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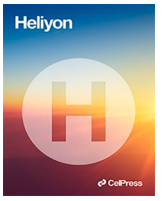

Machine learning predictors of risk of death within 7 days in patients with non-traumatic subarachnoid hemorrhage in the intensive care unit: A multicenter retrospective study

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A R T I C L E I N F O

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A B S T R A C T

Non-traumatic subarachnoid hemorrhage (SAH) is a critical neurosurgical emergency with a high mortality rate, imposing a significant burden on both society and families. Accurate prediction of the risk of death within 7 days in SAH patients can provide valuable information for clinicians, enabling them to make better-informed medical decisions. In this study, we developed six machine learning models using the MIMIC III database and data collected at our institution. These models include Logistic Regression (LR), AdaBoosting (AB), Multilayer Perceptron (MLP), Bagging (BAG), Gradient Boosting Machines (GBM), and Extreme Gradient Boosting (XGB). The primary objective was to identify predictors of death within 7 days in SAH patients admitted to intensive care units. We employed univariate and multivariate logistic regression as well as Pearson correlation analysis to screen the clinical variables of the patients. The initially screened variables were then incorporated into the machine learning models, and the performance of these models was evaluated. Furthermore, we compared the performance differences among the six models and found that the MLP model exhibited the highest performance with an AUC of 0.913. In this study, we conducted risk factor analysis using Shapley values to identify the factors associated with death within 7 days in patients with SAH. The risk factors we identified include Gcsmotor, bicarbonate, wbc, spo2, heartrate, age, nely, glucose, aniongap, GCS, rbc, sysbp, sodium, and gcseys. To provide clinicians with a useful tool for assessing the risk of death within 7 days in SAH patients, we developed a web calculator based on the MLP machine learning model.

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1. Introduction

Non-traumatic subarachnoid hemorrhage (SAH) is a common and fatal neurosurgical condition, with ruptured aneurysms accounting for approximately 85 % of cases and a mortality rate that can reach up to 45 % [1]. The main risk factors include sudden hypertension [2], smoking, and excessive alcohol consumption [3,4]. Early mortality in SAH is extremely high, with rates reaching 50 % within one month and up to 35 % within 7 days [5,6]. Patients with SAH admitted to the ICU are often in critical condition, and identifying the risk of death within 7 days and high mortality risk predictors at an early stage is crucial for guiding treatment decisions. Usually, the information available to us at the time of patient admission is very limited, with only the patient's vital signs, Glasgow Coma Scale(GCS), and laboratory tests. This study attempts to find predictors associated with patient death within 7 days by collecting this information.

However, the vast amount of information available at the time of admission for SAH patients can present significant challenges when using traditional statistical methods. Machine learning (ML) algorithms have been widely adopted to handle medical big data and are well-suited to address such challenges [7–11]. Although previous studies have developed prognostic models for patients with subarachnoid hemorrhage (SAH), their discriminative ability was limited (the area under the receiver operating characteristic curve [AUC] was 0.76), which hinders their effectiveness in clinical practice [12]. Moreover, there is a lack of research on predicting mortality within 7 days of onset in patients with SAH, we first selected six machine learning algorithms with good performance and identified the optimal algorithm applicable to our study to construct a prediction model for 7-day mortality in SAH patients.

Thus, the objective of this study was to utilize ML algorithms to identify highly effective predictors of early mortality (within 7 days) in SAH patients in the ICU, as well as externally validate the machine learning algorithm models. Moreover, we developed a user-friendly web calculator to aid clinicians in predicting the risk of death within 7 days for patients at an early stage.

2. Objects and methods

2.1. Study subjects and data Sources

In this study, we retrospectively collected a total of 548 patients diagnosed with SAH, comprising 341 cases in the training set and 207 cases in the test set.

The training set patient data was obtained from the MIMIC-III database (Medical Information Mart for Intensive Care III), a large multicenter database of critical care data published by the MIT (Massachusetts Institute of Technology) Computational Physiology Laboratory. The database contains comprehensive information, including basic demographic data, diagnostic and treatment information, laboratory test data, and care record data, on nearly 60,000 patients at Beth Israel Deaconess Medical Center from 2008 to 2012 [13]. To access the MIMIC-III database, we completed a web-based course provided by the National Institutes of Health (NIH), obtained the Collaborative Institutional Training Initiative (CITI Program) completion report certificate (certification number:

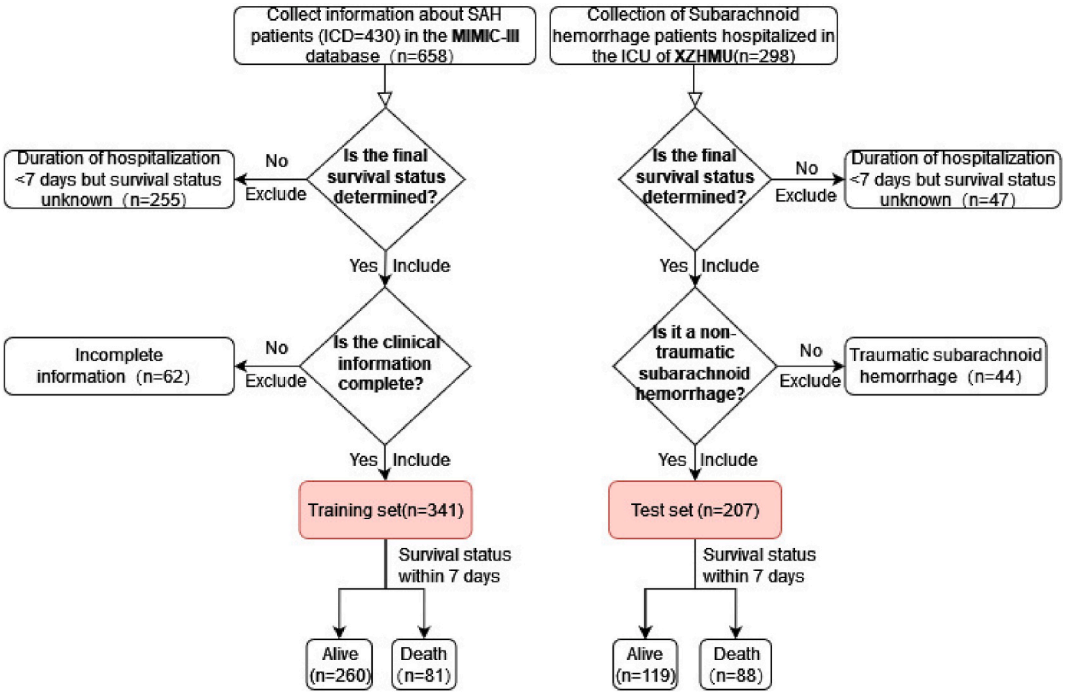

Fig. 1. Flowchart of data filtering process.

11771857), and submitted a complete application. The data extraction was conducted using Structured Query Language (SQL) [14] based on PostgreSQL (UC Berkeley version 9.6). The current data extraction was mainly from two systems: MetaVision and CareVue. In this study, only data recorded within 24 h after admission of some patients were extracted from the MetaVision system for analysis to improve the consistency and reliability of the data.

The test set for external validation of the model comprised 207 patients admitted and diagnosed with SAH at the ICU of XZHMU between January 2021 and December 2022.

The Ethics Committee of XZHMU reviewed the study (ethics number XYFY2022-KL457-01), and the Institutional Review Boards of Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center approved the creation and use of the MIMIC-III database. Informed consent was not required.

