21.00,119.00]	36.00[19.00,96.00]	62.00[28.00,239.00]	< 0.001
Alp,median[IQR],(U/L)		88.00[58.00,140.00]	87.00[58.00,139.00]	90.00[60.00,142.00]	0.231
Ast,median[IQR],(U/L)		70.00[35.00,214.00]	58.00[31.00,159.00]	123.00[54.00,482.00]	< 0.001
Tbil,median[IQR],(mg/dl)		1.00[0.50,2.90]	0.90[0.50,2.20]	1.80[0.70,6.20]	< 0.001
NEUT,median[IQR],(k/uL)		10.94[7.11,16.69]	10.94[7.10,16.80]	10.88[7.57,16.18]	0.689
NEUT%,median[IQR],%		83.00[73.70,88.30]	83.00[73.70,88.30]	82.00[73.70,88.10]	0.562
Lymphocyte,median[IQR],(k/uL)		0.89[0.49,1.58]	0.93[0.52,1.60]	0.84[0.44,1.57]	0.114
Mg,median[IQR],(mEq/L)		2.00[1.70,2.30]	2.00[1.70,2.30]	2.00[1.80,2.30]	0.005

Red pS pSA\_AKI persistent Sev pSA\_AKI persistent severe sepsis-associated acute kidney injury, SOFA score sequential organ failure assessment, RRT renal replacement therapy, RR respiratory rate, MAP mean arterial pressure, APTT activated partial thromboplastin time, PT prothrombin time, BUN blood urea nitrogen, WBC white blood cell count, RBC red blood cell count,  $\Delta Scr$  changes in serum creatinine within 24 h after ICU admission, Ast aspartate transaminase, Alt alanine transaminase, Alp alkaline phosphatase, ICU intensive care unit, TBIL total bilirubin, Mg magnesium, NEUT neutrophil count, NEUT% neutrophil percentage, INR international normalized ratio, SBP systolic blood pressure, DBP diastolic blood pressure, FIB fibrinogen

## Log(sCAR) and Log(LAR) are independent risk factors for persistent severe SA-AKI

In the training set, the selected five factors PAR, LAO, sCAR, LAR, BAR and their logarithmic forms were subjected to univariate and multivariate logistic regression analyses to determine which were independent predictors of persistent severe SA-AKI. As shown in Table 3, we first performed a univariate logistic regression analysis. The results showed that the P values of PAR, LAO, SAR, LAR, BAR, Log (SAR), Log (BAR), Log (LAR), Log (PAR), Log (LAO) were all less than 0.05. We then included these variables in the multivariate logistic regression analysis and found that Log (SAR) and Log (LAR) were independent prognostic predictors of persistent severe SA-AKI. Finally, the Log (sCAR) \_ Log (LAR) score was established based on multivariate logistic regression analysis.

## **ROC curve analysis**

In the training set, to more accurately assess the predictive value of these variables for persistent severe SA-AKI more accurately, ROC curve analysis was performed for the Log(sCAR), Log(LAR), Log(sCAR)\_ Log(LAR) score, SOFA score, and  $\Delta$ Scr. The area under the curve (AUC) for five variables is depicted in (Fig. 2a). The Log(sCAR)\_Log(LAR) score exhibited the highest AUC at 0.71 (95% CI 0.68–0.74), with  $\Delta$ Scr following at 0.70 (95% CI 0.67-0.74). Log(sCAR) showed an AUC of 0.69 (95% CI 0.65-0.72), while SOFA score and log(LAR) had AUCs of 0.66 (95% CI 0.63-0.70) and 0.65 (95% CI 0.62-0.68), respectively. To evaluate the ability of the Log(sCAR)\_Log(LAR) score's predictive capability for persistent severe SA-AKI more precisely, we have determined its sensitivity, specificity, cutoff point, and Youden's index. At the optimal threshold of

## Table 2 Baseline table of the validation set

Variables	Category	All (n=268)	pSA_AKI 0 ( <i>n</i> = 168)	pSA_AKI 1 ( <i>n</i> = 100)	р
Infection_Sites,n(%)	Abdominal_infection	70(26.12)	42(25.00)	28(28.00)	0.140
	Other	16(5.97)	12(7.14)	4(4.00)	
	Pneumonia	163(60.82)	98(58.33)	65(65.00)	
	Urinary_tract_infection	19(7.09)	16(9.52)	3(3.00)	
Gender,n(%)	No	108(40.30)	69(41.07)	39(39.00)	0.738
	Yes	160(59.70)	99(58.93)	61(61.00)	
Hypertension,n(%)	No	162(60.45)	100(59.52)	62(62.00)	0.688
	Yes	106(39.55)	68(40.48)	38(38.00)	
Coronary_heart_disease,n(%)	No	230(85.82)	142(84.52)	88(88.00)	0.430
,	Yes	38(14.18)	26(15.48)	12(12.00)	
Chronic heart failure,n(%)	No	248(92.54)	155(92.26)	93(93.00)	0.824
/ / /	Yes	20(7.46)	13(7.74)	7(7.00)	
Diabetes.n(%)	No	198(73.88)	127(75.60)	71(71.00)	0.408
	Yes	70(2612)	41(24 40)	29(29,00)	
Cerebrovascular disease $n(\%)$	No	205(76 49)	130(77 38)	75(75,00)	0.657
	Yes	63(23 51)	38(22.62)	25(25.00)	0.007
Chronic nulmonary disease n(%)	No	249(92.91)	155(92.26)	94(94,00)	0 592
enionic_painonaly_alsease, (///	Voc	19(7.09)	13(774)	6(6,00)	0.552
Malignant cancer n(%)	No	246(01 70)	15(7.7-7)	91(91,00)	0.716
Manghant_cancel,n(70)	Voc	270(21.72)	13(774)	9(9,00)	0.710
Chronic liver disease n(%)	No	22(0.21)	145(86 31)	76(76.00)	0.032
Chronic_liver_disease,n(%)	No	ZZT(82.40)	22(12.60)	70(70.00)	0.032
Depth in bospital $p(0())$	No	47(17.54)	23(13.09) 142(05.12)	24(24.00)	< 0.001
Death_in_nospital,n(%)	NO	202(75.57)	145(65.12)	39(39.00)	< 0.001
Depth in $ C  + r(0/)$	ies	00(24.05)	23(14.00)	41(41.00)	< 0.001
Death_In_ICO,n(%)	NO	203(75.75)	143(85.12)	60(60.00)	< 0.001
	Yes	65(24.25)	25(14.88)	40(40.00)	.0.001
RR1, <i>n</i> (%)	No	181(67.54)	144(85.71)	37(37.00)	< 0.001
	Yes	87(32.46)	24(14.29)	63(63.00)	
Mechanical_ventilation, <i>n</i> (%)	No	3/(13.81)	22(13.10)	15(15.00)	0.662
	Yes	231(86.19)	146(86.90)	85(85.00)	
Vasopressor,n(%)	No	66(24.63)	38(22.62)	28(28.00)	0.323
	Yes	202(75.37)	130(77.38)	72(72.00)	
qSOFA score, <i>n</i> (%)	2	149(55.60)	87(51.79)	62(62.00)	0.104
	3	119(44.40)	81(48.21)	38(38.00)	
Lactate,median[IQR],(mmol/L)		3.20[1.80,5.20]	3.40[2.10,5.80]	2.60[1.50,4.30]	0.014
Age,median[IQR],(years)		67.00[55.00,76.00]	66.00[56.00,74.00]	67.00[53.00,77.00]	0.934
Length_of_hospital_stay,median[IQR],(d)		10.00[5.00,17.00]	9.00[5.00,15.00]	13.00[7.00,21.00]	0.001
Length_of_icu_stay,median[IQR],(d)		7.00[4.00,13.00]	6.00[3.00,11.00]	10.00[5.00,18.00]	< 0.001
WBC,median[IQR],(k/uL)		13.44[7.98,18.13]	13.61[8.25,18.06]	12.40[7.38,18.59]	0.722
RBC,mean(±SD),(k/uL)		$3.80 \pm 0.92$	$3.89 \pm 0.90$	$3.65 \pm 0.94$	0.043
Hemoglobin,mean(±SD),(g/uL)		115.44±26.85	$117.99 \pm 26.20$	111.16±27.38	0.044
Platelets,median[IQR],(k/uL)		156.00[90.00,223.00]	155.00[83.00,222.00]	165.00[93.00,223.00]	0.763
Alt,median[IQR],(U/L)		28.20[17.50,57.00]	26.40[17.00,48.80]	33.60[20.30,79.00]	0.073
Ast,median[IQR],(U/L)		41.00[23.50,83.00]	38.70[23.10,68.30]	48.10[25.90,121.10]	0.072
Alp,median[IQR],(U/L)		84.80[61.20,122.10]	84.00[62.40,122.10]	86.60[61.00,120.40]	0.955
TBIL,median[IQR],(mg/dl)		15.35[9.60,24.14]	14.40[9.52,24.11]	16.80[10.30,24.71]	0.403
Albumin,median[IQR],(g/dl)		29.70[26.20,33.60]	30.10[26.30,33.50]	29.50[25.60,33.80]	0.321
BUN,median[IQR],(mg/dl)		35.06[22.96,54.30]	31.42[20.92,44.61]	43.27[28.76,72.20]	< 0.001
Creatinine,median[IQR],(mg/dl)		121.20[80.40,223.90]	102.20[79.30,165.40]	192.40[91.20,387.80]	< 0.001

