Original Article

Development of SAB model for predicting mortality in intensive care unit after aortic aneurysm surgery

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Background: Aortic aneurysm (AA) patients after vascular surgery are at high risk of death, some of them need intensive care. Our aim was to develop a simplified model with baseline data within 24 hours of intensive care unit (ICU) admission to early predict mortality.

Methods: Univariate analysis and least absolute shrinkage and selection operator were used to select important variables, which were then taken into logistic regression to fit the model. Discrimination and validation were used to evaluate the performance of the model. Bootstrap method was conducted to perform internal validation. Finally, decision clinical analysis curve was used to test the clinical usefulness of the model.

Results: We obtained baseline data of 482 AA patients from Medical Information Mart for Intensive Care III database, 33 (6.8%) of whom died in ICU. Our final model contained three variables and was called SAB model based on initials of three items [Sepsis, Anion gap, Bicarbonate (SAB)]. Area under the curve of SAB was 0.904 (95% CI: 0.841–0.967) while brier score was 0.043 (95% CI: 0.028–0.057). After internal validation, corrected area under the curve was 0.898 and brier score was 0.045, which showed good prediction ability of SAB model. The model can be assessed on https://vascularmodel.shinyapps.io/AorticAneurysm/.

Conclusions: SAB model derived in this study can be easily used to predict in-ICU mortality of AA patients after surgery precisely.

Keywords: Aortic aneurysm (AA); intensive care unit (ICU); prediction model

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Introduction

Aortic aneurysm (AA) is a disease about the dilation of aorta, larger than one and a half times of normal vessel diameter. According to anatomical classification, it can be divided into abdominal aortic aneurysm (AAA), thoracic aortic aneurysm (TAA) and thoracoabdominal aortic aneurysm (TAAA). The in-hospital mortality rate of AA varies widely from 2 to 20 percent (1-4), while the mortality of TAA is the highest among these three types (5,6). Under normal circumstances, the treatment options for patients with AA include open repair surgery (ORS) and

endovascular aneurysm repair (EVAR). After the operation, the patients will have many complications because of organ ischemia or aortic repair surgery (7). Common complications include acute renal failure, endoleaks, graft rupture, graft thrombosis and so on (8,9). Some patients suffered from more than one complication and some needed a secondary intervention (10). For example, a thrombus at the edge of the anastomosis after surgery can block the distal artery and cause organ ischemia. Some of the abdominal aorta aneurysm that needs to be cut above the level of the renal artery can cause kidney ischemia. Most seriously, anastomotic leakage may occur in artificial blood vessels, which cause internal hemorrhage. Once internal hemorrhage occurs, a second operation should be performed immediately or the patient will die (11,12). Due to these complications, the post-operative mortality rate is still between 5 to 10 percent (5,13).

Therefore, when postoperative AA patient's condition is unstable, it is vital to transfer them to intensive care unit (ICU) for health support and observation. However, ICU admission can cost a lot and sometimes is a waste of hospital resource. A recent study indicated that ICU admission was often unnecessary after EVAR (14). If a patient's mortality after operation is known before admission to ICU, surgeons can make a more suitable and accurate treatment plan and choose when to leave ICU. The establishment of predicting model can help doctors predict the ICU mortality rate quickly. Simplified acute physiology score II (SAPSII) and sequential organ assessment (SOFA) are widely used to measure the severity of ICU patients. It was proved that SAPSII and SOFA can indicate the mortality in ruptured AAA within 48 hours (15). But sometimes these models are cumbersome to use, model especially and easily measuring the mortality of AA patients after surgery is still to be built. We present the following article in accordance with the TRIPOD reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1660).

Methods

Data source & ethical statement

We used the data obtained from the Medical Information Mart for Intensive Care III (MIMIC-III) database (16). The MIMIC-III database is open to the public free of charge and it uses international classification of diseases, 9th revision (ICD-9) diagnostic code for the determination of patients' condition. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Population selection

Firstly, we used ICD-9 code including 4411, 4412, 4413, 4414, 4416 and 4417 to select the study cohort diagnosed as AA (4411: thoracic aneurysm, ruptured; 4412: thoracic aneurysm without mention of rupture; 4413: abdominal aneurysm, ruptured; 4414: abdominal aneurysm without mention of rupture; 4416: thoracoabdominal aneurysm, ruptured; 4417: thoracoabdominal aneurysm, without mention of rupture). The studying cohort including rupture or non-rupture type, elective or urgent type. By using ICD-9 code 3844 (Resection of vessel with replacement, aorta, abdominal), 3845 (Resection of vessel with replacement, thoracic vessels), 3973 (Endovascular implantation of graft in thoracic aorta) and 3971 (Endovascular implantation of other graft in abdominal aorta), we selected the cohorts who received vascular surgery. Patients or the ICU admission were excluded meeting the following criteria: (I) who didn't have surgery before admitting to ICU; (II) for those who had multiple ICU admissions, we only remained the first admission record; (III) of whom ICU stay were less than 24 hours; (IV) who lacked of anion gap record in the first day of ICU admission; (V) who were younger than 18.

Data extraction and data processing

We extracted the admission baseline data of selected study cohort, which included general condition, comorbidity, vital signs on admission, laboratory indicators, surgery-related indications and severity scores. In the vital signs on admission, heart rate, systolic blood pressure, diastolic blood pressure, respirate rate and percutaneous oxygen saturation (SpO_2) were all the average values of the data collected on the first day of ICU after surgery. In laboratory indicators, the anion gap, bicarbonate, creatinine, blood urea nitrogen, partial thromboplastin time (PTT), international standard ratio (INR), prothrombin time (PT), white blood cell count and platelet count were defined as the maximum and minimum values of data collected on the first day. In the surgery-related indications, way of surgery (ORS, EVAR and mixed), extracorporeal circulation used, bypass surgery used, ventilation used in the first day of ICU, urine output in first day of ICU were also collected. Outcome was defined as in-ICU mortality. Above data extraction were conducted on PostgreSQL software (version 10.12, www.postgresql.org).

Statistical analysis

In the baseline data of patients, continuous variables with abnormal distribution of the two groups were represented by the median with interquartile range (IQR), compared with Kruskal Wallis test. The categorical variables were expressed as percentage, compared with Chi-square tests. Single imputation was then performed for the whole dataset based on the complete conditional specification and predictive mean matching method was used to fill the missing value.

