

Novel inflammatory biomarkers enhance prediction of sepsis-associated acute kidney injury: a machine learning approach

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Abstract

Background: Sepsis-associated acute kidney injury (S-AKI) is a common complication of sepsis, and early identification can improve patient prognosis. This study incorporated novel inflammatory markers as features to construct a model and employed 6 machine learning methods to predict the occurrence of S-AKI.

Methods: A total of 3613 patients with sepsis were included in this study. Novel inflammatory markers, including neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, systemic inflammatory response index, systemic immune-inflammation index, systemic inflammatory aggregate index, lactate-to-albumin ratio, and prognostic nutritional index, along with demographic characteristics, clinical conditions, and routine laboratory results, were used to construct the model. The machine learning methods employed included logistic regression, support vector machine, random forest (RF), extreme gradient boosting (XGBoost), and ensemble methods (RF+XGBoost). Model performance and stability were evaluated using 5-fold cross-validation. Model performance was assessed using the area under the receiver-operating characteristic curve, sensitivity, specificity, accuracy, precision, recall, and F1 score. Additionally, SHapley Additive exPlanations values were used to interpret the predictive model.

Results: In the final algorithm group, the ensemble model of RF and XGBoost (0.843; 95% confidence interval: 0.820–0.866) was higher than those of other models. Among the single models, the XGBoost model exhibited the highest sensitivity (0.856) and F1 score (0.780), indicating its stronger ability to identify patients who will develop S-AKI, albeit at the expense of lower specificity (0.667). The 4 most influential features for XGBoost were mechanical ventilation, mean arterial pressure, blood urea nitrogen level, and sequential organ failure assessment score. Among the 3 novel inflammatory markers, lactate-to-albumin ratio showed the greatest effect.

Conclusion: We successfully developed machine learning methods to predict S-AKI, highlighting the importance of novel inflammatory markers in model construction. This breakthrough offers novel perspectives for feature selection in the future development of related predictive models.

Keywords: Acute kidney injury, Artificial intelligence, Machine learning, Prediction, Sepsis

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

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Introduction

Sepsis is a systemic inflammatory response syndrome characterized by an imbalance in the immune response due to an infection, leading to multiple organ dysfunction. Among the most prevalent complications, sepsis-associated acute kidney injury (S-AKI) is frequently observed in patients with sepsis.^[1,2] The occurrence of S-AKI is associated with adverse long-term outcomes.

A study involving 1243 patients with septic shock revealed that, according to the Kidney Disease: Improving Global Outcomes criteria, more than two-thirds of patients developed AKI within the first 7 days. Although some patients experienced only brief episodes of AKI, those whose kidney function did not improve had lower survival rates. In contrast, patients with S-AKI who experienced recovery of kidney function, even if incomplete, had survival rates similar to those of patients who did not develop AKI.^[3] Therefore, early identification and intervention in S-AKI are expected to reduce the extent of kidney damage and improve patient prognosis.

Currently, the clinical diagnosis of AKI relies on serum creatinine levels and urine output. However, by the time creatinine levels increase significantly and urine output decreases sharply, the kidneys have already sustained severe damage.^[4] As a result, early identification and intervention in S-AKI are crucial.

Machine learning can efficiently process and analyze large volumes of complex medical data, automate decision-making, and continuously optimize and adapt to complex environments, thereby providing more accurate results. Zeng et al.^[5] developed a predictive model for AKI following cardiac surgery using machine learning methods. Zhang et al. developed a machine learning predictive model for S-AKI in patients with sepsis based on demographic information, laboratory results, and vital signs. However, because of the relatively low correlation of the included features, the overall predictive accuracy of the model was not high.^[6]

In recent years, novel inflammatory markers derived from conventional indicators have shown strong predictive power for various diseases. Studies have found that routine peripheral blood-derived inflammatory markers, such as the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), systemic inflammatory response index (SIRI), systemic immune-inflammation index (SII), and systemic inflammatory aggregate index (AISI), can be used to assess the immune status of patients. These markers have unique advantages in predicting outcomes for specific patient groups, such as those with sepsis, acute respiratory distress syndrome, or postoperative infections.^[7–10] In addition, Chen et al. found that the lactate-to-albumin ratio (LAR) was better at predicting organ dysfunction and mortality in patients with sepsis.^[11, 12] The prognostic nutritional index (PNI) uses serum albumin levels and peripheral blood total lymphocyte counts to assess overall immune and nutritional status. Kyo et al. found that PNI values are significantly associated with the mortality rate in patients with sepsis and that PNI can help predict sepsis outcomes.^[13, 14]

Therefore, to enhance the discriminatory ability of the model, we combined the aforementioned novel inflammatory markers related to sepsis with patient demographic characteristics, laboratory results, and clinical symptoms to construct a machine learning prediction model for S-AKI after hospital admission in patients with sepsis.

Methods

Research design

This retrospective cohort study involved 3613 patients with sepsis. We obtained data from the Medical Information Mart for Intensive Care (MIMIC)-IV database,^[15] which is developed and maintained by the Laboratory for Computational Physiology at the Massachusetts Institute of Technology. Zhang Y extracted the data after the completion of online training (certification number 64967484) and passing the required examination. Informed consent was not required because the data were deidentified.