## Table 2 (continued)

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Variables	Category	All (n=268)	pSA_AKI 0 ( <i>n</i> = 168)	pSA_AKI 1 ( <i>n</i> = 100)	р
Potassium,median[IQR],(mEq/L)		4.11[3.70,4.58]	4.01[3.54,4.42]	4.28[3.89,4.78]	< 0.001
Sodium,median[IQR],(mEq/L)		138.90[134.90,143.40]	139.60[135.80,143.50]	137.90[132.90,141.80]	0.073
Chloride,median[IQR],(mEq/L)		103.10[98.60,107.20]	103.50[99.25,107.20]	101.90[97.70,106.70]	0.272
Calciuml,median[IQR],(mEq/L)		2.02[1.92,2.17]	2.03[1.92,2.17]	2.01[1.90,2.14]	0.259
Mg,median[IQR],(mEq/L)		0.83[0.73,0.95]	0.83[0.73,0.93]	0.84[0.75,1.00]	0.249
Lactic_dehydrogenase,median[IQR],(mmol/	L)	362.80[263.00,502.00]	340.00[259.00,454.00]	404.00[292.00,576.00]	0.012
NEUT,median[IQR],(k/uL)		11.21[6.69,16.43]	11.87[6.94,16.46]	9.88[6.46,15.99]	0.478
NEUT%,median[IQR],%		87.40[82.00,92.30]	87.50[81.50,92.20]	87.30[83.00,92.50]	0.344
Lymphocyte,median[IQR],(k/uL)		0.73[0.45,1.20]	0.78[0.48,1.29]	0.71[0.40,1.18]	0.159
INR,median[IQR]		1.23[1.13,1.40]	1.20[1.12,1.39]	1.29[1.16,1.45]	0.022
$\Delta$ Scr,median[IQR],(mg/dL)		22.30[8.10,52.50]	19.50[7.50,39.00]	32.50[12.20,75.80]	< 0.001
MAP,median[IQR],(mmHg)		68.67[57.00,87.33]	68.67[56.67,83.67]	70.00[58.00,90.33]	0.786
Heart_rate,median[IQR],(beats/min)		116.00[95.00,130.00]	118.00[96.00,131.00]	114.00[92.00,125.00]	0.119
SBP,median[IQR],(mmHg)		98.00[79.00,121.00]	97.00[78.00,119.00]	100.00[82.00,130.00]	0.317
DBP,median[IQR],(mmHg)		55.00[45.00,66.00]	56.00[45.00,67.00]	55.00[45.00,66.00]	0.924
RR,median[IQR],(times/min)		28.00[23.00,32.00]	28.00[23.00,34.00]	27.00[22.00,32.00]	0.075
Bicarbonate,median[IQR],(mEq/L)		20.39[16.81,23.13]	20.49[17.34,23.63]	19.74[16.24,22.00]	0.051
FIB,median[IQR],(mg/dL)		4.73[3.21,6.43]	4.43[3.19,6.00]	5.09[3.30,6.56]	0.102
APTT,median[IQR],(s)		30.80[26.80,36.30]	30.60[26.40,36.00]	31.70[28.20,37.40]	0.133
PT,median[IQR],(s)		13.80[12.60,15.60]	13.50[12.50,15.50]	14.30[13.00,16.00]	0.050
Aniongap,median[IQR],(s)		15.40[11.81,19.55]	14.94[11.48,18.84]	15.86[12.90,20.23]	0.051

pS pSA\_AKI persistent severe sepsis-associated acute kidney injury, SOFA score sequential organ failure assessment, RRT renal replacement therapy, RR respiratory rate, MAP mean arterial pressure, APTT activated partial thromboplastin time, PT prothrombin time, BUN blood urea nitrogen, WBC white blood cell count, RBC red blood cell count, *ΔScr* changes in serum creatinine within 24 h after ICU admission, Ast aspartate transaminase, Alt alanine transaminase, Alp alkaline phosphatase, ICU intensive care unit, TBIL total bilirubin, Mg magnesium, NEUT neutrophil count, NEUT% neutrophil percentage, INR international normalized ratio, SBP systolic blood pressure, DBP diastolic blood pressure, FIB fibrinogen

## Table 3 Training set: logistic regression analysis

Variables	Univaria	Univariate				Multivariate				
	β	S.E	Z	Р	OR (95%CI)	β	S.E	Z	Р	OR (95%CI)
PAR	- 0.01	0.00	- 4.40	<.001	0.99 (0.99 ~ 0.99)	- 0.00	0.00	- 1.81	0.071	1.00 (0.99~1.00)
BAR	0.03	0.01	5.90	<.001	1.04 (1.02~1.05)	0.00	0.02	0.08	0.933	1.00 (0.97~1.04)
LAO	0.23	0.05	4.91	<.001	1.26 (1.15~1.38)	- 0.11	0.11	- 0.99	0.324	0.90 (0.72~1.11)
LAR	0.01	0.00	5.88	<.001	1.01 (1.01~1.01)	- 0.00	0.00	- 0.23	0.819	1.00 (1.00~1.00)
scar	1.08	0.12	9.13	<.001	2.96 (2.34~3.73)	- 0.13	0.32	- 0.41	0.681	0.88 (0.47~1.65)
Log(sCAR)	1.02	0.10	10.77	<.001	2.78 (2.31~3.35)	1.19	0.29	4.02	<.001	3.27 (1.84~5.84)
Log(BAR)	0.55	0.09	6.39	<.001	1.73 (1.46~2.04)	- 0.25	0.25	- 0.98	0.326	0.78 (0.47~1.28)
Log(LAR)	0.54	0.06	8.93	<.001	1.72 (1.53~1.94)	0.41	0.11	3.88	<.001	1.51 (1.23~1.86)
Log(PAR)	- 0.34	0.07	- 4.58	<.001	0.71 (0.62~0.82)	- 0.12	0.16	- 0.76	0.448	0.88 (0.64~1.21)
Log(LAO)	0.44	0.08	5.76	<.001	1.55 (1.34~1.80)	0.24	0.18	1.28	0.201	1.27 (0.88~1.81)

