Development and Validation of a Clinical Prediction Model for Elderly Patients with Preoperative mild cognitive impairment: A Prospective Cohort Study

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Abstract

Background

Mild cognitive impairment (MCI) in elderly patients undergoing surgery is neglected easily by clinicians and families. Preoperative patients with MCI are more likely to suffer from postoperative cognitive dysfunction and postoperative delirium, so an effective MCI prediction method has important implications for ameliorating perioperative cognitive function.

Objective

This study is designed to construct a predictive model to provide a novel approach for preoperative MCI diagnosis in geriatric patients.

Methods

Patients over 65 years old who underwent elective surgery with general anesthesia were screened. Patients were randomly divided into training cohort \((n = 258)\) and test cohort \((n = 49)\) by the ratio of 8:2, and baseline demographic variables and characteristics of the patients in the different cohort were compared. The least absolute shrinkage and selection operator (LASSO) regression was used to identify risk factors in the training cohort. A nomogram was constructed based on the logistic regression. Receiver operating characteristic (ROC) curves and calibration charts were drawn in the training cohort and test cohort respectively to evaluate the diagnostic value of the prediction model. The decision curve analysis (DCA) was used to value the clinical utility of the prediction model.

Results

In this study, a total of 307 elderly surgical patients were enrolled, including 137 patients with MCI and 170 patients with normal cognitive function. Multivariate analysis showed that history of more than two operations, higher urea nitrogen, lack of education, body mass index (BMI) < 24kg/m\(^2\) and lower albumin/globulin ratio were the independent risk factors for preoperative MCI. The C statistic of the prediction model in the training cohort and test cohort was 0.754 (95%CI, 0.695–0.812) and 0.708 (95%CI, 0.559–0.856) respectively. The threshold probability of the net benefit ranged from 45–81% in the DCA.

Conclusions

The independent risk factors for preoperative MCI in elderly patients were two or more operations, higher blood urea nitrogen level, shorter years of education, BMI < 24kg/m\(^2\), and lower albumin/globulin ratio.
The predictive model has a certain diagnostic value for preoperative MCI in elderly patients, and provides a novel method for anesthetists to evaluate preoperative cognitive function in elderly patients.

**Introduction**

Mild cognitive impairment (MCI) is defined as a heterogeneous clinical syndrome which presents a significant change in cognitive function and deficits on neuropsychological testing but a relatively intact functionality. As the population ages, an ever-increasing number of people are at high risk for MCI. By the 2020 US census, the prevalence of MCI was 22.7%, namely, 12.23 million people had MCI in 2020, which will increase to 21.55 million in 2060 [1]. In a follow-up study, MCI patients were 21% more likely to develop mild Alzheimer’s disease in the next year, but not normal cognition [2].

MCI has not received enough attention from clinicians and families. It is estimated that the prevalence of MCI in elderly patients over 65 years old who receive outpatient surgery is about 16.1% [3] and about 18% in elderly patients who receive elective surgery, among which undiagnosed MCI is as high as 37%, and the proportion of MCI in patients over 65 years old who receive thoracic surgery is as high as 49.5% [4]. The percentage of undiagnosed MCI in emergency surgery patients even was about 50% [5]. Some studies have confirmed that nearly 38.6% of elderly patients over 60 with preoperative cognitive abnormalities should be paid attention to by clinicians [6]. The complex diagnosis process of MCI is the main reason for its low diagnosis rate.

Nevertheless, the diagnosis of MCI is a complicated task in some instances, given that it is essential to differentiate it from the manifestations of dementia and the cognitive changes of aging. The routine diagnosis of MCI depends on which cognitive and functional questionnaires are used, and the sensitivity and specificity of these questionnaires determine the presence or absence of MCI [7]. It is no doubt that the screening of MCI in elderly patients takes clinicians a long time and great effort and requires close cooperation from the patient. Significantly, preoperative patients with MCI are more likely to suffer from postoperative neurological complication which further aggravate the degree of brain damage in patients with MCI and accelerate the progression of MCI to dementia. Therefore it is necessary to find a new tool to screen patients at high risk for mild cognitive impairment.

