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Establishment and validation of a nomogram of postoperative delirium in patients undergoing cardiac surgery: a retrospective study of MIMIC-IV

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Abstract

Objective To establish a nomogram for predicting the occurrence of postoperative delirium (POD) in patients undergoing cardiac surgery.

Materials and methods Data from 5379 patients were retrieved from the Medical Information Mart for Intensive Care (MIMIC-IV) database and divided into a training set and a validation set at a 7:3 ratio. Multivariate logistic regression was conducted to identify independent predictors and establish nomograms to predict the occurrence of POD. The area under the receiver operating characteristic curve (AUC), calibration curve, and decision curve analysis (DCA) were used to evaluate the accuracy and reliability of the model.

Results A total of 5379 post-cardiac surgery patients were included in the study, with 258 patients in the training set and 113 patients in the validation set developing POD. Multivariate logistic regression analysis identified seven independent predictors: age, partial pressure of carbon dioxide (PCO2), glucose, white blood cell count (Wbc), stroke, anemia and chronic obstructive pulmonary disease (COPD). The prediction model demonstrated good discrimination, with an AUC of 0.702 (95 CI: 0.671–0.734) in the training set and 0.711 (95 CI: 0.7662 – 0.761) in the validation set. The calibration curve of the prediction model closely matched the ideal curve in both the training set and the validation set. In addition, the DCA curve demonstrated that the nomogram has better clinical applicability.

Conclusion We constructed a nomogram for the personalized prediction of delirium in post-cardiac surgery patients, demonstrating satisfactory performance and clinical utility. This tool may help clinicians initiate preventive interventions for POD.

Keywords Cardiac surgery, Postoperative delirium, Nomogram, MIMIC-IV, ICU

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Introduction

Postoperative delirium (POD) is a common complication, characterized by changes and fluctuations in consciousness, attention, perception, cognition, and thought disorders during acute episodes [1]. According to the literature, patients undergoing cardiac surgery are at particularly high risk due to the nature of the disease process and the inflammatory environment caused by myocardial injury and cardiopulmonary bypass during surgery, with the incidence of POD ranging from 12.4–52% [2–4]. Notably, patients who experience delirium have prolonged hospital stays, increased healthcare costs, cognitive and social dysfunction, and even higher mortality rates [5–7].

Early diagnosis and management of delirium after cardiac surgery are crucial for patient survival and prognosis. Some researchers have identified the risk factors for delirium after cardiac surgery, but no predictive model has been established [8–11].

A nomogram, used to predict the incidence of outcome events, is a numerical estimation of several clinicopathological parameters [12]. This study aims to create a predictive model using potential risk factors through retrospective analysis of large clinical databases, to enable early identification of delirium after cardiac surgery.

Methods

Data source

The retrospective cohort analysis utilized the MIMIC-IV version 2.2 database [13]. The author of this study, Gang Liao (ID: 12855703), registered for and completed the online training program of the NIH Cooperative Agreement, and obtained approval from the Institutional Review Board at the Massachusetts Institute of Technology. He can access the MIMIC-IV database and obtain the data, having received the necessary certification.

Study population

Patient information was extracted from the MIMIC IV database based on the following inclusion criteria: (1) patients admitted to the ICU after cardiac surgery; (2) demographic data (gender, age, marital status); (3) vital signs, laboratory data, and ventilator data on the first day; (4) disease severity scores: logistic organ dysfunction system (LODS), simplified acute physiology score II (SAPS II), and Sequential Organ Failure Assessment (SOFA); (5) other comorbidities. Exclusion criteria included: (1) age < 18 years; (2) patients with schizophrenia or dementia; (3) patients receiving cardiopulmonary resuscitation; or (4) missing data for research variables. The flowchart of the selection process is presented in Fig. 1.

