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Predicting postoperative cognitive dysfunction in older cardiac surgery patients: An integrated machine learning approach with a visual nomogram

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Abstract

Objectives

This study integrated machine learning algorithms to identify key risk factors for postoperative cognitive dysfunction (POCD) in older cardiac surgery patients. This study aimed to develop a predictive nomogram to assist clinicians and nurses in identifying high-risk patients and implementing targeted interventions.

Methods

A prospective cohort study was conducted with 353 older cardiac surgery patients admitted to the surgical intensive care unit (ICU). Data on demographics, laboratory results, and clinical characteristics were collected. The least absolute shrinkage and selection operator (LASSO) regression was applied to determine the most relevant predictors for POCD. These predictors were incorporated into a multivariate logistic regression model to construct a predictive nomogram. Model performance was assessed using receiver operating characteristic (ROC) curve analysis, calibration curves, and decision curve analysis.

Results

POCD was observed in 49.86% of patients. Seven independent predictors were identified: surgical approach, pre-existing comorbidities, operation duration, intraoperative blood loss, sleep quality score during ICU stay, Acute Physiology and Chronic Health Evaluation II (APACHE II), and self-care ability. These predictors were incorporated into the predictive nomogram; it demonstrated robust predictive performance with an area under the ROC curve (AUC) of 0.786. The nomogram exhibited excellent calibration and discrimination. Decision curve analysis confirmed its clinical utility across a broad range of threshold probabilities.

Conclusions

A precise and effective nomogram was developed using the surgical approach, Underlying comorbidities, operation duration, blood loss, ICU sleep quality, APACHE II, and self-care ability as predictors of POCD in older cardiac surgery patients.

Implications for Clinical Practice

This nomogram provides a valuable tool for early detection and prevention of POCD, enabling clinicians to make informed decisions and tailor interventions. Its application can help reduce the incidence of POCD, ultimately improving patient outcomes and quality of care.

Introduction

Cardiac surgery frequently involves extracorporeal circulation, frequent surgical operations, hypothermia, and hemodynamic instability, all of which contribute to a high incidence of postoperative cognitive

dysfunction (POCD), reported to affect up to 40% of patients (Polunina et al., 2014). POCD is characterized by a decline in cognitive functions, including learning, memory, language, perception, attention, executive ability, and abstract thinking following anesthesia and operation, which may appear within a week to several months postoperatively (Deiner and Silverstein, 2009).

Cognitive impairment is a prevalent complication among older patients undergoing cardiac surgery, with an incidence as high as 31.2%, significantly higher than other surgical procedures (Zhang et al., 2021). The POCD is a prevalent neurocognitive complication that significantly impacts recovery and nursing outcomes in older patients undergoing surgical procedures and anesthesia for diverse medical conditions. The heightened susceptibility to POCD in older patients may be attributed to age-related degeneration of the central nervous system, impaired autoregulatory function of cerebral blood flow, and increased vulnerability to cerebral hypoperfusion, particularly during cardiac procedures, which can disrupt neurotransmitter function (Selnes et al., 1999). POCD significantly diminishes the quality of life and independence, leading to increased healthcare costs, prolonged hospitalization, and a significant socioeconomic burden. Furthermore, older patients with POCD face a heightened risk of 1-year mortality (Goettel et al., 2017; Tarasova et al., 2021). However, its impact on older cardiac surgical patients is often underestimated (Arefayne et al., 2023). As the global population ages, the incidence of cardiac disease among older individuals rises steadily. This trend has been accompanied by prolonged hospitalization, higher mortality rates, and increased complication rates in these patients (Bowry et al., 2015). While most patients with POCD regain normal cognitive function within one postoperative month, a subset develops permanent POCD **(Yazit et al., n.d.)**. Prolonged POCD can severely hinder recovery, reduce self-care capacity, and limit participation in social or occupational activities, ultimately worsening patient prognosis and increasing postoperative mortality (Perbet et al., 2018).

The POCD has garnered increasing attention over the past decade as a significant postoperative complication. Various risk factors have been identified that contribute to the development of POCD, including advanced age, low educational attainment, history of cerebrovascular disease without residual deficits, prolonged surgical duration, type of surgery, pre-existing cognitive decline, poor functional capacity, multiple comorbidities, disease severity, and postoperative respiratory complications **(Li and Liu, 2018;** Needham et al., 2017). Given its multifactorial nature and the increasing prevalence in older cardiac surgery patients, there is an urgent need for an accurate and practical risk prediction tool to facilitate early identification and tar geted interventions.