OR odds ratio, 95% CI 95% confidence index, PAR platelet–albumin ratio, sCAR secrum creatinine–albumin ratio, LAR Lactic–dehydrogenase–albumin ratio, BAR, BUN– albumin ratio, LAO Lactate–albumin ratio

1.259, the Log(sCAR)\_Log(LAR) score demonstrated 68% sensitivity, 66% specificity, and a Youden's index of 0.34.We also performed ROC curve analysis on the above five variables in the validation set, and found that

the AUC of Log (sCAR) \_ Log (LAR) score was also the highest [AUC = 0.68, 95% CI (0.61–0.76)] (Fig. 2b). At the optimal threshold of 3.295, the Log(sCAR)\_ Log(LAR) score demonstrated 54% sensitivity, 80.4% specificity, and a Youden's index of 0.34.



**Fig. 2** deltaScr changes in serum creatinine within 24 h after ICU admission, logSAR\_logLAR Log(SAR)\_Log(LAR)score,SAR, secrum creatinine– albumin ratio; LAR, lactic–dehydrogenase–albumin ratio, SOFA score sequential organ failure assessment, (**a**) training set: the ROC curves for the ability of the Log(sCAR), Log(LAR), Log(sCAR)\_Log(LAR) score, SOFA score,  $\Delta$ Scr in predicting persistent severe SA-AKI in patients with SA-AKI. **b** validation set: the ROC curves for the ability of the Log(sCAR), Log(LAR), Log(sCAR)\_Log(LAR), Log(sCAR)\_Log(LAR) score, SOFA score, deltaScr in predicting persistent severe SA-AKI in patients with SA-AKI.

Variables	Low Log(sCAR)_Log(LAR) score (n = 849)	High Log(sCAR)_Log(LAR) score (n=639)	р	
pSA_AKI,n(%)	125(14.72)	266(41.63)	< 0.001	
Vasopressor_use, <i>n</i> (%)	100(11.78)	188(29.42)	< 0.001	
Death_in_ICU,n(%)	167(19.67)	211(33.02)	< 0.001	
Death_in_hospital,n(%)	233(27.44)	271(42.41)	< 0.001	
RRT, <i>n</i> (%)	84(9.89)	272(42.57)	< 0.001	
SOFA score,median[IQR]	4.00[2.00,5.00]	5.00[3.00,8.00]	< 0.001	
$\Delta$ Scr, median[IQR],(mg/dL)	0.20[0.10,0.40]	0.50[0.30,0.90]	< 0.001	
Creatinine,median[IQR],(mg/dL)	0.90[0.70,1.20]	2.00[1.40,3.00]	< 0.001	

Table 4 Training set: differences between the high Log(sCAR)\_Log(LAR) score group and the low Log(sCAR)\_Log(LAR) score group

Training set: differences between the high Log(sCAR)\_Log(LAR) score group and the low Log(sCAR)\_Log(LAR) score group. pSA-AKI persistent severe sepsis-associated acute kidney injury ∆Sc changes in serum creatinine within 24 h after ICU admission, SOFA score sequential organ failure assessment, RRT renal replacement therapy

## Differences between high and low Log(sCAR)\_Log(LAR) score groups

In the training set, using the optimal Log(sCAR)\_ Log(LAR) score threshold(1.259), the population was divided into high and low Log(sCAR)\_Log(LAR) score groups. The high-Log(sCAR)\_Log(LAR) score group exhibited significantly higher rates of adverse outcomes compared to the low-Log(sCAR)\_Log(LAR) score group, including persistent severe SA-AKI (266(41.63)% vs. 125(14.72)%, P<0.001), need for RRT (272(42.57)% vs. 84(9.89)%, P<0.001), hospital mortality (271(42.41)% vs. 233(27.44)%, P<0.001), ICU mortality (211(33.02)% vs. 167(19.67)%, P<0.001), and Vasopressor use (188(29.42)% vs. 100(11.78)%, P<0.001). The high-Log(sCAR)\_ Log(LAR) score group also had higher SOFA scores (5.00 (3.00–8.00) vs. 4.00 (2.00–5.00), P<0.001),  $\Delta$ Scr (0.50 (0.30–0.90) vs. 0.20 (0.10–0.40), P<0.001), and serum creatinine levels (2.00 (1.40–3.00) vs. 0.90 (0.70–1.20) mg/dl, P<0.001) (Table 4). In the validation set, according to the optimal threshold of Log (sCAR) \_ Log (LAR) score (3.295), we divided Log (sCAR) \_ Log (LAR) score into high Log (sCAR) \_ Log (LAR) score and low Log (sCAR) \_ Log (LAR) score, In the validation set, the high Log (SAR) \_ Log (LAR) score group had a higher

probability of using mechanical ventilation treatment (67 (78.82)% vs. 164 (89.62)%, P = 0.017), RRT (43(50.59)% vs. 44(24.04)%, P<0.001), persistent severe SA-AKI (52(61.18)% vs. 48(26.23)%, P<0.001),  $\Delta$ Scr (46.00 [19.90, 104.80] vs. 17.00 [6.40, 32.20], P<0.001), and serum creatinine levels (282.00 [201.00, 425.50] vs. 93.00 [67.30, 129.60], P<0.001) (Supplementary materials TableS1).

## Ability of the Log(sCAR)\_Log(LAR) score to predict persistent severe SA-AKI

In the training set, to evaluate whether the Log(sCAR)\_ Log(LAR) score improves risk prediction beyond individual clinical variables, a baseline multivariate logistic regression model was developed. Variables with p values <0.05 were identified through univariate logistic regression analysis (Table 5) and underwent collinearity analysis before multivariate logistic regression. The Variance Inflation Factor (VIF) indicated potential multicollinearity for the INR, Chloride, and Sodium (Table 6), leading to their exclusion. Subsequent multivariate logistic regression analysis showed SOFA score, PT,  $\Delta$ Scr, Tbil, Chronic liver disease, and Vasopressor use were independently associated with persistent severe SA-AKI (Table 7). A base prediction model was created using these factors and compared to a model including the Log(sCAR)\_Log(LAR) score. The predictive model with the Log(sCAR)\_Log(LAR) score had an AUC of 0.78 (0.76-0.81), which was significantly higher than the base model's AUC of 0.77 (0.75–0.79; p=0.03) (Fig. 3a). The NRI and IDI were then calculated to assess the predictive enhancement by adding the Log(sCAR)\_Log(LAR) score. The NRI of the two models (Fig. 4a) indicated no difference, suggesting that the Log(sCAR)\_Log(LAR) score did not significantly enhance the predictive ability. The IDI result of the predictive model, after incorporating the Log(sCAR)\_Log(LAR) score, was 0.03 [95% CI 0.01-0.04], indicating a 3% improvement in predictive ability compared to the base model. DCA confirmed the enhanced clinical utility of the updated model (Fig. 5a). Despite an NRI of 0, suggesting no significant predictive difference at the 0.5 cutoff, the IDI>0 indicated an overall improvement. In the validation set, we still use the six variables screened in the training set to build a basic clinical prediction model. The AUC of the updated model in the validation set was 0.73 (0.66-0.80), which was significantly higher than that of the base model's (0.67 (0.59–0.73), p=0.04 (Fig. 3b). However, the NRI of the updated model remained 0 (Fig. 4b), The IDI for the updated model was 0.08 [95% CI 0.04-0.12]. DCA confirmed the enhanced clinical utility of the updated model (Fig. 5b) in the validation sets. Furthermore, DCA was also performed to determine the clinical utilities of the Log(sCAR)\_Log(LAR) score. The results indicated **Table 5**Identification of risk factors for persistent severe sepsis-<br/>associated acute kidney injury patients via univariate regression<br/>analysis