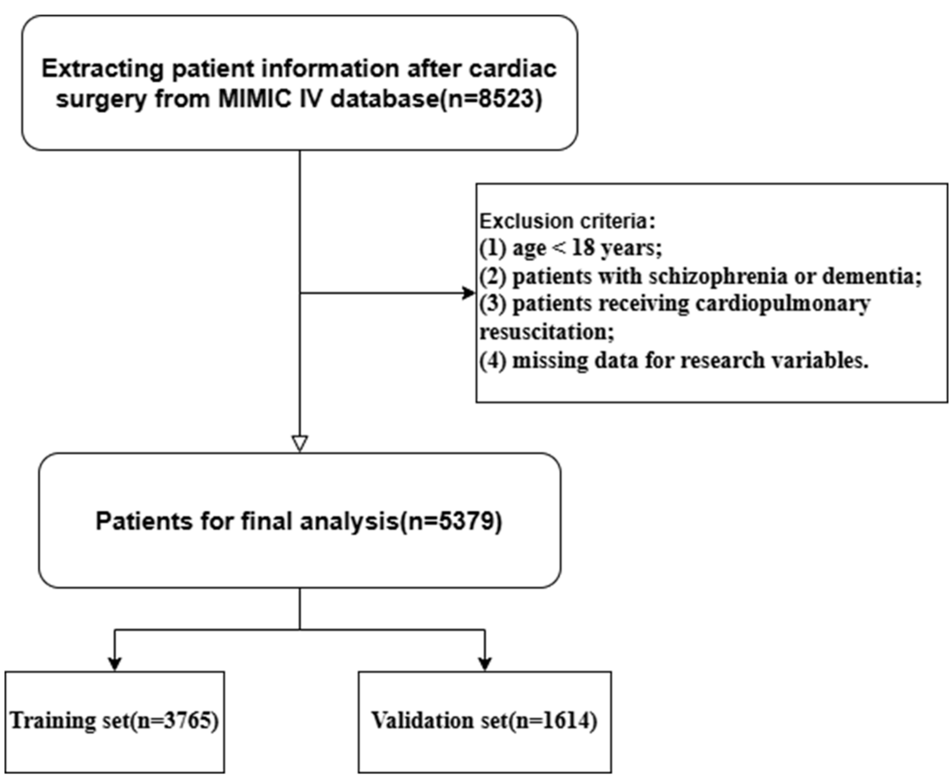

Fig. 1 Flow diagram for patient selection

Statistical analysis

The study population was divided into two groups based on their delirium assessments. The Pearson chi-square test was employed to compare the classified data. All statistical analyses were performed using R software with the Table 1, compareGroups, regplot, pROC, rms, and ggDCA packages.

To develop a predictive nomogram, patients were randomly assigned to a training set and a validation set in a 7:3 ratio using R software (version 4.2.0). The risk factors for the nomogram were selected through multivariate logistic regression, where the variable had a p-value < 0.05. In the training and validation sets, the performance of the nomograms was evaluated using the AUC. Additionally, the calibration curve is used to assess the consistency between the model's predictions and actual outcomes, while DCA is conducted to evaluate the clinical utility of the nomogram.

In this study, all statistical analyses were performed using R software (version 4.2.0), and $P < 0.05$ was considered statistically significant.

Results

Patient clinical data

A total of 5,379 patients were included in the analysis, among which 371 experienced delirium following cardiac surgery. Demographic and clinical characteristics are detailed in Table 1. Patients older than 73 years, with glucose levels exceeding 180 mg/dL or below 140 mg/dL, who have a history of stroke, anemia and COPD, are more likely to experience delirium.

Risk prediction nomogram development

Initially, multivariate logistic regression analysis was performed in the training group, selecting factors with a p-value less than 0.05 as independent predictors of POD. Ultimately, seven predictors were identified: age, PCO2, glucose, Wbc, stroke, anemia and COPD. These data are presented in Table 2.

The nomogram used to predict the probability of POD is constructed using a logistic regression model (Fig. 2). By summing the scores of each variable, the overall score can be calculated to assess the likelihood of delirium in patients. For example, a patient aged ≥ 73 years receives 53 points, a normal range of PCO2 scores 0 points, glucose levels below 140 mg/dL receive 53 points, Wbc greater than 10^9/L scores 53 points, a prior history of stroke scores 100 points, a history of anemia scores 78 points, and a history of COPD scores 79 points. The total score was 416, indicating that the estimated risk of POD in this instance was 0.66.

Predictive accuracy and net benefit of the nomogram

The AUC values for the training set and the validation set are 0.702 (95CI: 0.671–0.734) and 0.711 (95CI: 0.662–0.761), respectively, indicating that the model demonstrates high accuracy. (Fig. 3)The calibration curve of the nomogram model closely approximates the ideal diagonal, demonstrating that the predicted values align well with the actual observed values. (Fig. 4) The DCA reveals that the model exhibits high clinical validity within threshold probability ranges of 0.02–0.81 for the training set and 0.03–0.17 for the validation set.(Fig. 5).