Model building

Admission baseline variables [excluded length of stay (LOS) of hospital and ICU, type of AA] that had statistical significance in univariate analysis were then put into least absolute shrinkage and selection operator (LASSO) to select the final model according to the LASSO results and clinical significance. The selected variables were then put into logistic regression to build a new prediction model. After that, two widely used models (SAPSII and SOFA) and the newly built model were used to calculate the discrimination and calibration in the original data. Discrimination was measured by area under the curve (AUC) while calibration was measured by Brier score and calibration curve. The following formula was used to calculate Brier score:

$$Brier\ score = \frac{1}{N}\sum_{t=1}^{N}(f_t - 0_t)^2 \quad [1]$$

In the formula, N represents the total number of predictions, f_t represents the actual results and 0_t presents the predicted probability of the model. Discrimination and calibration, also with net reclassification improvement (NRI) and integrated discrimination improvement (IDI) were used as indicators to compare the prediction ability of the newly built model with the other models. NRI could be measured as:

$$NRI = Sensitivity^{New\ model} + Specificity^{New\ model} - Sensitivity^{Old\ model} - Specificity^{Old\ model} \quad [2]$$

NRI can reflect the ability improvement in true classification of the new model compared to the old model. And IDI can be measured as:

$$IDI = (P_{New,events} - P_{Old,events}) - (P_{New,non-events} - P_{Old,non-events}) \quad [3]$$

$P_{new,\ events}$ and $P_{old,\ events}$ represent mean probability of mortality (or outcome events) predicted by the new and old model in outcome-occurrence group, while $P_{new,\ non\text{-}events}$ and $P_{old,\ non\text{-}events}$ represent mean probability of mortality (or outcome events) predicted by the new and old model in outcome-nonoccurrence group. IDI can reflect change of predicted probability between the new and old model, and a higher IDI means a better prediction ability of the new model. Then internal validation was conducted, optimism bootstrap method with 1,000 repetition was used to correct the AUC, brier score and calibration curve. In order to evaluate the risk stratification ability of the SAB model, the study cohort had been divided into 5 groups based on the predicted probability: (I) 0–20%; (II) 20–40%; (III) 40–60%; (IV) 60–80%; (V) 80–100%. And the actual number of deaths and death rates were counted in each group to show whether if SAB model can identify the high-risk group. Then a decision clinical analysis (DCA) curve was conducted to estimate the clinical usefulness and net benefit. For its convenient application in clinic, we presented the newly built model as a website. Finally, we also performed an external validation of SAB model in a large ICU cohort (31,645 patients) to investigate whether SAB model can also be equally applicable in non-aorta ICU patients. The result of external validation is not shown in text and many more regressions were run than can be included in the article. The interested reader can find them in Appendix 1. Above data were analyzed with R software (version.3.6.1; The R Project for Statistical Computing, TX, USA; http://www.r-project.org).

Results

At first, 609 patients with 667 ICU admission records were identified from MIMIC-III. After selection, 127 patients and 185 ICU records were excluded and at last, 482 AA patients [33 patients (6.85%) died in ICU] and 482 ICU records were enrolled in this study. The enrollment flowchart is shown in *Figure 1*. Rupture cases make up 14.5% of the entire cohort. Emergency and urgent type make up 31.3% of the entire cohort. *Table 1* shows the baseline data of patients. In the univariate analysis of patients' baseline data categorized according to clinical outcome, as for general condition, LOS of ICU, in-hospital death, type of AA, rupture of AA, age and gender had statistical significances. As for comorbidity, sepsis and coagulopathy disorders had statistical significances. As for vital signs on admission, the mean of heart rate, systolic blood pressure, respirate rate and SpO_2 had statistical significances. In laboratory indicators, both maximum and minimum value of anion gap, bicarbonate, creatinine, blood

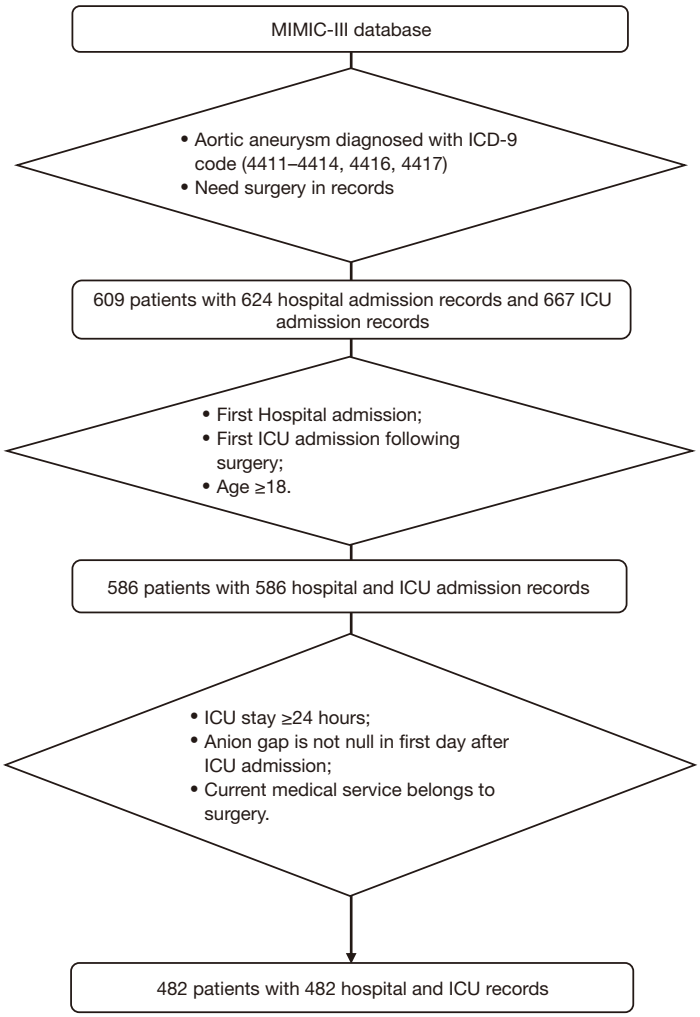

Figure 1 Flow chart of the study population. MIMIC-III, Medical Information Mart for Intensive Care III; ICD-9, International Classification of Diseases, 9th revision; ICU, intensive care unit.

