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Research article

Development and validation using NHANES data of a predictive model for depression risk in myocardial infarction survivors

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ABSTRACT

Background: Depression after myocardial infarction (MI) is associated with poor prognosis. This study aimed to develop and validate a nomogram to predict the risk of depression in patients with MI.

Methods: This retrospective study included 1615 survivors of MI aged >20 years who were selected from the 2005–2018 National Health and Nutrition Examination Survey database. The 899 subjects from the 2005–2012 survey comprised the development group, and the remaining 716 subjects comprised the validation group. Univariate and multivariate analyses identified variables significantly associated with depression. The least absolute shrinkage and selection operator (LASSO) binomial regression model was used to select the best predictive variables.

Results: A full predictive model and a simplified model were developed using multivariate analysis and LASSO binomial regression results, respectively, and validated using data from the validation group. The receiver operator characteristic curve and Hosmer–Lemeshow goodness of fit test were used to assess the nomogram's performance. The full nomogram model included 8 items: age, BMI, smoking, drinking, diabetes, exercise, insomnia, and PIR. The area under the curve for the development group was 0.799 and for the validation group was 0.731, indicating that our model has good stability and predictive accuracy. The goodness of fit test showed a good model calibration for both groups. The simplified model includes age, smoking, PIR, and insomnia. The AUC of the simplified model was 0.772 and 0.711 in the development and validation groups, respectively, indicating that the simplified model still possessed good predictive accuracy.

Conclusion: Our nomogram helped assess the individual probability of depression after MI and can be used as a complement to existing depression screening scales to help physicians make better treatment decisions.

1. Introduction

Patients suffering from depressive symptoms after MI are at an increased risk of adverse events and death [1, 2, 3]. Therefore, it is important to identify patients with MI at risk of depression early and take preventive measures, not only to treat those who have already experienced depressive symptoms [4]. Presently, various depression-screening tools are available to effectively identify those who are already suffering from depression [5, 6]. However, most of these scale options are based on the subject's independent choice, and thus are somewhat subjective in their assessment of depressive symptoms. In addition, most of these scales focus on the mental and psychological aspects of the patient, therefore their ability to identify those who do not yet present with depressive symptoms is limited. Several objective factors such as body mass index (BMI), hypertension, and diabetes have previously been observed to be strongly associated with depression [7, 8, 9]. Extensive research has shown that alcohol consumption, smoking, insomnia, and lack of exercise are significantly associated with the risk of depression [10, 11, 12, 13, 14]. Additionally, some simple demographic information, such as age, gender, marital status, educational level, and income level, are important factors for depression [15, 16].

A nomogram enables the simplification of traditional predictive model formulae into a single numerical estimate of the probability of an event, helping to inform clinical decision making during clinical consultations for individual patients' situations [17]. Currently, few clinical predictive models regarding the risk of depression in MI survivors exist. Therefore, the specific goal of this study was to use the National Health and Nutrition Examination Surveys (NHANES) database to investigate objective predictors of depression in MI survivors and to develop and validate a nomogram for predicting the depression risk in patients with MI.

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2. Methods

2.1. Study design

This was a retrospective study based on the 2005–2018 NHANES database. The NHANES is a nationally representative survey conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention to assess the health and nutritional status of non-institutionalized, community-dwelling adults and children in the United States [18]. Written informed consent was signed by all study participants. NHANES is an open database, so ethical approval was waived.

2.2. Study population

A total of 1712 self-reported >20-year-old MI survivors were selected from the 2005–2018 NHANES. Ninety-seven individuals who lacked information on the depression scale were excluded, and we ultimately selected 1615 subjects for the study. A total of 899 subjects from the 2005–2012 survey comprised the development group, and 716 subjects from the 2013–2018 survey comprised the validation group.

2.3. Depression and candidate predictor variables

The Patient Health Questionnaire-9 (PHQ-9) scale is a nine-item depression-screening tool with each of the nine items rated from 0 (not at all) to 3 (nearly every day), giving a total score between 0 and 27 based on the subject's responses to questions about the frequency of depressive symptoms in the past 2 weeks [19]. We defined having symptoms of depression at the time of survey participation as a score of ≥10 on the PHQ-9 [20, 21]. The participants' demographic characteristics were obtained through a self-reported questionnaire and included age, gender (male or female), race (non-Hispanic White, non-Hispanic Black, Mexican American, other Hispanic, and other Race), education (less than high school, high school, and more than high school), marriage status (married, single, never married; “single” was defined as divorced or widowed). Hypertension was defined by self-report or blood pressure >140/90 mmHg. Diabetes was defined as glycohemoglobin ≥6.5% or self-report. BMI was calculated as the weight in kilograms divided by the square of height in meters (kg/m^2). Drinking status (no, light, moderate, heavy) was defined by self-report, and if subjects reported drinking five or more drinks on more than 10 days in the past 12 months, we defined current drinking status as “heavy”; if they drank five or more drinks on fewer than 10 days in the past 12 months, then the current drinking status was defined as “moderate”; if they reported drinking <12 drinks in their lifetime, they were defined as “no”; others were defined as “light” [22]. Smoking status was defined by self-report, and each participant was classified as a non-smoker, ex-smoker, or current smoker. The exercise conditions were divided into no exercise, ≥10 min of moderate-intensity exercise for ≤3 days, and 10 min of moderate-intensity exercise for >3 days. Insomnia was based on the participant's self-report. The poverty to income ratio (PIR) was calculated by dividing family (or individual) income by the poverty guidelines specific to the survey year and state [23].