Patient selection

We included 3613 patients from the MIMIC-IV database. The inclusion criteria were as follows: (1) age >18 years and (2) first admission diagnosed as sepsis. The exclusion criteria were a history of malignancy, long-term use of immunosuppressive drugs, hematologic malignancies, and liver cirrhosis with Child-Pugh class C.

Data collection and preprocessing

We used structured query language in Navicat Premium (version 15.4, PremiumSoft, Hong Kong, China) to extract demographic characteristics, laboratory results, and clinical conditions of the

included patients from the MIMIC database. Additionally, novel inflammatory markers were calculated based on the patients' laboratory results. The specific formulas for these markers are as follows:

- $NLR = \text{neutrophil count (absolute)} / \text{lymphocyte count (absolute)}$
- $MLR = \text{monocyte count (absolute)} / \text{lymphocyte count (absolute)}$
- $SIRI = \text{neutrophil count (absolute)} \times \text{monocyte count (absolute)} / \text{lymphocyte count (absolute)}$
- $SII = \text{platelet count (absolute)} \times \text{neutrophil count (absolute)} / \text{lymphocyte count (absolute)}$
- $AISI = \text{platelet count (absolute)} \times \text{neutrophil count (absolute)} \times \text{monocyte count (absolute)} / \text{lymphocyte count (absolute)}$
- $PNI = 10 \times \text{serum albumin (g/dL)} + 0.005 \times \text{lymphocyte count (cells/mm}^3\text{)}$
- $LAR = \text{lactate} / \text{albumin (g/dL)}$

These inflammatory markers were calculated based on the relevant laboratory results available in the database.

Missing values

For missing data imputation, we used a 2-step strategy: Variables with >20% missing values were excluded from the analysis. Variables with ≤20% missing values were imputed using multivariate imputation by chained equations via the fancyimpute package. This method preserves the correlation structure across variables and reduces bias compared with mean or median imputation.

Statistical analysis

Statistical analysis and modeling were conducted using Python 3.11.5 (Python Software Foundation) and its scientific computing libraries. Continuous variables were first tested for normality using the Shapiro–Wilk test. Normally distributed variables are presented as mean ± standard deviation, whereas nonnormally distributed variables are expressed as medians with interquartile ranges. Categorical variables are presented as number and percentage (n [%]).

For group comparisons, the Student's *t*-test was used for normally distributed continuous variables, whereas the Mann–Whitney *U* test was applied for nonnormally distributed data. Categorical variables were compared using the chi-square test or Fisher's exact test depending on the data characteristics and sample size. A 2-tailed *P* value <0.05 was considered statistically significant.

Machine learning

We constructed and evaluated the performance of 6 models: logistic regression, decision tree, random forest (RF), support vector machine (SVM), extreme gradient boosting (XGBoost), and an ensemble model (RF + XGBoost). The evaluation metrics were the area under the receiver-operating characteristic curve (AUC) and its 95% confidence interval (CI), which were used to measure the ability of the models to discriminate between positive and negative samples.

Logistic regression is a linear model suitable for binary classification problems that estimates the probability of an event occurring based on a linear combination of features. Logistic regression performs well when there is a linear relationship between

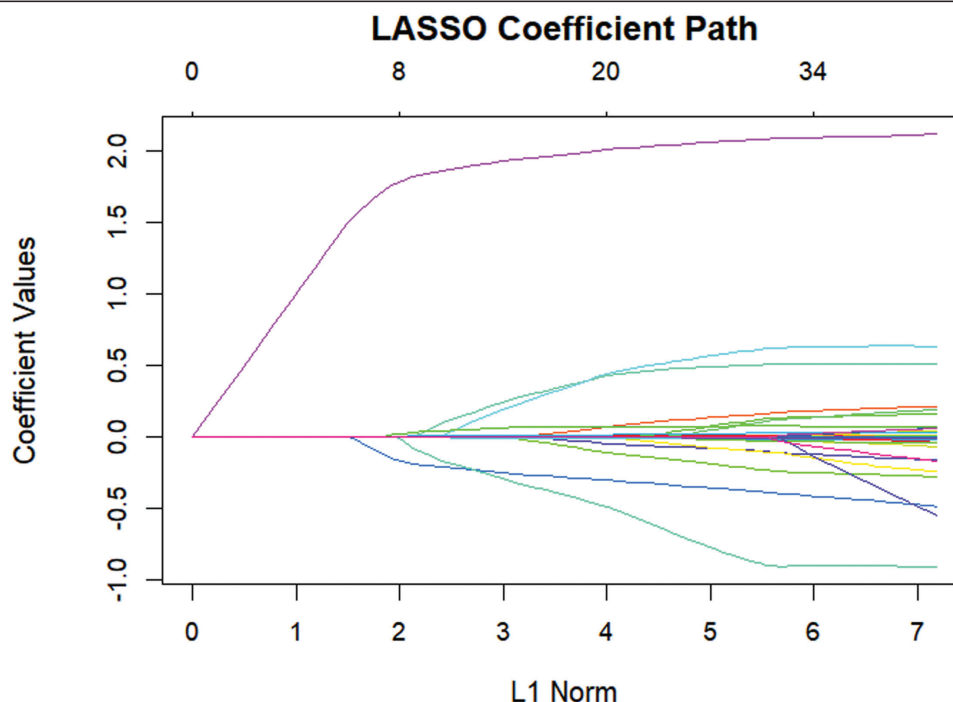


Figure 1. Screening of variables based on LASSO regression. The variation characteristics of the coefficient of variables. LASSO, least absolute shrinkage and selection operator.

the features and the target variable. However, its performance may be limited when dealing with nonlinear relationships.^[16] A decision tree classifies data by conditionally splitting features to construct a tree structure with the leaf nodes providing the final classification result. However, a single decision tree is prone to overfitting and tends to have poor generalization ability. For complex or high-dimensional data, model stability may be insufficient, leading to less reliable predictions.