2.2. Data collection

To select the training set data, we employed PostgreSQL (UC Berkeley version 9.6) and Structured Query Language (SQL) [14] to extract comprehensive clinical information, such as basic information, vital signs, and laboratory test data, from the MIMIC-III database for each patient. By applying the International Classification of Diseases, 9th edition (ICD-9) code = 430, we identified 658 patients.

Data inclusion and exclusion criteria for the test set: The diagnosis of SAH was confirmed by a neurosurgeon after a computed tomography scan and reviewed by a radiologist. Inclusion criteria were as follows: (1) confirmed diagnosis of non-traumatic subarachnoid hemorrhage; (2) first hospitalization and admission to the intensive care unit. Exclusion criteria were as follows: (1) traumatic subarachnoid hemorrhage; (2) incomplete clinical data and inadequate ancillary tests; (3) previous history of serious underlying diseases, such as severe heart disease, liver and kidney insufficiency, etc.; (4) those who voluntarily give up treatment within 7 days.

The data collection process for the training and test sets is depicted in Fig. 1.

2.3. Determination of patients' outcome

In this retrospective study, the primary outcome was the occurrence of mortality within 7 days of admission to the ICU for SAH patients. Previous research indicates that the 7-day mortality rate for SAH patients is approximately 35 % [6]. The study aimed to identify high-risk patients for early mortality, which would enable physicians to provide timely interventions and inform the patient's family about the patient's condition, thereby reducing physician-patient conflicts and the burden of disease.

2.4. Inclusion of variables

In this study, clinical data of SAH patients were retrospectively collected, and the final data included basic information about patients, such as gender and age; vital signs such as temperature, heart rate, respiration, blood pressure, and GCS at the time of admission; in addition, laboratory test data of enrolled patients were collected, such as blood routine (white blood cells, Wbc; red blood cells, Rbc; Hemoglobin; Hematocrit; Platelets; neutrophil to lymphocyte ratio, NLR), coagulation function (partial thromboplastin time, Ptt; international normalized ratio, Inr; prothrombin time Pt), blood biochemistry (Creatinine; blood urea nitrogen, BUN; Chloride; Potassium; Sodium; Glucose) and blood gas analysis (potential of hydrogen, Ph; partial pressure of carbon dioxide, Pco2; Pulse Oxygen Saturation, Spo2; Aniongap; Bicarbonate). These indicators have been reported in previous studies to potentially correlate with survival prognosis in patients with cerebral hemorrhage [9–11,15–17].

2.5. Statistical processing and ML algorithms for model construction and validation

This study was statistically analyzed using R software (version 3.6.1) and Python software (version 3.4.3). Package CBCgrps (version 2.8.2); corrplot (version 0.92) in R. pandas(version 1.4.1); scikit-learn (version 1.1.1); streamlit (version 1.8.1); numpy (version 1.20.3); matplotlib (version 3.5.1); joblib(version 1.1.0); shap(version 0.41.0); seaborn (version 0.11.2) in Python. In this study, all variables in the training and test sets were statistically analyzed. Continuous variables were expressed as median and interquartile range IQR and compared using the Mann-Whitney *U* test, and categorical variables were expressed as frequencies (percentages, %) and compared using chi-square tests. Correlations between the two variables were analyzed using Pearson correlation analysis; variables that were statistically different from the outcome were identified using univariate and multifactorial logistic regression. A two-sided $P < 0.05$ was considered a statistically significant difference.

We used six machine learning methods to build models in the training set, namely LR, AB, MLP, BAG, GBM, and XGB. The performance of the models was subsequently tested in the test set, and the evaluation of model performance was done by the area under the subject's working characteristic curve (AUC), and the precision-recall (PR) curve was used to evaluate the imbalance data The accuracy of different ML algorithm models and the calibration curve was used to evaluate the prediction performance of different models. In addition, we calculated Accuracy, Sensitivity, Specificity, and F1-score for each of the six models to further evaluate the models. For the best-performing models, we determined and reported the importance of the model parameters by plotting Shapley additive interpretation (SHAP) plots.

To facilitate clinical use, we constructed an accessible web calculator.

3. Results

3.1. Baseline characteristics

After screening, a total of 548 patients were included in this study, 341 in the training set and 207 in the test set; mortality within 7 days was 31 % in all patients, compared to 24 % in the training set and 43 % in the test set. The median age of patients in this study was 61 (50.75,71) years, and in terms of gender distribution, there were 233 (43 %) males and 315 (57 %) females. More details about the baseline characteristics of patients' GCS scores, vital signs, and laboratory indicators are presented in Table 1. Results after comparing baseline characteristics between the two groups suggested that GCS, Gcsmotor, Gcseys, Heartrate, Meanbp, Resprate, Tempc, Spo2, Aniongap, Bicarbonate, Creatinine, Glucose, Chloride Hematocrit, Hemoglobin, Platelet, Ptt, Inr, Pt, Sodium, Bun, Wbc, and NLR were statistically different between the two groups (two-sided $P < 0.05$).

3.2. Variable filtering

To exclude redundant and non-relevant variables, we used logistic regression analysis and Pearson correlation analysis to screen the variables. As shown in Table 2, the univariate logistic regression analysis suggested that: GCS, Gcsmotor, Gcsverbal, Gcseyes, Heartrate, Sysbp, Diasbp, Resprate, Tempc, Spo2, Aniongap, Bicarbonate Creatinine, Glucose, Potassium, Sodium, Wbc, Rbc, Ph, and NLR were statistically associated with patient death within 7 days ($P < 0.05$); further multivariate regression analysis of the results from the above univariate analysis suggested that Gcsmotor (OR0.796,95 % CI 0.596–0.992, $p = 0.043$), Spo2 (OR0.96, 95 % CI 0.932–0.99, $p = 0.009$), Bicarbonate (OR0.861, 95 % CI 0.755–0.982, $p = 0.025$), Potassium (OR0.368, 95 % CI 0.153–0.885, $p = 0.026$), Wbc (OR0.924, 95 % CI 0.867–0.985, $p = 0.015$), Rbc (OR2.047, 95 % CI 1.229–3.411, $p = 0.006$), Ph (OR0.01, 95 % CI 0–0.932, $p = 0.047$), and NLR (OR1.045,95%CI 1.012–1.079, $p = 0.006$) were statistically associated with patient death within 7 days and suggest that these factors may be independent risk factors for patient death.

The strength of the correlation between variables was evaluated using a heat map generated through Pearson correlation analysis. Our findings indicated that Age, GCS, Gcsmotor, Gcsverbal, Gcseyes, Heartrate, Meanbp, Spo2, Bicarbonate, Chloride, Glucose,

Table 1
Comparison of baseline data for training and test sets.