Nomograms offer a user-friendly, visual method for predicting individual risk by integrating independent variables into a single, quantifiable score **(Ohori et al., 2009)**. This tool efficiently represents the relationship between multiple predictors and outcomes, enabling clinicians to make personalized, evidence-based decisions regarding patient care. By stratifying patients into high- and low-risk groups, nomograms support the development of precise intervention strategies. They have been extensively applied to predict disease incidence, recurrence, and overall health outcomes (Han et al., 2024; Huang et al., 2016). However, to the best of our knowledge, no nomogram currently exists for predicting POCD risk in older cardiac surgery patients. This study represents a novel effort to develop such a tool by

integrating a nomogram with machine learning techniques (specifically the least absolute shrinkage and selection operator [LASSO] regression) to identify and quantify significant risk factors for POCD. The resulting model aims to provide clinicians with a reliable, convenient instrument for early risk assessment and intervention, ultimately guiding postoperative care and improving patient outcomes.

Methods

Study design and patients

This single-center, prospective cohort study was conducted in a tertiary hospital's surgical intensive care unit (ICU) in southeast China between October 2021 and June 2022. The study population comprised cardiac surgery patients aged 60 years or older. The adequate sample size for the prediction study was estimated based on the number of outcome events, with at least ten positive outcome events (POCD cases) required per predictor variable to ensure model accuracy and feasibility.

The events per variable (EPV) ratio was considered for developing the risk prediction model, adhering to the established guideline of 10 EPVs per predictor (Riley et al., 2019). The sample size (N) was calculated by multiplying the number of predictor variables by ten and dividing the result by the expected incidence of POCD cases. Predictor variable selection followed a rigorous, multi-step approach, incorporating an extensive literature review, data synthesis, and expert consultation. The process accounted for factors such as the feasibility of data collection and its relevance to the geriatric cardiac surgical population. Ultimately, ten predictor variables, including age and perioperative parameters, were anticipated for inclusion in the final binary logistic regression model. According to the research findings of Zhang et al. (Zhang et al., 2021), the incidence of POCD following cardiac surgery in older patients was 31.2%. Based on this incidence, the required sample size was calculated as 321 cases. Assuming a 10% loss to follow-up, the final estimated sample size was adjusted to 356 cases. Ultimately, 353 participants were enrolled and completed the study.

Inclusion criteria and exclusion criteria

Inclusion criteria: 1) age ≥ 60 years; 2) ICU stay ≥ 48 hours; 3) clear consciousness and normal communication ability upon ICU discharge; 4) those who underwent cardiac surgery involving extracorporeal circulation.

Exclusion criteria: 1) history of mental illness or substance abuse; 2) cardiopulmonary resuscitation or cardiac arrest; 3) conditions potentially affecting cognition, such as pulmonary encephalopathy, hepatic encephalopathy, diabetic hyperosmolar coma, or unexplained coma; 4) hearing, visual, or communication impairments; 5) refusal to cooperate with cognitive scale testing.

Data collection and variable screening

Clinical data, including patient demographics and perioperative parameters, were systematically collected. Moreover, surgical details such as procedure type, operation duration(min), bypass time (min), etc. were recorded. All variables included in the study are listed in Appendix S1. The variables are defined in Appendix S2. Continuous variables were normalized using the minimum-maximum value method. Predictor variables were selected through LASSO regression (10-fold cross-validation) employing R's “glmnet” package.

Data collection

The researchers conducted two rounds of comprehensive training for the nurses to assess cognitive impairment, delirium, and sleep conditions to collect accurate and consistent data. Only nurses who demonstrated proficiency by correctly performing assessments during training were authorized to conduct clinical evaluations. All participating nurses successfully passed the competency assessment. Clinical assessments were conducted at the patient’s bedside during their ICU stay. Three days after ICU discharge, the follow-up nurse (responsible for data collection) performed cognitive assessments in the ward using the mini-mental state examination (MMSE). If any questions arose regarding the assessment, the nurse consulted the attending physician or primary psychiatrist for clarification. Patient conditions were meticulously documented on a record sheet, particularly for those unsuitable for assessment. The following assessment scales were used in the study:

Mini-mental state examination (MMSE)

The MMSE is a widely recognized cognitive screening tool that assesses areas such as orientation to time and place, language (retelling, naming, understanding instructions), mental arithmetic, immediate and short-term auditory word memory, and structural imitation. The maximum score is 30 points, with lower scores indicating more severe cognitive impairment. A score of < 27 points suggests cognitive dysfunction, while a score of 27–30 points is considered normal (Folstein et al., 1975).

Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)

The CAM-ICU assesses changes in consciousness, attention deficits, and confusion in thinking. It is a highly accurate screening tool for delirium with a brief average assessment time of 2 minutes. The CAM-ICU has become the gold standard for ICU delirium screening. A systematic review showed its sensitivity to be 80.0%, specificity 95.9%, and diagnostic odds ratio 103.2 (Gusmao-Flores et al., 2012).

Richards-Campbell Sleep Questionnaire (RCSQ)

The RCSQ evaluates sleep quality through five items; each scored out of 100. The previous night’s sleep status is measured using a visual analog scale, with the average score of all items calculated. A score of

75 points or higher indicates better sleep quality. The questionnaire has demonstrated strong reliability, with a content validity index of 0.840, an intraclass correlation coefficient for retest reliability of 0.912 (3-hour interval), and a Cronbach's α of 0.874 (Yang et al., 2017).

Statistical analysis

Continuous variables were presented as means and standard deviations; categorical variables were expressed as absolute values and percentages. The t-test was used to compare continuous variables between groups, and the chi-square test was applied to categorical data.

The LASSO regression was employed to identify potential risk factors for POCD in older cardiac surgery patients, with the optimal λ value determined via 10-fold cross-validation. Variables with $P < 0.05$ in binary logistic regression were included in the final model. The model's performance was assessed using the area under the receiver operating characteristic curve (AUC). Internal validation was conducted through 1000 bootstrap resamples. A calibration curve was generated to evaluate the agreement between predicted and observed values. A coefficient-based nomogram was established to facilitate clinical implementation. Decision curve analysis (DCA) assessed clinical utility and net benefit. Statistical significance was set at a P value < 0.05.

Results

Baseline demographics and clinical characteristics

A total of 646 patients were recruited between October 2021 and June 2022. Among them, 176 developed cognitive impairment 3 days after being transferred from the surgical ICU, while 177 did not (Fig. 1).

Screening for predictive factors

A total of 34 candidate variables were initially collected (see **Supplementary Materials**). Using LASSO regression analysis, 12 variables with non-zero coefficients were identified as potential predictors (Figs. 2A and 2B). These included: occurrence of delirium, sedation after extubation, use of analgesics, surgical method, underlying comorbidities, cardiac function classification, operation duration (min), intraoperative blood loss (mL), worst sleep score during ICU stay, APACHE II, maximum blood glucose level(mmol/L), and self-care ability. These 12 variables were subsequently included in a multivariate logistic regression analysis. The results identified the following independent predictors of POCD in older cardiac surgery patients: surgical method, underlying comorbidities, operation duration, intraoperative blood loss, sleep score during ICU stay, APACHE II, and self-care ability (Table 1).

Table 1
Multivariate analysis of predictors selected by LASSO regression procedure

Variables	OR(odds ratio)	95%CI	P
Whether delirium occurs			
No	1.000		
Yes	2.502	0.948–6.602	0.064
Sedation after extubation			
No	1.000		
Yes	2.099	0.999–4.410	0.050
Whether to use analgesics			
No	1.000		
Yes	0.545	0.289–1.029	0.061
Surgical method			
Coronary Artery Bypass Grafting	1.000		
Valve replacement	2.539	1.218–5.293	0.013
Aortic dissection	5.096	1.039–24.995	0.045
Others (cardiac tumor resection, pericardial stripping, atrioventricular septal repair, etc.)	0.935	0.265–3.302	0.917
Combination of 2 heart surgeries	3.340	0.954–11.693	0.059
Underlying comorbidities			
None	1.000		
hypertension	5.071	1.958–13.136	0.001
diabetes	2.079	0.581–7.435	0.260
Cerebral infarction	2.114	0.337–13.277	0.424
other	3.215	1.285–8.041	0.013

Variables	OR(odds ratio)	95%CI	P
Whether delirium occurs			
Mixed multiple	7.528	2.445–23.178	< 0.001
Heart function classification			
I	1.000		
II	0.310	0.068–1.416	0.131
III	0.487	0.104–2.288	0.362
IV	2.760	0.277–27.491	0.387
Operation time(min)	0.992	0.989–0.996	< 0.001
Intraoperative blood loss(ml)	1.002	1.001–1.003	0.004
Worst sleep score during ICU stay	0.975	0.963–0.988	< 0.001
APACHE Ⅱ	1.066	1.009–1.127	0.023
Maximum blood glucose level(mmol/L)	1.080	0.998–1.170	0.056
Self-care ability score	0.965	0.950–0.980	< 0.001

Development of the Risk prediction model

A predictive nomogram was constructed using the identified independent predictors **(Fig. 3A**). In this model, a higher total score corresponded to an increased risk of POCD. The ROC curve analysis demonstrated an AUC of 0.786, indicating robust predictive performance (Fig. 3B).

