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ORIGINAL RESEARCH

Developing a Nomogram to Predict the Risk of Delirium in ICU Patients: A Retrospective Cohort Study

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Background: Delirium is a prevalent and severe neuropsychiatric syndrome commonly observed among critically ill patients in the intensive care unit (ICU). Despite its substantial clinical impact, effective tools for predicting delirium risk remain limited. This study aimed to develop and validate a nomogram to predict the risk of delirium in ICU patients, integrating clinical, demographic and laboratory parameters for individualized risk assessment.

Methods: A retrospective cohort study was conducted involving 964 ICU patients admitted between January 2020 and December 2023. Comprehensive clinical data were collected, and delirium was assessed using the Confusion Assessment Method for the ICU (CAM-ICU). Predictive variables were identified using Least Absolute Shrinkage and Selection Operator (LASSO) regression, followed by multivariate logistic regression analysis. A nomogram was constructed based on significant predictors and validated using calibration curves, receiver operating characteristic (ROC) curves, and decision curve analysis (DCA).

Results: Among the 964 ICU patients, 186 (19.3%) developed delirium. Eight predictors were identified as independent risk factors for delirium, including drug abuse, alcohol abuse, male sex, maximum potassium (potassium_max), minimum chloride (chloride_min), length of hospital stay, maximum blood urea nitrogen (BUN_max), and minimum hematocrit (hematocrit_min). The nomogram demonstrated good discrimination with an area under the ROC curve (AUC) of 0.732 (95% CI: 0.690–0.773) and satisfactory calibration. DCA confirmed the clinical utility of the model, showing a net benefit across a wide range of risk thresholds.

Conclusion: This study developed a robust and clinically applicable nomogram for predicting ICU delirium risk, integrating key clinical and laboratory variables. The nomogram can aid ICU clinicians in implementing timely preventive interventions to improve patient outcomes.

Keywords: delirium, intensive care unit, nomogram, logistic model, risk assessment

Introduction

Delirium is a common and severe neuropsychiatric syndrome that frequently occurs in critically ill patients admitted to the ICU.[1] It is characterized by an acute onset of confusion, inattention, and fluctuating levels of consciousness. Delirium affects a substantial proportion of ICU patients, with reported incidence rates ranging from 20% to 80%, depending on the population and underlying comorbidities.[2–4]

The development of delirium in ICU patients has been associated with numerous adverse outcomes, including increased mortality, prolonged hospital and ICU stays, higher rates of long-term cognitive impairment, and greater healthcare costs.[2,5,6] For example, patients who develop delirium are more likely to experience complications such as mechanical ventilation dependence and ICU-acquired weakness, which further exacerbate their prognosis.[1,2] In a study involving elderly patients undergoing hip replacement, the follow-up mortality rate was significantly higher in those with both preoperative and postoperative delirium (80%) than in those with only postoperative delirium (38%) and those without delirium (24%), with a p value of 0.02.[7] A study pooled data from prospective studies and randomized controlled trials (2015–2020) and demonstrated that ICU delirium was associated with a significant mean increase in length of stay

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of 4.77 days in the ICU and 6.67 days in the hospital.[8] Despite these significant clinical implications, delirium often goes underdiagnosed or misdiagnosed due to its fluctuating and heterogeneous presentation.[9]

Regarding the pathogenesis of delirium, inflammatory responses triggered by factors such as surgery may promote the occurrence of delirium by affecting the central nervous system, eg, disrupting the blood-brain barrier and causing neurological dysfunction.[10] Similarly, inflammatory responses are also an important driving factor in the pathogenesis of postoperative cognitive decline (POCD). The study by Glumac et al found that preoperative administration of dexamethasone can mitigate surgery-induced inflammation to reduce cognitive complications.[11] Cotae et al reviewed preventive strategies for early POCD in emergency surgical patients, including anti-inflammatory interventions to mitigate neuroinflammation and reduce incidence.[12] Taken together, these findings underscore that inflammatory responses may play a key role in the pathogenesis of delirium, as they do in POCD.

Efforts to predict the occurrence of delirium have identified a wide range of risk factors, including advanced age, pre-existing cognitive impairment, systemic inflammation, hypoalbuminemia, mechanical ventilation, and prolonged ICU stays.[6,13,14] Various predictive tools and scoring systems have been developed to identify high-risk patients, but many lack precision and generalizability across diverse ICU populations.[1,2,15] While machine learning models and biomarkers have shown promise in improving predictive accuracy, their clinical applicability remains limited due to their complexity and lack of validation in real-world settings.[16]

Nomograms, as graphical predictive tools, have gained popularity in recent years due to their ability to integrate multiple risk factors into a user-friendly and individualized prediction model.[17,18] Several studies have applied nomograms to predict specific ICU complications, such as postoperative delirium following cardiac surgery or delirium in patients with specific conditions like sepsis or acute pancreatitis.[2,3,13] However, most existing models are condition-specific and fail to account for the diverse etiologies and presentations of delirium in the general ICU population. Furthermore, few models have undergone external validation, limiting their practical utility.[9,15]

In this study, we aim to address the gaps in current research by developing and validating a comprehensive nomogram for predicting delirium risk in ICU patients. We hypothesized that integrating clinical, demographic, and laboratory parameters via LASSO and logistic regression would enable the development of a robust nomogram to predict delirium risk in a general ICU population, thereby facilitating timely interventions, improving patient outcomes, and providing a practical tool for clinicians to optimize care for high-risk patients.

Methods

Study Population

This retrospective cohort study enrolled critically ill patients admitted to the intensive care units (ICUs) of Ningbo Medical Center Lihuili Hospital between January 2020 and December 2023. The inclusion and exclusion criteria were designed to ensure the homogeneity and representativeness of the study population. Adult patients aged 18 years or older who were admitted to the ICU with medical, surgical, or trauma-related conditions and had an expected ICU stay exceeding 24 hours were eligible for inclusion. Only patients with available complete clinical and laboratory data and who were able to undergo delirium assessment were included.

Exclusion criteria included patients with pre-existing neurological diseases, such as dementia, Parkinson's disease, or traumatic brain injury, as well as those with psychiatric disorders, such as schizophrenia or major depressive disorder, that could interfere with the evaluation of delirium. Patients with severe sensory deficits, including blindness or deafness, or significant language barriers were also excluded. Additionally, patients under palliative care or with an expected survival of less than 48 hours, as well as those who declined consent or whose legal representatives refused participation, were excluded from the study.