urea nitrogen had statistical significances; maximum value of PTT, INR and white blood cell count had statistical significances; minimum value of PT and platelet count had statistical significances. In surgery-related indicators, extracorporeal circulation used and urine output in first day of ICU had statistical significances. In severity score, SAPSII and SOFA had statistical significances. To build a new model, we used cross-validation of logistic regression of LASSO to screen all the statistically significant baseline variables (excluded LOS of hospital and ICU, type of AA) of 482 patients. *Figure 2* shows the relationship between penalty coefficient λ and the continuous decrease of variables in the model. Finally, we got the final model with 3 variables and the penalty coefficient λ is 0.0545. The 3 variables included sepsis, anion gap^{maximum} and bicarbonate^{minimum}. Then we put these variables into multivariable logistic regression to fit the model. Our final model was called SAB model based on initials of three items [Sepsis, Anion gap, Bicarbonate, (SAB)]. *Table 2* shows the variables and coefficients included in SAB model. Then we conducted the receiver operating characteristic (ROC) curves to show the prediction abilities of SAB model, SOFA and SAPSII on the clinical outcome in AA patients, which are shown in *Figure 3*. Among these three indicators, the SAB model had the best prediction ability on the clinical outcome. The AUC of SAB was 0.904 [95% confidence interval (CI): 0.841–0.967]. The second was SAPSII of which the AUC was 0.823 (95% CI: 0.752–0.893). The SOFA had the worse ability and its AUC was 0.776 (95% CI: 0.686–0.867). Then, we used the original data to

Table 1 Baseline data of AA after vascular surgery

Candidate variables	ICU-survival group (N=449)	ICU-death group (N=33)	P value
General condition			
Admission type			<0.001***
Elective	321 (71.5%)	10 (30.3%)	
Emergency	119 (26.5%)	23 (69.7%)	
Urgent	9 (2.0%)	0 (0.0%)	
LOS of hospital	8.83 (6.24, 14.15)	9.92 (4.04, 17.61)	0.763
LOS of ICU	3.02 (1.83, 6.33)	10.04 (2.59, 17.92)	<0.001***
In-hospital death	3 (0.7%)	33 (100.0%)	<0.001***
Type of aortic aneurysm			<0.001***
Abdominal aneurysm without mention of rupture	124 (27.6%)	10 (30.3%)	
Abdominal aneurysm, ruptured	38 (8.5%)	12 (36.4%)	
Thoracic aneurysm without mention of rupture	238 (53.0%)	5 (15.2%)	
Thoracic aneurysm, ruptured	7 (1.6%)	2 (6.1%)	
Thoracoabdominal aneurysm, ruptured	9 (2.0%)	2 (6.1%)	
Thoracoabdominal aneurysm, without mention of rupture	33 (7.3%)	2 (6.1%)	
Rupture of aortic aneurysm	54 (12.0%)	16 (48.5%)	<0.001***
Age (years)	69.89 (60.42, 77.18)	77.26 (70.76, 82.71)	<0.001***
Male	289 (64.4%)	15 (45.5%)	0.047*
Comorbidity			
Sepsis	6 (1.3%)	7 (21.2%)	<0.001***
Chronic pulmonary diseases	105 (23.4%)	8 (24.2%)	1
Coagulopathy disorders	73 (16.3%)	12 (36.4%)	0.007**
Congestive heart failure	9 (2.0%)	1 (3.0%)	1
Renal failure	43 (9.6%)	6 (18.2%)	0.2
Fluid and electrolyte disorders	96 (21.4%)	9 (27.3%)	0.567
Vital signs on admission			
Heart rate, mean (bpm)	81.08 (73.55, 87.67)	89.28 (79.36, 93.31)	0.001**
Systolic blood pressure, mean (mmHg)	111.83 (106.55, 120.72)	106.77 (103.78, 123.19)	0.045*
Diastolic blood pressure, mean (mmHg)	57.09 (52.52, 61.98)	59.56 (55.40, 64.51)	0.09
Respirate rate, mean (1/min)	16.45 (14.98, 18.40)	18.61 (16.38, 20.14)	0.002**
SpO_2, mean (%)	98.04 (97.01, 98.94)	97.53 (96.33, 98.35)	0.01*
Laboratory indicators			
Anion gap, maximum (mEq/L)	12.00 (11.00, 14.00)	17.00 (16.00, 22.00)	<0.001***
Anion gap, minimum (mEq/L)	11.00 (9.00, 12.00)	13.00 (12.00, 16.00)	<0.001***
Bicarbonate, maximum (mEq/L)	25.00 (23.00, 27.00)	22.00 (20.00, 25.00)	<0.001***

Table 1 *(continued)*

Table 1 *(continued)*

Candidate variables	ICU-survival group (N=449)	ICU-death group (N=33)	P value
Bicarbonate, minimum (mEq/L)	23.00 (21.00, 25.00)	17.00 (15.00, 21.00)	<0.001***
Creatinine, maximum (mg/dL)	1.00 (0.80, 1.30)	1.80 (1.20, 2.10)	<0.001***
Creatinine, minimum (mg/dL)	0.90 (0.70, 1.10)	1.10 (0.80, 1.40)	0.001**
Blood urea nitrogen, maximum (mg/dL)	17.00 (14.00, 22.00)	27.00 (21.00, 35.00)	<0.001***
Blood urea nitrogen, minimum (mg/dL)	15.00 (12.00, 19.00)	18.00 (16.00, 29.00)	<0.001***
PTT, maximum (sec)	40.70 (33.60, 51.70)	64.80 (38.80, 113.00)	0.001**
PTT, minimum (sec)	31.20 (28.00, 35.80)	31.30 (25.10, 36.80)	0.355
INR, maximum	1.40 (1.30, 1.70)	1.70 (1.30, 2.32)	0.026*
INR, minimum	1.20 (1.10, 1.30)	1.20 (1.08, 1.30)	0.056
PT, maximum (sec)	15.60 (14.40, 17.25)	16.90 (14.57, 19.40)	0.07
PT, minimum (sec)	13.70 (13.10, 14.60)	13.40 (12.47, 14.00)	0.021*
White blood cell count, maximum (K/μL)	12.40 (9.70, 15.50)	14.60 (10.30, 17.60)	0.034*
White blood cell count, minimum (K/μL)	9.00 (6.80, 11.40)	9.60 (5.30, 11.40)	0.863
Platelet count, maximum (K/μL)	174.50 (136.00, 219.00)	174.00 (138.00, 218.00)	0.828
Platelet count, minimum (K/μL)	126.00 (94.00, 161.25)	86.00 (61.00, 126.00)	<0.001***
Surgery-related indications			
Way of surgery			0.79
Endovascular	59 (13.1%)	3 (9.1%)	
Mixed	15 (3.3%)	1 (3.0%)	
Open	375 (83.5%)	29 (87.9%)	
Extracorporeal circulation used	245 (54.6%)	8 (24.2%)	0.001**
Bypass surgery used	26 (5.8%)	2 (6.1%)	1
Ventilation used in first day of ICU	408 (90.9%)	29 (87.9%)	0.795
Urine output in first day of ICU (mL)	1,945.00 (1,250.00, 2,850.00)	895.00 (311.00, 1,397.00)	<0.001***
Severity score			
GCS	15.00 (14.00, 15.00)	15.00 (15.00, 15.00)	0.185
SAPSII	34.00 (27.00, 43.00)	51.00 (44.00, 66.00)	<0.001***
SOFA	5.00 (3.00, 7.00)	9.00 (7.00, 12.00)	<0.001***