Model Performance

The prediction performance of the developed nomogram is presented in Fig. 4. The calibration curve revealed strong agreement between the predicted and observed values, demonstrating the model's accuracy (Fig. 4A). Moreover, DCA indicated that the expected threshold probabilities for most patients exceeded the two extreme reference lines within the 0–1 range, underscoring the model's clinical applicability and utility (Fig. 4B). Internal validation was performed using 1000 bootstrap resamples to determine the consistency of the model's predicted probabilities (Fig. 4C).

Discussion

This study successfully developed a novel nomogram to predict the risk of POCD in older cardiac surgical patients. The model exhibited excellent predictive value, with intense discrimination and calibration capabilities. Moreover, the nomogram demonstrated substantial clinical practicality, providing an objective tool for clinical nurses to assess POCD risk. Its implementation could facilitate the early identification of high-risk patients, thereby contributing to strategies aimed at reducing the incidence of POCD in older cardiac surgical patients.

In this study, the incidence of POCD in older cardiac surgery patients was 49.86%, higher than the 31.2% determined by Zhang et al. (Zhang et al., 2021). This discrepancy may be attributed to our ICU admitting some older cardiac surgery patients for temporary postoperative observation. Furthermore, due to our hospital's high volume of surgical operations, stable patients were typically transferred back to the ward within 3–4 days to increase bed turnover, which could have led to a higher recorded incidence. However, these patients could not be followed up due to time and personal constraints. Future studies could address this limitation. Moreover, as the number of cardiac surgeries and the incidence of heart disease in older individuals continue to rise, the incidence of POCD may also increase.

Surgical procedures, especially cardiac surgery, are linked to higher levels of neuronal damage and neurodegeneration markers, such as total-Tau and neurofilament light chain (NfL) (Florido-Santiago et al., 2023). These effects, including hypoxemia and disruption of the blood-brain barrier, seem to be caused by the entire surgical procedure, not just by inhaled anesthesia, as was previously assumed (Deiner et al., 2020). Patients with underlying, though clinically silent, neurodegenerative diseases may experience a significant “second hit” that accelerates the neurodegenerative process, contributing to cognitive decline following these interventions (Sadlonova et al., 2022). Although the incidence of cognitive impairment post-ICU discharge has decreased over time, long-term follow-ups have revealed persistent cognitive deficits, with 80% of ICU survivors affected after 1 year and 45% after 2 years in some studies. Surgical neuroinflammatory damage and altered cerebral blood flow may predispose older surgical patients to long-term POCD (Arefayne et al., 2023).

Previous studies investigating factors influencing the development of POCD in cardiac surgery have reported considerable variability, with heterogeneity arising from differences in study populations and methodologies (Zhang et al., 2021) (Florido-Santiago et al., 2023). This study identified several predictive factors for POCD, including the type of surgery, pre-existing health conditions, operation duration, intraoperative blood loss, ICU sleep scores, APACHE II score, and self-care ability score. These factors highlight the need for heightened attention to older cardiac surgery patients at higher risk for POCD. Several previous studies have identified surgical risks, operation time, and various cardiovascular risk factors as predictors of POCD (Florido-Santiago et al., 2023). Common risk factors include advanced age, lower education level, preoperative cognitive impairment, prior stroke, diabetes, poor functional status, prolonged intraoperative duration, and the depth of anesthesia **(Miles et al., 2018)**. The clinical consequences of POCD may vary depending on the surgery type and assessment timing. Moreover,

complex vascular or neurological procedures may have similar perioperative cognitive effects as those seen after cardiac surgery (Suraarunsumrit et al., 2024). In summary, older patients undergoing extensive cardiac surgery are at risk for long-term POCD, with both patient- and operation-related factors contributing to this outcome. The prevalence of cognitive impairment following cardiac surgery in older patients may be linked to the potential progression toward dementia, highlighting the need for comprehensive long-term cognitive assessments (Florido-Santiago et al., 2023). Many identified risk factors are modifiable; however, these patients frequently experience cognitive decline without adequate attention, such as insufficient focus on sleep quality or self-care ability during their ICU stay.