2.4. Statistical analysis

All continuous variables were presented as the mean ± standard deviation, and Student's *t* test or the Kruskal–Wallis Rank Sum Test was used for comparisons between groups. Categorical variables were presented as frequency or percentage, and the chi-square test or Fisher's exact test was performed to detect group differences. We used univariate and multivariate logistic regression to estimate the risk of depression in survivors with MI. Because of the unequal selection probabilities of NHANES complex sampling and oversampling of the selected overall subgroup, NHANES sample weights were used in the logistic regression analysis to obtain nationally representative estimates. Odds ratio (OR) and 95% confidence interval (CI) were presented as effect estimates. This study used two methods to establish a predictive model and to verify internal validation. First, a full model including age, BMI, diabetes, drinking, smoking, PIR, insomnia and exercise was fitted based on the results of multivariate logistic regression. Second, we built a simplified model by filtering the optimal predictive variables from the risk factors through the least absolute shrinkage and selection operator (LASSO) binomial regression [24].

The receiver operator characteristic (ROC) curves were used to evaluate the discriminative performance of the nomogram, and the C statistic was measured to assess the accuracy of prediction. The Hosmer–Lemeshow goodness of fit test in the multiple logistic regression was performed to assess the model calibration [25], and calibration curves were plotted. In the validation group, the performance of the model building, identification and calibration were assessed using the same methods mentioned above. All the analyses were performed using R software version 4.1.1 (R Foundation for Statistical Computing, Vienna, Austria) and the statistical software package EmpowerStats (http://www.empowerstats.com, X&Y solutions, Inc, Boston, MA). Values of $p < 0.05$ were considered indicative of statistical significance.

3. Results

3.1. Baseline clinical characteristics

In this study, 1615 eligible subjects, with a mean age of 66.9 ± 12.2 years, including 1076 males (66.6%) and 539 females (33.4%), were divided into a development group (n = 899) and a validation group (n = 716). Of the 1615 subjects, 276 were assessed as having depressive symptoms, 153 in the development group and 123 in the validation group. As shown in Table 1, there were significant differences in race, education, and diabetes between the development and validation groups.

3.2. Association of candidate predictive variables with depression

The results of the logistic regression analysis among these potential predictors were presented in Table 2. Univariate logistic regression analysis demonstrated that BMI (OR: 1.1, 95% CI: 1.0–1.1, $P < 0.001$) was positively associated with depressive symptoms and PIR (OR: 0.7, 95% CI: 0.5–0.8, $P < 0.001$) was inversely associated with depressive symptoms. Further multivariate logistic regression analysis revealed that people with diabetes (OR: 1.8, 95% CI: 1.1–3.1, $p = 0.027$) and Insomnia (OR: 2.5, 95% CI: 1.5–4.2, $p < 0.001$) had a higher risk of depression. Light alcohol drinkers (OR: 2.7, 95% CI: 1.5–4.8, $p < 0.001$) had the highest risk of depression. However, age (OR: 0.9, 95% CI: 0.9–1.0, $P < 0.001$) was inversely associated with depressive symptoms. In addition, ex-smokers (OR: 0.5, 95% CI: 0.3–1.0, $P = 0.040$) with <3 days of moderate-intensity exercise (OR: 0.4, 95% CI: 0.2–1.0, $P = 0.038$) per week had the lowest risk for depressive symptoms.

3.3. Prediction of depression in the development and validation groups

In the development and validation groups, 153 (17.02%) and 123 (17.18%) participants were identified as having depressive symptoms, respectively. First, we constructed a full model with eight independent predictive variables based on the results of the multivariate regression analysis. As shown in Figure 1A, a full nomogram model, including age, BMI, diabetes, drinking, smoking, insomnia, exercise, PIR could predict the risk of depression in MI survivors. Each variable was assigned a specific score on a rating scale. The scores of each variable were summed and a vertical line was drawn downward at the location of the total score to obtain the predicted probability of depression. Higher total scores indicated a higher probability of depression. Second, the simplified model was built by the optimal predictive features screened by the LASSO binomial regression. As shown in Figure 2A, the partial likelihood deviance (binomial deviance) curve was plotted versus log (lambda). Dotted vertical lines were drawn at the optimal values by using the

Table 1. Clinical and demographic data for development and validation group.