0.6% of patients had unknown value for heart rate (mean); 1.0% for systolic blood pressure (mean) and diastolic blood pressure (mean); 0.6% for respirate rate (mean); 0.6% for SpO_2 (mean); 0.2% for platelet count; 2.1% for PTT; 2.3% for PT; 2.3% for INR; 0.4% for white blood cell count; 1.7% for urine output on first day; 0.6% for GCS score. *, P<0.05; **, P<0.01; ***, P<0.001. AA, aortic aneurysm; ICU, intensive care unit; LOS, length of stay; SpO_2, percutaneous oxygen saturation; PTT, partial thromboplastin time; INR, international standard ratio; PT, prothrombin time; GCS, Glasgow Coma Scale; SAPSII, simplified acute physiology score II; SOFA, sequential organ failure assessment.

evaluate the calibration of SAB model, SOFA and SAPSII. The results showed that the Brier score of SAB model was 0.043 (95% CI: 0.028–0.057), which was smaller than that of SAPSII (0.057, 95% CI: 0.040–0.073) and SOFA (0.056, 95% CI: 0.039–0.072), indicating more accuracy prediction ability of SAB model. Calibration curve of SAB model

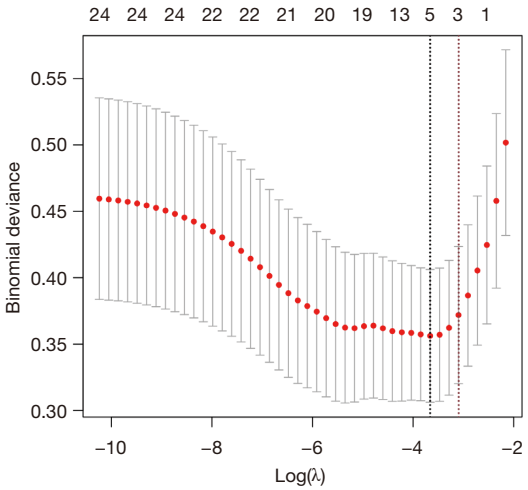

Figure 2 Cross-validation of logistic regression with LASSO. Lower abscissa represents the continuous increase of penalty coefficient λ, and the upper represents the continuous decrease of variables in the model from left to right. The ordinate represents corresponding binomial deviation (or minimum mean cross-validated error) of each model. The black dotted line represents the model with the least binomial deviation while the red one represents the model including three variables we selected in this study. Line segment of each model represents 95% CI of binomial deviation. LASSO, least absolute shrinkage and selection operator; CI, confidence interval.

Table 2 Variables and coefficients included in SAB model

Variables	Estimate	Standard error	Z value	P value
Intercept	−3.157	2.390	−1.321	0.187
Sepsis	2.385	0.733	3.253	0.001**
Anion gap, maximum	0.248	0.065	3.790	<0.001***
Bicarbonate, minimum	−0.166	0.079	−2.099	0.036*

*, P<0.05; **, P<0.01; ***, P<0.001. SAB, Sepsis, Anion gap, Bicarbonate.

is shown in *Figure 4*. For internal validation, optimism bootstrap method with 1,000 repetitions was conducted. The adjusted AUC of SAB model was 0.898 (0.822 for SAPSII and 0.775 for SOFA) and the adjusted Brier scores was 0.045 (0.057 for SAPSII and 0.057 for SOFA). Other results of parameters of calibration curve in original cohort and results of internal validation are showed in *Table 3*. In

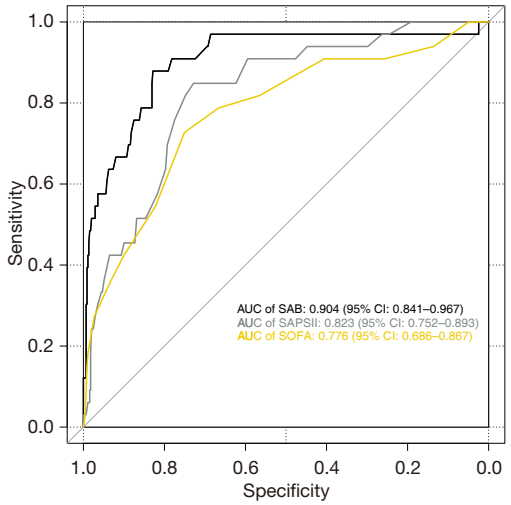

Figure 3 ROC curves of SAB models and traditional scores. ROC, receiver operating characteristic; SAB, Sepsis, Anion gap, Bicarbonate; AUC, area under the curve; CI, confidence interval; SAPSII, simplified acute physiology score II; SOFA, sequential organ failure assessment.

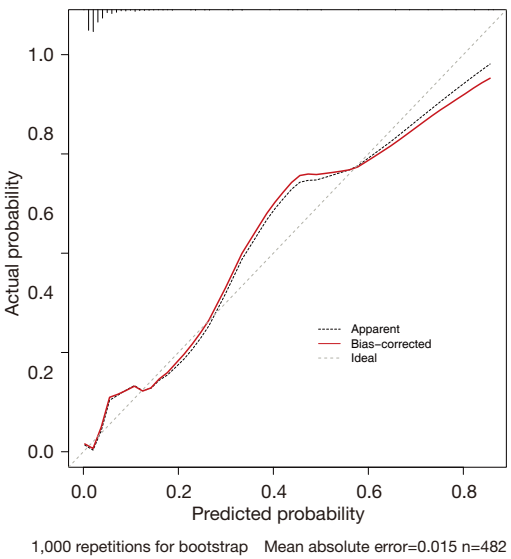

Figure 4 Calibration curves of SAB model. Calibration curve shows the mean predicted probability of outcome against the observed proportion of clinical outcomes. SAB, Sepsis, Anion gap, Bicarbonate.

order to evaluate the improvement of prediction ability of SAB model compared with SAPSII and SOFA, NRI (continuous) and IDI were used. Compared to SAPSII, the NRI (continuous) of SAB model was 0.695 (95%