Variables	β	S.E	Z	Р	OR (95%CI)
Gender					
Female					1.00 (Reference)
Male	- 0.01	0.12	- 0.12	0.902	0.99 (0.78~1.25
Infection Sites					
Abdominal_infection					1.00 (Reference)
Other	- 0.39	0.20	- 1.99	0.046	0.68 (0.46~0.99)
Pneumonia	- 0.25	0.24	- 1.07	0.285	0.78 (0.49~1.23)
Urinary_tract_infec- tion	- 0.26	0.25	- 1.07	0.285	0.77 (0.47~1.25)
Race					
Asian					1.00 (Reference)
Black	- 0.31	0.36	- 0.85	0.394	0.73 (0.36~1.50)
Hispanic	- 0.44	0.45	- 0.96	0.335	0.65 (0.27~1.57)
Other	- 0.22	0.41	- 0.53	0.594	0.80 (0.36~1.79)
White	- 0.26	0.30	- 0.85	0.394	0.77 (0.43 ~ 1.39)
Hypertension					
No					1.00 (Reference)
Yes	- 0.33	0.12	- 2.79	0.005	0.72 (0.57~0.91)
Coronary heart disease					
No					1.00 (Reference)
Yes	- 0.16	0.14	- 1.14	0.255	0.85 (0.64~1.12)
Chronic heart failure					
No					1.00 (Reference)
Yes	- 0.12	0.13	- 0.91	0.362	0.89 (0.69~1.15
Chronic liver disease					
No					1.00 (Reference)
Yes	0.84	0.12	6.99	<.001	2.31 (1.83~2.93)
Diabetes					
No					1.00 (Reference)
Yes	- 0.29	0.14	- 2.10	0.036	0.75 (0.57~0.98
Chronic pulmonary disea	ise				
No					1.00 (Reference)
Yes	- 0.11	0.14	- 0.76	0.449	0.90 (0.68~1.19
Malignant cancer					
No					1.00 (Reference)
Yes	- 0.35	0.16	- 2.10	0.036	0.71 (0.51~0.98
Cerebrovascular disease					
No					1.00 (Reference)
Yes	- 0.18	0.19	- 0.96	0.339	0.84 (0.58~1.20)
Vasopressor use					
No					1.00 (Reference)
Yes	0.74	0.14	5.35	<.001	2.10 (1.60~2.76
Mechanical ventilation					
No					1.00 (Reference)
Yes	0.26	0.12	2.13	0.033	1.30 (1.02 ~ 1.65)
Age	- 0.02	0.00	- 4.47	<.001	0.98 (0.98~0.99
SOFA score	0.20	0.02	9.62	<.001	1.22 (1.18~1.28)
Aniongap	0.09	0.01	8.15	<.001	1.09 (1.07~1.12)

Table 5	(continued)
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Variables	β	S.E	Z	Ρ	OR (95%CI)
Chloride	- 0.03	0.01	- 4.21	<.001	0.97 (0.95 ~ 0.98)
Sodium	- 0.02	0.01	- 2.34	0.020	0.98 (0.96~0.99)
Potassium	0.15	0.07	2.25	0.024	1.16 (1.02 ~ 1.32)
WBC	0.01	0.01	1.13	0.259	1.01 (1.00~1.02)
PT	0.03	0.01	6.00	<.001	1.03 (1.02~1.05)
INR	0.40	0.06	6.64	<.001	1.49 (1.33~1.68)
∆Scr	1.36	0.13	10.33	<.001	3.90 (3.01 ~ 5.04)
MAP	- 0.00	0.00	- 0.05	0.957	1.00 (1.00 ~ 1.00)
Heart rate	0.01	0.00	2.44	0.015	1.01 (1.01 ~ 1.01)
SBP	- 0.00	0.00	- 1.29	0.197	1.00 (0.99~1.00)
DBP	- 0.00	0.00	- 0.32	0.748	1.00 (0.99~1.00)
RR	0.02	0.01	2.33	0.020	1.02 (1.01 ~ 1.03)
Bicarbonate	- 0.07	0.01	- 6.25	<.001	0.93 (0.91 ~ 0.95)
Calciuml	- 0.09	0.05	-1.61	0.107	0.92 (0.83~1.02)
FIB	- 0.01	0.00	- 2.53	0.012	0.99 (0.99~0.99)
APTT	0.00	0.00	1.62	0.104	1.00 (1.00~1.01)
Hemoglobin	- 0.04	0.02	- 1.91	0.056	0.96 (0.91 ~ 1.00)
RBC	- 0.16	0.07	- 2.40	0.016	0.85 (0.74~0.97)
Alt	0.01	0.00	5.11	<.001	1.01 (1.01 ~ 1.01)
Alp	0.00	0.00	1.60	0.109	1.00 (1.00 ~ 1.00)
Ast	0.01	0.00	5.47	<.001	1.01 (1.01 ~ 1.01)
Tbil	0.05	0.01	7.06	<.001	1.06 (1.04~1.07)
NEUT	- 0.00	0.01	- 0.34	0.733	1.00 (0.98~1.01)
NEUT%	- 0.00	0.00	- 0.37	0.715	1.00 (0.99~1.01)
Lymphocyte	0.02	0.04	0.51	0.613	1.02 (0.94~1.11)
Mg	0.40	0.11	3.62	<.001	1.49 (1.20~1.85)

OR, odds ratio; 95% CI, 95% confidence index; pSA\_AKI persistent severe sepsisassociated acute kidney injury, SOFA score sequential organ failure assessment, *RRT* renal replacement therapy, *RR* respiratory rate, *MAP* mean arterial pressure, *APTT* activated partial thromboplastin time, *PT* prothrombin time, *BUN* blood urea nitrogen, *WBC* white blood cell count, *RBC* red blood cell count, *ΔScr* changes in serum creatinine within 24 h after ICU admission, *Ast* aspartate transaminase, *Alt* alanine transaminase, *Alp* alkaline phosphatase, *ICU* intensive care unit, *TBIL* total bilirubin, *Mg* magnesium, *NEUT* neutrophil count, *NEUT%* neutrophil percentage, *INR* international normalized ratio, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *FIB* fibrinogen

that the Log(sCAR)\_Log(LAR) score was clinically useful in both the training set and the validation set (Fig. 6). Adding the Log(sCAR)\_Log(LAR) score to this model improves the performance of the base model for predicting persistent severe SA-AKI. Overall, the new model with the Log(sCAR)\_Log(LAR) score showed superior discrimination and clinical utility.