In this study, a nomogram was developed to predict the incidence of postoperative cognitive dysfunction in older cardiac surgery patients, using seven independent predictors of cognitive impairment. A nomogram is a graphical representation of a complex mathematical formula, which provides the advantage of estimating individual risk based on patient characteristics. It incorporates continuous and categorical variables and visually represents how each variable influences the predicted outcome, enhancing readability and clinical utility. The seven clinical predictors used in the model are frequently utilized, easily accessible, and routinely assessed in the ICU, making the model highly applicable and feasible for clinical practice, enabling early prediction of cognitive impairment risk.

The AUC is a key indicator of a model's discrimination ability. A higher AUC suggests better prediction performance (Carter et al., 2016). In this study, the model's AUC exceeded 0.7 in training and validation cohorts, demonstrating a strong discrimination ability for distinguishing between patients with and without subsyndromal delirium, indicating good predictive performance. The calibration curve confirmed that the model's predictions were closely aligned with observed outcomes, thereby enhancing the model's accuracy and reliability. Moreover, DCA evaluates the net benefit of using a specific model, guiding model selection in clinical practice. This method supports the early identification of patients at risk of poor outcomes and helps prevent unnecessary treatments for patients at lower risk. Overall, this study demonstrated the clinical validity of the model (Vickers, 2006).

The nomogram developed in this study is straightforward and has strong predictive ability, making it a valuable tool for routine clinical assessment of POCD. Early identification of risk factors, developing risk-disease relationship maps using modern technology, and timely intervention adjustment can help address the challenge of accurately diagnosing cognitive dysfunction in clinical settings. For example, interventions aimed at improving sleep quality and circadian rhythm could reduce the risk of cognitive impairment (Wilcox et al., 2024). Given the high incidence and risks of postoperative cognitive impairment in older cardiac surgery patients, it is crucial to emphasize the role of clinical staff in identifying relevant risk factors and incorporating routine monitoring of cognitive impairment. Furthermore, healthcare professionals should focus on proactive care, shifting from reactive interventions after symptoms arise to targeted prevention before cognitive impairment develops.

Limitations

Firstly, participants were recruited from a single hospital due to time, resource, and economic constraints. Future research should include external validation with larger multicenter cohorts to assess the model's performance further. Secondly, the analysis did not include certain variables potentially linked to POCD, such as anesthesia type and duration. Thirdly, although some older cardiac surgery patients may experience prolonged cognitive impairment after ICU discharge, this study only assessed patients 3 days post-transfer. Moreover, extensive multicenter clinical studies are needed to determine the optimal risk factors for prediction models and improve predictive accuracy.

Conclusion

A nomogram was developed and validated to predict the risk of postoperative cognitive impairment in older cardiac surgery patients. The nomogram includes accessible and assessable clinical parameters, offering significant predictive value and clinical utility. It incorporates key risk factors such as surgical method, pre-existing conditions, operation duration, intraoperative blood loss, sleep quality score during ICU stay, APACHE II, and self-care ability. This model can be incorporated into clinical workflows to support decision-making, enhance quality of care, and improve strategies for preventing postoperative cognitive impairment in older cardiac surgery patients.

Declarations

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Ethics statement

This study adhered to the ethical standards of the Declaration of Helsinki and was approved by the First Affiliated Hospital of Zhejiang University School of Medicine (approval number 2021-068). Clinical staff informed eligible patients of the purpose of the study and obtained informed consent from all patients included in the study.

Clinical trial registration

Clinical Trial number: ChiCTR2100046093. Website: www.chictr.org.cn/guide.html.

Declaration of competing interest

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

Author Contribution

The authors have no relevant affiliations or financial involvement with any organisation or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending or royalties.Ming Sang designed this study, collected and analysed data and drafted the manuscript; Jianhua Wei designed this study, revised the manuscript and supervised this study; Fengxia Weng and Ping Zhang collected and analysed the data; Sirui Wang and Yanan Leng analysed the data, interpreted the results and reviewed the manuscript. All authors read and approved the final manuscript.