Table 3 Discrimination and calibration of models in internal validation

Evaluation index	SAB model	SAPSII	SOFA
Discrimination			
AUC (95% CI)	0.904 (0.841–0.967)	0.823 (0.752–0.893)	0.776 (0.686–0.867)
Adjusted AUC†	0.898	0.822	0.775
Calibration			
Brier score (95% CI)	0.043 (0.028–0.057)	0.057 (0.040–0.073)	0.056 (0.039–0.072)
Adjusted brier score†	0.045	0.057	0.057
Intercept (95% CI)	4.914E-09 (–1.628E-07 to 1.332E-08)	–1.018E-10 (–6.683E-08 to 1.159E-08)	5.859E-12 (–6.422E-08 to 3.814E-08)
Adjusted intercept†	–0.081	0.035	0.061
Slope (95% CI)	1.000 (1.000–1.000)	1.000 (1.000–1.000)	1.000 (1.000–1.000)
Adjusted slope†	0.953	1.008	1.018

†, corrected indexes were calculated with optimism bootstrap method with 1,000 repetitions. SAB, Sepsis, Anion gap, Bicarbonate; AUC, area under the curve; CI, confidence interval; SAPSII, simplified acute physiology score II; SOFA, sequential organ failure assessment.

Table 4 Improvement in prediction ability of SAB model compared with SAPSII and SOFA

Evaluation items	Compared to SAPSII	P value	Compared to SOFA	P value
NRI (continuous) (95% CI)	0.695 (0.369–1.020)	<0.001***	0.744 (0.418–1.069)	<0.001***
IDI (95% CI)	0.217 (0.090–0.345)	<0.001***	0.229 (0.118–0.340)	<0.001***

***, P<0.001. SAB, Sepsis, Anion gap, Bicarbonate; SAPSII, simplified acute physiology score II; SOFA, sequential organ failure assessment; NRI, net reclassification improvement; IDI, integrated discrimination improvement; CI, confidence interval.

Table 5 Risk stratification by prediction results of SAB model

Prediction result interval of SAB model	0–20%	20–40%	40–60%	60–80%	80–100%
Number	445	17	6	6	8
In-ICU death	14 (3.1%)	5 (29.4%)	4 (66.7%)	5 (83.3%)	5 (62.5%)
In-hospital death	17 (3.8%)	5 (29.4%)	4 (66.7%)	5 (83.3%)	5 (62.5%)

SAB, Sepsis, Anion gap, Bicarbonate; ICU, intensive care unit.

CI: 0.369–1.020; P<0.001) and IDI was 0.217(95% CI: 0.090–0.345; P<0.001), which had statistical significances. While comparing to SOFA, the NRI (continuous) of SAB model was 0.744 (95% CI: 0.418–1.069; P<0.001) and IDI was 0.229 (95% CI: 0.118–0.340; P<0.001), which also had statistical significances. The results of NRI and IDI are showed in *Table 4*. The risk stratification ability of SAB model is shown in *Table 5*. It was shown that SAB model could stratified the high-risk group. The death rate was 66.7% in 40–60% group, 83.3% in 60–80% group and 62.5% in 80–100% group. If a patient's predicted probability is higher than 40%, he/she should be paid more attention in clinic. To show the clinical usefulness of SAB model, the DCA (*Figure 5*) was built based on the continuum of potential thresholds of ICU-death (x axis) and the net benefit of using SAB model to risk stratify patients (y axis) relative to assuming that no AA patient will die in ICU. The curve of SAB model showed that SAB model provided a net benefit across the range of ICU-death compared with the positive group in which every patient underwent surgery. Finally, a website based on this model is showed in *Figure 6*. If the clinical doctor input the patients'

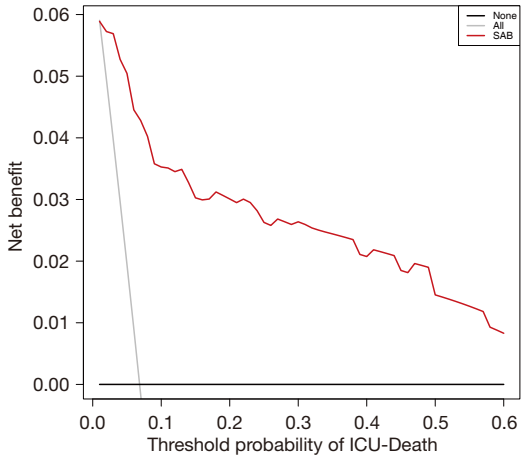

Figure 5 DCA curve for SAB model. DCA, decision clinical analysis. SAB, Sepsis, Anion gap, Bicarbonate.

data of sepsis, anion gap^{maximum} and bicarbonate^{minimum}, the website will calculate the ICU-mortality and show the results immediately.

Discussion

This research used the recorded data in MIMIC-III to develop SAB model by using logistic regression with LASSO. SAB model was proved to have good prediction ability for ICU-death of AA patients (AUC higher than 0.8 in the original data and after internal validation), good calibration (Brier score was 0.043 in original data and 0.045 after internal validation), improvement in prediction ability compared to SOFA and SAPSII scores [both NRI (continuous) >0; both IDI >0; both P<0.05]. This research also validated better clinical usefulness across the range of