### Ability of the Log(sCAR)\_Log(LAR) score to predict RRT

To test the ability of the Log (SAR)  $\_$  Log (LAR) score to predict RRT, we used the same method as that used to predict persistent severe SA-AKI. The AUC (95% CI) of the Log (SAR)  $\_$  Log (LAR) score-predicted RRT was 0.78(0.76–0.82), the best cut-off was 1.44, the sensitivity

Table 6	Variance inf	lation fac	tors of	the vari	ables in	the
predictiv	re model					

Variables	VIF
Chloride	14.78
Sodium	11.17
INR	10.19
PT	9.93
Bicarbonate	8.14
Aniongap	8.00
Alt	3.74
Ast	3.59
Tbil	1.53
SOFA score	1.41
Chronic_liver_disease	1.37
Age	1.33
Hypertension	1.26
ΔScr	1.25
Heart_rate	1.21
RBC	1.21
Potassium	1.19
FIB	1.16
Vasopressor_use	1.16
Mg	1.13
Diabetes	1.10
RR	1.10
Malignant_cancer	1.07

SOFA score sequential organ failure assessment, RR respiratory rate, PT prothrombin time, RBC red blood cell,  $\Delta Scr$  changes in serum creatinine within 24 h after ICU admission, Ast aspartate transaminase, Alt alanine transaminase, TBIL total bilirubin, Mg magnesium, INR international normalized ratio, FIB fibrinogen

was 70.5%, and the specificity was 74.1%. In the training set, univariate logistic regression (Supplementary materials TableS2), multicollinearity analysis (Table S3), and multivariate logistic regression analysis (Table S4) showed that  $\Delta$ Scr, serum magnesium ions, serum potassium ions, anion gap, chronic liver disease, complications of malignant tumors, use of vasopressors, and SOFA score were independently associated with RRT.

A basic clinical prediction model was constructed based on the above eight variables, and the performance of the clinical model was improved after adding Log (SAR) \_ Log (LAR) score to the basic prediction model. The AUC of the prediction model including the Log (SAR) \_ Log (LAR) score was 0.85, which was significantly higher than that of the underlying prediction model (AUC = 0.83; P = 0.001) (Fig. 7a). Moreover, the IDI of the two prediction models is 0.043, which shows that compared with the basic prediction model, the prediction ability of the model after adding the Log (SAR) \_ Log (LAR) score is improved by 4.3%. DCA further confirmed that the clinical practicability of the new model

Variables	β	S.E	Z	Р	OR (95%CI)
Intercept	- 3.23	0.82	- 3.93	<.001	0.04 (0.01 ~ 0.20)
Hypertension					
No					1.00 (Reference)
Yes	- 0.01	0.15	- 0.09	0.925	0.99 (0.74~1.31)
Chronic liver dise	ease				
No					1.00 (Reference)
Yes	0.37	0.15	2.43	0.015	1.44 (1.07~1.93)
Diabetes					
No					1.00 (Reference)
Yes	- 0.13	0.16	- 0.83	0.405	0.87 (0.64~1.20)
Malignant cance	er				
No					1.00 (Reference)
Yes	- 0.21	0.18	- 1.12	0.263	0.81 (0.57~1.17)
Vasopressor use					
No					1.00 (Reference)
Yes	0.39	0.16	2.36	0.018	1.47 (1.07~2.02)
Age	0.00	0.00	0.00	0.997	1.00 (0.99~1.01)
SOFA score	0.10	0.03	3.76	<.001	1.10 (1.05 ~ 1.16)
Aniongap	0.01	0.02	0.91	0.364	1.01 (0.98~1.05)
Potassium	- 0.02	0.07	- 0.28	0.777	0.98 (0.85~1.13)
PT	0.01	0.01	2.38	0.017	1.01 (1.01 ~ 1.02)
∆Scr	0.94	0.14	6.63	<.001	2.55 (1.93~3.36)
Heart rate	0.00	0.00	1.08	0.281	1.00 (1.00~1.01)
RR	0.01	0.01	1.67	0.095	1.01 (1.00~1.03)
Bicarbonate	- 0.02	0.02	- 1.37	0.170	0.98 (0.95~1.01)
FIB	0.00	0.00	0.78	0.433	1.00 (1.00 ~ 1.00)
RBC	- 0.07	0.08	- 0.89	0.372	0.93 (0.80~1.09)
Alt	0.00	0.00	0.17	0.867	1.00 (1.00 ~ 1.00)
Ast	0.00	0.00	1.30	0.192	1.00 (1.00 ~ 1.00)
Tbil	0.02	0.01	2.00	0.045	1.02 (1.01 ~ 1.04)
Mg	0.19	0.12	1.60	0.109	1.21 (0.96~1.54)

**Table 7** Multivariate analysis of risk factors for persistent severesepsis-associated acute kidney injury

OR, odds ratio; 95% CI, 95% confidence index, SOFA score sequential organ failure assessment, *RR* respiratory rate, *PT* prothrombin time, *RBC* red blood cell, *ΔScr* changes in serum creatinine within 24 h after ICU admission, *Ast* aspartate transaminase, *Alt* alanine transaminase, *TBIL* total bilirubin, *Mg* magnesium, *FIB* fibrinogen

after adding Log (SAR) \_ Log (LAR) score was stronger (Fig. 8a). In the validation set, after using the variables screened in the training set to construct the basic clinical prediction model and adding the Log (SAR) \_ Log (LAR) score, the performance of the clinical model is improved like the training set (Figs. 7b, 8b).

## Sensitivity analysis

We used sensitivity analysis to assess the stability of Log (SAR) \_ Log (LAR) score in predicting persistent severe SA-AKI. The results showed that after adjusting

for covariates, the Log (SAR) \_ Log (LAR) score could still predict persistent severe SA-AKI in the training and validation sets (all P<0.05, Tables8, 9, Supplementary materials Table S5). To further validate the ability of the Log(sCAR)\_Log(LAR) score's predictive power for secondary clinical outcomes, we tested its ability to predict RRT incidence, ICU mortality, and hospital mortality. Multivariate logistic or Cox regression analyses confirmed that the Log(sCAR)\_Log(LAR) score independently predicted all secondary outcomes across different models (Tables8, 9, Supplementary materials Table S5). Furthermore, we assessed the Log(sCAR)\_ Log(LAR) score's ability to forecast different definitions of persistent severe SA-AKI. The Log(sCAR)\_Log(LAR) score demonstrated effective prediction of SA-AKI at 48 h, 72 h, and prior to discharge, with consistent outcomes across various models (Tables8, 9, Supplementary materials Table S5). The Log (sCAR) \_Log (LAR) Log(sCAR) Log(LAR) score exhibited substantial predictive capability in multiple validation sets for persistent severe SA-AKI definitions. The AUC (95% CI) ranged from 0.61 (0.59-0.64) at 48 h to 0.60 (0.57-0.63) at 72 h and 0.59 (0.56-0.61) at discharge.

Subgroup analyses were examined to determine the Log(sCAR)\_Log(LAR) score's effectiveness in predicting persistent severe SA-AKI, considering factors such as Gender, Age, Hypertension, Coronary heart disease, Chronic heart failure, Diabetes, Cerebrovascular disease, Chronic pulmonary disease, Malignant cancer, Chronic liver disease, Race, and Infection sites. The forest plot shows that the Log(sCAR)\_Log(LAR) score effectively predicts persistent severe SA-AKI across most subgroups (P<0.05, Fig. 9), except for Asian patients. The trial set's subgroup analysis revealed significant interactions (p<0.05) for Diabetes, Chronic liver disease, and Vasopressure\_use. Stratified analysis and model adjustment with additional covariates confirmed the predictive ability of the Log(sCAR)\_ Log(LAR) score's predictive ability within these stratified groups (P<0.05)(Supplementary materials TableS6). The differences are also statistically significant in the various subgroups within the validation set (P<0.05, Supplementary materials Figure S1). In the validation set, various definitions of persistent severe SA-AKI were examined: 48 h (OR: 2.12, 95% CI 1.70–2.63; P<0.05, Supplementary materials Figure S2), 72 h (OR: 1.93, 95% CI 1.57-2.38; P<0.05, Supplementary materials Figure S3), and continuation until hospital discharge (OR: 1.83, 95% CI 1.48-2.25; P<0.05, Supplementary materials Figure S4). Subgroup analysis was performed for each definition. The Log(sCAR)\_Log(LAR) score was confirmed as an independent predictor of persistent severe SA-AKI.