Discussion

In this study, we retrospectively analyzed data from 5,379 patients who had undergone cardiac surgery using the MIMIC IV database. Age, PCO2, glucose levels, Wbc, history of stroke, anemia, and COPD were utilized to calculate the probability of POD, assisting clinicians in identifying high-risk patients and adjusting treatment plans.

Delirium is characterized by acute brain dysfunction or alterations in mental state, placing all patients at risk, particularly the elderly and vulnerable populations. Anemia is prevalent among the elderly; however, previous studies have indicated that there is no correlation between anemia and delirium in this population. In contrast, our study found that the rate of delirium in patients with anemia was 1.516 times higher than that in patients without anemia ($P = 0.005$). This discrepancy may be attributed to the inclusion of younger individuals in our data set, which could explain the differing results [14, 15].

The occurrence of delirium following cardiac surgery is believed to be associated with disturbances in cerebral circulation due to cardiopulmonary bypass, embolic load, and insufficient perfusion [16, 17]. Cardiopulmonary bypass during cardiac surgery can induce a systemic inflammatory response. Previous studies have documented the relationship between biomarkers of systemic inflammation (such as IL-6, IL-8, and C-reactive protein) and delirium [18, 19]. Research has indicated that the potential endogenous anticoagulant activity of inflammatory markers is associated with delirium during critical illness [20]. The systemic inflammatory response can release potentially neurotoxic pro-inflammatory mediators by activating microglia in the brain, thereby contributing to the onset of delirium. Similarly, our study found that the likelihood of POD in patients with a normal white blood cell count following cardiac surgery is only 0.556 times that of patients with a high white blood cell count ($P = 0.036$).

Patients who have suffered a stroke are particularly susceptible to delirium [21, 22]. The likelihood of cerebral embolism following cardiac surgery, particularly during coronary artery bypass grafting, is over 100 times greater than that of off-pump surgery, significantly contributing

Table 1 Characteristics of the included patients (stratified by delirium risk)

	[ALL]	Without Delirium risk	With Delirium risk	*p*.overall
	N **= 5379**	***N*** **= 5008**	***N*** **= 371**	
Age: years				<0.001
≥73	1805 (33.6%)	1599 (31.9%)	206 (55.5%)	
18–63	1688 (31.4%)	1625 (32.4%)	63 (17.0%)	
63–73	1886 (35.1%)	1784 (35.6%)	102 (27.5%)	
Gender				0.014
Female	1438 (26.7%)	1318 (26.3%)	120 (32.3%)	
Male	3941 (73.3%)	3690 (73.7%)	251 (67.7%)	
BMI				0.046
Normal weight	806 (15.0%)	735 (14.7%)	71 (19.1%)	
Overweight or obese	4528 (84.2%)	4232 (84.5%)	296 (79.8%)	
underweight	45 (0.84%)	41 (0.82%)	4 (1.08%)	
Marital_status				0.001
Divorced	403 (7.49%)	373 (7.45%)	30 (8.09%)	
Married	3553 (66.1%)	3333 (66.6%)	220 (59.3%)	
Single	918 (17.1%)	852 (17.0%)	66 (17.8%)	
Widowed	505 (9.39%)	450 (8.99%)	55 (14.8%)	
Heart_rate: beats/min				0.026
<60	15 (0.28%)	12 (0.24%)	3 (0.81%)	
>100	191 (3.55%)	184 (3.67%)	7 (1.89%)	
60–100	5173 (96.2%)	4812 (96.1%)	361 (97.3%)	
MBP: mmHg				0.034
<60	16 (0.30%)	13 (0.26%)	3 (0.81%)	
>75	2318 (43.1%)	2175 (43.4%)	143 (38.5%)	
60–75	3045 (56.6%)	2820 (56.3%)	225 (60.6%)	
Resp_rate: breaths/min				1.000
>12	5370 (99.8%)	4999 (99.8%)	371 (100%)	
8–12	9 (0.17%)	9 (0.18%)	0 (0.00%)	
Temperature: celsius				0.997
≥37	1008 (18.7%)	939 (18.8%)	69 (18.6%)	
36–37	4371 (81.3%)	4069 (81.2%)	302 (81.4%)	
PH:				0.602
<7.35	3994 (74.3%)	3719 (74.3%)	275 (74.1%)	
>7.45	8 (0.15%)	7 (0.14%)	1 (0.27%)	
7.35–7.45	1377 (25.6%)	1282 (25.6%)	95 (25.6%)	
pO2:mmHg				<0.001
<80	1167 (21.7%)	1040 (20.8%)	127 (34.2%)	
>100	2725 (50.7%)	2584 (51.6%)	141 (38.0%)	
80–100	1487 (27.6%)	1384 (27.6%)	103 (27.8%)	
pCO2: mmHg				0.153
<35	8 (0.15%)	6 (0.12%)	2 (0.54%)	
>45	3975 (73.9%)	3703 (73.9%)	272 (73.3%)	
35–45	1396 (26.0%)	1299 (25.9%)	97 (26.1%)	
Lactate: mmol/L				0.008
>2	3828 (71.2%)	3541 (70.7%)	287 (77.4%)	
0–2	1551 (28.8%)	1467 (29.3%)	84 (22.6%)	
Calcium: mmol/L				0.252
<1.16	4731 (88.0%)	4395 (87.8%)	336 (90.6%)	
>1.31	6 (0.11%)	6 (0.12%)	0 (0.00%)	
1.16–1.31	642 (11.9%)	607 (12.1%)	35 (9.43%)	
Glucose: mg/dL				0.001
<140	531 (9.87%)	492 (9.82%)	39 (10.5%)	
>180	2298 (42.7%)	2107 (42.1%)	191 (51.5%)	