RF is an ensemble learning method based on bagging that constructs multiple decision trees and combines them using a voting mechanism to improve predictive performance. This approach effectively mitigates overfitting from a single decision tree, offering strong robustness and generalization ability. It is particularly well-suited for handling high-dimensional and complex data.^[17]

SVM classifies samples by finding the optimal hyperplane that separates different classes. The use of kernel functions allows the SVM to be extended to nonlinear classification problems, enabling it to handle more complex decision boundaries by mapping the data into a higher dimensional space.^[18]

XGBoost is a gradient boosting tree model that uses an incremental optimization algorithm offering both efficiency and powerful learning capabilities. It is well-suited for handling nonlinear relationships and complex data, effectively capturing feature interactions. Additionally, XGBoost includes regularization mechanisms to prevent overfitting, thereby enhancing model stability and generalization ability.^[19]

We used 5-fold cross-validation to train and tune the models, ensuring robust performance and mitigating overfitting. This method involved splitting the dataset into 5 subsets, training the model on 4 subsets, testing it on the remaining one, and repeating this process 5 times. The performance metrics were then averaged to provide a more reliable estimate of the model's ability to generalize to unseen data. Model performance was comprehensively evaluated using the following metrics on the independent test set: the AUC, accuracy, sensitivity (recall), specificity, precision,

and the F1 score (the harmonic mean of precision and recall). To assess clinical utility, decision curve analysis was performed to quantify the net benefit across a range of probability thresholds. To interpret the predictions of the optimal model and identify the most influential features, we employed SHapley Additive exPlanations (SHAP) values. The ensemble model combined the output probabilities of RF and XGBoost using a weighted averaging approach to enhance predictive performance and stability.

Variable selection

To address potential multicollinearity among the derived inflammatory markers and routine laboratory indicators, we applied least absolute shrinkage and selection operator (LASSO) regression for feature selection. This method imposes L1 regularization to shrink less relevant coefficients to zero, thus reducing model complexity and enhancing interpretability. The model was implemented using LassoCV from Python's scikit-learn library, with the optimal regularization parameter (λ) determined by minimizing the mean squared error through 10-fold cross-validation. A total of 27 features with nonzero coefficients were retained for subsequent model development.

Results

We used 27 variables selected through LASSO regression as features for machine learning (LASSO results are shown in Figs. 1 and 2). After data preprocessing, 3613 eligible patients with sepsis from the MIMIC-IV database were randomly divided into training and internal testing sets using a stratified sampling strategy at a ratio of 70:30. Stratification was based on the binary outcome variable (occurrence of S-AKI) to ensure both sets maintained similar proportions of positive and negative cases. The training set was used for model construction and 5-fold cross-validation to optimize hyperparameters and prevent overfitting, while all data

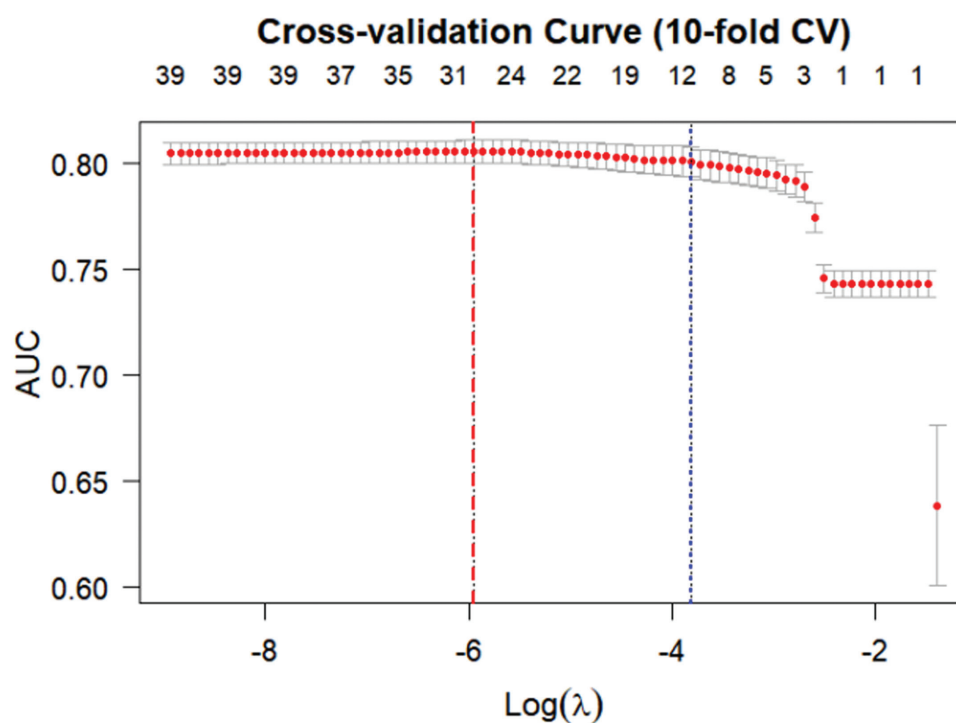


Figure 2. Screening of variables based on LASSO regression. The selection process of the optimum value of the parameter λ in the LASSO regression model by the cross-validation method. LASSO, least absolute shrinkage and selection operator.