Variables	Total (n = 548)	Train group (n = 341)	Test group (n = 207)	P
group, n (%)				<0.001
Live	379 (69)	260 (76)	119 (57)	
Death	169 (31)	81 (24)	88 (43)	
gender, n (%)				0.787
Female	315 (57)	194 (57)	121 (58)	
Male	233 (43)	147 (43)	86 (42)	
age, Median (Q1,Q3) (year)	61 (50.75, 71)	59 (49, 70)	63 (52.5, 72)	0.042
mingcs, Median (Q1,Q3)	13 (5, 15)	15 (12, 15)	3 (3, 8)	<0.001
gcsmotor, Median (Q1,Q3)	4 (1, 6)	5 (4, 6)	1 (1, 3)	<0.001
gcsverbal, Median (Q1,Q3)	1 (1, 4)	1 (0, 5)	1 (1, 2)	0.086
gcseyes, Median (Q1,Q3)	1 (1, 3)	2 (1, 3)	1 (1, 3)	<0.001
heartrate, Median (Q1,Q3) (bpm)	92 (81, 106)	98 (88, 111)	83 (78, 95.5)	<0.001
sysbp, Median (Q1,Q3) (mmHg)	160 (143, 177.25)	161 (145, 177)	157 (138.5, 177)	0.062
diasbp, Median (Q1,Q3) (mmHg)	87 (77, 96)	88 (77, 97)	86 (79, 94.5)	0.299
meanbp, Median (Q1,Q3) (mmHg)	100 (79, 115)	109 (99, 122)	70 (57, 83.5)	<0.001
resprate, Median (Q1,Q3) (bpm)	22 (19, 27)	25 (22, 29)	19 (16, 20)	<0.001
tempc, Median (Q1,Q3) (°C)	37.2 (36.7, 37.8)	37.6 (37.1, 38.1)	36.7 (36.5, 37)	<0.001
spo2, Median (Q1,Q3) (mmHg)	96 (92, 106)	95 (92, 97)	133 (94.3, 173)	<0.001
aniongap, Median (Q1,Q3) (mmol/L)	14 (11, 17)	16 (14, 18)	9.9 (8.5, 12.4)	<0.001
bicarbonate, Median (Q1,Q3) (mmol/L)	22.7 (20, 24.9)	22 (19, 24)	23.8 (21.65, 25.65)	<0.001
creatinine, Median (Q1,Q3) (umol/L)	69 (53, 88.4)	70.7 (61.9, 97.2)	58 (47, 70)	<0.001
chloride, Median (Q1,Q3) (mmol/L)	104 (101, 108)	103 (101, 106)	107 (103, 111)	<0.001
glucose, Median (Q1,Q3) (mmol/L)	9.2 (7.6, 11.53)	9.4 (8, 11.9)	8.6 (6.95, 10.9)	<0.001
hematocrit, Mean ± SD(%)	34.21 ± 5.96	33.24 ± 5.43	35.8 ± 6.46	<0.001
hemoglobin, Mean ± SD(g/L)	115.68 ± 20.46	113.64 ± 19.05	119.04 ± 22.24	0.004
platelet, Median (Q1,Q3) (10^9/L)	228 (174, 289)	250 (203, 317)	199 (150, 247)	<0.001
potassium, Median (Q1,Q3) (mmol/L)	3.6 (3.2, 3.9)	3.5 (3.2, 3.8)	3.6 (3.2, 3.9)	0.256
ptt, Median (Q1,Q3) (sec)	26.7 (24.4, 30.92)	27.6 (24.6, 37.5)	25.6 (24.1, 27.95)	<0.001
inr, Median (Q1,Q3)	1.1 (1, 1.2)	1.2 (1.1, 1.3)	0.99 (0.96, 1.08)	<0.001
pt, Median (Q1,Q3) (sec)	12.8 (11.6, 13.9)	13.4 (12.6, 14.3)	11.4 (10.85, 12.3)	<0.001
sodium, Median (Q1,Q3) (mmol/L)	141 (139, 144)	142 (139, 145)	140 (138, 144)	0.001
bun, Median (Q1,Q3) (mmol/L)	5.3 (4.08, 7.1)	5.4 (4.3, 7.5)	4.91 (3.92, 6.4)	0.005
wbc, Median (Q1,Q3) (10^9/L)	13.1 (10, 17.15)	14 (10.3, 17.9)	12 (9.1, 15.95)	<0.001
rbc, Median (Q1,Q3) (10^12/L)	3.9 (3.32, 4.4)	3.82 (3.32, 4.34)	3.98 (3.33, 4.46)	0.073
ph, Median (Q1,Q3)	7.42 (7.37, 7.46)	7.43 (7.38, 7.46)	7.41 (7.37, 7.45)	0.098
pco2, Median (Q1,Q3) (mmol/L)	36.2 (33, 41)	36 (32, 41)	36.8 (33.25, 40.85)	0.726
NPR, Median (Q1,Q3)	8.6 (4.9, 14)	7 (3.6, 11.7)	12.3 (7.6, 20.85)	<0.001

Table 2
The result of Univariate and Multivariate logistic regression analysis for training set.

Characteristics	Category	Univariate logistic analysis		Multivariate logistic analysis	
		OR (95 % CI)	P value	OR (95 % CI)	P value
Gender	Female	Ref	Ref	Ref	Ref
	Male	1.395 (0.845–2.302)	0.193	\	\
Age	\	1.023 (1.005–1.041)	0.013	1.025 (0.998–1.052)	0.07
GCS	\	0.907 (0.853–0.965)	0.002	0.94 (0.861–1.026)	0.168
Gcsmotor	\	0.555 (0.482–0.64)	<0.001	0.769 (0.596–0.992)	0.043
Gcsverbal	\	0.6 (0.507–0.711)	<0.001	0.876 (0.648–1.184)	0.389
Gcseyes	\	0.384 (0.287–0.513)	<0.001	0.797 (0.476–1.333)	0.387
Heartrate	\	1.03 (1.017–1.044)	<0.001	1.013 (0.992–1.035)	0.224
Sysbp	\	1.01 (1–1.02)	0.046	1.002 (0.988–1.015)	0.823
Resprate	\	1.033 (1.001–1.067)	0.046	1.031 (0.987–1.078)	0.171
Tempc	\	1.359 (1.009–1.831)	0.043	1.008 (0.655–1.553)	0.971
Spo2	\	0.966 (0.944–0.988)	0.002	0.96 (0.932–0.99)	0.009
Aniongap	\	1.217 (1.122–1.32)	<0.001	1.049 (0.914–1.204)	0.498
Bicarbonate	\	0.823 (0.761–0.891)	<0.001	0.861 (0.755–0.982)	0.025
Creatinine	\	1.006 (1.001–1.01)	0.019	1.002 (0.997–1.006)	0.399
Glucose	\	1.193 (1.116–1.276)	<0.001	1.082 (0.99–1.181)	0.081
Potassium	\	0.393 (0.221–0.697)	0.001	0.368 (0.153–0.885)	0.026
Sodium	\	1.111 (1.062–1.163)	<0.001	1.031 (0.964–1.104)	0.373
Wbc	\	1.05 (1.015–1.086)	0.005	0.924 (0.867–0.985)	0.015
Rbc	\	1.869 (1.323–2.64)	<0.001	2.047 (1.229–3.411)	0.006
Ph	\	0.006 (0–0.147)	0.002	0.01 (0–0.932)	0.047
NLR	\	1.057 (1.025–1.09)	<0.001	1.045 (1.012–1.079)	0.006
Meanbp	\	1 (0.992–1.009)	0.968	\	\
Hematocrit	\	1.012 (0.966–1.059)	0.622	\	\
Hemoglobin	\	1.001 (0.988–1.014)	0.886	\	\
Diasbp	\	1.003 (0.99–1.016)	0.669	\	\
Ptt	\	1 (0.993–1.008)	0.89	\	\
Inr	\	1.159 (0.845–1.591)	0.36	\	\
Chloride	\	0.976 (0.935–1.019)	0.272	\	\
Bun	\	1.058 (0.999–1.12)	0.053	\	\
Platelet	\	0.998 (0.995–1)	0.058	\	\
Pco2	\	1.002 (0.969–1.037)	0.892	\	\
Pt	\	1.021 (0.98–1.064)	0.312	\	\

Platelet, Sodium, Wbc, Rbc, Ph, and NLR were highly correlated with the outcome variable. Please refer to Figs. 2 and 3 for detailed results.