Some studies have found that education, age, gender, stroke history, neighborhood socioeconomic status, diabetes, apolipoprotein ε4 carrier and body mass index (BMI) could be used as risk factors to construct a predictive model for cognitive decline, with a sensitivity of 75% and specificity of 81% [8]. Another study on the elderly in China used 10 risk factors to construct an MCI prediction model with a sensitivity of 86.6% and specificity of 76.5% [9]. However, these studies have focused on the elderly in the community and little attention has been paid to hospitalized elderly patients. Only one cross-sectional study on preoperative MCI risk factors in elderly patients undergoing orthopedic surgery showed that atherosclerosis, ASA grade 3 and plasma cholesterol level had predictive effects on MCI [10]. However, only MMSE, which has insufficient sensitivity to detect MCI, as the neuropsychological tools applied may underestimate the prevalence of preoperative MCI. With MMSE, MoCA contains more sophisticated
sections making it more difficult, with a higher percentage of error and sensitivity for the elderly with MCI [11]. So we used MMSE and MoCA to screen MCI for improving the accuracy of the diagnosis of MCI. Subsequently, our study constructed and examined a novel predictive model which could be used for elderly who are going to undergo surgery and evaluated clinical application.

Materials And Methods

Source of data

The data of the study were collected in Tianjin Third Central Hospital between June 2020 and March 2021. The study was approved by the Ethics Committee of Tianjin Third Central Hospital (approval number: IRB021-002-01).

Patients

The study included elderly patients aged 65 years or older with American Society of Anesthesiologists (ASA) physical status II or who underwent elective surgery with general anesthesia.

The exclusion criteria were as follows: (1) having a history of dementia, psychiatric or any other central nervous system (CNS) disease; (2) having a history of cerebrovascular diseases with or without cognitive dysfunction; (3) using sedatives or antidepressants for a long time; (4) long-term alcohol or drug dependence; (5) severe liver and kidney dysfunction; (6) participated in other clinical trials within a month; (7) patients who received two or more elective surgery with general anesthesia during the study and whose results of the first surgery have been recorded.

Outcome assessment

The endpoint of our study was MCI before surgery. A single researcher trained in the use of tools previously performed a cognitive assessment to screen MCI patients before surgery. The diagnostic criteria were as follows: (1) patient or his/her family members stated that he/she had memory loss symptoms within six months; (2) Montreal Cognitive Assessment (MoCA) scores were higher than 14 and lower than 26; (3) Mini-Mental State Examination (MMSE) score < 27; (4) Dementia scale results showed that the patient could not be diagnosed as dementia; (5) Scores of the daily living ability scale range from 16 to 21 [12].

Predictors

Demographic, laboratory tests obtained before surgery and comorbidity disease data were collected including age, sex, body mass index, ASA grade, education, blood routine examination, liver and kidney function, hypertension, diabetes, coronary heart disease and the history of surgery.

Data analysis

All analyses were performed using R version 4.1.2 and SPSS 25. Missing data were handled by single imputation with the linear regression method. Variables that might be related to MCI were selected by
referring to relevant literature, clinical guidelines and relevant scientific knowledge. Data were checked for normality analysis using Shapiro-Wilk tests and the results showed that they were all non-normality. Continuous variables were reported as medians with interquartile ranges (IQRs) and categorical variables were reported as whole numbers and proportions. Patients included in the study were randomly divided in a ratio of 8:2. Data set of about 80% of the patients was used as a training set to build the preoperative MCI prediction model, and another part of the data set was used as a validation cohort to evaluate the prediction model. Patients in the training and prediction sets were compared to determine baseline similarity between the training and validation cohorts. The Mann-Whitney U test was applied for the data, such as age, education, laboratory test and history of surgery. The sex, ASA grade and comorbidity were analyzed using the Pearson Chi-squared test. The least absolute shrinkage and selection operator (LASSO) regression was applied to select risk factors in the training cohort. According to cross-validation results, lambda = 1SE was used to determine the risk factors. Multivariate analysis was performed using a regression model in the training set. A nomogram was constructed by the results of multivariate analysis. C statistic equivalent to the area under the Receiver operating characteristic (ROC) curve [13] was used to evaluate the consistency between prediction results and observation results. Calibration was used to evaluate the discriminant ability of prediction models in the training set and validation set respectively by the 1000 bootstrap resampling procedure which was used to reduce bias caused by over-fitting [14]. The decision curve analysis (DCA) was used to value the clinical utility of the prediction model and corresponding net benefits for a range of risk thresholds was plotted.

Results

Patient Selection

There were 396 patients aged 65 years or older with ASA physical status II or who underwent elective surgery with general anesthesia. After using the excluded criteria, 307 patients were included in the study (Fig. 1).