standardization and oversampling procedures were performed exclusively within this set. The test set, which was kept completely independent, was used only to evaluate the final generalization performance of the trained models. To ensure reproducibility, a random split was conducted using the scikit-learn train_test_split function with a fixed random seed (42).

As shown in Table 1, P values for continuous variables (such as age, white blood cell count, and neutrophil count) between the training and testing sets were all >0.05 . This indicates that these variables were evenly distributed between the 2 sets, and the data splitting process maintained the randomness and representativeness of the variables. For categorical variables (such as sex, hypertension, and diabetes), the P values were also >0.05 , suggesting no statistically significant differences between the 2 groups.

We used 6 machine learning methods—logistic regression, SVM, decision tree, RF, XGBoost, and an ensemble model (RF + XGBoost)—to construct predictive models and performed 5-fold cross-validation on the training set. The 27 selected variables were used as input features. The AUC values for the 6 methods are shown in Fig. 3.

As shown in Fig. 3, the ensemble learning methods and tree-based models (such as RF and XGBoost) performed exceptionally well in this task and were particularly suited for handling complex feature data. In contrast, simpler models (such as decision trees and SVM) demonstrated lower performance and may require parameter optimization for further improvement. Among the single models, the XGBoost model exhibited the highest sensitivity (0.856) and F1 score (0.780), indicating its stronger ability to identify patients who will develop S-AKI, albeit at the expense of lower specificity (0.667). (We present the cross-validation results for the XGBoost model in the Supplementary Material, <https://links.lww.com/ECCM/A109> to evaluate its performance and stability.)

To identify the most influential features in the predictive model, we present the SHAP summary plot for the top 15 features in the XGBoost model. SHAP analysis enhances model interpretability by quantifying the contribution of each feature to the prediction. The results highlighted that mechanical ventilation was the most important predictor of AKI, and its use significantly increased the risk of AKI. Other important predictors included albumin (with lower levels associated with higher risk), Acute Physiology and Chronic Health Evaluation (APACHE) score, and age, both of which showed positive correlations with increased risk. These findings confirm that the model's decisions rely heavily on key clinical indicators, such as mechanical ventilation, albumin, APACHE score, and age, which align with clinical reasoning and support the model's practical utility and reliability.

Figures 4 and 5 reveal how each feature value influenced the model's predictions. In addition, through SHAP dependence plots, it was possible to identify high-risk patient groups, such as those using mechanical ventilation (vent flag = 1) or those with high Sequential Organ Failure Assessment scores (>10).

Discussion

In this study, we collected demographic information, laboratory results, and vital signs of patients in the MIMIC-IV database. The laboratory results, including complete blood counts and biochemical markers, were obtained from the first results within 24 hours after admission. Vital signs such as blood pressure and heart rate were recorded on the first day, with the average value used if multiple measurements were available. The outcome was AKI occurrence within 7 days, based on the Kidney Disease: Improving Global Outcomes criteria.

To avoid feature redundancy and multicollinearity, we used LASSO regression to select features most closely associated with