Based on these findings, we decided to include the results of the univariate logistic regression analysis in our machine learning algorithm for further analysis.

3.3. Performance comparison of six ML algorithms

In order to obtain an optimal prediction model, we utilized six different ML algorithms, including LR, AB, MLP, BAG, GBM, and XGB, in this study. We compared the performance of the six algorithms and performed external validation on independent datasets that were separate from the training set. Fig. 4(A and B) shows that the MLP algorithm model had higher AUC values compared to the other five algorithms in both the training set (AUC = 0.977) and the test set (AUC = 0.913). In addition, the PR curves for the MLP machine learning algorithm had the highest area under the curve: 0.946 for the training set and 0.733 for the test set [Fig. 5(A and B)]. The calibration curve plots for the different machine learning algorithms [Fig. 6(A and B)] showed that the MLP algorithm had the highest coherence with the ideal prediction curve in both the training and test sets. We also utilized a radar plot that visualizes the comprehensive performance of the six machine learning algorithms simultaneously, as shown in Fig. 7 and Table 3. The results indicated that the MLP algorithm had the best performance.

Therefore, we selected the MLP algorithm to screen the predictors of death within 7 days in SAH patients. To understand the performance of the MLP algorithm model, we use 5-fold cross-validation as a resampling method in the training set data to perform internal validation. In each iteration, every 4 folds were used as a training subset, and the remaining 1 fold was processed to adjust the hyperparameters. The validation results showed that the MLP algorithm had good predictive power, with an average AUC value of 0.90 $\pm$ 0.028, as detailed in Fig. 8. Additionally, Fig. 9(A and B) shows the confusion matrix of the optimal classifier in MLP.

3.4. Interpretability analysis

In order to explain the MLP model more intuitively and concisely, we introduce SHAP in the article [18]. The feature density scatter plot shows us which variables influence the final output of the model; each row on the vertical coordinate represents a feature, and the horizontal coordinate is the SHAP value. The red dots represent the higher feature values and the blue dots represent the lower feature

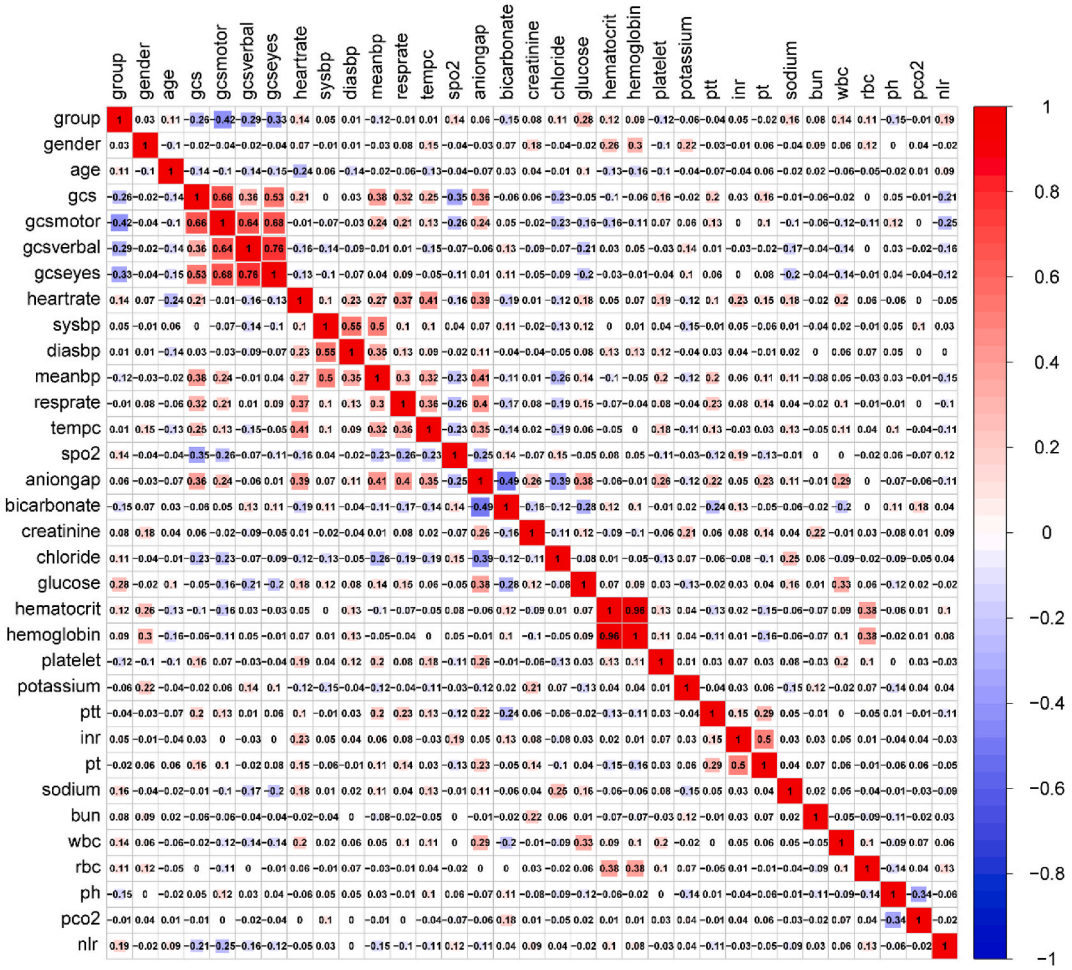

Fig. 2. Pearson correlation analysis among variables.

values. The results suggest that lower Gcsmotor and Gcsverbal scores, as well as lower Bicarbonate levels, Wbc values, and Spo2, and higher Heartrates, have high SHAP values, indicating a higher likelihood of death in patients with SAH.; More details are shown in Fig. 10(A); Fig. 10(B) depicts the importance ranking of each covariate in the final prediction model development. Fig. 11(A and B) illustrates the interpretation of the MLP model for two case predictions. Red features in the figure indicate an increased risk of death, while blue features indicate a decreased risk of death. The length of the arrow reflects the extent of influence on the predicted mortality.

3.5. Creation of the web calculator

In this study, we developed a web-based online calculator (https://ml-hemorrhage-web-hemorrhage-web-edugwe.streamlit.app/) (shown in Fig. 12) using the MLP algorithm model to facilitate the use of the model by clinicians. The calculator predicts the probability of death within 7 days based on clinical characteristic variables of patients with SAH, which can be easily inputted into the tool.

4. Discussion

In this study, we collected data on 956 patients, but excluded 408 cases due to incomplete information and uncertainty about the outcome of death, leaving 548 cases for analysis. Among these cases, we included data from an independent test set in the ICU of our institution. Using the MLP algorithm, we successfully constructed a predictive model for death within 7 days in patients with SAH. We visualized the model using SHAP analysis and demonstrated its use with a web-based online calculator (Fig. 12). Our results suggest that factors such as Gcsmotor, Bicarbonate, Wbc, Spo2, Heartrate, Age, NLR, Glucose, Aniongap, GCS, Rbc, Sysbp, Sodium, and Gcseyes at the time of patient admission can suggest an extremely poor general status after the onset of SAH and an elevated risk of death within 7 days of its occurrence. Furthermore, the MLP classifier significantly improved the discriminatory performance of predicting whether SAH patients would die within 7 days.