Characteristics Of The Patients

There were 307 patients included in the study according to the included and excluded criteria and 137 patients (44.6%) were diagnosed with preoperative MCI. These patients finally were randomly divided into the training cohort \( (n = 258) \) and validation cohort \( (n = 49) \). In the training cohort, the median patient age was 69 years (IQR, 67–73 years), 43.4% (112 of 258) were female, and 46.5% (120 of 258) patients had preoperative MCI. In the validation cohort, the median patient age was 70 years (IQR, 66–72 years), 53.1% (26 of 49) were female, and 34.7% (17 of 49) patients had preoperative MCI. There were no statistical differences between the training cohort and the validation cohort in demographic, laboratory test results and comorbidity disease data, etc. The characteristics of the patients in the two cohorts are shown in Table 1.
Table 1
Characteristics of patients in the training and validation cohort.

<table>
<thead>
<tr>
<th></th>
<th>Training cohort (n = 258)</th>
<th>Validation cohort (n = 49)</th>
<th>t/Z/χ²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No[n(%)]</td>
<td>138(53.5%)</td>
<td>32(65.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes[n(%)]</td>
<td>120(46.5%)</td>
<td>17(34.7%)</td>
<td>2.33</td>
<td>0.127</td>
</tr>
<tr>
<td>Age[years, median(IQR)]</td>
<td>69(67,73)</td>
<td>70(66,72)</td>
<td>-0.76</td>
<td>0.449</td>
</tr>
<tr>
<td>Education[years,median(IQR)]</td>
<td>9(9,12)</td>
<td>9(9,12)</td>
<td>-0.73</td>
<td>0.465</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male[n(%)]</td>
<td>146(56.6%)</td>
<td>23(46.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female[n(%)]</td>
<td>112(43.4%)</td>
<td>26(53.1%)</td>
<td>1.55</td>
<td>0.213</td>
</tr>
<tr>
<td>BMI ≥ 24 kg/m²</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No[n(%)]</td>
<td>107(41.5%)</td>
<td>19(38.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes[n(%)]</td>
<td>151(58.5%)</td>
<td>30(61.2%)</td>
<td>0.12</td>
<td>0.725</td>
</tr>
<tr>
<td>ASA Classification</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[n(%)]</td>
<td>172(66.7%)</td>
<td>36(73.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[n(%)]</td>
<td>86(33.3%)</td>
<td>13(26.5%)</td>
<td>0.87</td>
<td>0.350</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No[n(%)]</td>
<td>133(51.6%)</td>
<td>29(59.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes[n(%)]</td>
<td>125(48.4%)</td>
<td>20(40.8%)</td>
<td>0.96</td>
<td>0.327</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No[n(%)]</td>
<td>200(77.5%)</td>
<td>34(69.4%)</td>
<td>0.15</td>
<td>0.220</td>
</tr>
<tr>
<td>Yes[n(%)]</td>
<td>58(22.5%)</td>
<td>15(30.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No[n(%)]</td>
<td>210(81.4%)</td>
<td>42(85.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes[n(%)]</td>
<td>48(18.6%)</td>
<td>7(14.3%)</td>
<td>0.52</td>
<td>0.470</td>
</tr>
</tbody>
</table>