Data Collection

Comprehensive clinical data were collected for all enrolled patients through electronic medical records and bedside assessments conducted by trained researchers. Variables were selected based on their clinical relevance to delirium pathogenesis or outcomes in ICU settings and data availability from routine electronic medical records to ensure feasibility and generalizability. Demographic information, including age, sex and weight, was recorded to account for basic patient characteristics. Medical history was meticulously documented, including pre-existing comorbidities such as congestive heart failure, hypertension, diabetes, and chronic kidney disease. Laboratory parameters included creatinine, chloride, sodium, glucose, inflammatory markers, electrolyte levels, blood urea nitrogen (BUN), hematocrit, hemoglobin, Potassium, and platelet counts, etc. For biochemical indicators with multiple measurements, both the minimum and maximum values were retained for subsequent analyses. Sequential Organ Failure Assessment (SOFA) scores were also were also gathered to assess disease severity and physiological status.

ICU length of stay, total hospital stay, the presence and severity of delirium and survival status were also recorded. Data collection occurred at predefined time points, including within 24 hours of ICU admission, daily during the ICU stay, and at the onset of delirium when applicable. A dedicated research team ensured the completeness and accuracy of collected data through regular quality checks and cross-referencing medical records.

Delirium Assessment

Delirium was assessed using the Confusion Assessment Method for the ICU (CAM-ICU), a widely recognized and validated tool for diagnosing delirium in critically ill patients. Assessments were conducted twice daily (morning and evening) by trained ICU nurses who had undergone standardized training to ensure consistency and reliability. Delirium was defined as the presence of acute changes or fluctuations in mental status, inattention, and either disorganized thinking or an altered level of consciousness.

Statistical Analysis

Statistical analyses were performed using R software (version 4.2.2) and SPSS (version 22.0). Descriptive statistics were used to summarize the data, with continuous variables expressed as means with standard deviations or medians with interquartile ranges, and categorical variables presented as frequencies and percentages. Univariate analyses were conducted to compare variables between patients in the delirium and non-delirium groups. Continuous variables were analyzed using t-tests or Mann–Whitney *U*-tests depending on distribution, while categorical variables were compared using chi-square tests or Fisher's exact tests.

To identify potential predictors of delirium, Least Absolute Shrinkage and Selection Operator (LASSO) regression was applied to reduce dimensionality and select the most relevant variables. The penalty parameter (λ) was determined through cross-validation to minimize binomial deviance, and only significant predictors were retained for further analysis. The selected variables were then included in a multivariate logistic regression model using the Enter method to identify independent risk factors for delirium. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to quantify the strength of associations. In all tests, a two-tailed $p < 0.05$ was considered to indicate a significant difference.

Based on the results of the logistic regression analysis, a nomogram was constructed to provide individualized risk estimates for delirium. The predictive performance of the nomogram was evaluated using calibration curves, which assessed the agreement between predicted and observed probabilities, and receiver operating characteristic (ROC) curves, with the area under the curve (AUC) quantifying discrimination ability. Decision curve analysis (DCA) was conducted to evaluate the clinical utility of the nomogram by comparing net benefits across different risk thresholds.

Results

Baseline Characteristics of Patients and Univariate Analysis

This study analyzed a total of 964 ICU patients, of whom 186 (19.3%) developed postoperative delirium, while 778 (80.7%) did not (Figure 1). Baseline demographic, clinical, and laboratory characteristics were compared between the two groups, and significant differences were identified by univariate analysis (Table 1).

Univariate analysis revealed several factors significantly associated with the occurrence of postoperative delirium. The two groups exhibited a comparable median age (73 years [IQR: 64–80.75] in the delirium group vs 74 years [IQR: 67–81] in the non-delirium group, $p = 0.123$). However, a significant difference in gender distribution was observed, with

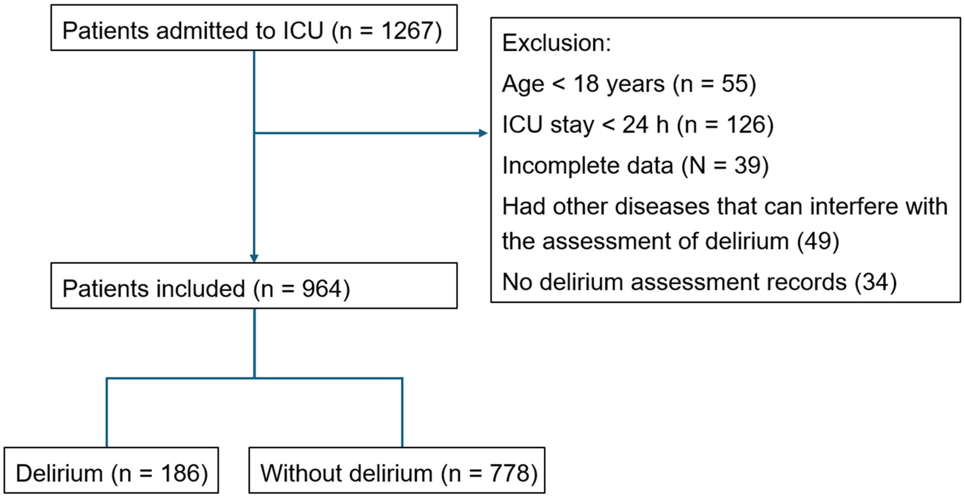

Figure 1 The flowchart of this study.

a higher proportion of males in the delirium group (68.8% vs 49.4%, $p < 0.001$), suggesting that male patients may be at a greater risk of developing delirium.

Among comorbidities, congestive heart failure ($p = 0.011$), peripheral vascular disease ($p = 0.044$), and other neurological disorders ($p = 0.033$) were more prevalent in patients who developed delirium. Fluid and electrolyte disorders ($p < 0.001$) were also significantly more common in the delirium group. Substance use disorders, including alcohol abuse ($p < 0.001$) and drug abuse ($p < 0.001$), were strongly associated with increased risk of delirium. Additionally, gender showed significant differences, with males being more likely to experience delirium ($p < 0.001$).