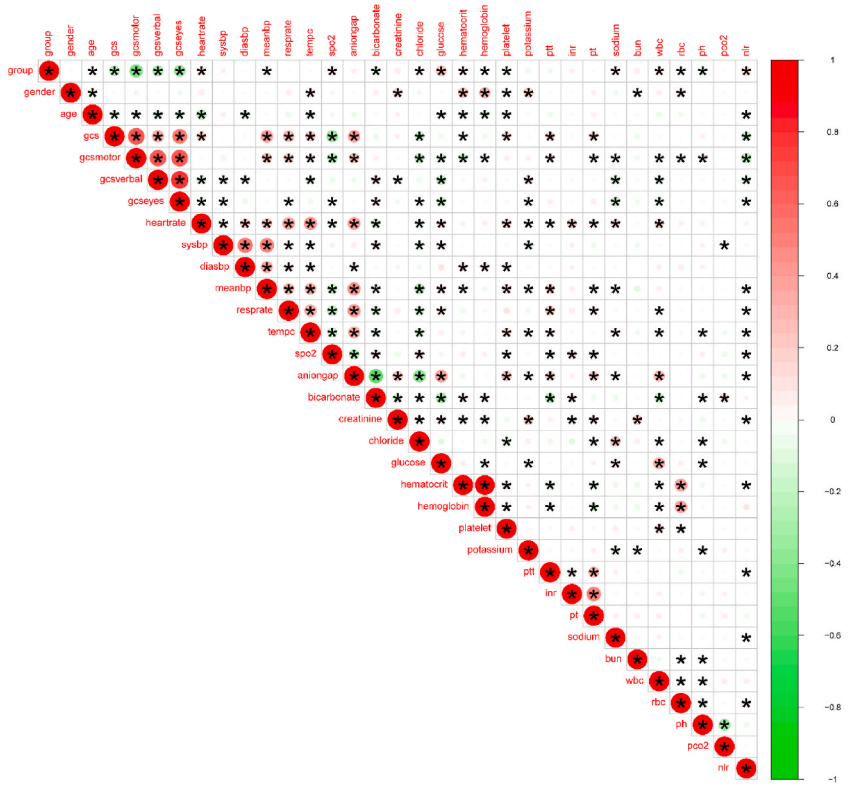

Fig. 3. Pearson correlation analysis, statistically significant indicators are marked with *.

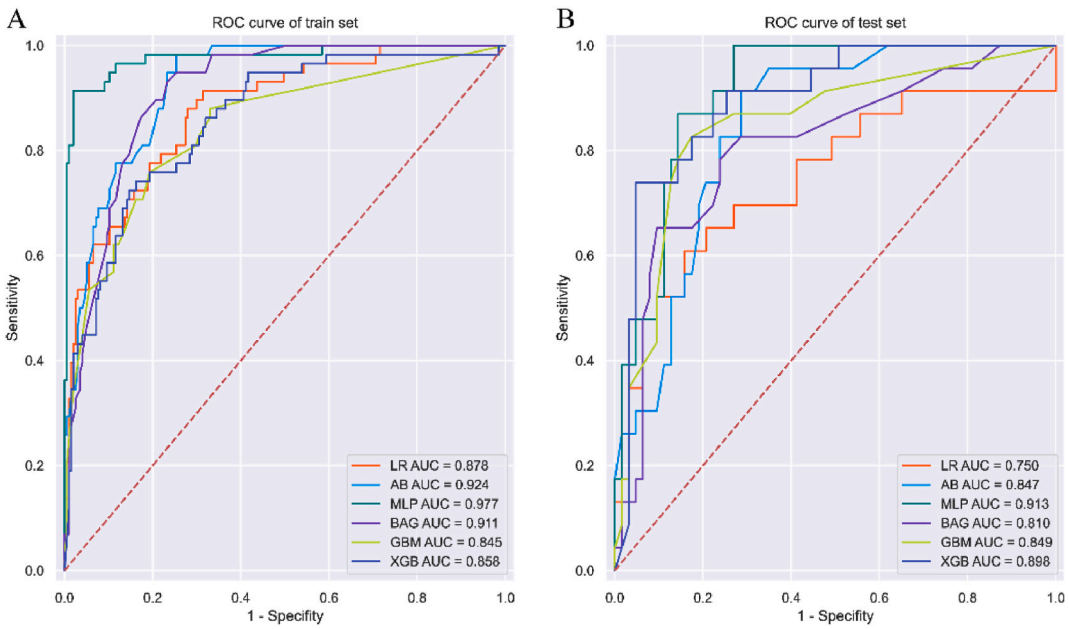

Fig. 4. ROC curve analysis of six ML algorithms for training set (A) and test set (B).

Although laboratory tests are conducted according to clinical requirements, processing the numerous data entries can be tedious from a comprehensive statistical analysis perspective. Previous research with medical big data has shown that machine learning algorithms generally outperform traditional statistical models [9], allowing for simultaneous analysis of a large number of variables and handling nonlinear relationships and complex interactions between variables [19]. In this study, we compared the performance of six

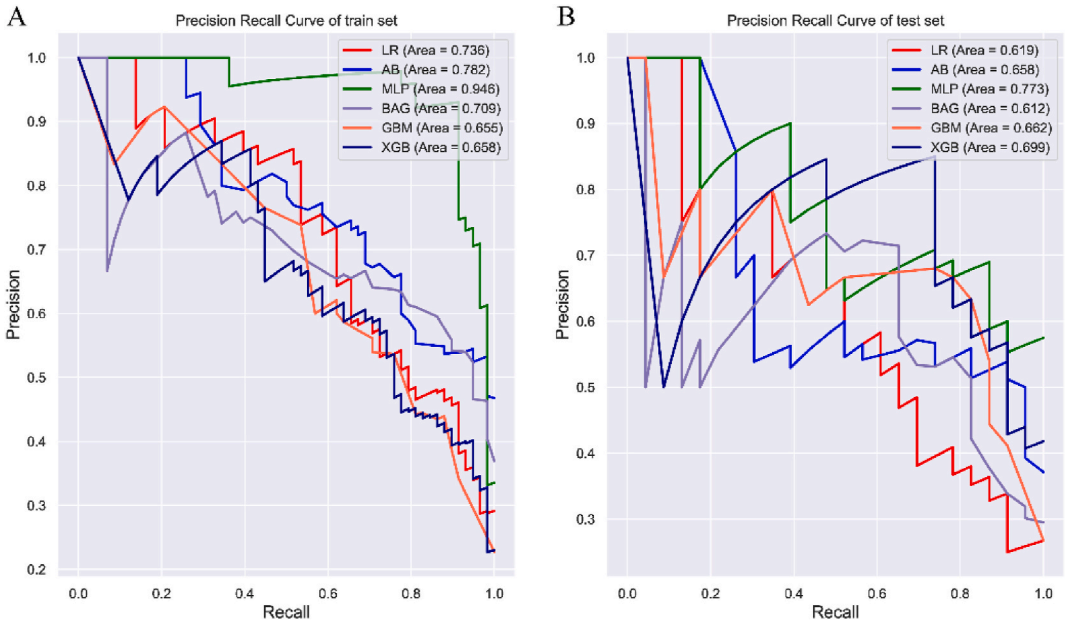

Fig. 5. Analysis of PR curves of six ML algorithms for training set (A) and test set (B).