Fig. 3 ROC curves of the base prediction model and the predictive model after adding the Log(sCAR)\_Log(LAR) score for the prediction of Persistent severe sepsis-associated acute kidney injury. **a** Training set: Model 1 base prediction model; Model 2 the predictive model after adding the Log(sCAR)\_Log(LAR) score; (**b**) Validation set: Model 1 base prediction model; Model 2 the predictive model after adding the Log(sCAR)\_Log(LAR) score; (**b**) Validation set: Model 1 base prediction model; Model 2 the predictive model after adding the Log(sCAR)\_Log(LAR) score; (**b**) Validation set: Model 1 base prediction model; Model 2 the predictive model after adding the Log(sCAR)\_Log(LAR) score



Fig. 4 NRI of the base prediction model and the predictive model after adding the Log(sCAR)\_Log(LAR) score for the prediction of persistent severe sepsis-associated acute kidney injury. **a** Training set: NRI of base prediction model and the predictive model after adding the Log(sCAR)\_Log(LAR) score for the prediction of persistent severe sepsis-associated acute kidney injury. **b** Validation set: NRI of base prediction model and the predictive model after adding the predictive model after adding the Log(sCAR)\_Log(LAR) score for the prediction of persistent severe sepsis-associated acute kidney injury.

## Kaplan-Meier curve

In the training set ,patients were classified on the basis of the optimal cutoff into low Log(sCAR)\_Log(LAR) score (<= 1.259, n=849) and high Log(sCAR)\_Log(LAR) score (> 3.295, n=639) groups. The Kaplan-Meier survival

analysis curve (Fig. 10) and Log Rank test statistic for survival time between these groups was 152.576, with HR=3.3895, 95% CI (2.757–4.143), and p=0. The Log Rank test indicated a significant difference in survival time between the groups, revealing that patients with a



**Fig. 5** DCA of the base prediction model and the predictive model after adding the Log(sCAR)\_Log(LAR) score for the prediction of persistent severe sepsis-associated acute kidney injury. **a** Training set: Model 1 base prediction model; Model 2 the predictive model after adding the Log(sCAR)\_Log(LAR) score. **b** Validation set: Model 1 base prediction model; Model 2 the predictive model after adding the Log(sCAR)\_Log(LAR) score. **b** Validation set: Model 1 base prediction model; Model 2 the predictive model after adding the Log(sCAR)\_Log(LAR) score.



Fig. 6 DCA of Log(sCAR)\_Log(LAR) score for the prediction of persistent severe sepsis-associated acute kidney injury. a Training set: DCA of Log(sCAR)\_Log(LAR) score for the prediction of persistent severe sepsis-associated acute kidney injury. b Validation set: DCA of Log(sCAR)\_ Log(LAR) score for the prediction of persistent severe sepsis-associated acute kidney injury.

high Log(sCAR)\_Log(LAR) score had significantly higher mortality than those with a low Log(sCAR)\_Log(LAR) score (P<0.0001).

## Discussion

This study is the first to explore the prediction ability of the sCAR and LAR for predict persistent severe SA-AKI and other clinical outcomes upon ICU admission. This study indicates that sCAR and LAR can independently predict persistent severe SA-AKI, and a Log(sCAR)\_Log(LAR) score was established on the basis of log(sCAR) and log(LAR). We found through univariate and multivariate logistic regression that the SOFA score, PT,  $\Delta$ Scr, Tbil, Chronic liver disease, and Vasopressor use were independent risk factors for persistent severe SA-AKI. A base prediction model was established based on these variables. The predictive model combined with the Log(sCAR)\_Log(LAR) score had better discrimination ability than the base prediction model, predictive ability, and clinical utility. In both the training and validation sets, the Log(sCAR)\_Log(LAR) score showed good predictive performance for persistent severe SA-AKI and other clinical outcomes (different definitions of persistent severe SA-AKI, RRT incidence, ICU mortality, and hospital mortality). The correlation between the Log(sCAR)\_ Log(LAR) score and persistent severe SA-AKI was



Fig. 7 ROC curves of the base prediction model and the predictive model after adding the Log(sCAR)\_Log(LAR) score for the prediction of RRT. a Training set: Base\_model base prediction model; SAR\_LAR represents the predictive model after adding the Log(sCAR)\_Log(LAR) score; (b) validation set: Model 1 base prediction model; Model 2 represents the predictive model after adding the Log(sCAR)\_Log(LAR) score



Fig. 8 DCA of base prediction model and the predictive model after adding the Log(sCAR)\_Log(LAR) score for the prediction of RRT. a Training set: Model 1 base prediction model; Model 2 the predictive model after adding the Log(sCAR)\_Log(LAR) score. b Validation set: Model 1 base prediction model; Model 2 predictive model after adding the Log(sCAR)\_Log(LAR) score

further confirmed using data from the electronic medical records of the First Affiliated Hospital of Harbin Medical University.

Early detection of persistent severe SA-AKI is crucial in clinical practice. Identifying at-risk patients and timely interventions can affect the progression from AKI to CKD [20]. Predicting short-term AKI reversibility aids in assessing the need for RRT and the timing of its initiation [21]. Some progress has been made using biomarkerbased approaches for the early identification of persistent SA-AKI [22]. Therefore, further research into biomarkerbased detection of SA-AKI subtypes is warranted.

Low albumin levels may significantly contribute to endothelial dysfunction; its production decreases, and its breakdown increases, exacerbating inflammation [23]. Recent studies have revealed a correlation between LDH and long-term mortality rates in hemodialysis patients [24]. In addition, LDH and low albumin levels are key indicators for predicting outcomes in critically ill patients [25, 26]. The LAR has also been

Madal	N	0.0	050/ 61		
Model	N	UK	95%CI	P value	
pSA_AKI1					
Crude Model	1488	2.11	[1.70,2.62]	0.000	
Adjusted Model 1	1488	1.83	[1.45,2.31]	0.000	
Adjusted Model 2	1488	1.48	[1.14,1.92]	0.004	
pSA_AKI2					
Crude Model	1488	1.92	[1.56,2.37]	0.000	
Adjusted Model 1	1488	1.71	[1.37,2.14]	0.000	
Adjusted Model 2	1488	1.53	[1.19,1.97]	0.001	
pSA_AKI3					
Crude Model	1488	1.83	[1.49,2.25]	0.000	
Adjusted Model 1	1488	1.57	[1.26,1.97]	0.000	
Adjusted Model 2	1488	1.31	[1.01,1.69]	0.040	
RRT					
Crude Model	1488	6.75	[5.13,8.88]	0.000	
Adjusted Model 1	1488	5.06	[3.77,6.77]	0.000	
Adjusted Model 2	1488	2.91	[2.08,4.07]	0.000	
pSA_AKI					
Crude Model	1488	4.13	[3.23,5.29]	0.000	
Adjusted Model 1	1488	3.21	[2.46,4.17]	0.000	
Adjusted Model 2	1488	2.15	[1.59,2.91]	0.000	

Table 8 Training set: multivariate logistic regression analyses for clinical outcomes