MCI, mild cognitive impairment; BMI, body mass index; WBCs, white blood cell count; RBCs, red blood cell count; Hb, hemoglobin; PLT, platelet count; MPV, mean platelet volume; Glu, blood glucose; ALB, albumin; GLOB, globulin; AG, Albumin to Globulin; ALT, alanine transaminase; AST, Aspartate Transaminase; TBil, total bilirubin; BUN, blood urea nitrogen; Scr, serum creatinine; UA, uric acid.
<table>
<thead>
<tr>
<th>Predictors Of Preoperative MCI</th>
<th>Training cohort ( (n = 258) )</th>
<th>Validation cohort ( (n = 49) )</th>
<th>( t/Z/\chi^2 )</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of two or more operations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No[n(%)]</td>
<td>220(85.3%)</td>
<td>44(89.8%)</td>
<td>0.70</td>
<td>0.403</td>
</tr>
<tr>
<td>Yes[n(%)]</td>
<td>38(14.7%)</td>
<td>5(10.2%)</td>
<td>-1.66</td>
<td>0.098</td>
</tr>
<tr>
<td>WBCs[x10^9/L, median(IQR)]</td>
<td>5.7(4.6,7.3)</td>
<td>5.4(4.3,6.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RBCs[x10^{12}/L, median(IQR)]</td>
<td>4.4(4.1,4.7)</td>
<td>4.4(4.1,4.8)</td>
<td>-0.17</td>
<td>0.865</td>
</tr>
<tr>
<td>Hb[g/L, median(IQR)]</td>
<td>136.5(127.0,146.3)</td>
<td>135.0(130.0,145.5)</td>
<td>-0.45</td>
<td>0.652</td>
</tr>
<tr>
<td>PLT[x10^9/L, median(IQR)]</td>
<td>200.5(165.0,246.0)</td>
<td>215.0(161.0,267.0)</td>
<td>-0.61</td>
<td>0.542</td>
</tr>
<tr>
<td>MPV[fL, median(IQR)]</td>
<td>8.6(8.2,9.5)</td>
<td>8.7(8.0,9.4)</td>
<td>-0.14</td>
<td>0.887</td>
</tr>
<tr>
<td>Glu[mmol/L, median(IQR)]</td>
<td>5.5(5.0,6.4)</td>
<td>6.0(5.1,7.2)</td>
<td>-1.96</td>
<td>0.050</td>
</tr>
<tr>
<td>ALB[g/L, median(IQR)]</td>
<td>42.8(39.9,45.5)</td>
<td>43.3(41.0,46.5)</td>
<td>-1.15</td>
<td>0.250</td>
</tr>
<tr>
<td>GLOB[g/L, median(IQR)]</td>
<td>25.9(23.7,28.2)</td>
<td>26.3(24.5,29.9)</td>
<td>-1.64</td>
<td>0.101</td>
</tr>
<tr>
<td>AG[median(IQR)]</td>
<td>1.7(1.5,1.8)</td>
<td>1.6(1.4,1.8)</td>
<td>-0.84</td>
<td>0.399</td>
</tr>
<tr>
<td>ALT[U/L, median(IQR)]</td>
<td>18.0(12.0,34.0)</td>
<td>18.0(12.5,55.0)</td>
<td>-0.27</td>
<td>0.785</td>
</tr>
<tr>
<td>AST[U/L, median(IQR)]</td>
<td>20.0(16.0,29.3)</td>
<td>21.0(17.0,34.5)</td>
<td>-1.25</td>
<td>0.213</td>
</tr>
<tr>
<td>TBil[umol/L, median(IQR)]</td>
<td>15.7(12.1,21.7)</td>
<td>13.9(12.2,19.8)</td>
<td>-1.23</td>
<td>0.220</td>
</tr>
<tr>
<td>BUN[mmol/L, median(IQR)]</td>
<td>5.3(4.5,6.6)</td>
<td>5.0(4.2,7.5)</td>
<td>-0.40</td>
<td>0.689</td>
</tr>
<tr>
<td>Scr[umol/L, median(IQR)]</td>
<td>72.5(63.0,85.0)</td>
<td>70.0(59.0,89.5)</td>
<td>-0.76</td>
<td>0.448</td>
</tr>
<tr>
<td>UA[umol/L, median(IQR)]</td>
<td>290.0(241.8,350.3)</td>
<td>296.0(238.0,366.5)</td>
<td>-0.35</td>
<td>0.727</td>
</tr>
</tbody>
</table>

MCI, mild cognitive impairment; BMI, body mass index; WBCs, white blood cell count; RBCs, red blood cell count; Hb, hemoglobin; PLT, platelet count; MPV, mean platelet volume; Glu, blood glucose; ALB, albumin; GLOB, globulin; AG, Albumin to Globulin; ALT, alanine transaminase; AST, Aspartate Transaminase; TBil, total bilirubin; BUN, blood urea nitrogen; Scr, serum creatinine; UA, uric acid.

Predictors Of Preoperative MCI

There were 24 factors included in the LASSO regression and 5 variables had nonzero coefficients in the training cohort. The factors included years of education, BMI \( \geq 24 \text{ kg/m}^2 \), a history of two or more operations, red blood cell count (RBCs), Albumin to Globulin (AG) and blood urea nitrogen (BUN) (Fig. 2).
The variables above were used for multivariate analysis. Years of education (OR = 0.78, 95%CI = 0.71–0.87), BMI ≥ 24 kg/m² (OR = 0.50, 95%CI = 0.29–0.87), a history of two or more operations (OR = 2.42, 95%CI = 1.10–5.32), RBCs (OR = 0.56, 95%CI = 0.29–1.08) and AG (OR = 0.27, 95%CI = 0.09–0.74) were included in the prediction model (Table 2).