Table 1 (continued)

	[ALL]	Without Delirium risk	With Delirium risk	p.overall
	N = 5379	N = 5008	N = 371	
140–180	2550 (47.4%)	2409 (48.1%)	141 (38.0%)	
Potassium: mmol/L				0.034
<3.5	7 (0.13%)	5 (0.10%)	2 (0.54%)	
>5.5	1939 (36.0%)	1819 (36.3%)	120 (32.3%)	
3.5–5.5	3433 (63.8%)	3184 (63.6%)	249 (67.1%)	
Sodium: mmol/L				0.009
<135	453 (8.42%)	406 (8.11%)	47 (12.7%)	
>145	10 (0.19%)	9 (0.18%)	1 (0.27%)	
135–145	4916 (91.4%)	4593 (91.7%)	323 (87.1%)	
Hemoglobin: g/dL				0.039
<9	4106 (76.3%)	3806 (76.0%)	300 (80.9%)	
>=9	1273 (23.7%)	1202 (24.0%)	71 (19.1%)	
Platelets: $\times10^9$/L				<0.001
<100	986 (18.3%)	888 (17.7%)	98 (26.4%)	
>300	45 (0.84%)	40 (0.80%)	5 (1.35%)	
100–300	4348 (80.8%)	4080 (81.5%)	268 (72.2%)	
White blood cell count:$\times10^9$/L				0.162
>10	4886 (90.8%)	4541 (90.7%)	345 (93.0%)	
4–10	493 (9.17%)	467 (9.33%)	26 (7.01%)	
Bun: mmol/L				<0.001
<8	49 (0.91%)	46 (0.92%)	3 (0.81%)	
>21	1475 (27.4%)	1339 (26.7%)	136 (36.7%)	
8–21	3855 (71.7%)	3623 (72.3%)	232 (62.5%)	
Creatinine: mg/dL				<0.001
<0.6	161 (2.99%)	152 (3.04%)	9 (2.43%)	
>1.2	1260 (23.4%)	1126 (22.5%)	134 (36.1%)	
0.6–1.2	3958 (73.6%)	3730 (74.5%)	228 (61.5%)	
Stroke:				<0.001
NO	5276 (98.1%)	4928 (98.4%)	348 (93.8%)	
Yes	103 (1.91%)	80 (1.60%)	23 (6.20%)	
MI:				0.010
NO	3884 (72.2%)	3638 (72.6%)	246 (66.3%)	
Yes	1495 (27.8%)	1370 (27.4%)	125 (33.7%)	
CHF:				<0.001
NO	4460 (82.9%)	4187 (83.6%)	273 (73.6%)	
Yes	919 (17.1%)	821 (16.4%)	98 (26.4%)	
Anemia:				<0.001
NO	2718 (50.5%)	2602 (52.0%)	116 (31.3%)	
Yes	2661 (49.5%)	2406 (48.0%)	255 (68.7%)	
Chronic Hepatitis:				1.000
NO	5298 (98.5%)	4933 (98.5%)	365 (98.4%)	
Yes	81 (1.51%)	75 (1.50%)	6 (1.62%)	
Chronic Kidney Disease:				<0.001
NO	4574 (85.0%)	4297 (85.8%)	277 (74.7%)	
Yes	805 (15.0%)	711 (14.2%)	94 (25.3%)	
COPD:				<0.001
NO	5166 (96.0%)	4827 (96.4%)	339 (91.4%)	
Yes	213 (3.96%)	181 (3.61%)	32 (8.63%)	
Diabetes:				0.724
NO	4934 (91.7%)	4596 (91.8%)	338 (91.1%)	
Yes	445 (8.27%)	412 (8.23%)	33 (8.89%)	
Alcohol abuse:				0.757

