Appendix 1 Supplementary method

Missing data handling

This study is based on the MIMIC database. Although demographic data was mostly complete, laboratory indicators had several missing values, which, if eliminated, would lead to the loss of crucial information, thus invalidating our modeling approach. The missing data is classified into missing completely at random (MCAR), missing at random (MAR), and not missing at random (NMAR) based on the cause of the missing values (68,69). To discover the nature of the data missing, the correlation matrix was performed to examine the correlation between missing values in the continuous variables (*Table S4*). To facilitate presentation, only significant variables such as weight, bicarbonate, calcium, serum sodium, creatinine, and base excess, were selected and their correlations were presented on the correlation matrix. The values ranged between −0.08 and 0.35, and a weak correlation could be observed between serum sodium and bicarbonate (0.35). Based on a comprehensive analysis, the missing data was deemed to be MCAR, and thus the missing values in the database were replaced with the method "norm. predict" in Multivariate Imputation by Chained Equation (MICE).

Details of the five assumptions in logistic regression

Assumption 1: appropriate outcome variable type

The statement appears to be correct in terms of meeting the first assumption of logistic regression, which requires a dichotomous outcome variable. The outcome variable in this study, death within 28 days, is binary, as it only has two possible outcomes: death or survival. Therefore, it satisfies the first assumption of logistic regression.

Assumption 2: linearity in the logit p (log OR)

The logistic regression model assumes a linear relationship between continuous variables and logit, which is an essential assumption. Two methods are commonly used to assess linearity: graphic visualization and the Box-Tidwell test.

Firstly, we performed restricted cubic spline analysis to explore potential nonlinear relationships between continuous variables and outcomes, a widely used method in this context (70-73). Our analysis did not reveal any significant nonlinearity relationship in the continuous variables, as shown in Figure 3 for both the lasso regression model and the binary logistic regression model.

Additionally, we performed the Box-Tidwell test to further validate our findings and ensure their robustness. As shown in *Figure 3*, all P-nonlinear >0.05, confirm that no significant nonlinearity relationship existed between the continuous variables and the outcome.

Assumption 3: multicollinearity

To diagnose multicollinearity, both the correlation coefficient and variance inflation factor (VIF) are useful metrics (29). First, Pearson and non-parametric Spearman correlation matrices are calculated to explore the possibility of multicollinearity in both continuous and bivariate analyses. Secondly, VIF values equal or greater than 5 indicate the presence of multicollinearity among variables (30). Importantly, neither the correlation matrix nor the VIF values revealed any significant multicollinearity between variables as shown in *Table 4* and *Figure S1*.

Assumption 4: independence of observations.

The assumption of independence in statistical analysis refers to the occurrence of positive events that are randomly distributed across different spaces, times, and populations (excluding the independent variables included in the model). In our study, the positive outcome is not influenced by the aforementioned factors. Therefore, we can assume that the independence hypothesis is approximately met.

Assumption 5: sample size

In this study, we employed one of the most recent techniques to calculate the sample size (27), and traditional methods that satisfy the criteria proposed by Peduzzi of event per variable (EPV) >10 suggest that 1,250 samples would be needed to achieve an EPV of 10 from the final selection of six variables and an event rate of 0.048. We failed to achieve sufficient statistical power. Acknowledging the limitations of the sample size, the validation of our conclusions will be required in future large-scale population studies.