Table 1 Baseline Characteristics of the Patients

Characteristics	Total (N=964)	Non-Delirium (N=778)	Delirium (N=186)	Test method	P value
Age, median (IQR)	74 (67, 81)	74 (67, 81)	73 (64, 80.75)	Mann–Whitney *U*-test	0.123
Sex, male, n (%)	512 (53.11)	384 (49.36)	128 (68.82)	Chi-square test	< 0.001
Weight, median (IQR)	76.55 (63.5, 90)	76.1 (63.5, 90.18)	77.25 (63.88, 89.98)	Mann–Whitney *U*-test	0.913
Congestive heart failure, n (%)	325 (33.71)	277 (35.60)	48 (25.81)	Chi-square test	0.011
Cardiac arrhythmias, n (%)	415 (43.05)	328 (42.16)	87 (46.77)	Chi-square test	0.254
Valvular disease, n (%)	141 (14.63)	114 (14.65)	27 (14.52)	Chi-square test	0.962
Pulmory circulation, n (%)	59 (6.12)	50 (6.43)	9 (4.84)	Chi-square test	0.417
Peripheral vascular, n (%)	92 (9.54)	67 (8.61)	25 (13.44)	Chi-square test	0.044
Hypertension, n (%)	552 (57.26)	445 (57.20)	107 (57.53)	Chi-square test	0.935
Paralysis, n (%)	37 (3.84)	31 (3.99)	6 (3.23)	Chi-square test	0.628
Other neurological, n (%)	98 (10.17)	87 (11.18)	11 (5.91)	Chi-square test	0.033
Chronic pulmory, n (%)	218 (22.61)	177 (22.75)	41 (22.04)	Chi-square test	0.836
Diabetes uncomplicated, n (%)	187 (19.40)	153 (19.67)	34 (18.28)	Chi-square test	0.668
Diabetes complicated, n (%)	61 (6.33)	46 (5.91)	15 (8.07)	Chi-square test	0.279
Hypothyroidism, n (%)	110 (11.41)	94 (12.08)	16 (8.60)	Chi-square test	0.180
Renal failure, n (%)	141 (14.63)	121 (15.55)	20 (10.75)	Chi-square test	0.096
Liver disease, n (%)	74 (7.68)	63 (8.10)	11 (5.91)	Chi-square test	0.315
Peptic ulcer, n (%)	3 (0.31)	3 (0.39)	0 (0)	Fisher's exact test	>0.999
Aids, n (%)	2 (0.21)	2 (0.26)	0 (0)	Fisher's exact test	>0.999
Lymphoma, n (%)	15 (1.56)	12 (1.54)	3 (1.61)	Fisher's exact test	>0.999
Metastatic cancer, n (%)	59 (6.12)	49 (6.30)	10 (5.38)	Chi-square test	0.638
Solid tumor, n (%)	28 (2.91)	21 (2.70)	7 (3.76)	Chi-square test	0.438

(*Continued*)

Table 1 (Continued).