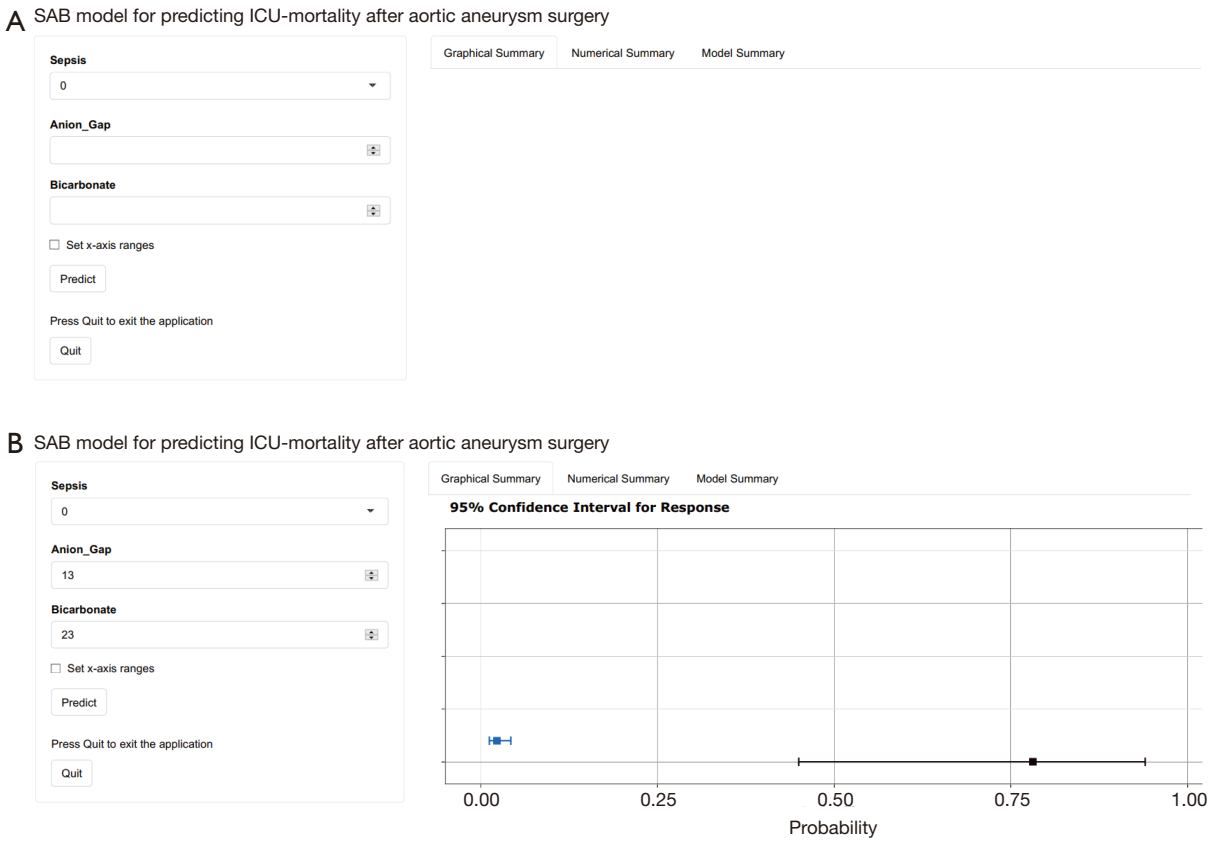

Figure 6 SAB model shown in website. The model can be assessed on https://vascularmodel.shinyapps.io/AorticAneurysm/. SAB, Sepsis, Anion gap, Bicarbonate.

ICU-death. This model only included 3 variables, which made it easy to obtain data. Besides, the website based on this model made it easy for clinical doctors in ICU to make rapid decision.

AA is a disease about pathological dilation of aorta. Different types of AA have different mortality. For AAA, it ranges from 2 to 10 percent (1,2); for TAAA, it ranges from 5 to 20 percent (4); while for TAA, it ranges from 5 to 11 percent (6). If AA ruptured, the 30-day mortality might rise over 30 percent (17,18) and the prognosis of aortic rupture is quite bad. For the patients who were more than 80 years old, more than 60% of EVAR patients sustained a complication (19). Renal failure is one of the most life-threatening complications. After receiving an urgent ruptured EVAR, the incidence rate of postoperative acute kidney injury (AKI) was more than 70% (20) and most occurred on the first day of ICU admission. In addition to renal failure, graft rupture is a common complication after repair surgery. According to EUROSTAR registry, the presence of graft migration, type 1 and type 3 endoleaks, and graft kink indicates graft rupture. Once the graft ruptures, the patient will bleed internally, which is life-threatening (8,9). Open repair is more dangerous than EVAR since the prognosis is worse. Most patients underwent open AAA repair had systemic inflammatory response syndrome (SIRS) (21). If these patients occurred infection, SIRS may develop into sepsis, and even worse when patients developed systemic hypoperfusion (22). Besides, there was a 3.8%, 38% and 64% incidence of multiorgan failure in the elective open AAA repair group, the urgent open AAA repair group and the ruptured AAA group (21). 5% of AA patients with multiorgan failure died before hospital discharge, which had higher incidence than the patients without organ dysfunction (23). The ICU-mortality of AAA patients was 2.36%, while TAA patients had the incidence of 9.43% (24). When patients are in unstable situation after surgery, surgeons will routinely transfer them to ICU. Therefore, it's important for doctors to evaluate the risk of mortality of AA patient in ICU in order to make a more suitable treatment plan. A scoring system such as SOFA and SAPSII can help doctors make the best decision. This study showed that both SOFA, SAPSII and SAB model had the prediction ability of mortality of AA patient in ICU, but SAB had the best discrimination (AUC =0.904, 95% CI: 0.841–0.967). Both SAPSII and SOFA scores require more than 10 variables, which makes it inconvenient to use. While SAB model only requires 3 indicators. What's more, the website has the advantages of visualization and quickness for calculate. In summary, we recommend that clinical doctors refer to our website to quickly assess the mortality of AA patients in ICU.

SAB model includes sepsis, the maximum of anion gap and the minimum of bicarbonate. Sometimes the treatment of infection is insufficient, which may lead to organ dysfunction or sepsis (25,26). Sepsis significantly increases the length of hospital stay and mortality in ICU patients. The reason for the significant increase in mortality due to sepsis is circulatory and cellular metabolic abnormalities (27). The mortality is related to the occurrence of septic shock. The mortality of septic shock was 27.9%, while those with non-septic shock was 16.0% (28). During follow-up or hospitalization, some AA patients died of sepsis (29,30). Because the AA repair surgery needs to create an opening in the blood vessel, this will lead to an increase in the rate of thrombosis. Besides, many studies prove that there is a strong relationship between sepsis and thrombosis, which significantly increases mortality (31).

Laboratory indicators can help doctors better understand the state of patients and help to accurately judge the prognosis. SAB model includes two indicators: the maximum of anion gap and the minimum of bicarbonate. Both the anion gap and bicarbonate in the serum is useful in the interpretation of acid-base disorders. This study proves that the maximum of anion gap has a positive correlation with ICU mortality. According to a multivariate analysis, the risk of ICU mortality may increase by 38% per 1 mEq/L increase in serum anion gap at hospital admission (32). Many patients underwent selective EVAR have AKI which has close relationship with mortality, and high dose of bicarbonate is proved to be an important preventive method (33,34). After AAA repair, bicarbonate can be used as a free radical scavenger and reduce renal tubular ischemia, which reduces the incidence of AKI (35,36).

Our study has several strengths. Firstly, we used machine learning LASSO to simplify the model and ensure the predictive ability. SAB model derived in this study only needs three variables, which is more convenient and quicker to use than SOFA and SAPSII. Secondly, SAB model is tested to have better prediction ability in both original data and internal validation. The discrimination and calibration of SAB model are better than the other two scoring systems (SAPSII and SOFA). Thirdly, we used DCA to test whether this model had clinical usefulness, and the result was quite good. Therefore, SAB model is convenient and has clinical application.