OR: Odds Ra OR, odds ratio; 95% CI, 95% confidence index; pSA\_AKI, persistent severe sepsis-associated acute kidney injury: defined as stage 3 AKI during an ICU stays over 72 h, including those who died or received RRT before 72 h; pSA\_AKI1, persistent severe sepsis-associated acute kidney injury: defined as sepsis-related acute kidney injury lasting at least 48 h; pSA\_AKI2, persistent severe sepsis-associated acute kidney injury: defined as sepsis-related acute kidney injury lasting at least 48 h; pSA\_AKI2, persistent severe sepsis-related acute kidney injury: defined as sepsis-related acute kidney injury lasting at least 72 h; pSA\_AKI3, persistent severe sepsis-related acute kidney injury control discharge, *RRT* Renal replacement therapy; Adjusted Model 1 was adjusted for the SOFA score, Hypertension, Chronic liver disease, Diabetes, Malignant cancer, Vasopressor use, Mechanical ventilation, Gender, and Age. Adjusted Model 2 was adjusted for Adjusted Model 1 plus Aniongap, Potassium, PT, \DeltaScr, Heart\_rate, RR, Bicarbonate, FIB, RBC, Alt, Ast, Tbil, and Mg

Table 9	Training set:	multivariate	Cox reares	sion analy	vses for	clinical	outcomes
Tuble 2	nunning set.	manufalle	COX regres	Sion analy	y 3C 3 101	chincui	outcomes

Model	Ν	HR	95%CI	P value
Death_in_ICU				
Crude Model	1488	1.85	[1.51,2.26]	0.000
Adjusted Model 1	1488	1.00	[0.82,1.23]	0.985
Adjusted Model 2	1488	1.00	[0.81,1.24]	0.986
Death_in_hospital				
Crude Model	1488	1.73	[1.45,2.06]	0.000
Adjusted Model 1	1488	0.93	[0.78,1.11]	0.398
Adjusted Model 2	1488	0.95	[0.79,1.14]	0.559

OR, HR: Hazard Ratio; 95% CI, 95% Confidence Interval. Adjusted Model 1 was adjusted for the SOFA score, Hypertension, Chronic liver disease, Diabetes, Malignant cancer, Vasopressor use, Mechanical ventilation, Gender, and Age. Adjusted Model 2 was adjusted for Adjusted Model 1 plus Aniongap, Potassium, PT, ΔScr, Heart\_ rate, RR, Bicarbonate, FIB, RBC, Alt, Ast, Tbil, and Mg

confirmed as a significant predictor of overall mortality in critically ill individuals with AKI [27]. Creatinine: the gold standard for the diagnosis of acute kidney injury. However, its levels are influenced by sex, age, diet, and hydration, often leading to an overestimation of renal function in critically ill patients [28–30]. In pediatric cardiac surgery patients, the urinary albumin-to-creatinine ratio (ACR) is an early diagnostic test for AKI, comparable to other biomarkers [31].

Previous research has examined High-density lipoprotein cholesterol (HDL-C) as a predictor of AKI in patients with severe sepsis-associated acute kidney

Variable	Count	Percent(%)	OR (95% CI)	P value	P for interaction
Gender			1		0.41
male	883	59.3	→ 4.58 (3.29 to 6.37)	< 0.001	
female	605	40.7	→ 3.71 (2.54 to 5.41)	< 0.001	
Age					0.284
<=65	838	56.3	→ 3.63 (2.65 to 4.97)	<0.001	
>65	650	43.7	← → 4.80 (3.21 to 7.17)	<0.001	
Hypertension					0.38
No	694	46.6	→ 3.66 (2.59 to 5.17)	< 0.001	
Yes	794	53.4	← → 4.57 (3.21 to 6.50)	< 0.001	
Diabetes					0.021
No	1101	74	→ 3.54 (2.68 to 4.67)	< 0.001	
Yes	387	26	7.42 (4.22 to 13.03)	< 0.001	
Chronic_heart_failure					0.167
No	1054	70.8	→ 3.70 (2.77 to 4.93)	< 0.001	
Yes	434	29.2	→ 5.48 (3.40 to 8.82)	< 0.001	
Chronic_pulmonary_disea	ise				0.088
No	1140	76.6	→ 3.67 (2.78 to 4.85)	< 0.001	
Yes	348	23.4	←→ 6.21 (3.64 to 10.60)	< 0.001	
Chronic liver disease					0.01
No	922	62	→ 5.31 (3.74 to 7.55)	< 0.001	
Yes	566	38	2.75 (1.93 to 3.94)	< 0.001	
Cerebrovascular disease					0.479
No	1304	87.6	► 4.00 (3.08 to 5.19)	< 0.001	
Yes	184	12.4	$\rightarrow$ 5 34 (2 51 to 11 34)	<0.001	
Coronary heart disease					0.12
No	1141	76.7	$\rightarrow$ 373 (2.83 to 4.92)	<0.001	
Yes	347	23.3	$\longmapsto 6.11 (3.50 \text{ to } 10.67)$	<0.001 ·	
Malignant cancer	•	2010			0.81
No.	1227	82.5	$\downarrow \rightarrow 4.08(3.12 \text{ to } 5.33)$	<0.001	0.01
Yes	261	17.5	4.44 (2.34  to  8.42)	<0.001	
Mechanical ventilation	201	11.0	1.11(2.01.00.12)	0.001	0.796
No	577	38.8	→ 3 94 (2 62 to 5 94)	<0.001	
Yes	911	61.2	$\longrightarrow 4.92 (3.10 \text{ to } 5.75)$	<0.001	
Race	011	01.2	4.22 (0.10 (0 0.10)	-0.001	0.483
Black	115	77	5 44 (2 14 to 13 79)	<0.001	0.100
White	1208	81.2	4 11 (3 12 to 5 40)	<0.001	
Asian	54	36	2 18 (0 64 to 7 40)	0.212	
Hispanic	48	3.2	16 43 (1 80 to 142 45)	0.011	
Other	63	12	+ 10.43 (1.03 to 142.43)	0.022	
Infection Sites	00	4.2	4.03 (1.25 to 15.05)	0.022	0.22
Other	050	63.9	4 50 (3 28 to 6 10)	<0.001	0.22
Dullei	218	14.7	5.97 (3.10 to 11.52)	<0.001	
Abdominal infection	127	0.2	> 3.56 (3.10 to 11.52)	0.012	
Abdominal_Intection	107	9.2	2.30 (1.23 to 5.32)	0.012	
Vecenness use	165	12.5	2.80 (1.43 to 5.47)	0.003	0.004
No.	1200	20.6		-0.001	0.004
Voc	200	10.4	4.04 (3.49 (0 6.18)	-0.001	
Querall	1499	10.4		<0.013	
Overdi	1400	100	4.13 (3.23 to 5.29)	<0.001	
		0	5 1 1.5		

Fig. 9 Training set: the subgroup analysis of the Log(sCAR)\_Log(LAR) score in persistent severe sepsis-associated acute kidney injury

injury (SA-AKI), but the results did not support this hypothesis. HDL-C showed no independent association with persistent severe SA-AKI and did not enhance the clinical model's predictive performance [32]. This study revealsthat the Log(sCAR)\_Log(LAR) score has a higher AUC and remains significantly associated with persistent severe SA-AKI after adjusting for multiple variables at hospital admission. These associations are consistent across subgroup analyses, secondary outcomes, and different primary endpoint definitions. Data from the validation set further validated the Log(sCAR)\_Log(LAR) score's connection with persistent severe SA-AKI. Thus, the Log(sCAR)\_Log(LAR) score is a more effective predictor of persistent severe SA-AKI. Its development and validation provide medical professionals with a valuable tool for predicting the persistence and severity of SA-AKI, aiding clinical decisions on renal replacement therapy timing and intensity, and facilitating close patient monitoring.