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Figures

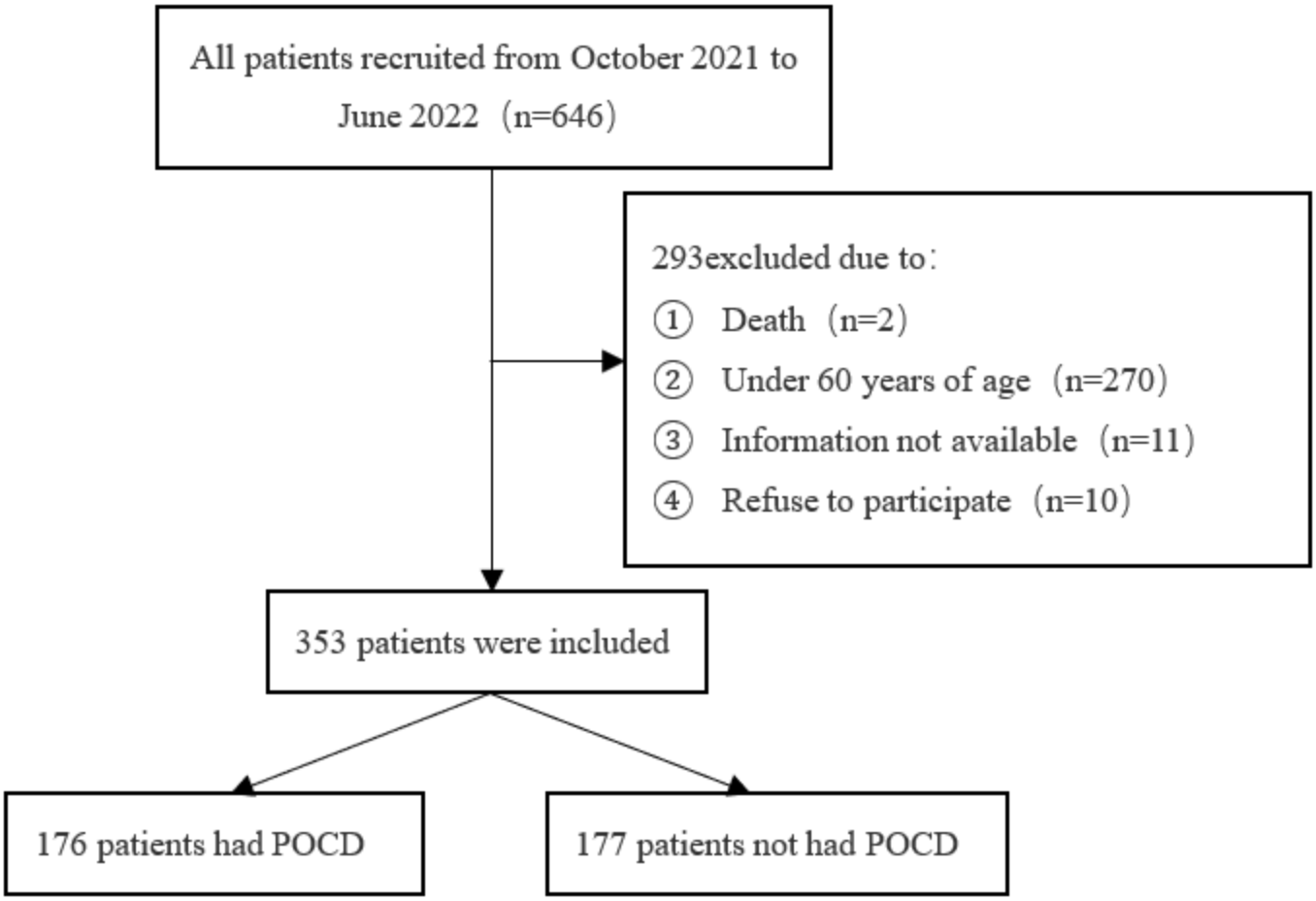


Figure 1

Flow chart of the constructing of the cohort for developing a POCD nomogram.