**Table 2**

<table>
<thead>
<tr>
<th>Risk Predictor</th>
<th>β</th>
<th>OR</th>
<th>95%CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education</td>
<td>-0.247</td>
<td>0.78</td>
<td>0.71–0.87</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI ≥ 24 kg/m²</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No [n(%)]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes [n(%)]</td>
<td>-0.693</td>
<td>0.50</td>
<td>0.29–0.87</td>
<td>0.015</td>
</tr>
<tr>
<td>History of two or more operations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.884</td>
<td>2.42</td>
<td>1.10–5.32</td>
<td>0.028</td>
</tr>
<tr>
<td>RBCs</td>
<td>-0.577</td>
<td>0.56</td>
<td>0.29–1.08</td>
<td>0.083</td>
</tr>
<tr>
<td>BUN</td>
<td>0.103</td>
<td>1.11</td>
<td>0.98–1.26</td>
<td>0.110</td>
</tr>
<tr>
<td>AG</td>
<td>-1.330</td>
<td>0.27</td>
<td>0.09–0.74</td>
<td>0.001</td>
</tr>
</tbody>
</table>

BMI, body mass index; RBCs, red blood cell count; BUN, blood urea nitrogen; AG, Albumin to Globulin.

**Development And Validation Of A Preoperative MCI Nomogram**

According to the odds ratio of the independent factors, a nomogram to predict preoperative MCI was developed (Fig. 3). The score of each predictor could be evaluated using the nomogram. The clinician could evaluate the patient’s probability of preoperative MCI by adding up all scores of the patient.

The 1000 bootstrap resampling procedure was used to evaluate the value of the nomogram. Calibration was used to evaluate the discriminant ability of prediction models in the validation cohort (Fig. 4). The area under ROC (AUC) of the nomogram in the training cohort and validation cohort were 0.754 (95%CI, 0.695–0.812) and 0.708 (95%CI, 0.559–0.856) respectively (Fig. 5). The DCA showed that the threshold probability of net benefit of the prediction model ranged from 45–81% (Fig. 6).

**Discussion**
Patients may be comparatively ignored by clinicians before diagnosis as an insidious onset of MCI. In addition, the diagnostic criteria of MCI in clinical practice rely on some cognitive screening measures such as MMSE or MoCA, which is an intricate task. Accordingly, we provide a new way to predict preoperative MCI of elderly by using multivariable logistic regression to develop the elderly patients with preoperative MCI prediction model and drawing the nomogram. Five variables could be used to predict the probability of elderly patients with preoperative MCI. The validation demonstrated that it had good discriminative and calibration capabilities.

Previous studies have found that education has a profound association with an individual's cognitive ability. The relationship between cognitive function and educational attainment demonstrates that dementia incidence is clearly linked to educational attainment [15]. Additionally, higher education is a protective factor for cognitive decline in MCI patients [16]. In the present study, our nomogram also indicated that the number of years of education is negatively related to the risk of MCI. Subsequent studies have indicated that memory training for MCI patients can significantly improve the cognitive decline of MCI patients, whose protective effect lasts for 2 years [17] And education can improve the cognitive function of the elderly before the onset of dementia and delay the onset of clinical manifestations in MCI patients [18]. Given all these results, we recommend cognitive training for older adults with preoperative MCI.

Generally speaking, being overweight is unhealthy. However, there seems to be an "obesity paradox" between overweight and cognitive function in elderly. Being overweight seems to be beneficial to the cognitive function of the elderly, while abdominal obesity may promote cognitive decline. [19]. The results of our study also found that normal or low BMI may indicate preoperative MCI in elderly patients. Obesity in older women is inversely associated with less brain atrophy and lower ischemic lesion loads [20], which may explain the protective effect of obesity on cognitive function. At the same time, studies have confirmed that leptin secreted by adipose tissue can avoid neuronal death, block neurotoxin damage to neurons, boost the secretion of BDNF, and then perform a neuroprotective role [21]. Nevertheless, the existence of an obesity paradox is still controversial. Judith M. Kronschnabl et al. [22] believed that there may be undiagnosed diseases that lead to the combined decline in weight and cognitive ability, while overweight itself does not affect cognition, and there is no so-called "obesity paradox". Based on the above reasons, the results of this study should be interpreted with caution.