Characteristics	Total (N=964)	Non-Delirium (N=778)	Delirium (N=186)	Test method	P value
Rheumatoid arthritis, n (%)	35 (3.63)	33 (4.24)	2 (1.08)	Chi-square test	0.038
Coagulopathy, n (%)	83 (8.61)	71 (9.13)	12 (6.45)	Chi-square test	0.243
Obesity, n (%)	30 (3.11)	25 (3.21)	5 (2.69)	Chi-square test	0.711
Weight loss, n (%)	59 (6.12)	48 (6.17)	11 (5.91)	Chi-square test	0.896
Fluid electrolyte, n (%)	307 (31.85)	267 (34.32)	40 (21.51)	Chi-square test	< 0.001
Blood loss anemia, n (%)	30 (3.11)	24 (3.09)	6 (3.23)	Chi-square test	0.921
Deficiency anemias, n (%)	20 (2.08)	18 (2.31)	2 (1.08)	Fisher's exact test	0.397
Alcohol abuse, n (%)	44 (4.56)	20 (2.57)	24 (12.90)	Chi-square test	< 0.001
Drug abuse, n (%)	21 (2.18)	10 (1.29)	11 (5.91)	Fisher's exact test	< 0.001
Psychoses, n (%)	11 (1.14)	10 (1.29)	1 (0.54)	Fisher's exact test	0.701
Depression, n (%)	60 (6.22)	49 (6.30)	11 (5.91)	Chi-square test	0.846
Aniongap_min, median (IQR)	13 (11, 15)	13 (11, 15)	12 (10, 14)	Mann–Whitney *U*-test	< 0.001
Aniongap_max, median (IQR)	15 (13, 18)	15 (13, 18)	14 (12, 16)	Mann–Whitney *U*-test	< 0.001
Bicarbote_min, median (IQR)	23 (21, 26)	23 (20, 26)	23 (21, 26)	Mann–Whitney *U*-test	0.483
Bicarbote_max, median (IQR)	25 (23, 28)	25 (23, 28)	25 (23, 28)	Mann–Whitney *U*-test	0.416
Creatinine_min, median (IQR)	0.9 (0.7, 1.4)	1 (0.7, 1.5)	0.9 (0.6, 1.2)	Mann–Whitney *U*-test	< 0.001
Creatinine_max, median (IQR)	1.1 (0.8, 1.625)	1.1 (0.8, 1.7)	1 (0.7, 1.3)	Mann–Whitney *U*-test	< 0.001
Chloride_min, median (IQR)	102 (98, 106)	102 (98, 106)	104 (100, 107)	Mann–Whitney *U*-test	< 0.001
Chloride_max, median (IQR)	106 (102, 110)	105 (102, 109)	108 (104, 110)	Mann–Whitney *U*-test	< 0.001
Glucose_min, median (IQR)	110 (93, 133)	111.5 (94, 135)	104.5 (92.25, 127.75)	Mann–Whitney *U*-test	0.038
Glucose_max, median (IQR)	158 (126, 198)	156 (124, 197)	164.5 (134.25, 199.75)	Mann–Whitney *U*-test	0.097
Hematocrit_min, mean (SD)	29.75 (6.00)	30.032 (6.00)	28.568 (5.86)	*t*-test	0.003
Hematocrit_max, median (IQR)	35 (31.3, 39)	35 (31.3, 38.6)	35 (31.85, 40)	Mann–Whitney *U*-test	0.187
Hemoglobin_min, median (IQR)	9.9 (8.6, 11.5)	10 (8.7, 11.6)	9.5 (8.4, 10.8)	Mann–Whitney *U*-test	0.003
Hemoglobin_max, median (IQR)	11.5 (10.3, 13)	11.5 (10.2, 13)	11.6 (10.5, 13.2)	Mann–Whitney *U*-test	0.131
Platelet_min, median (IQR)	194 (137, 265)	198 (139, 268)	175 (129.5, 235.75)	Mann–Whitney *U*-test	0.011
Platelet_max, median (IQR)	226 (169, 308)	228 (171, 311)	214.5 (159.25, 280.25)	Mann–Whitney *U*-test	0.074
Potassium_min, median (IQR)	3.7 (3.4, 4.1)	3.8 (3.4, 4.1)	3.7 (3.4, 3.98)	Mann–Whitney *U*-test	0.025
Potassium_max, median (IQR)	4.4 (4, 5)	4.4 (4, 4.9)	4.6 (4.2, 5.3)	Mann–Whitney *U*-test	< 0.001
PTT_min, median (IQR)	28.5 (25.2, 33.8)	28.3 (24.93, 33.8)	29.45 (26.23, 33.9)	Mann–Whitney *U*-test	0.014
PTT_max, median (IQR)	31.25 (27, 43.05)	30.9 (26.8, 41.78)	32.65 (27.33, 49.25)	Mann–Whitney *U*-test	0.030
INR_min, median (IQR)	1.2 (1.1, 1.4)	1.2 (1.1, 1.4)	1.2 (1.1, 1.4)	Mann–Whitney *U*-test	0.668
INR_max, median (IQR)	1.3 (1.2, 1.7)	1.3 (1.1, 1.7)	1.4 (1.2, 1.7)	Mann–Whitney *U*-test	0.372
PT_min, median (IQR)	13.8 (12.8, 15.2)	13.8 (12.8, 15.3)	13.65 (12.8, 14.98)	Mann–Whitney *U*-test	0.600
PT_max, median (IQR)	14.3 (13.2, 16.5)	14.3 (13.2, 16.6)	14.25 (13.3, 16.25)	Mann–Whitney *U*-test	0.959
Sodium_min, median (IQR)	137 (134, 140)	137 (134, 140)	137 (135, 140)	Mann–Whitney *U*-test	0.630
Sodium_max, median (IQR)	140 (137, 142)	140 (137, 142)	140 (138, 143)	Mann–Whitney *U*-test	0.329
BUN_min, median (IQR)	19.5 (14, 33)	21 (15, 35)	17 (12, 25)	Mann–Whitney *U*-test	< 0.001
BUN_max, median (IQR)	22 (16, 37)	23.5 (17, 40)	20 (14, 28)	Mann–Whitney *U*-test	< 0.001
WBC_min, median (IQR)	9.7 (7.3, 13.1)	9.6 (7.2, 13)	9.95 (7.8, 14)	Mann–Whitney *U*-test	0.161
WBC_max, median (IQR)	12.3 (8.9, 16.6)	12.2 (8.8, 16.4)	13.2 (9.53, 16.9)	Mann–Whitney *U*-test	0.064
LOS hospital, median (IQR)	9 (5, 17)	8 (5, 16)	12 (8, 17)	Mann–Whitney *U*-test	< 0.001
LOS_ICU, median (IQR)	2 (1, 5)	2 (1, 5)	3 (2, 6)	Mann–Whitney *U*-test	0.006
SOFA, median (IQR)	4 (2, 6)	3.5 (2, 6)	4 (2, 5)	Mann–Whitney *U*-test	0.124

Laboratory parameters also demonstrated significant differences. Patients with delirium had lower minimum anion gap ($p < 0.001$), maximum anion gap ($p < 0.001$), and minimum creatinine ($p < 0.001$). Maximum creatinine levels ($p < 0.001$) and minimum chloride levels ($p < 0.001$) were significantly different between groups. Among hematologic markers, lower minimum hemoglobin ($p = 0.003$), minimum hematocrit ($p = 0.003$), and platelet counts

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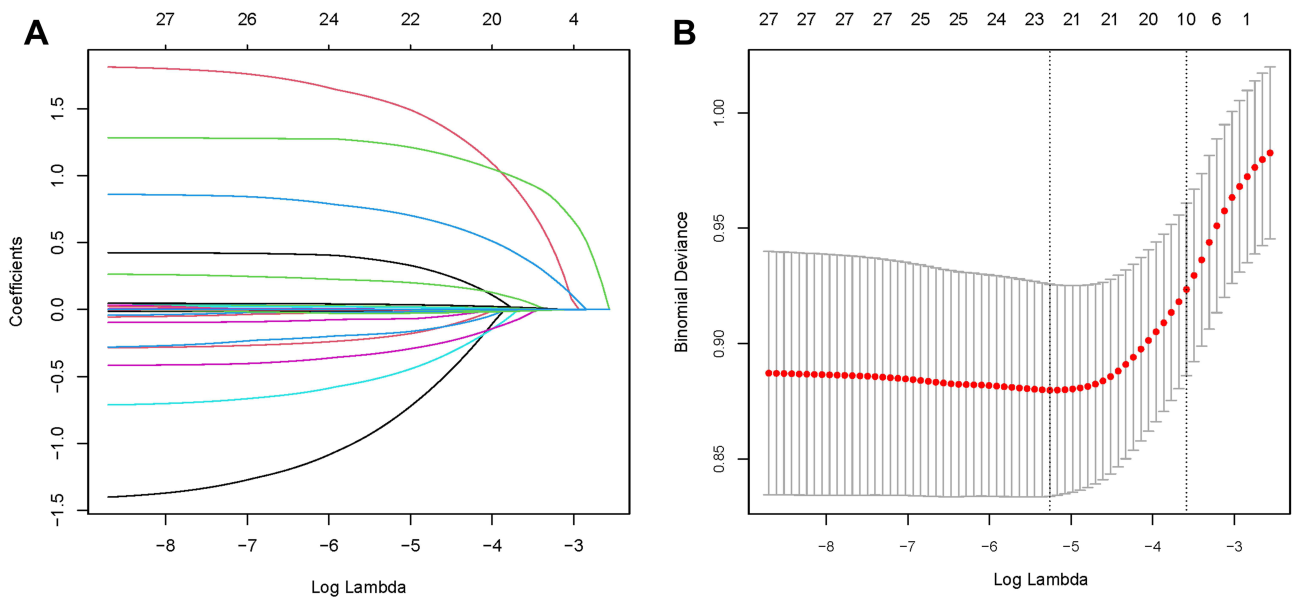