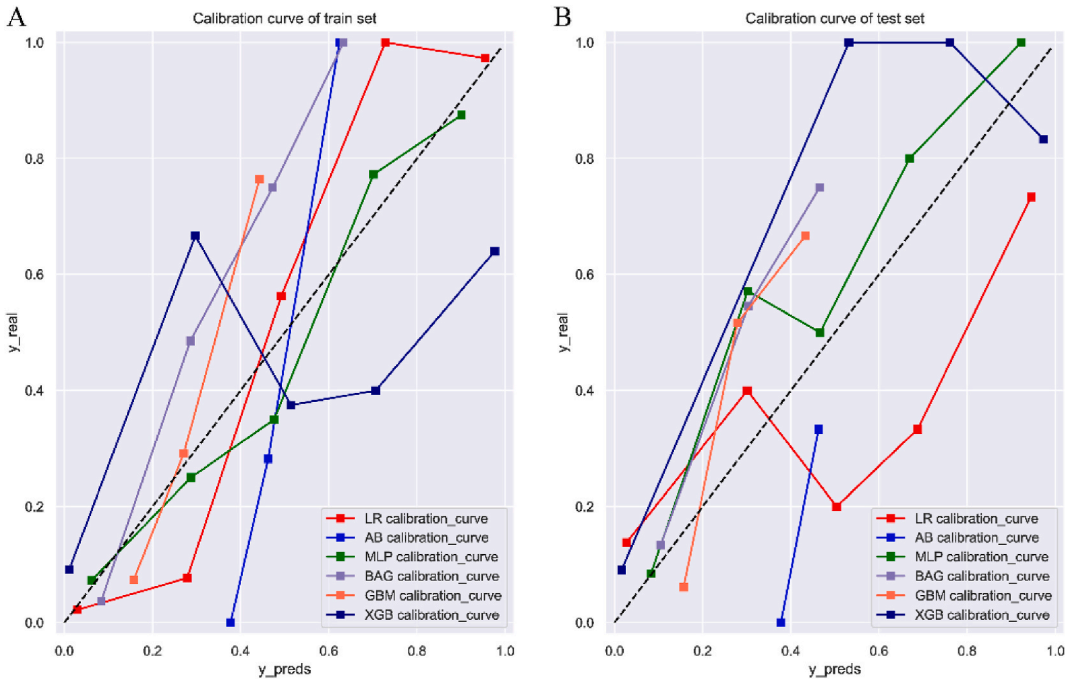

Fig. 6. Comparison of calibration curves of six ML algorithms for the training set (A) and test set (B).

ML algorithms, including LR, AB, MLP, BAG, GBM, and XGB, to model the survival outcomes of the study data. Our results showed that the MLP model performed the best, with an AUC of 0.913, accuracy of 0.895, sensitivity of 0.739, specificity of 0.952, and F1 score of 0.86 for external validation in the test set. The comparison of model effectiveness is detailed in Table 3, and the average ROC value of the MLP model during internal validation was 0.90 ± 0.028.

MLP is one of the simplest forms of artificial neural networks; it simulates the properties of the nervous system and biological learning functions through an adaptive process and is a general function approximation method that can be used to fit complex functions or to solve classification problems, and is considered a standard supervised learning algorithm in the field of pattern recognition [20–22]. We offer SHAP analysis, a novel technique to interpret multiple black-box ML models that have previously been

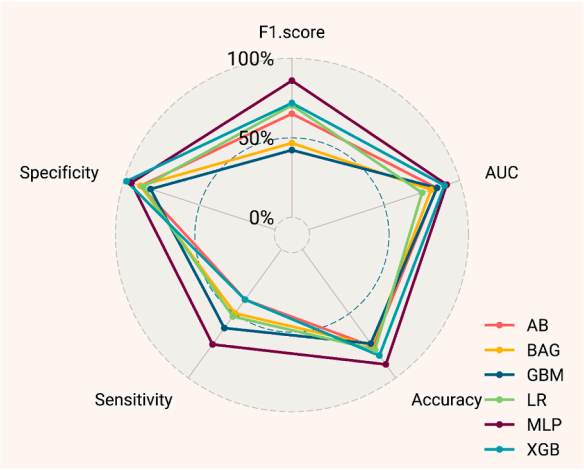

Fig. 7. Radar plot of six ML methods.

Table 3
Performance comparison of six machine learning (ML)models.

Model	F1 score	AUC	Accuracy	Sensitivity	Specificity
AB	0.652	0.847	0.756	0.391	0.889
LR	0.705	0.75	0.779	0.522	0.873
BAG	0.467	0.81	0.744	0.498	0.892
MLP	0.86	0.913	0.895	0.739	0.952
GBM	0.423	0.849	0.733	0.612	0.824
XGB	0.719	0.898	0.826	0.391	0.984

verified based on their interpretability performance, to interpret the outcomes of machine learning algorithms. When compared to other methods, it has a strong theoretical foundation and allows for both local and global interpretability [23–25]. The model prediction results can be explained effectively by the SHAP analysis utilized in this study, and its intuitive depiction is more appealing [26]. A web-based calculator was further constructed to estimate the probability of death within 7 days in spider blood patients to better utilize the model.

Previously, some scholars also constructed the same type of model and got good results. However, in comparison, our model performs quite well in terms of AUC, accuracy, and specificity, which is better than the results in the articles by other scholars [7,10,11, 27,28]. And the performance in terms of sensitivity was slightly worse than the articles by Esther Wu et al. [11] and Han et al. [27]. Overall, the performance of the model we developed is higher than that of similar studies. Supplementary Table 1 shows more information about these articles.

The model in this study incorporates a range of clinical indicators, among which we believe that the GCS motor score correlates most strongly with patient survival outcomes. Teasdale and Jennett first created the GCS score in 1974, and it is now frequently used to assess the severity of the illness and the prognosis of SAH patients [29–31]. The Glasgow Coma Scale (GCS) is a widely used tool to evaluate the severity of traumatic brain injury. It is based on three subscale scores: eye-opening score (range 1–4), verbal score (range 1–5), and motor score (range 1–6). The total GCS score ranges from 3 to 15, with a score of 3–8 indicating severe impairment, a score of 9–12 indicating moderate impairment, and a score of 13–15 indicating mild impairment [29]. Our study indicates that there is a significant association between the patient's likelihood of dying and a lower GCS motor score. This result is consistent with the findings of Selioutski et al. [31]. In the present study, GCS verbal scores also played a significant role in the model. However, previous studies have shown conflicting results regarding the impact of GCS verbal scores on patient survival scores [31–33]. the main reason for the disagreement was whether the patient was extubated at the time of scoring, and if extubation had been performed, the GCS verbal score could not be accurately assessed [34]. Cevik et al. believed that if a complete GCS score was successfully obtained, then the GCS verbal score could be a good predictor of patient survival [32]. To overcome the issue of inaccurate assessment of GCS verbal scores due to extubation, we conducted a comprehensive GCS evaluation at the time of patient admission, before tracheal intubation. Thus, our study effectively avoids this limitation and enhances the accuracy of our findings. Accordingly, we recommend that an accurate GCS score be promptly obtained upon patient admission to ensure the precision of predictions when applying our study's model. Furthermore, our study highlights the significance of patient heart rate as an essential factor in predicting outcomes. Specifically, we found that for every 3 beats/min increase in mean heart rate, the likelihood of adverse outcomes increased by 10.4 %. Conversely, every 3 beats increase in HR-ARV (heart rate variability) corresponded to a 1.1 % increase in the likelihood of hematoma enlargement and a 1.1 % increase in adverse outcomes. These findings underscore the critical importance of closely monitoring heart rate in SAH patients and taking appropriate interventions to mitigate potential adverse outcomes [35,36].