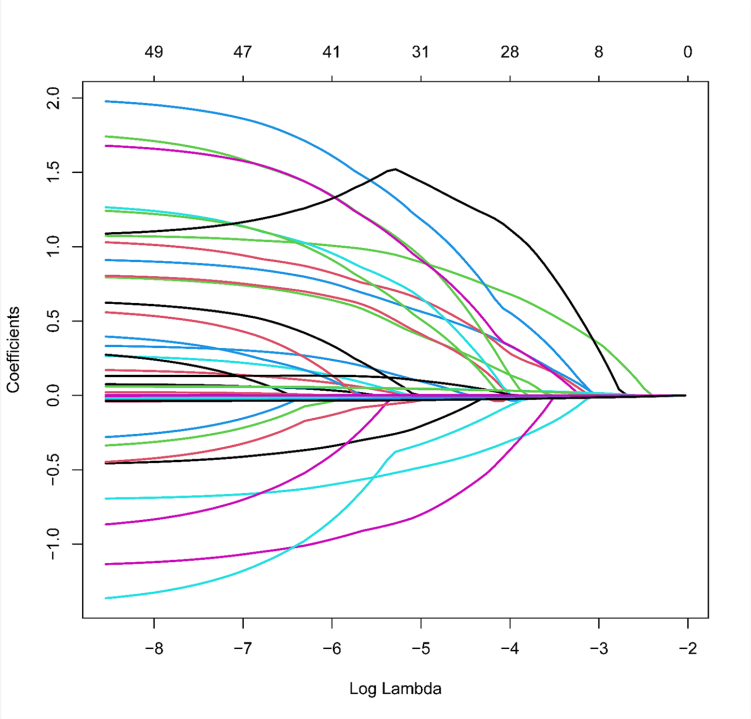


Figure2A.png

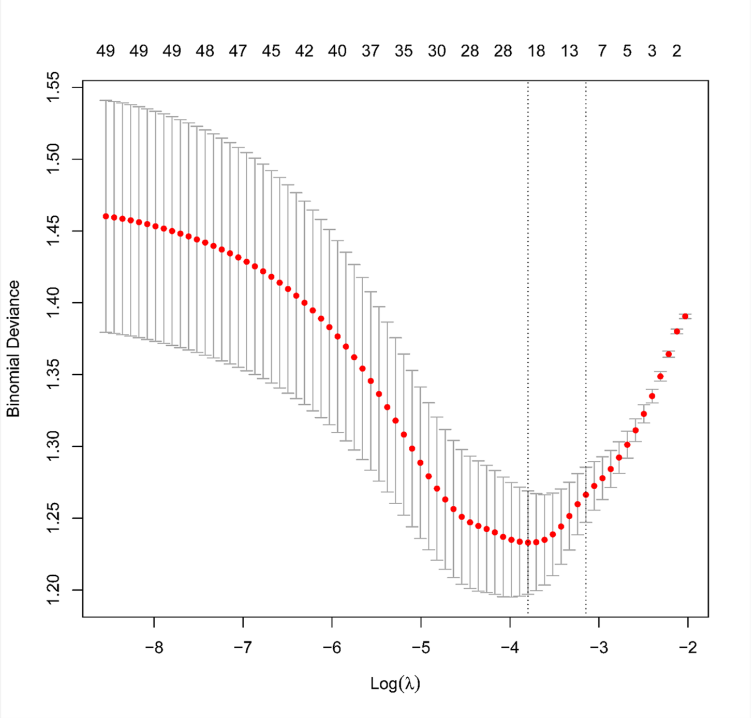


Figure2B.png

Figure 2

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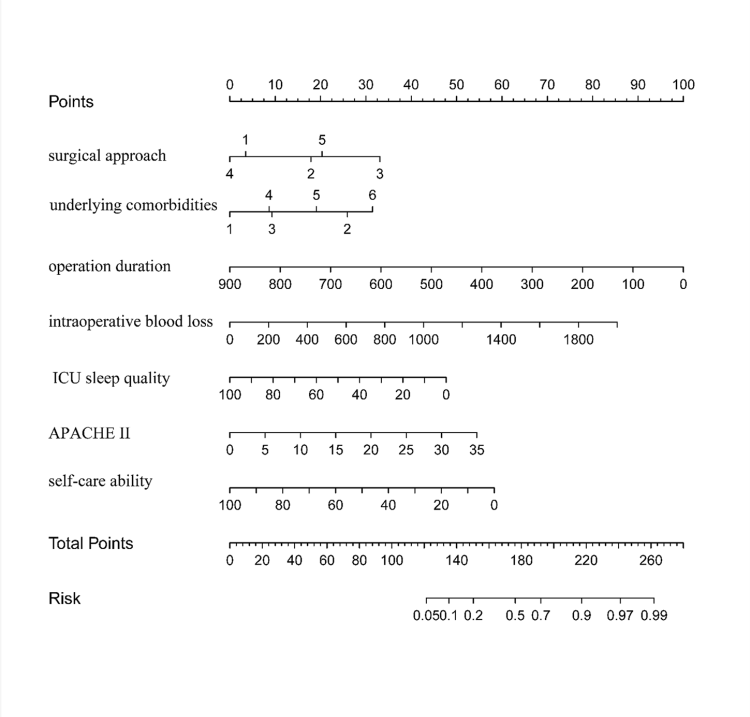