Figure 2 Selection of delirium-associated variables using the LASSO regression model. (**A**) Coefficient path plot of the LASSO regression, illustrating the changes in coefficients of variables across different Log Lambda values. As the regularization strength increases, certain coefficients shrink to zero, enabling variable selection. (**B**) Binomial deviance of the LASSO regression model as a function of Log Lambda, based on 10-fold cross-validation. The optimal value of the parameter λ is determined using cross-validation.

($p = 0.011$) were observed in the delirium group. Length of ICU stay ($p = 0.006$) and overall hospital stay ($p < 0.001$) were significantly longer in patients with delirium, indicating its impact on resource utilization and outcomes.

LASSO Regression Results

The LASSO regression was performed to select variables with the strongest association with delirium (Figure 2). As λ increased, coefficients of less relevant variables shrank to zero, leaving only significant predictors. The cross-validation curve identified the optimal λ value that minimized binomial deviance. At the optimal λ, 8 variables were selected as potential predictors to be included in the multivariate logistic regression analysis.

Multivariate Logistic Regression Analysis

Multivariate logistic regression analysis was conducted to identify independent risk factors for delirium in ICU patients. The analysis retained 8 significant predictors: drug abuse, alcohol abuse, male gender, potassium_max, chloride_min, Length of hospital stay, BUN_max and hematocrit_min. The forest plot visually presents the odds ratios and 95% confidence intervals for the variables included in the logistic regression model (Figure 3). It highlights the relative contributions of each factor to the risk of delirium, with drug abuse and alcohol abuse showing the strongest associations.

Nomogram Model Construction and Evaluation

A nomogram was constructed based on the results of the multivariate logistic regression analysis (Figure 4). The variables included in the model were drug abuse, alcohol abuse, gender, maximum potassium level, minimum chloride level, length of hospital stay, maximum BUN level, and minimum hematocrit level. These variables were selected for their significant contributions to the risk of delirium, as determined by their regression coefficients. Each variable was assigned a specific score, and the total score was calculated by summing these individual contributions. The total score was then mapped to a predicted probability of delirium using the nomogram.

Model Performance Evaluation

The receiver operating characteristic (ROC) curve (Figure 5) was used to evaluate the discrimination ability of the nomogram. The area under the ROC curve (AUC) was 0.732 (95% CI: 0.690–0.773), reflecting high predictive accuracy.

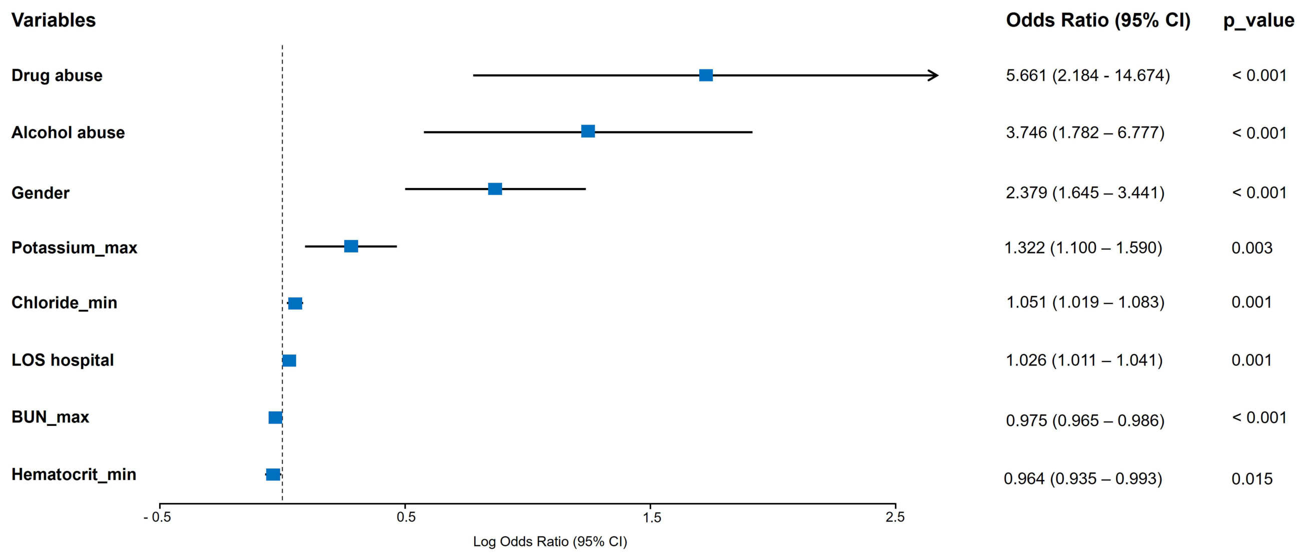

Figure 3 Forest plot of multivariate logistic regression for delirium-associated factors in ICU patients.

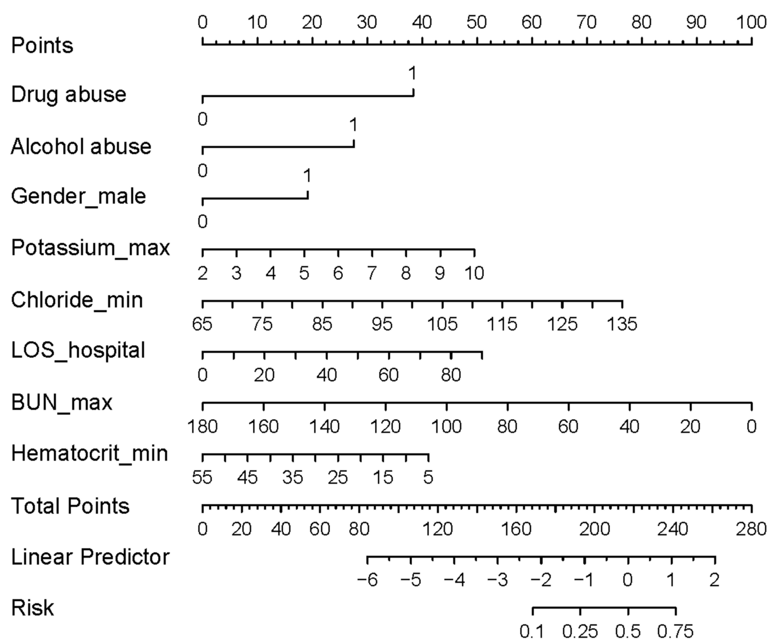

Figure 4 Nomogram constructed based on the results of multivariate logistic regression analysis. Predictors included drug abuse, alcohol abuse, gender, potassium_max, chloride_min, length of hospital stay, BUN_max, and hematocrit_min.