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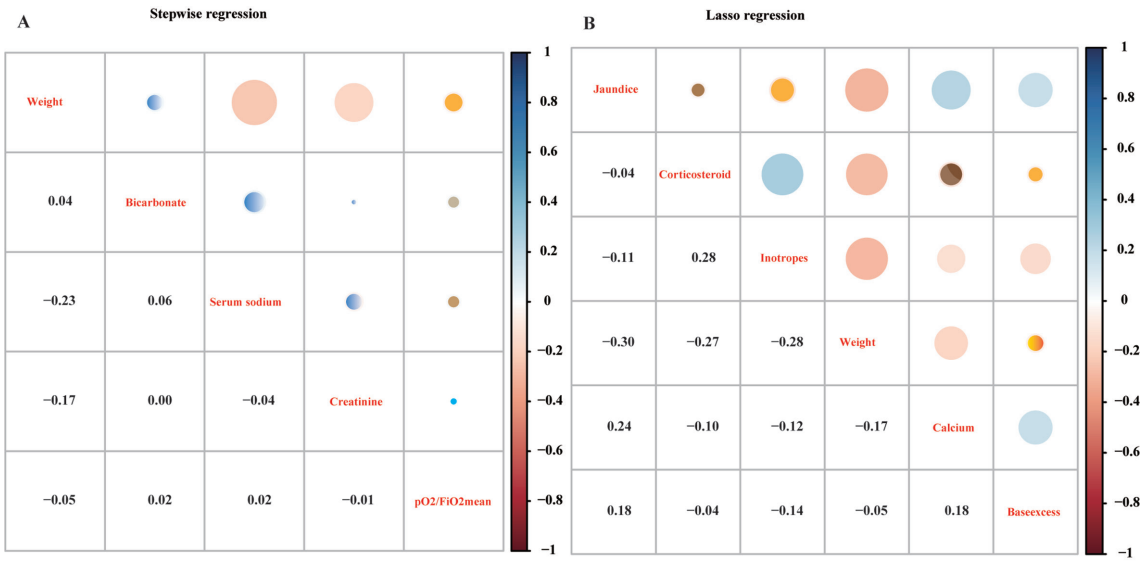

Figure S1 Pearson and nonparametric Spearman correlation matrices among variables in the models.

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Table S1 Neonatal Sequential Organ Failure Assessment (nSOFA) Components and Scoring[†]

Component	nSOFA Scores				
Respiratory score	0	2	4	6	8
Criteria	Not intubated or intubated, SpO2/FiO2≥300	Intubated, SpO2/FiO2<300	Intubated, SpO2/FiO2<200	Intubated, SpO2/FiO2<150	Intubated, SpO2/FiO2<100
Cardiovascular score	0	1	2	3	4
Criteria[§]	No inotropes and no Systemic corticosteroid treatment	No inotropes and systemic corticosteroid treatment	1 inotrope and no systemic corticosteroid treatment	≥2 inotropes or 1 inotrope and systemic corticosteroid treatment	≥2 inotropes and systemic corticosteroid treatment
Hematologic score	0	1	2	3	NA
Criteria[¶]	Platelet count[‡] ≥150×10^9	Platelet count (100–149)×10^9	Platelet count <100×10^9	Platelet count <50×10^9	

[†], Score range, 0 (best) to 15 (worst). [‡], SI conversion factor: To convert platelet count to ×10^9/L, multiply by 1. [§], Medications considered as inotropic or vasoactive included dopamine, dobutamine, epinephrine, norepinephrine, vasopressin, and phenylephrine. [¶], Most recent platelet count available to the clinician. FiO2, fraction of inspiratory oxygen; SpO2, peripheral oximetric saturation; NA, not applicable.

Table S2 The correlation between missing values in all continuous variables

Variables	Weight	Bicarbonate	Calcium	Serum sodium	Creatinine	Base excess
Weight	1	0.3	0.04	0.3	–0.03	0.09
Bicarbonate	0.3	1	0.1	0.35	0.07	0.06
Calcium	0.04	0.1	1	0.1	0.12	–0.08
Serum sodium	0.3	0.35	0.1	1	0.07	0.06
Creatinine	–0.03	0.07	0.12	0.07	1	0.06
Base excess	0.09	0.06	–0.08	0.06	0.06	1

Table S3 Performance of the developed models and nSOFA

Models	AUC	Sensitivity	Specificity	Accuracy
Stepwise	0.784	0.998	0.037	0.952
Lasso	0.924	0.991	0.439	0.965
nSOFA	0.807	0.998	0.096	0.955

AUC, area under the receiver operating characteristic curve; Lasso, the least absolute shrinkage and selection operator; nSOFA, the neonatal sequential organ failure assessment score.

Table S4 The NRI and IDI estimate of the developed models and nSOFA.

Models	NRI		IDI	
	Estimate (95% CI), %	P value	Estimate (95% CI), %	P value
Stepwise regression and nSOFA	8.41 (–10.34, 27.15)	0.379	3.95 (–1.84, 9.74)	0.181
Lasso algorithm and stepwise regression	52.95 (35.70, 70.21)	<0.001	30.93 (21.94, 39.92)	<0.001
Lasso algorithm and nSOFA	53.64 (38.85, 68.43)	<0.001	26.98 (19.06, 34.89)	<0.001

nSOFA, the neonatal sequential organ failure assessment score; Lasso, the least absolute shrinkage and selection operator; NRI net reclassification improvement; IDI integrated discrimination improvement.

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