Table 1 (continued)

	[ALL]	Without Delirium risk	With Delirium risk	*p*.overall
	***N*=5379**	***N*=5008**	***N*=371**	
NO	5304 (98.6%)	4937 (98.6%)	367 (98.9%)	
Yes	75 (1.39%)	71 (1.42%)	4 (1.08%)	
Nicotine Dependence:				<0.001
NO	4092 (76.1%)	3846 (76.8%)	246 (66.3%)	
Yes	1287 (23.9%)	1162 (23.2%)	125 (33.7%)	
Ventilator service time in ICU, days:				<0.001
<5	1893 (35.2%)	1804 (36.0%)	89 (24.0%)	
>10	1763 (32.8%)	1573 (31.4%)	190 (51.2%)	
5–10	1723 (32.0%)	1631 (32.6%)	92 (24.8%)	
Length of ICU stay, days:				<0.001
<5	1963 (36.5%)	1910 (38.1%)	53 (14.3%)	
>10	1513 (28.1%)	1286 (25.7%)	227 (61.2%)	
5–10	1903 (35.4%)	1812 (36.2%)	91 (24.5%)	
LODS:				<0.001
<4	2317 (43.1%)	2192 (43.8%)	125 (33.7%)	
>=4	3062 (56.9%)	2816 (56.2%)	246 (66.3%)	
SAPS II:				<0.001
<36	2561 (47.6%)	2450 (48.9%)	111 (29.9%)	
>=36	2818 (52.4%)	2558 (51.1%)	260 (70.1%)	
SOFA:				0.002
<5	2631 (48.9%)	2479 (49.5%)	152 (41.0%)	
>=5	2748 (51.1%)	2529 (50.5%)	219 (59.0%)	

BMI: body mass index; MI: myocardial infarction; CHF: congestive heart failure; COPD: chronic obstructive pulmonary disease; LODS: logistic organ dysfunction system; SAPS II: simplified acute physiology score II; SOFA: Sequential Organ Failure Assessment

Table 2 Multivariate logistic analysis of the training group

variables	OR	95%CI	*P* value
Age 18–63 (Reference category is Age ≥ 73)	0.346	0.240–0.493	1.20E-06
Age 63–73 (Reference category is Age ≥ 73)	0.592	0.449–0.776	0.001
pCO2 35–45 (Reference category is pCO2 < 35)	0.111	0.019–0.797	0.045
Glucose 140–180 (Reference category is Glucose < 140)	0.616	0.419–0.923	0.042
WBC 4–10 (Reference category is WBC > 10)	0.556	0.341–0.864	0.036
Stroke Yes (Reference category is Stroke NO)	3.526	2.061–5.869	7.04E-05
Anemia Yes (Reference category is Anemia NO)	1.516	1.185–1.948	0.005
COPD Yes (Reference category is COPD NO)	1.808	1.165–2.751	0.023