At the optimal cutoff point of 0.207, the model achieved a sensitivity of 0.618 and a specificity of 0.735, demonstrating a reasonable balance between correctly identifying patients with delirium and avoiding false positives.

The calibration of the nomogram was evaluated using a calibration curve (Figure 6), which compared the predicted probabilities of delirium with the observed probabilities. The "Ideal" line represented perfect calibration, while the "Apparent" and "Bias-corrected" lines illustrated the actual performance of the model. The calibration curve demonstrated good agreement between predicted and observed probabilities, indicating that the nomogram was well-calibrated for predicting delirium in the training cohort.

The clinical utility of the nomogram was assessed using decision curve analysis (DCA) (Figure 7). The DCA curve showed that the nomogram provided a higher net benefit across a wide range of risk thresholds compared to the "All"

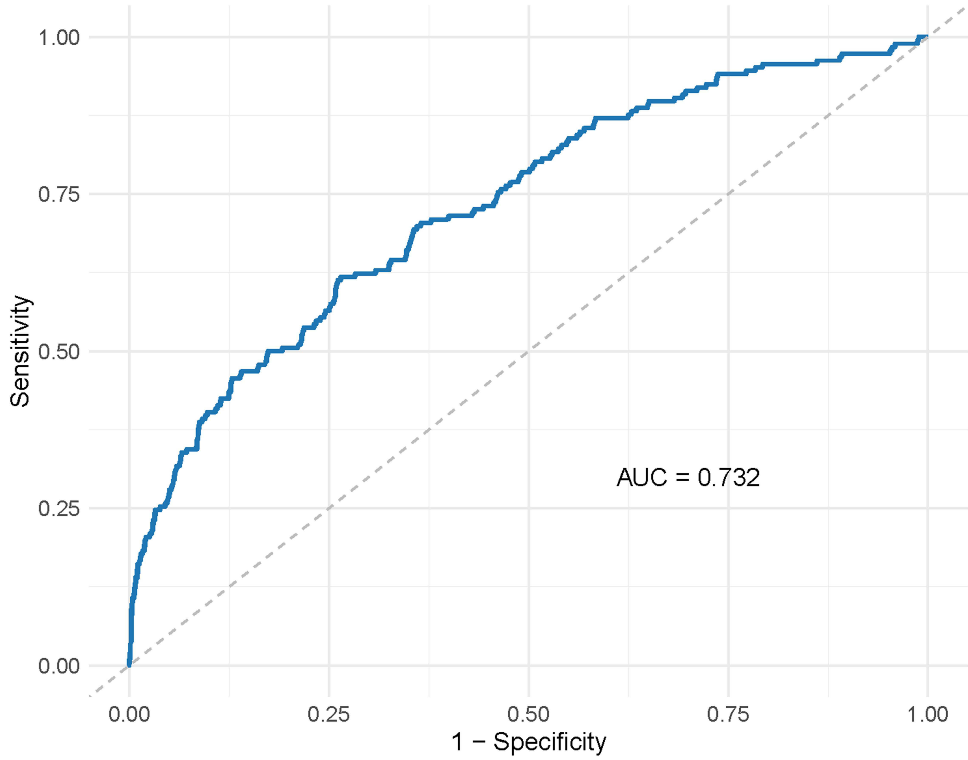

Figure 5 Receiver operating characteristic (ROC) curve and area under the ROC curve (AUC) of the nomogram for predicting delirium in ICU patients. ROC: receiver operating characteristic; AUC: area under the ROC curve.