However, research also has limitations. Firstly, this

study design was a retrospective study and it can't include more sensitivity or specialist-recommending factor for predicting mortality. And the clinical outcome was set as all-cause mortality other than death directly related to AA, other complications associated with AA or non-return to independent living because we couldn't have access to the patient's clinical end point and do further follow up due to the limitation of database. Secondly, our study lacked data of blood gas analysis because there was too much lacking data for them, which may damage the sake and accuracy of the model. As a result, we didn't include data of blood gas analysis though there were many variables that had value to predict the outcome. Thirdly, due to the limitation of the database, we couldn't include preoperative variables which we thought can make our model more diversified and had more predictive power. Fourthly, we only included AA patients from single center, which needs more external validation.

Conclusions

We developed SAB model for in-ICU mortality of AA after surgery using the data from MIMIC-III database. SAB model had better predictive ability than SOFA and SAPSII. Clinical doctors can use our website to predict the mortality rate and choose a more suitable treatment plan.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/apm-21-1660). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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Aims

To investigate whether if SAB model can also be equally applicable in most of ICU patients (not just restricted on aortic aneurysm patients).

Methods

From MIMIC database, we included 31,645 patients for external validation of SAB model. The inclusion criteria didn't set special restriction on the type of disease at the aim of validating if the model can be equally applicable in most of ICU patients. Patients or the ICU admission were excluded meeting the following criteria: (I) for those who had multiple ICU admissions, we only remained the first admission record; (II) of whom ICU stay less than 24 hours; (III) who lacked of anion gap or bicarbonate record in the first day of ICU admission; (IV) who were younger than 18. The disease spectrum and baseline data of the selected external validation group are shown in *Tables S1*,*S2*.

Then, prediction result of each individual was calculated based on SAB model derived from the group of aortic aneurysm patients. Two widely used models (SAPSII and SOFA) and the SAB model were used to calculate the discrimination and calibration. Discrimination was measured by AUC while calibration was measured by Brier score and calibration curve, which are shown in *Table S3* and *Figure S1*.

Results

In external validation of SAB model in the large ICU cohort, the results had shown that the discrimination of the model didn't reach great level (AUC <0.75), and was lower than SAPSII and SOFA. *Figure S1* shows the calibration curve (dotted line) of SAB model in external validation group, which is below on the ideal line, meaning that the model may overestimated the mortality of patients in clinical use.

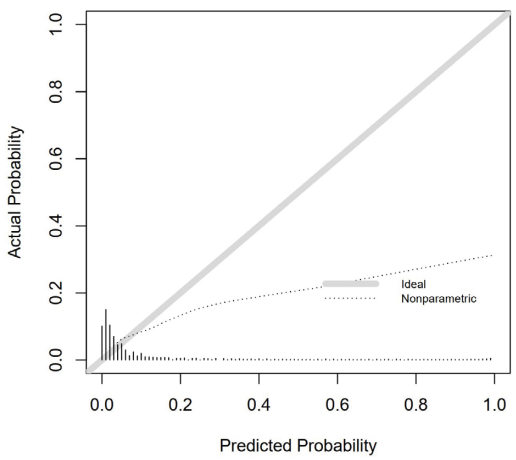

Figure S1 Calibration curve of SAB model in external validation group. Calibration curve shows the mean predicted probability of outcome against the observed proportion of clinical outcomes. SAB, Sepsis, Anion gap, Bicarbonate.

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Table S1 Disease spectrum and prevalence of external validation group

Disease	Number (%)
Coronary atherosclerosis of native coronary artery	2,588 (8.2%)
Subendocardial infarction, initial episode of care	1,286 (4.1%)
Unspecified septicemia	1,142 (3.6%)
Aortic valve disorders	882 (2.8%)
Intracerebral hemorrhage	757 (2.4%)
Acute respiratory failure	685 (2.2%)
Subarachnoid hemorrhage	450 (1.4%)
Mitral valve disorders	407 (1.3%)
Acute myocardial infarction of other inferior wall, initial episode of care	380 (1.2%)
Acute myocardial infarction of other anterior wall, initial episode of care	379 (1.2%)
Pneumonia, organism unspecified	374 (1.2%)
Pneumonitis due to inhalation of food or vomitus	348 (1.1%)
Congestive heart failure, unspecified	342 (1.1%)
Acute kidney failure, unspecified	292 (0.9%)
Acute pancreatitis	268 (0.8%)
Cerebral embolism with cerebral infarction	258 (0.8%)
Cerebral artery occlusion, unspecified with cerebral infarction	246 (0.8%)
Hemorrhage of gastrointestinal tract, unspecified	224 (0.7%)
Other pulmonary embolism and infarction	224 (0.7%)
Subdural hemorrhage following injury without mention of open intracranial wound, with no loss of consciousness	206 (0.7%)
Septicemia due to Escherichia coli (E. coli)	204 (0.6%)
Secondary malignant neoplasm of brain and spinal cord	203 (0.6%)
Atrial fibrillation	201 (0.6%)
Diverticulosis of colon with hemorrhage	174 (0.5%)
Alcoholic cirrhosis of liver	155 (0.5%)
Paroxysmal ventricular tachycardia	146 (0.5%)
Other postoperative infection	144 (0.5%)
Hemorrhage complicating a procedure	139 (0.4%)
Subdural hemorrhage following injury without mention of open intracranial wound, unspecified state of consciousness	138 (0.4%)
Dissection of aorta, thoracic	136 (0.4%)
Subdural hemorrhage	134 (0.4%)
Malignant neoplasm of upper lobe, bronchus or lung	127 (0.4%)
Mitral valve insufficiency and aortic valve stenosis	127 (0.4%)
Methicillin susceptible Staphylococcus aureus septicemia	126 (0.4%)
Acute on chronic systolic heart failure	125 (0.4%)