This research has several limitations. Discrepancies exist between the validation and training data sets; for instance, the high Log(sCAR)\_Log(LAR) score cohort in the validation set shows lower rates of mechanical ventilation, RRT, and shorter hospital and ICU stays. These disparities may stem from the limited sample size. Replacing lactate dehydrogenase, albumin, and serum creatinine with the Log(sCAR)\_Log(LAR) score in the base model showed no significantly difference between the models (training set: P=0.488; validation set: P=0.065)( supplementary materials Tables S9, S10



Fig. 10 Trainine set: Kaplan–Meier plots for the low-Log(sCAR)\_Log(LAR) score group and high Log(sCAR)\_Log(LAR) score group.logSAR\_logLAR\_ binary = 0 represents the low Log(sCAR)\_Log(LAR) score; logSAR\_logLAR\_binary = 1 represents the high Log(sCAR)\_Log(LAR) score

and Figures S5, S6). Similarly, the Log(sCAR)\_Log(LAR) score was not significantly different from the  $\Delta$ Scr score (training set: P=0.619, validation set: P=0.166), indicating that while the Log(sCAR)\_Log(LAR) score is somewhat relevant in diagnosing Persistent Severe Sepsis-Associated Acute Kidney Injury (SA-AKI), its importance is limited (supplementary materials Table S7,Table S8). The biological significance and mechanisms of Log(sCAR)\_Log(LAR) need further elucidation. Future research should validate the predictive value of the Log(sCAR)\_Log(LAR) score's predictive value in a more diverse patient population and examine its applicability across various ethnicities and regions.

## Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s40001-024-02269-6.

Additional file 1: Table S1: Validation set: differences between the high Log\_Logscore group and the low Log\_Logscore group. pSA-AKI, Persistent SevereSepsis-Associated Acute Kidney Injury; ΔScr, Changes in serum creatinine within 24 h after ICU admission,qSofa score, quick Sequential Organ Failure Assessment, RRT,renal replacement therapyTable S2 Identification of risk factors for Persistent RRT using univariate regression analysis. OR, odds ratio; 95% CI, 95% confidence index; pSA\_AKI Persistent Severe

Sepsis-Associated Acute Kidney Injury, SOFA score Seguential Organ Failure Assessment, RRT Renal replacement therapy, RR Respiratory rate, MAP mean arterial pressure, APTT Activated partial thromboplastin time, PT Prothrombin time, BUN Blood urea nitrogen, WBC White blood cell count, RBC Red blood cell count,  $\Delta$ Scr Changes in serum creatinine within 24 h after ICU admission, Ast Aspartate transaminase, Alt Alanine transaminase, Alp Alkaline phosphatase, ICU Intensive care unit,TBIL Total bilirubin,Mg Magnesium, NEUT neutrophil count,NEUT% Neutrophil percentage, INR International normalized ratio, SBP Systolic blood pressure, DBP Diastolic Blood pressure, FIB fibrinogen TableS3 Variance inflation factors of variables in the predictive model .Sofa score Sequential Organ Failure Assessment, RR Respiratory rate, PT Prothrombin time, RBC Red blood cell, ∆Scr Changes in serum creatinine within 24 h after ICU admission, Ast Aspartate transaminase, Alt Alanine transaminase, TBIL Total bilirubin, Mg Magnesium, INR International normalized ratio, FIB Fibrinogen, SBP Systolic Blood Pressure ; TableS4 Multivariate analysis of risk factors for persistent severe sepsis-associated acute kidney injury OR: odds ratio, CI: confidence interval, Sofa score sequential organ failure assessment, RR: respiratory rate, RBC: red blood cell, ∆Scr: changes in serum creatinine within 24 h after ICU admission, Ast: aspartate transaminase, Alt: alanine transaminase, TBIL: total bilirubin, Mg: magnesium, FIB: fibrinogen, SBP Systolic Blood Pressure, APTT Activated partial thromboplastin time; Table S5 Validation set: multivariate logistic regression analyses for clinical outcomes. OR: odds ratio; 95% CI, 95% confidence interval. pSA\_AKI, persistent severe sepsis-associated acute kidney injury: defined as stage 3 AKI during an ICU stays over 72 h, including those who died or received RRT before 72 h; pSA\_AKI1, persistent severe sepsis-associated acute kidney injury: defined as sepsis-related acute kidney injury lasting at least 48h; pSA\_ AKI2, persistent severe sepsis-associated acute kidney injury: defined as sepsis-related acute kidney injury lasting at least 72h; pSA\_AKI3, persistent severe sepsis-associated acute kidney injury: defined as sepsis-related acute kidney injury persisting until discharge ;RRT, Renal replacement therapy; Adjusted Model 1 was adjusted for the SOFA

score, Hypertension, Chronic liver disease, Diabetes, Malignant cancer, Vasopressor use, Mechanical ventilation, Gender, and Age, Adjusted Model 2 was adjusted for Adjusted Model 1 plus Aniongap, Potassium, PT, ∆Scr, Heart rate, RR, Bicarbonate, FIB, RBC, Alt, Ast, Tbil, and Mg. TableS6 Trainine set: stratified analysis. TableS7 Training set: the delong test for Log, Log, Log\_Logscore, SOFA score, ∆Scr in predicting persistent severe SA-AKI in patients with SA-AKI.Sofa\_score,Sequential Organ Failure Assessment,∆Scr Changes in serum creatinine within 24 h after ICU admission, sCAR, secrum creatinine-albumin ratio: LAR.Lactic-dehydrogenase-albumin ratio. TableS8 Validation set: the delong test for Log, Log\_Logscore, SOFA score,  $\Delta$ Scr in predicting persistent severe SA-AKI in patients with SA-AKI.qSofa\_score,quick Sequential Organ Failure Assessment,∆Scr Changes in serum creatinine within 24 h after ICU admission,sCAR, secrum creatinine-albumin ratio; LAR,Lactic-dehydrogenase-albumin ratio. Figure S1 Validation set: the subgroup analysis of the Log\_Logscore in Persistent Severe Sepsis-Associated Acute Kidney Injury. Figure S2 Training set: the subgroup analysis of the Log\_Logscore in Defined as persistent severe sepsis-related acute kidney injury lasting for 48 h. Figure S3 Training set: the subgroup analysis of the Log\_Logscore in Defined as persistent severe sepsis-related acute kidney injury lasting for 72 h. FigureS4 Training set: the subgroup analysis of the Log\_Logscore in Defined as persistent severe sepsis-related acute kidney injury prior to discharge. FigureS5 Training set: the ROC curves for Model1, Model2 in predicting persistent severe SA-AKI in patients with SA-AKI.Model1 the base predictive model after adding the Log\_Logscore; Model2 the base predictive model after adding the Creatinine, Albumin, Lactic\_dehydrogenase. Figure S6 Validation set: the ROC curves for Model 1, Model 2 in predicting persistent severe SA-AKI in patients with SA-AKI. Model 1 the base predictive model after adding the Log\_Logscore; Model 2 the base predictive model after adding the creatinine, albumin, and lactic\_dehydrogenase

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#### Author contributions

X.L.,Y.J.,W.L.,J.L.conceived and designed research; X.L.,D.L.,Y.W.,R.D.performed experiments; X.L.,C.L. analyzed data, interpreted results of experiments, prepared figures and drafted the manuscript;X.L.D.L.,Y.W.,R.D.edited and revised manuscript

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### Availability of data and materials

All data generated or analyzed during this study are included in this article and its Supplementary data files. Further enquiries can be directed to the corresponding author.

## Declarations

#### Ethics approval and consent to participate

This study was approved by the Ethical Committee of the First Affiliated Hospital of Harbin Medical University (No. MR-23-24-039837).

### **Consent for publication**

My co-authors have all contributed to approve of this submission.

### **Competing interests**

The authors declare no competing interests.

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