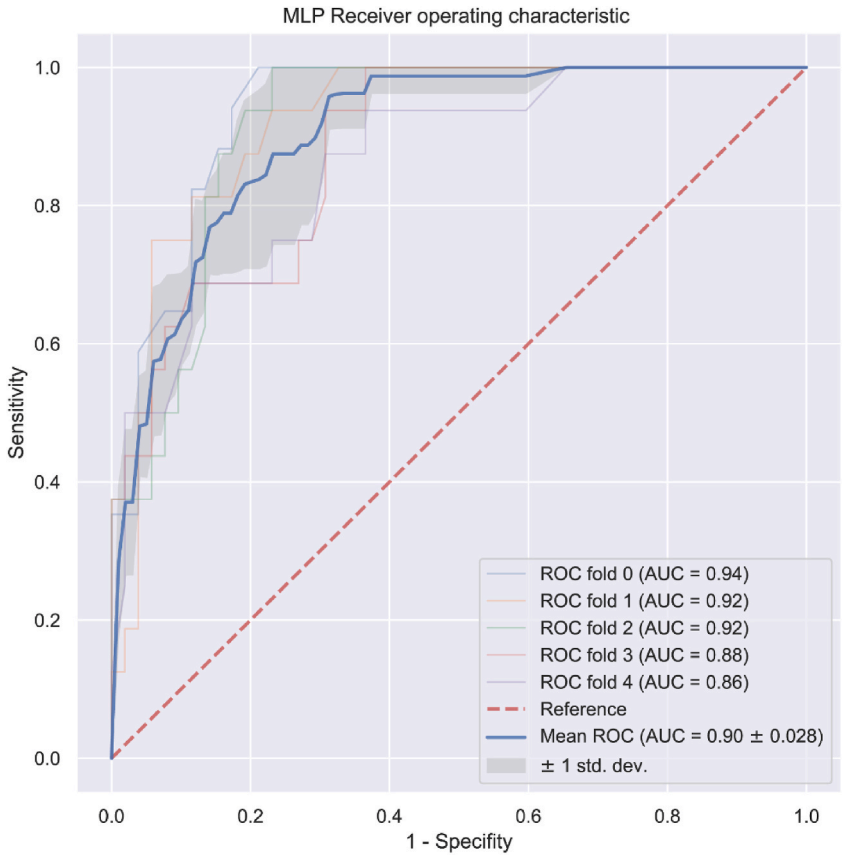

Fig. 8. ROC plot of MLP machine learning model 5-fold cross-validation results.

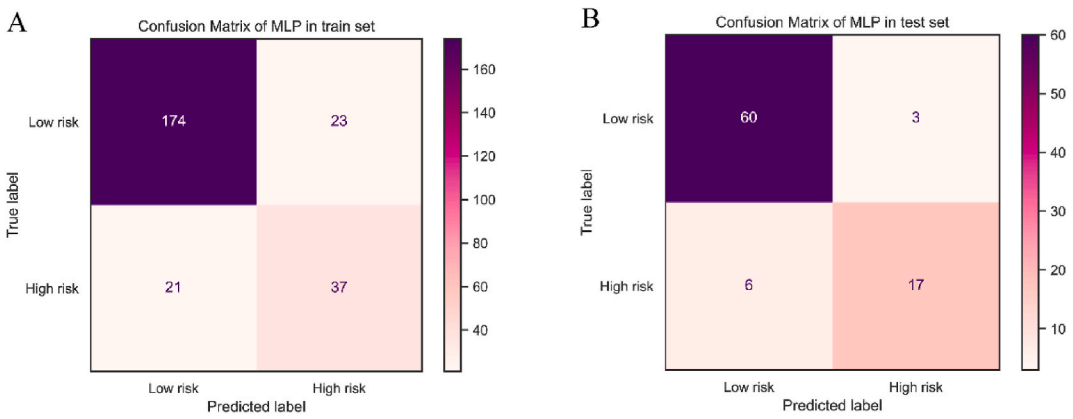

Fig. 9. Confusion matrix of MLP model in training set(A) and test set(B).

The bicarbonate level in the patient's blood gas analysis results at admission played a very critical role in this study, and it is believed that a lower bicarbonate level may indicate a worse condition for the patient and an increased risk of death within 7 days. This may be related to a transient lactic acidosis due to increased systemic vascular resistance in patients after sah, which in turn leads to severe neurogenic pulmonary edema [37,38]. This result is consistent with Tian et al.'s study, which also identified bicarbonate as an important predictor of SAH prognosis. Specifically, irreversible neuronal apoptosis was found to play a key role in both short- and long-term prognosis after SAH, in addition to general cell necrosis [39]. Our study revealed that SpO2 levels in blood gas analysis results are strongly associated with the risk of fatal events in patients within 7 days (P = 0.009 OR 0.96 (0.932–0.99). This finding may be attributed to cerebral hypoxia, a condition in which providing sufficient oxygen to the brain is crucial, and the partial pressure of oxygen must be adequate [40]. Therefore, monitoring SpO2 levels in SAH patients could help predict the risk of fatal events within 7

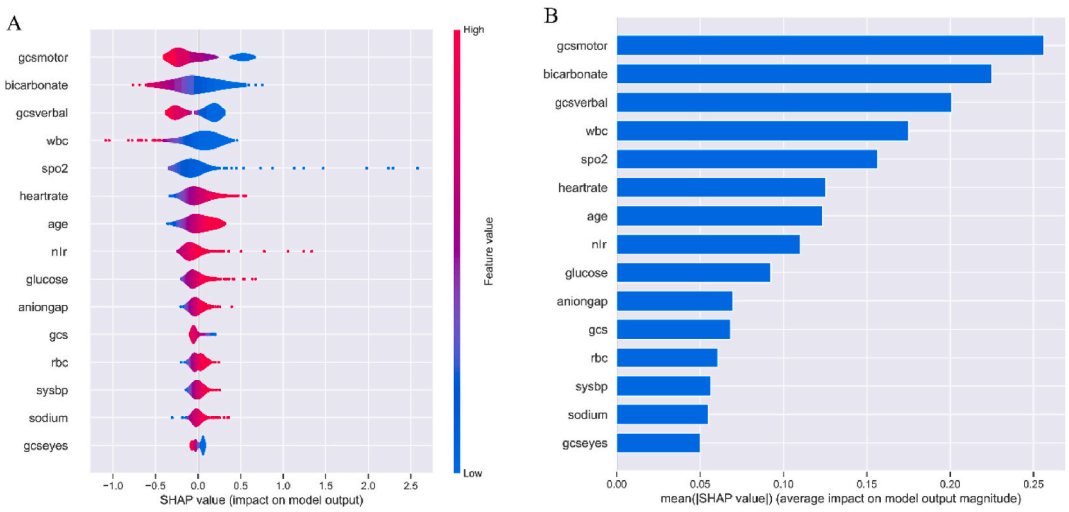

Fig. 10. Scatter plot of variables for SHAP analysis (A) and importance ranking plot (B).