Table 1
Baseline Characteristics of the 2 Groups

Variables	All	Training Set (n = 2529)	Test Set (n = 1084)	P
Age (years)	66.00 (52.00–79.00)	66.00 (52.00–80.00)	66.00 (51.00–79.00)	0.546
WBC ($\times 10^9/L$)	14.00 (9.30–19.20)	13.80 (9.20–19.30)	14.30 (9.60–19.00)	0.294
Monocytes abs ($\times 10^9/L$)	0.59 (0.32–0.96)	0.59 (0.32–0.97)	0.58 (0.32–0.91)	0.333
Platelet ($\times 10^9/L$)	216.00 (148.00–304.00)	216.00 (148.96–301.00)	217.50 (148.00–311.00)	0.456
CRP (mg/L)	138.00 (135.00–141.00)	138.00 (135.00–141.00)	138.00 (135.00–141.00)	0.830
Albumin (g/dL)	2.90 (2.40–3.40)	2.90 (2.40–3.40)	2.90 (2.50–3.40)	0.640
MLR	0.59 (0.34–1.00)	0.60 (0.33–1.00)	0.58 (0.35–1.00)	0.864
APACHE score	1459.88 (529.39–3232.36)	1438.65 (525.47–3252.20)	1522.28 (539.57–3219.81)	0.571
LAR	0.68 (0.43–1.13)	0.68 (0.43–1.12)	0.67 (0.43–1.14)	0.948
SOFA score	52.15 (38.00–72.00)	53.00 (38.00–73.00)	51.39 (38.00–70.35)	0.232
Creatinine (mg/dL)	6.00 (3.59–9.00)	6.00 (3.70–9.00)	6.74 (3.88–9.18)	0.065
BUN (mg/dL)	1.00 (0.70–1.60)	1.00 (0.70–1.60)	1.00 (0.70–1.50)	0.107
pH	20.00 (12.00–35.00)	20.00 (12.00–36.00)	19.00 (12.00–34.00)	0.110
Bicarbonate (mmol/L)	7.36 (7.28–7.43)	7.36 (7.28–7.42)	7.36 (7.28–7.42)	0.904
Anion gap	22.00 (19.00–25.00)	22.00 (19.00–25.00)	23.00 (20.00–25.00)	0.161
APTT (s)	14.00 (12.00–17.00)	14.00 (12.00–17.00)	14.00 (12.00–17.00)	0.066
PT (s)	32.20 (28.10–39.97)	32.38 (28.20–40.40)	32.00 (28.00–39.05)	0.246
Avg mean arterial pressure (mm Hg)	14.90 (13.10–18.40)	15.00 (13.10–18.60)	14.90 (13.00–18.10)	0.304
Hematocrit (%)	72.88 (66.07–81.00)	72.77 (66.06–80.84)	73.00 (66.20–81.56)	0.264
Sex (male)	33.30 (29.50–37.40)	33.30 (29.50–37.40)	33.30 (29.40–37.40)	0.604
Hypertension flag	1742 (48.2%)	1211 (47.9%)	531 (49.0%)	0.568
Diabetes flag	446 (12.3%)	303 (12.0%)	143 (13.2%)	0.338
Urinary infection flag	248 (6.9%)	168 (6.6%)	80 (7.4%)	0.465
Heart failure flag	148 (4.1%)	107 (4.2%)	41 (3.8%)	0.595
Copd flag	179 (5.0%)	118 (4.7%)	61 (5.6%)	0.256
Vent flag	114 (3.2%)	69 (2.7%)	45 (4.2%)	0.032
AKI stage	1462 (40.5%)	1028 (40.6%)	434 (40.0%)	0.759
	1791 (49.6%)	1254 (49.6%)	537 (49.5%)	1.000

Data are n (%) or median (IQR).

APACHE, Acute Physiology and Chronic Health Evaluation; APTT, activated partial thromboplastin time; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; IQR, interquartile range; LAR, lactate-to-albumin ratio; MAP, mean arterial pressure; MLR, monocyte-to-lymphocyte ratio; PT, prothrombin time; SOFA, Sequential Organ Failure Assessment; WBC, white blood cell.

the occurrence of AKI in patients with sepsis, simplifying model complexity and reducing the negative impact of weakly correlated variables and multicollinearity between derived indicators. Additionally, we integrated 5 machine learning algorithms, each optimized through parameter tuning, to maximize predictive efficiency for the risk of S-AKI.

In the final algorithm group, both XGBoost (AUC: 0.835; 95% CI: 0.812–0.859) and the ensemble model of RF and XGBoost (AUC: 0.843; 95% CI: 0.820–0.866) demonstrated superior performance in predicting S-AKI within 7 days of admission. Notably, XGBoost achieved the highest sensitivity (0.856) and F1 score (0.780) among all models, indicating its exceptional capability to identify patients at risk of S-AKI—a critical attribute for an early warning system aimed at minimizing missed cases. This high sensitivity, however, came at the cost of a lower specificity (0.667). A lower positive predictive value (precision: 0.717) suggests that when the XGBoost model predicts a high risk of AKI, approximately 28% of these alerts might be false positives. This trade-off underscores a key clinical consideration: the value of early detection must be weighed against the resources and potential patient anxiety incurred by false alarms. In contrast, the ensemble model demonstrated the most balanced performance profile (accuracy: 0.758, sensitivity: 0.733, and specificity: 0.782), offering a more conservative and potentially more readily actionable risk assessment. Therefore, while XGBoost may serve as an excellent screening tool to “rule out” low-risk patients (given its high negative predictive value), its direct integration into clinical practice may require

careful calibration of the decision threshold or combination with other clinical assessments to manage the false positive rate. Future multicenter studies with larger sample sizes are warranted to refine these models, validate their generalizability, and thoroughly assess their utility and impact in diverse real-world clinical settings.

The mechanisms underlying S-AKI are complex and multifactorial, involving inadequate renal perfusion, inflammatory responses, coagulation disorders, and ischemia/reperfusion injury. These factors contribute to kidney dysfunction in patients with sepsis by disrupting normal kidney function through a combination of hemodynamic changes, immune system activation, and microvascular injury. The interplay between these mechanisms leads to progressive damage to renal tissues, making S-AKI a critical and challenging condition to predict and manage.^[20–24]

Currently, the primary diagnostic indicators of AKI in clinical practice are serum creatinine levels and urine output. However, creatinine levels are influenced by various factors such as muscle mass, dehydration, and dietary protein intake. Furthermore, when serum creatinine levels increase significantly, kidney damage is often already advanced. Urine output may be more sensitive than creatinine, as during the early stages of AKI, when the glomerular filtration rate rapidly declines to zero, urine production decreases swiftly, even leading to anuria for several hours. This can be detected quickly through clinical monitoring. However, urine output is easily influenced by factors such as the overall body fluid status, heart function, and diuretic use, which can hinder its interpretation when assessing kidney function.^[25] Therefore, it