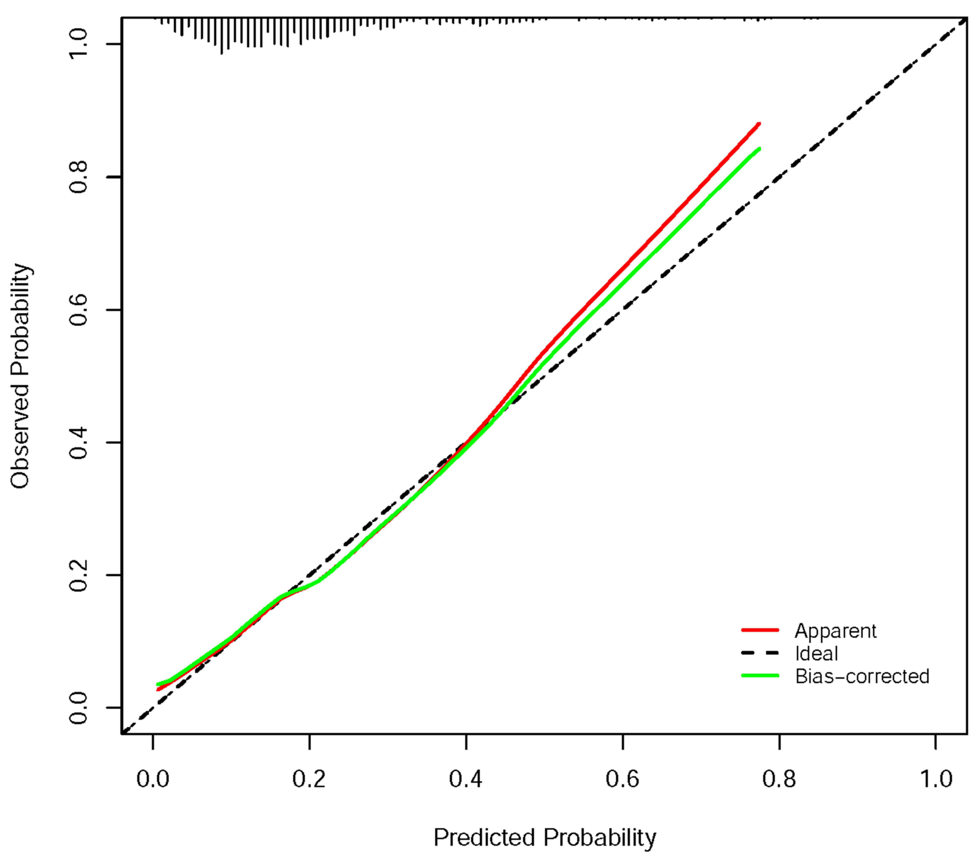

Figure 6 Calibration curve for assessing the consistency between the predicted probabilities and the actual probabilities of delirium occurrence based on the nomogram.

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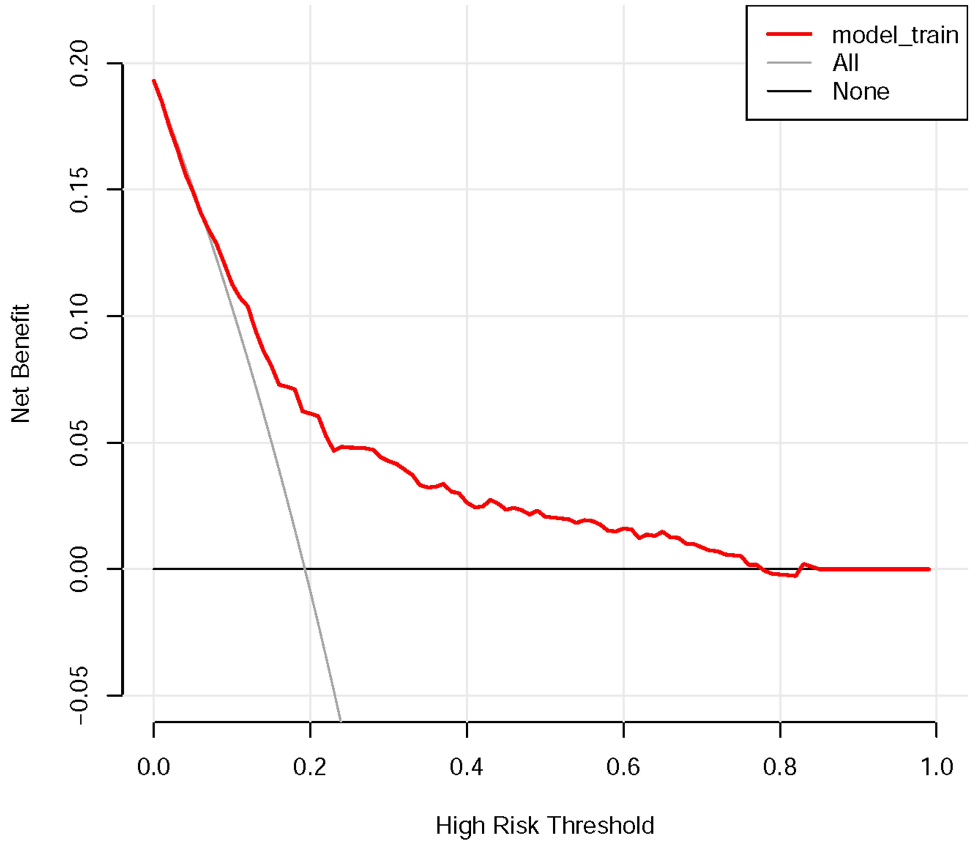

Figure 7 DCA curve for evaluating the clinical applicability of the nomogram. DCA: decision curve analysis.

(treat all patients) and "None" (treat no patients) strategies. As shown in the DCA curve of nomogram, a net clinical benefit was achieved when the threshold probability was below 0.8.

Discussion

The main finding of this study is that we developed and validated a robust nomogram incorporating eight independent risk factors—drug abuse, alcohol abuse, male sex, maximum potassium level, minimum chloride level, length of hospital stay, maximum BUN, and minimum hematocrit—for predicting delirium risk in ICU patients, with satisfactory discrimination (AUC = 0.732), calibration, and clinical utility.

The Nomogram developed in this study demonstrated several strengths. By integrating multiple clinical, demographic, and laboratory variables, it provided a comprehensive and individualized risk prediction for ICU delirium. The model exhibited high predictive accuracy, as indicated by the ROC-AUC, and good calibration, as evidenced by the agreement between predicted and observed probabilities. These features underscore the model's ability to offer precise and reliable predictions, making it a practical tool for predicting postoperative delirium in ICU patients, enabling early identification of high-risk individuals and informing preventive strategies. Moreover, its visual presentation simplifies interpretation for healthcare professionals, facilitating its adoption in routine clinical workflows. Such characteristics align with the growing recognition of nomograms as user-friendly and effective predictive tools in critical care settings.[2,19,20]

The findings of this study are consistent with previous research on ICU delirium while also offering unique insights. For example, Wang et al developed a nomogram to predict postoperative delirium in cardiac surgery patients, achieving an AUC of 0.852.[20] While their model demonstrated higher predictive accuracy, it was specific to a surgical cohort, whereas our model targets a broader ICU population, enhancing its generalizability.

This study identified several independent risk factors for ICU delirium, as detailed above. These findings are consistent with prior research while also offering novel perspectives into the interplay of these factors in delirium pathophysiology, bridging the existing understanding and new observations to deepen our comprehension of this complex syndrome.