It is widely accepted that surgical procedures can affect cognition. Though half of elderly patients with cancer surgery can recover their cognitive function to the previous level after surgery but 12% of patients still suffer from cognitive decline [23]. In our study, we compared patients with and without two or more operations and found patients with two or more operations were 1.7 times more likely to have preoperative MCI. Post-surgical neuroinflammation can transfer to the brain through cellular and humoral pathways that can result in synaptic impairment, neuronal dysfunction and death, and impaired neurogenesis that can ultimately lead to neurodegeneration and dementia [24, 25].
Nutritional imbalance is common in elderly and may cause decreased AG and anemia. AG was correlated with MoCA score in the elderly, and higher AG was usually associated with good cognitive function, which may be related to the cognitive impact of nutritional status [26]. Elderly people with low serum albumin levels were more likely to suffer from cognitive impairment [27]. About 90% of the plasma amyloid binds to albumin, which can no longer accumulate and deposit in the central nervous system (CNS) to form amyloid plaques, which may explain the protective effect of albumin on cognitive function [28]. Anemia caused by a nutritional imbalance can reduce blood supply to peripheral tissues and leads to chronic hypoxia. Such process in the brain causes chronic hypoxia of neurons, promotes amyloid accumulation, activates the inflammatory response of the nervous system, and promotes neuronal apoptosis with insufficient blood supply to the cerebral cortex [29]. When comparing MRI images of adult brain structures with RBC distribution width and hemoglobin level, it could be found that anemia was related to the reduction of hippocampus volume, and this effect was more obvious in women [30].

There are some limitations of the study. First, our study was a single central study that could not represent all elderly patients undergoing surgery. Second, the validation did not perform in an external database though we used 1000 bootstrap resampling procedure to reduce bias caused by over-fitting. Third, other related factors such as lipoprotein, amount of daily activity, and presence or absence of sleep disorders were not included in the study, which may have reduced the diagnostic value of the model.

In summary, given its increased incidence and difficulty in diagnosis, we developed a nomogram to predict the preoperative MCI in elderly and validate its diagnostic value to provide a novel approach for preoperative MCI diagnosis in geriatric patients.

Abbreviations

Mild cognitive impairment: MCI; Least absolute shrinkage and selection operator: LASSO; Receiver operating characteristic: ROC; Decision curve analysis: DCA; Body mass index: BMI; American Society of Anesthesiologists: ASA; Central nervous system: CNS; Montreal Cognitive Assessment: MoCA; Mini-Mental State Examination: MMSE; Interquartile ranges: IQRs; Red blood cell count: RBCs; Albumin to Globulin: AG; Blood urea nitrogen: BUN

Declarations

Authors’ contributions

Yuanyuan Zhang, Xin X and Haiyun Wang designed the study, Yuanyuan Zhang conducted all statistical analyses and data visualization and wrote the manuscript. Chenyi Yang and Yun Li contributed to study design and helped with statistical analyses, Xinyi Wang and Zhuo Yang helped with statistical analyses. All authors revised the manuscript and approved the final version.

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Availability of data and materials

The dataset used for the current study can be available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The protocol for the clinical trial was approved by the institutions and each participant or their legal representative gave informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References


**Figures**
Figure 1

Flow chart of the study. CNS, central nervous system; MCI, mild cognitive impairment.
Figure 2

Lasso regression was used to select variables. (A) Tuning parameter ($\lambda$) selection using LASSO penalized logistic regression with 10-fold cross-validation. (B) LASSO coefficient profiles of the radiomic features.
Figure 3

Nomogram to predict the probability of preoperative MCI. Clinicians could use the nomogram to find the point of each variable, add the points of all variables to find the total point and find the probability of MCI. BMI, body mass index; RBCs, red blood cell count; Hb, hemoglobin; AG, Albumin to Globulin; MCI, mild cognitive impairment.
Figure 4

Calibration of the nomogram in validation cohort. The predictive performance of the nomogram was evaluated in validation cohort by the 1000 bootstrap resampling procedure. The X axes presents the predictive probability and the Y axes presents actual probability.
Figure 5

Receiver operating characteristic curve of the nomogram in validation cohort. The AUC of the nomogram was 0.708 (95% CI: 0.559–0.856) in the validation cohort. ROC, receiver operating characteristic; AUC, area under ROC.
Figure 6

The DCA curve for the prediction models. The threshold probability value was ranged from 45% to 81%.