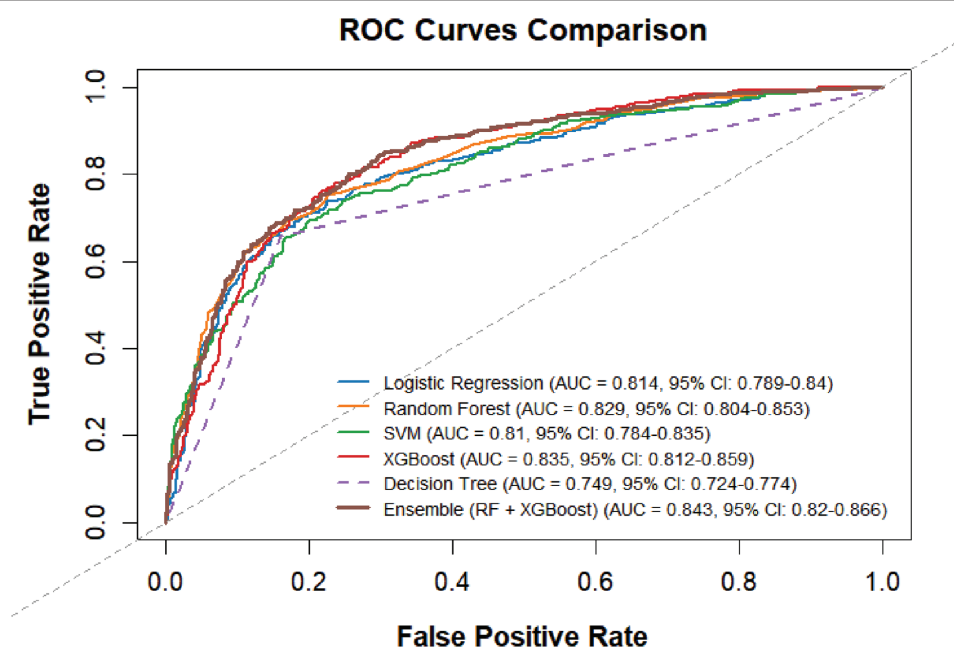


Figure 3. Receiver-operating characteristic curve (ROC) and area under the curve (AUC) values of different classification models. CI, confidence interval; RF, random forest; SVM, support vector machine; XGBoost, extreme gradient boosting.

is crucial to identify new biomarkers or diagnostic methods that can detect kidney injury early, allowing for prompt intervention.

Several novel biomarkers have been identified to assess the occurrence of AKI. These include soluble urokinase plasminogen activator receptor,^[26] NLR,^[27] insulin-like growth factor-binding protein 7 and tissue inhibitor of metalloproteinase 2,^[28, 29] neutrophil gelatinase-associated lipocalin,^[30] and kidney injury molecule-1.^[31] In addition, renal ultrasound can assess kidney blood flow and perfusion by measuring the resistance index at the level of the interlobar arteries. Studies have shown that the resistance index in patients with AKI is significantly higher than that in the control group. Ultrasound offers advantages such as being noninvasive, simple, rapid, and available at the bedside, making it a promising tool for the early diagnosis of S-AKI in the future.^[32] However, the clinical use of these diagnostic biomarkers remains limited. Therefore, in this study, we focused on the use of novel inflammatory markers derived from readily accessible routine laboratory tests to construct the predictive model.

In this model, we incorporated novel markers, such as NLR, MLR, SIRI, SII, AISI, PNI, and LAR. However, after performing LASSO regression for feature selection, only 3 features—MLR, AISI, and LAR—remained for model construction. Among these, LAR had a significant impact. In critically ill patients, elevated lactate levels indicate inadequate organ perfusion, a mechanism underlying AKI. Furthermore, lactate level is an independent risk factor for S-AKI.^[33, 34] Previous studies have shown that hypoalbuminemia increases the risk of AKI; however, the exact mechanisms are unclear.^[35] As a result, some studies have combined lactate and albumin levels to assess the risk and prognosis of S-AKI. These studies found that an elevated LAR within 12 hours before and after sepsis diagnosis is an independent risk factor for the development of S-AKI in patients with sepsis. Moreover, LAR has been identified as a prognostic risk factor for AKI in critically ill patients.^[36, 37] In the SHAP plot of this model, as the LAR increased, the risk of S-AKI significantly increased. This indicates that higher LAR values are strongly associated with a higher probability of S-AKI, reflecting worsened organ perfusion and greater systemic inflammation.

The SHAP values show how this feature contributed to the model's prediction, with higher LAR values driving the model's output toward predicting a higher risk of S-AKI in patients with sepsis.

In our model, each feature contributed either to an increase or decrease in the risk of developing S-AKI. Mechanical ventilation had the greatest impact, which may be associated with several factors. Patients who require mechanical ventilation typically have severe underlying conditions, and hypoxia caused by respiratory failure can lead to impaired renal microcirculation. Additionally, mechanical ventilation can trigger neurohormonal changes and inflammatory responses, both of which increase the risk of AKI. Collectively, these factors contribute to an increased risk of AKI in mechanically ventilated patients.^[38] In addition, factors such as mean arterial pressure, decreased albumin levels, and increased sequential organ failure assessment and APACHE scores are all associated with the occurrence of S-AKI.