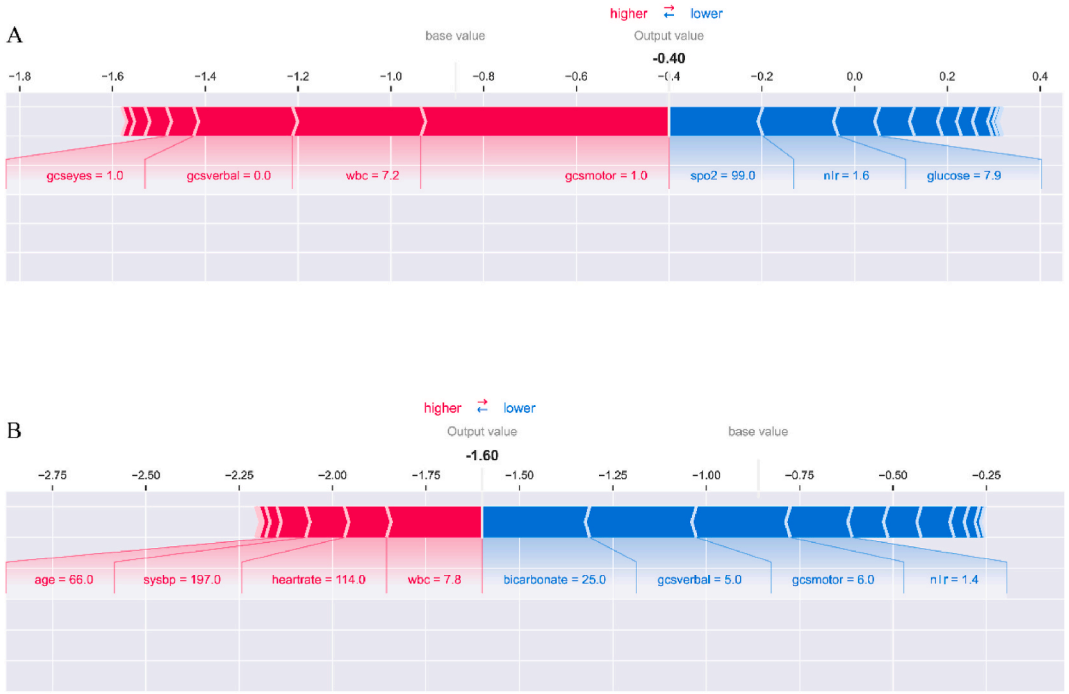

Fig. 11. Interpretation of the SHAP model for two case predictions, Fig. 11A for high risk and Fig. 11B for low risk.

days.

Our findings suggest that the risk of early death in SAH patients can be indicated by certain tests in clinical practice, including Wbc count, Rbc count, NLR, blood Glucose, and Potassium [40]. The underlying mechanism may be related to the local inflammatory response triggered by the entry of blood components into the subarachnoid space during the acute phase of SAH, leading to a downstream inflammatory cascade. This, in turn, activates central resident immune cells and chemotaxis of inflammatory cytokines, resulting in a large influx of peripheral inflammatory cells into the subarachnoid cavity during the subacute and chronic phases [41, 42]. The neutrophil-to-lymphocyte ratio (NLR) is a valuable biomarker for assessing the inflammatory response after SAH and correlates with prognosis, where the more severe the inflammatory response, the more severe the neurological damage [43–45]. Conversely, low levels of red blood cells (Rbc) were associated with more severe SAH outcomes, possibly due to impaired brain oxygenation [46]. Stress hyperglycemia is a common occurrence with an incidence of over 50 %, and it has been associated not only with the severity of intracerebral hemorrhage but also with an independent risk for neurological deficits and prognosis in patients with

Fig. 12. Web calculator for predicting death within 7 days for SAH patients.

intracerebral hemorrhage [47,48]. The hyperglycemic state affects brain tissue energy metabolism, leading to acidosis due to the accumulation of lactate, inducing oxidative stress, aggravating nerve cell injury, and worsening the prognosis in patients with intracerebral hemorrhage. Additionally, hyperglycemia levels have been linked to brain edema and neuronal apoptosis, and it has been reported to cause severe damage to the blood-brain barrier by lowering water channel proteins [49–51].

Treatment (such as surgery) was not individually evaluated for each patient but rather assumed that they received the most appropriate drug or surgical treatment available. The goal of this study was not to determine the best treatment but rather to identify predictors of mortality assuming that SAH patients received optimal treatment. Additionally, the baseline table results indicate that several variables in the training set and test set are statistically different from each other ($P < 0.05$), which may be due to the fact that the training set is from the MIMIC-III database in the United States, while the test set is from an independent medical institution in China, and the two datasets are independent of each other. In addition, patient mortality was higher in the real-world test set data than in the training set data, and this was not compared in this paper. Because the main purpose of the study was to explore the effect of each variable on the mortality outcome of patients with SAH and to explore the association between each variable and the outcome, and no further analysis of the differences with the between-group variables was performed.

5. Limitations

The present study represents a novel and comprehensive exploration of improved ML methods for predicting mortality within 7 days in patients with SAH, utilizing a multicenter, externally validated study with high confidence in the results. Nonetheless, several limitations still exist in this study. Firstly, retrospective studies are prone to selection bias. Secondly, although we collected variables related to patients with spider blood as comprehensively as possible, some variables were not available in time, such as Hunt-Hess classification [52], which determines the severity of SAH patients, mFisher score [53], which predicts vasospasm, and mRs score at admission [54], which may limit the generalizability of this study, and we regret this absence and may consider adding these important variables in subsequent studies. Lastly, important ancillary tests, such as computerized tomography (CT) information, were not entirely collected, which may have resulted in missing important variables of interest. Future studies should aim to address these limitations to further refine this model.

6. Conclusions

In this study, we developed a multilayer perceptron (MLP) model for predicting mortality and performed rigorous validation using an external validation set of SAH patients. Our model results suggest that Gcsmotor, Bicarbonate, Wbc, Spo2, Heartrate, Age, NLR, Glucose, Aniongap, GCS, Rbc, Sysbp, Sodium, and Gcseyes are key factors that help identify and classify patients at higher risk of death upon admission. The MLP algorithm-based network calculator constructed in this study can effectively predict the risk of death within 7 days in patients with SAH and aid physicians in making treatment decisions.

Funding statement

Not applicable.

Data availability statement

Data included in article/supp. material/referenced in article.

Additional information

No additional information is available for this paper.

Ethics approval and consent to participate

Written approval for this study was obtained from the Ethics Committee of The Affiliated Hospital of Xuzhou Medical University (ethics number: XYFY2022-KL457-01), and the creation and use of the MIMIC-III database were approved by the Institutional Review Boards of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center, and informed consent was not required.

CRediT authorship contribution statement

Longyuan Gu: Writing - original draft. **Hongwei Hu:** Data curation. **Shinan Wu:** Validation, Writing - original draft. **Fengda Li:** Data curation, Formal analysis. **Zeyi Li:** Data curation, Software, Supervision. **Yaodong Xiao:** Data curation. **Chuanqing Li:** Data curation. **Hui Zhang:** Data curation. **Qiang Wang:** Supervision, Writing - original draft, Writing - review & editing. **Wenle Li:** Writing - original draft, Writing - review & editing. **Yuechao Fan:** Supervision, Writing - original draft, Writing - review & editing.

Declaration of competing interest

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

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Not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e23943.

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