Table S1 *(continued)*

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Table S1 *(continued)*

Disease	Number (%)
Poisoning by aromatic analgesics, not elsewhere classified	125 (0.4%)
Acute and subacute necrosis of liver	124 (0.4%)
Acute and chronic respiratory failure	122 (0.4%)
Cirrhosis of liver without mention of alcohol	119 (0.4%)
Diabetes with ketoacidosis, type I (juvenile type), uncontrolled	119 (0.4%)
Streptococcal septicemia	118 (0.4%)
Chronic or unspecified duodenal ulcer with hemorrhage, without mention of obstruction	116 (0.4%)
Other septicemia due to gram-negative organisms	113 (0.4%)
Abdominal aneurysm without mention of rupture	112 (0.4%)
Cerebral aneurysm, non-ruptured	111 (0.4%)
Infection and inflammatory reaction due to other vascular device, implant, and graft	110 (0.3%)
Chronic or unspecified gastric ulcer with hemorrhage, without mention of obstruction	108 (0.3%)
Human immunodeficiency virus disease	108 (0.3%)
Obstructive chronic bronchitis with (acute) exacerbation	108 (0.3%)
Thoracic aneurysm without mention of rupture	106 (0.3%)
Acute myocardial infarction of unspecified site, initial episode of care	105 (0.3%)
Malignant neoplasm of other parts of bronchus or lung	105 (0.3%)
Occlusion and stenosis of carotid artery without mention of cerebral infarction	105 (0.3%)
Alcohol withdrawal	104 (0.3%)
Acute on chronic diastolic heart failure	98 (0.3%)
Cholangitis	97 (0.3%)
Other convulsions	95 (0.3%)
Acute myocardial infarction of inferoposterior wall, initial episode of care	94 (0.3%)
Acute vascular insufficiency of intestine	93 (0.3%)
Acute and subacute bacterial endocarditis	92 (0.3%)
Acute myocardial infarction of anterolateral wall, initial episode of care	91 (0.3%)
Blood in stool	88 (0.3%)
Malignant neoplasm of liver, primary	86 (0.3%)
Benign neoplasm of cerebral meninges	85 (0.3%)
Intestinal or peritoneal adhesions with obstruction (postoperative) (post infection)	85 (0.3%)
Ventricular fibrillation	77 (0.2%)
Closed fracture of base of skull with subarachnoid, subdural, and extradural hemorrhage, with loss of consciousness of unspecified duration	75 (0.2%)
Other diseases of trachea and bronchus	75 (0.2%)
Acute kidney failure with lesion of tubular necrosis	74 (0.2%)

Table S1 *(continued)*

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Table S1 *(continued)*

Disease	Number (%)
Atherosclerosis of native arteries of the extremities with gangrene	72 (0.2%)
Acute myeloid leukemia, without mention of having achieved remission	71 (0.2%)
Closed fracture of intertrochanteric section of neck of femur	70 (0.2%)
Atrioventricular block, complete	69 (0.2%)
Diverticulitis of colon (without mention of hemorrhage)	69 (0.2%)
Other specified cardiac dysrhythmias	69 (0.2%)
Unspecified disease of pericardium	68 (0.2%)
Acute myocardial infarction of inferolateral wall, initial episode of care	66 (0.2%)
Malignant neoplasm of cardia	66 (0.2%)
Urinary tract infection, site not specified	64 (0.2%)
Rheumatic heart failure (congestive)	62 (0.2%)
Secondary malignant neoplasm of bone and bone marrow	62 (0.2%)
Grand mal status	61 (0.2%)
Accidental puncture or laceration during a procedure, not elsewhere classified	60 (0.2%)
Intestinal infection due to Clostridium difficile	60 (0.2%)
Secondary malignant neoplasm of lung	59 (0.2%)
Congenital insufficiency of aortic valve	58 (0.2%)
Subarachnoid hemorrhage following injury without mention of open intracranial wound, with no loss of consciousness	58 (0.2%)
Malignant neoplasm of lower lobe, bronchus or lung	56 (0.2%)
Hepatic encephalopathy	55 (0.2%)
Malignant neoplasm of kidney, except pelvis	55 (0.2%)
Other complications due to other vascular device, implant, and graft	55 (0.2%)
Other specified septicemias	55 (0.2%)
Malignant neoplasm of head of pancreas	54 (0.2%)
Ostium secundum type atrial septal defect	54 (0.2%)
Pneumococcal septicemia (streptococcus pneumoniae septicemia)	54 (0.2%)
Poisoning by benzodiazepine-based tranquilizers	54 (0.2%)
Diabetes with ketoacidosis, type II or unspecified type, uncontrolled	53 (0.2%)
Morbid obesity	52 (0.2%)
Subarachnoid hemorrhage following injury without mention of open intracranial wound, with loss of consciousness of unspecified duration	52 (0.2%)
Other	12,372 (39.1%)

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Table S2 Baseline data of external validation group

Candidate variables	ICU-survival group (N=29,093)	ICU-death group (N=2,552)	P value
General condition			
LOS of hospital	7.73 (4.84, 13.00)	5.55 (2.44, 11.15)	<0.001***
LOS of ICU	2.42 (1.58, 4.46)	4.72 (2.29, 9.31)	<0.001***
In-hospital death	1,009 (3.5%)	2,531 (99.2%)	<0.001***
Admission type			<0.001***
Elective	4,804 (16.5%)	94 (3.7%)	
Emergency	23,499 (80.8%)	2,372 (92.9%)	
Urgent	790 (2.7%)	86 (3.4%)	
Age (years)	65.00 (52.00, 77.00)	72.00 (59.00, 81.00)	<0.001***
Male	16,579 (57.0%)	1,349 (52.9%)	<0.001***
Comorbidity			
Sepsis	1,853 (6.4%)	657 (25.7%)	<0.001***
Laboratory indicators			
Anion gap, maximum (mEq/L)	15.00 (12.00, 17.00)	18.00 (15.00, 21.00)	<0.001***
Anion gap, minimum (mEq/L)	12.00 (11.00, 14.00)	14.00 (12.00, 17.00)	<0.001***
Bicarbonate, maximum (mEq/L)	25.00 (23.00, 27.00)	24.00 (20.00, 27.00)	<0.001***
Bicarbonate, minimum (mEq/L)	23.00 (20.00, 25.00)	20.00 (16.00, 24.00)	<0.001***
Severity score			
GCS	15.00 (14.00, 15.00)	15.00 (13.00, 15.00)	<0.001***
SAPSII	33.00 (25.00, 41.00)	50.00 (39.00, 61.00)	<0.001***
SOFA	3.00 (2.00, 5.00)	7.00 (4.00, 10.00)	<0.001***

0.4% of patients had unknown value for GCS score; ICU, intensive care unit; LOS, length of stay; GCS, Glasgow Coma Scale; SAPSII, simplified acute physiology score II; SOFA, sequential organ failure assessment. ***, P<0.001.

Table S3 Discrimination and calibration of models in external validation

Evaluation index	SAB model	SAPSII	SOFA
Discrimination, AUC (95% CI)	0.7223 (0.7113–0.7333)	0.7983 (0.7895–0.8072)	0.7302 (0.7191–0.7413)
Calibration, brier score	0.070 (0.067–0.072)	0.065 (0.063–0.067)	0.067 (0.065–0.069)

AUC, area under the curve; CI, confidence interval; SAB, Sepsis, Anion gap, Bicarbonate; SAPSII, simplified acute physiology score II; SOFA, sequential organ failure assessment.

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