In contrast to the model of Zhang et al., in which the top-ranking features were temperature, heart rate, and hemoglobin, our model focused on predicting AKI within the first 7 days of hospital admission for patients with sepsis. In contrast, the model of Zhang et al. emphasized the dynamic changes that occur 12, 24, 36, and 48 hours before the onset of S-AKI. Therefore, their model likely places more emphasis on dynamic indicators that show substantial variation over time. The novel markers we included in our model also play a crucial role, offering new directions for feature selection in future model development. This not only underscores the importance of these indicators for clinicians but also highlights the need for early intervention. By focusing on such markers, clinicians can initiate proactive treatments, potentially reducing the incidence of S-AKI and improving patient prognosis.

Limitations

This study has several limitations. First, this was a retrospective study. Future prospective experiments are needed to confirm the validity of the results. Second, we constructed an S-AKI predictive

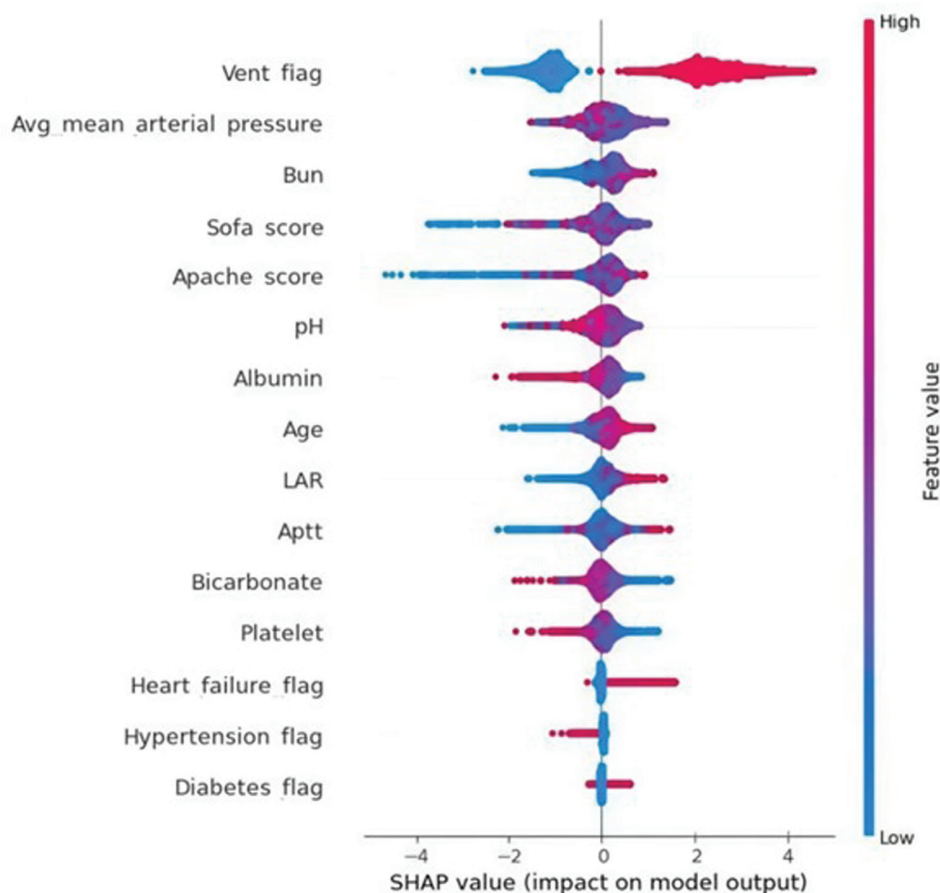


Figure 4. The SHAP summary plot for the top 15 features in the XGBoost model. In this plot, the higher the SHAP value for a feature, the greater the likelihood of developing AKI. For each patient, a point is created for each feature attribute value in the model. These points are assigned to a feature's line, and they are vertically stacked to represent the density of feature values. Points are colored based on the corresponding feature values: red indicates higher values, and blue indicates lower values. Positive SHAP values indicate that the feature increases the likelihood of the model predicting the positive class (eg, AKI). Negative SHAP values suggest that the feature decreases this probability (eg, AKI). Example: For the feature vent flag (whether mechanical ventilation is used), red (higher values) corresponds to positive SHAP values, indicating that mechanical ventilation increases the risk of AKI. Conversely, lower values (blue) would correspond to negative SHAP values, reducing the probability of AKI. AKI, acute kidney injury; BUN, blood urea nitrogen; LAR, lactate-to-albumin ratio; SHAP, SHapley Additive exPlanations; XGBoost, extreme gradient boosting.

model using data from the MIMIC-IV database. Although the dataset was large, it lacked external data validation. Although we adjusted the relevant model parameters to reduce internal learning rate bias, external data validation will be necessary in the future. Finally, we only collected data from the first 24 hours after patient admission, which led to the exclusion of many key features due to missing data, potentially impacting model accuracy.

Conclusion

This study developed an early warning model for S-AKI by combining novel indicators, such as LAR, NLR, and AISI. The model demonstrated good performance in predicting the occurrence of S-AKI and provided new insights into feature selection in future models.

Conflict of interest statement

The authors declare no conflict of interest.