Figure3A.png

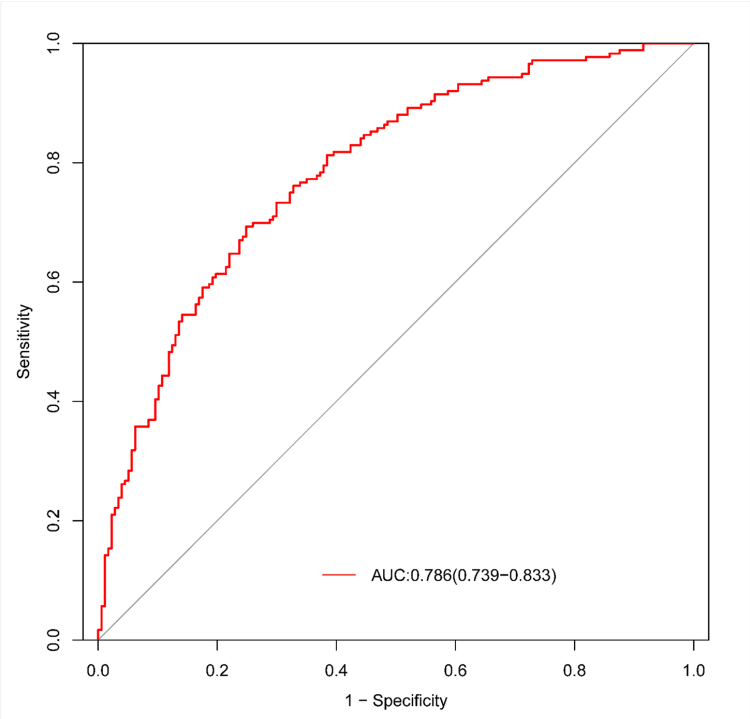


Figure3B.png

Figure 3

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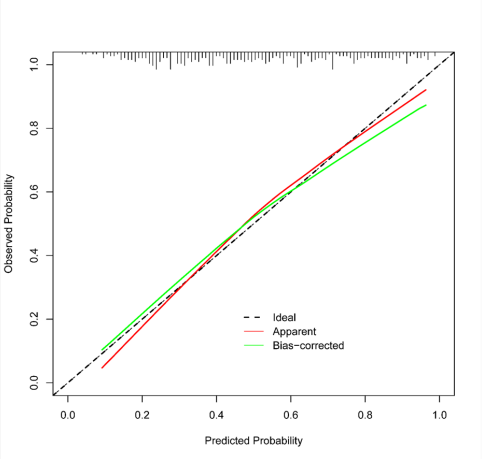


Figure4A.png

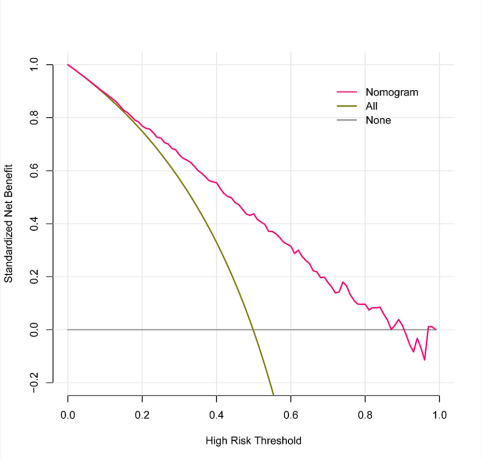


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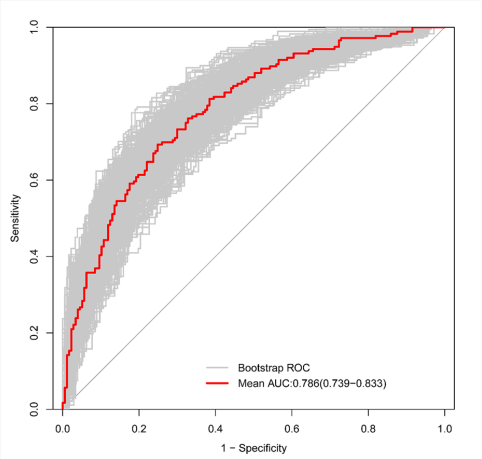


Figure4C.png

Figure 4

Legend not included with this version

Supplementary Files

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- AppendixS1.docx
- AppendixS2.docx