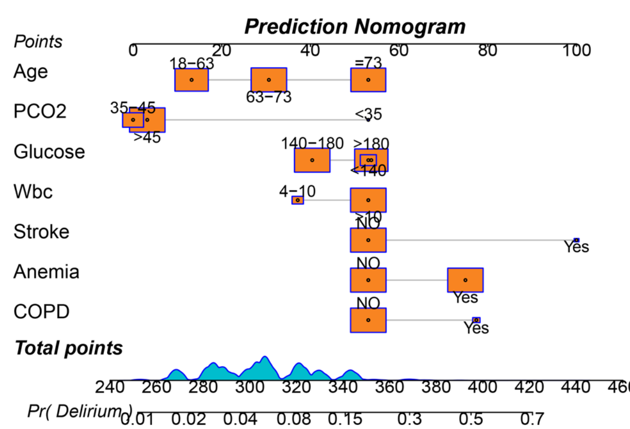

Fig. 2 Nomogram of postoperative delirium in patients undergoing cardiac surgery

to declines in neurocognitive function and the occurrence of delirium postoperatively [23, 24]. The most prevalent type of stroke following heart valve surgery is subdural hemorrhage, with an occurrence probability of approximately 2.0% [25, 26]. In patients with subdural hematomas postoperatively, the integrity of the blood-brain barrier may be compromised, potentially exacerbating neuroinflammatory responses and ultimately leading to delirium [27, 28].

Postoperative patients with COPD and respiratory failure often require prolonged mechanical ventilation, necessitating the use of sedation as a standard therapeutic intervention. However, sedative administration is associated with significant adverse effects, including hypotension, respiratory depression, hallucinations, withdrawal symptoms, impaired cerebral perfusion, and neurological dysfunction. These complications can contribute to extended ICU stays, prolonged mechanical ventilation, and an elevated risk of delirium, ultimately impacting patient recovery and clinical outcomes [29,

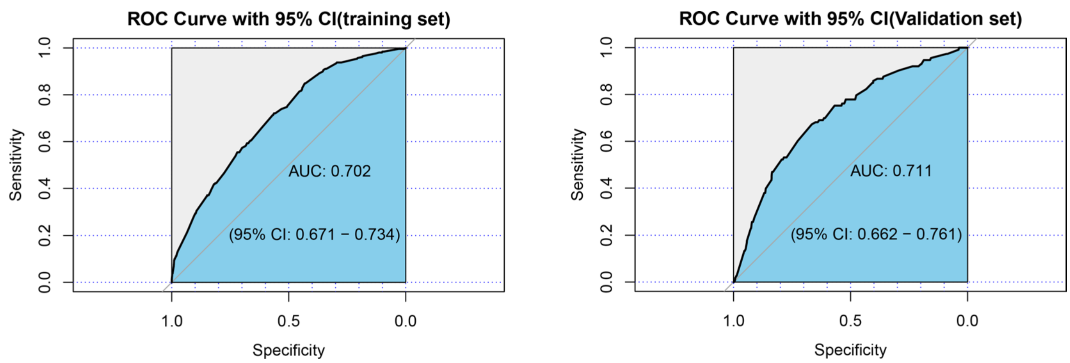

Fig. 3 ROC curves for the nomogram. Left: Training group; Right: Validation group