Author contributions

Zhang Y was responsible for acquiring the database, data extraction, curation, validation, and wrote the original draft of

the manuscript. Han X conceived, designed, and supervised the study. Lu S and Zeng Y performed formal analysis and investigation. Zhou Z conducted statistical analyses and created visualizations. Xu X and Fan M assisted in methodology development and project administration. Yan X and Zhu Y reviewed and edited the manuscript, and provided critical intellectual content. All authors have reviewed and approved the final manuscript.

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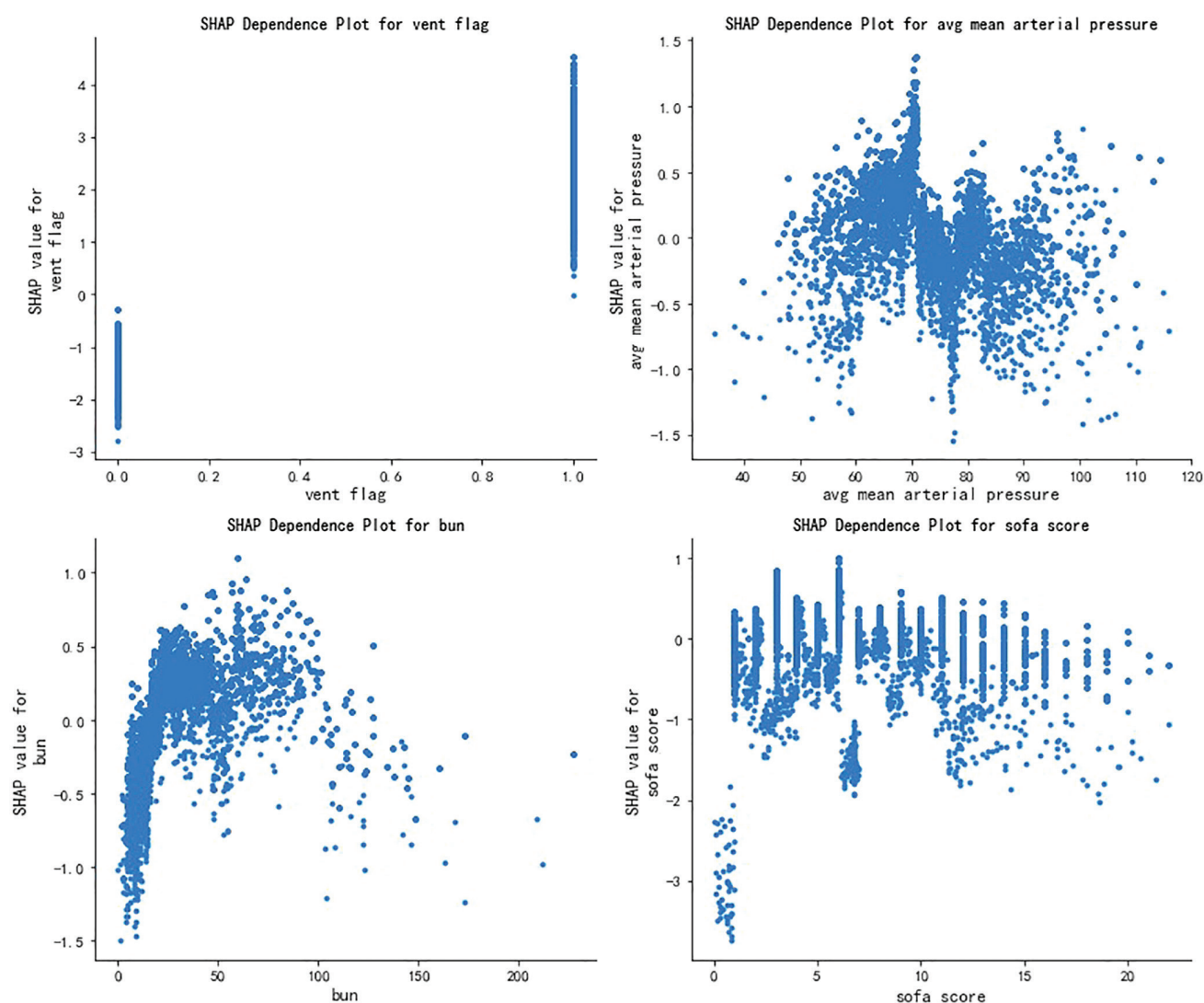


Figure 5. The SHAP Dependence Plot for 4 key features in the XGBoost model. X-axis: The feature value, vent flag, indicates whether mechanical ventilation was used (0 = not used, 1 = used). Y-axis: The SHAP value, representing the feature's influence on model prediction. When the vent flag = 1 (indicating mechanical ventilation was used), the SHAP value is significantly positive, suggesting the use of mechanical ventilation notably increases model prediction of the positive class (high risk of AKI). Conversely, when the vent flag = 0 (mechanical ventilation not used), the SHAP value is negative, indicating that patients who did not require mechanical ventilation have a lower risk of AKI. AKI, acute kidney injury; SHAP, SHapley Additive exPlanations; SOFA, sequential organ failure assessment; XGBoost, extreme gradient boosting.

Ethical approval of studies and informed consent

All the data were sourced from the MIMIC-IV database. Zhang Y extracted data after completing online training (certification number 64967484) and passing the exam on the website. The ethics activities of MIMIC-IV have been approved.

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