Substance abuse has long been recognized as a significant predictor of delirium due to its adverse effects on neurotransmitter regulation and cognitive reserve.[21,22] Chronic alcohol use, for example, has been linked to alterations in gamma-aminobutyric acid (GABA) and glutamate pathways, which may predispose patients to delirium in the ICU setting.[22] Similarly, drug abuse exacerbates systemic inflammation and compromises neurocognitive function, increasing the risk of delirium.[2,19] A study aimed at evaluating the incidence of delirium in patients with blunt traumatic brain injury (TBI) associated with drug or alcohol abuse revealed that individuals testing positive for stimulants (OR: 1.340, $P = 0.018$), tricyclic antidepressants (OR: 3.107, $P = 0.019$), or cannabinoids (OR: 1.326, $P \leq 0.001$) had a significantly higher risk of delirium.[23]

The association between male gender and delirium risk has been reported in multiple studies, with hormonal differences, higher rates of comorbidities, and differences in healthcare-seeking behavior proposed as contributing factors.[24] Male sex has been identified as a significant risk factor for neuropsychiatric disorders in both humans and animal models, while estrogen may offer protective effects in individuals with potential cognitive impairment (20). A study investigating the influence of sex differences on postoperative delirium (POD) in adult patients undergoing cardiac valve surgery identified male sex as a significant risk factor for POD (OR: 2.213, $P = 0.037$).[25] Almashari et al conducted a retrospective analysis of the incidence and risk factors for POD in elderly patients, including 108 patients (72 males). Their findings revealed significant associations between POD and advanced age, male sex, diabetes, hypertension, congestive heart failure, and chronic kidney disease.[26] Our findings align with these observations, further supporting the inclusion of gender as a predictor in delirium risk models.

The brain operates in a highly complex environment, requiring precise regulation of electrolytes.[27] Electrolyte imbalances, including elevated potassium and chloride levels, have been identified as significant predictors of delirium. These findings align with studies suggesting that electrolyte disturbances impair neuronal function, contributing to acute cognitive dysfunction.[20,28] Moreover, correcting electrolyte imbalances has been shown to shorten the duration of delirium.[29] Although these studies emphasize the role of electrolytes as a risk factor for postoperative delirium, the specific impact of different electrolytes remains controversial. Some studies suggest that disturbances in potassium or sodium levels may contribute to postoperative delirium.[30] For instance, Wang et al studied 582 patients undergoing orthopedic surgery and found that imbalances in sodium and calcium were independent risk factors for POD.[31] In our study, disruptions in potassium and chloride levels were associated with the occurrence of postoperative delirium. Therefore, while electrolyte imbalances are implicated, the exact mechanisms by which specific electrolytes contribute to postoperative delirium remain unclear.

Prolonged hospitalization was strongly associated with delirium, likely due to extended exposure to ICU stressors, sedatives, and invasive procedures.[32] These findings are in line with previous research highlighting the cumulative burden of critical illness as a key driver of delirium.[19,33] Štubljar et al reported that patients with delirium had significantly longer hospital stays ($p = 0.002$) and ICU stays ($p = 0.032$) compared to no n-delirium patients.[32]

Lower BUN and hematocrit levels were inversely associated with the risk of delirium. In contrast to our findings, some previous studies have demonstrated an association between higher BUN levels and delirium.[34,35] For example, a study investigating the relationship between BUN levels and delirium risk in elderly critically ill patients without kidney disease found that the maximum BUN level exhibited the strongest non-linear positive association with the odds of delirium.[34] This discrepancy may reflect differences in study populations or methodologies, underscoring the need for further research to elucidate the complex relationships between these variables and the pathophysiology of delirium.

Our findings on hematocrit levels are consistent with previous studies. Jang et al reported significantly lower hematocrit levels in patients with delirium, although hematocrit was not identified as an independent risk factor for delirium.[35] In contrast, Krzych et al conducted a large-scale study investigating risk factors for postoperative delirium in cardiac surgery patients, and multivariate analysis identified lower hematocrit as an independent risk factor for delirium.[36]

Some previous studies have identified risk factors for predicting ICU delirium that differ from those in this study. Al-Hoodar et al identified sepsis and metabolic acidosis as key predictors of delirium in Omani ICU patients.[19] In Jang's study, depression, musculoskeletal disorders, traumatic brain injury, elevated levels of WBC, BUN, AST, and CRP, as well as decreased levels of potassium and phosphorus, were identified as independent risk factors for delirium.[35] Similarly, findings from Pan et al indicated that the use of sedatives, length of ICU stay, and physical restraints were independent risk factors for delirium.[37] Discrepancies between studies may be attributed to differences in study design, patient demographics, sample size, and data collection methods. These results underscore the importance of considering a wide range of clinical and laboratory variables when assessing delirium risk and provide a robust basis for developing predictive models.

Additionally, some studies have utilized imaging data to predict the risk of delirium, such as white matter changes (WMC) and atrophy.[38] However, the feasibility of incorporating such approaches into routine clinical practice may be limited. By contrast, our model focuses on readily available clinical variables, making it more practical for widespread use.

Several limitations of this study must be acknowledged. First, the relatively small sample size and single-center design may limit the generalizability of the findings. Second, the inclusion of ICU patients with highly diverse admission diagnoses (eg, medical, surgical, and trauma-related conditions) introduces heterogeneity, as different underlying diseases are associated with varying baseline risks of delirium. This diversity may affect the model's performance across specific subgroups, as the pathophysiological mechanisms and risk profiles for delirium can differ substantially between, for example, post-surgical patients and those with acute medical illnesses. Third, the exclusion of certain potential predictors, such as biomarkers of neuroinflammation or genetic predispositions, may have impacted the model's predictive power. Fourth, the reliance on internal validation without external testing restricts the model's applicability to broader populations. Finally, the use of clinical and laboratory data at specific time points may not fully capture the dynamic nature of delirium risk in critically ill patients. Addressing these limitations in future studies will be critical to optimizing the nomogram's utility and effectiveness.

Conclusion

This study developed and validated a nomogram model to predict the risk of delirium in ICU patients. By integrating key clinical, demographic, and laboratory variables, the model demonstrated high predictive accuracy and good calibration, providing a practical tool for individualized risk assessment. The Nomogram is applicable in ICU settings for a broad population of critically ill patients. The findings highlight the nomogram's value in identifying high-risk patients early, thereby enabling timely preventive interventions and improving patient outcomes.

Data Sharing Statement

The datasets used or analysed during the current study are available from the corresponding authors on reasonable request.

Ethics Approval and Consent to Participate

The present study followed the Declaration of Helsinki. This study was approved by the Ethics Committee of Ningbo Medical Center Lihuili Hospital (No. KY2025SL008-01), and written informed consent was obtained from all subjects participating in the trial, and their information was stored and used for research anonymously. This study was in accordance with the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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