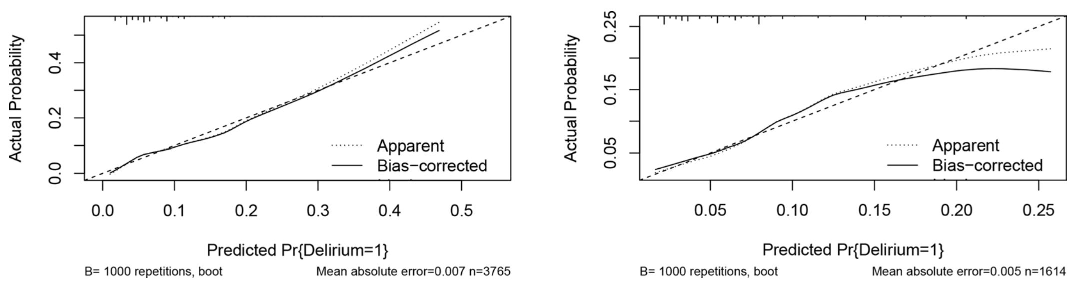

Fig. 4 Calibration curve Left: Training group; Right: Validation group

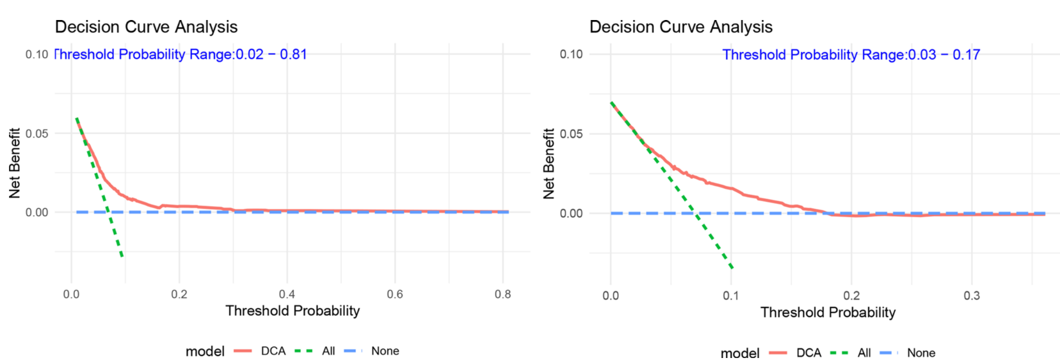

Fig. 5 Decision curve analysis Left: Training group; Right: Validation group

30]. Particularly for patients undergoing cardiac surgery, a history of COPD prior to the procedure may result in prolonged mechanical ventilation or respiratory infections postoperatively, which appears to contribute to the development of delirium and may even decrease patient survival rates [31]. Additionally, our research findings indicate that patients with low carbon dioxide levels postoperatively have a higher likelihood of experiencing delirium. This is consistent with recent evidence and supports the recommendation that patients at high risk for delirium should reduce or avoid postoperative hypocapnia [32].

The management of glucose levels is crucial for patients following cardiac surgery. Research indicates that glucose levels should ideally be maintained between 140 and 180 mg/dL for perioperative patients in the ICU [33, 34]. A recent retrospective study found that preoperative acute hyperglycemia was associated with POD in patients undergoing non-cardiac surgery [34]. Furthermore, Leif Saager et al. reported that stringent control of glucose levels through hyperinsulinemia increases the risk of delirium following cardiac surgery [35]. These findings align with our results: maintaining glucose levels between 140 and 180 mg/dL in patients following cardiac surgery is associated with a reduced likelihood of delirium.

Delirium in the ICU is associated with respiratory failure, shock, metabolic disorders, decreased compliance, prolonged mechanical ventilation, extended hospitalization, increased use or withdrawal of sedatives, and an unfavorable sleep environment [36, 37]. Therefore, it is especially important to evaluate the risk factors for delirium in ICU patients at an early stage, identify high-risk individuals, and mitigate the likelihood of delirium by decreasing ICU hospitalization duration.

This study has several limitations. Firstly, this is a retrospective observational study, which carries inherent biases. Secondly, for individuals with null variables, we employed direct elimination methods, which may introduce some bias in the results. Thirdly, we limited data collection to samples collected during the initial ICU admission. Additionally, these findings are derived from a single-center cohort and require validation in future studies involving multiple centers.

Conclusion

This study demonstrates that older age, lower partial pressure of carbon dioxide, abnormal glucose levels (both too high and too low), elevated white blood cell counts, stroke, anemia, and COPD are risk factors for POD. The AUC, calibration curve, and DCA demonstrate that the nomogram exhibits high accuracy and reliability. This nomogram provides a visual and personalized tool for clinicians to detect and identify high-risk patients experiencing delirium after cardiac surgery at an early stage, allowing for interventions that may reduce the incidence of delirium.

Abbreviations

POD	Postoperative delirium
MIMIC-IV	Medical Information Mart for Intensive Care
AUC	Area under the receiver operating characteristic curve
DCA	Calibration curve, and decision curve analysis
PCO2	Partial pressure of carbon dioxide
Wbc	White blood cell count
COPD	Stroke, anemia, chronic obstructive pulmonary disease
LOS_ICU	length of stay in the intensive care unit
LODS	Logistic organ dysfunction system
SAPS II	Simplified acute physiology score II
SOFA	Sequential Organ Failure Assessment

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Author contributions

This work was written by Huaxian-Mei and Gang-Liao who contributed equally to this work. Data were collected by Gang-Liao, Statistical analysis by Baning-Ye and Mingxiang-Wen. Jianquan-Li approved the final version of this manuscript. All the authors have read and agreed to the published version of the manuscript.

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Data availability

Publicly available datasets were analyzed in this study. This data can be found here: https://physionet.org/content/mimiciv/2.2.

Declarations

Ethics approval and consent to participate

Use of the MIMIC database was approved by the Beth Israel Women's Deaconess Medical Center and the MIT Institutional Review Board, and all patient information in the database is anonymized and therefore does not require informed consent. We completed online courses and exams and gained access to the database (ID: 12855703).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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