	All	Development	Validation	*p*-value
Number	1615	899	716	
Age (years)	66.9 ± 12.2	66.9 ± 12.6	66.8 ± 11.6	0.952
BMI (kg/m^2)	30.1 ± 6.9	30.0 ± 6.5	30.3 ± 7.4	0.408
PIR	2.1 ± 1.4	2.1 ± 1.4	2.1 ± 1.4	0.894
Gender (n, %)				0.521
Male	1076 (66.6)	605 (67.3)	471 (65.8)	
Female	539 (33.4)	294 (32.7)	245 (34.2)	
Race (n, %)				<0.001
Non-Hispanic White	911 (56.4)	545 (60.6)	366 (51.1)	
Non-Hispanic Black	301 (18.6)	166 (18.5)	135 (18.9)	
Mexican American	158 (9.8)	85 (9.5)	73 (10.2)	
Other Hispanic	128 (7.9)	62 (6.9)	66 (9.2)	
Other Race	117 (7.2)	41 (4.6)	76 (10.6)	
Education (n, %)				<0.001
Less than high school	572 (35.4)	365 (40.6)	207 (28.9)	
High school	412 (25.5)	221 (24.6)	191 (26.7)	
More than high school	631 (39.1)	313 (34.8)	318 (44.4)	
Marriage (n, %)				0.320
Married	824 (51.0)	473 (52.6)	351 (49.0)	
Single	617 (38.2)	335 (37.3)	282 (39.4)	
Never married	174 (10.8)	91 (10.1)	83 (11.6)	
Hypertension (n, %)				0.347
No	349 (21.6)	202 (22.5)	147 (20.5)	
Yes	1266 (78.4)	697 (77.5)	569 (79.5)	
Diabetes (n, %)				0.012
No	967 (59.9)	563 (62.6)	404 (56.4)	
Yes	648 (40.1)	336 (37.4)	312 (43.6)	
Drinking (n, %)				0.136
No	688 (42.6)	377 (41.9)	311 (43.4)	
Light	740 (45.8)	418 (46.5)	322 (45.0)	
Moderate	155 (9.6)	92 (10.2)	63 (8.8)	
Heavy	32 (2.0)	12 (1.3)	20 (2.8)	
Smoking (n, %)				0.217
Non-smoker	532 (32.9)	280 (31.1)	252 (35.2)	
Ex-smoker	699 (43.3)	402 (44.7)	297 (41.5)	
Current smoker	384 (23.8)	217 (24.1)	167 (23.3)	
Insomnia (n, %)				0.143
No	946 (58.6)	541 (60.2)	405 (56.6)	
Yes	669 (41.4)	358 (39.8)	311 (43.4)	
Exercise (n, %)				0.668
0	1136 (70.3)	638 (71.0)	498 (69.5)	
≤3	267 (16.5)	149 (16.6)	118 (16.5)	
>3	212 (13.1)	112 (12.5)	100 (14.0)	
Depression (n, %)				0.932
No	1339 (82.9)	746 (83.0)	593 (82.8)	
Yes	276 (17.1)	153 (17.0)	123 (17.2)	

BMI, body mass index; PIR, poverty to income ratio.

Table 2. Univariate and multivariate logistic regression analysis of predictors for depression.

Variable	Univariate		Multivariate	
	OR (95%CI)	*p*-value	OR (95%CI)	*p*-value
Age	1.0 (0.9, 1.0)	<0.001	0.9 (0.9, 1.0)	<0.001
BMI	1.1 (1.0, 1.1)	<0.001	1.0 (1.0, 1.1)	0.024
PIR	0.7 (0.5, 0.8)	<0.001	0.8 (0.7, 1.0)	0.049
Race				
Non-Hispanic White	1.0		1.0	
Non-Hispanic Black	2.5 (1.3, 4.6)	0.004	1.4 (0.7, 2.9)	0.374
Mexican American	1.8 (0.6, 4.9)	0.264	1.4 (0.4, 4.5)	0.562
Other Hispanic	2.7 (1.0, 7.1)	0.051	1.8 (0.6, 5.5)	0.292
Other Race	1.4 (0.5, 3.6)	0.503	0.9 (0.3, 2.5)	0.814
Education				
Less than high school	1.0		1.0	
High school	0.6 (0.3, 1.0)	0.048	0.8 (0.4, 1.5)	0.535
More than high school	0.4 (0.3, 0.7)	0.002	0.7 (0.4, 1.3)	0.299
Marriage				
Married	1.0		1.0	
Single	1.9 (1.2, 3.0)	0.006	1.7 (1.0, 2.9)	0.069
Never married	1.2 (0.6, 2.4)	0.692	0.6 (0.3, 1.5)	0.281
Diabetes				
No	1.0		1.0	
Yes	2.2 (1.4, 3.3)	<0.001	1.8 (1.1, 3.1)	0.027
Drinking				
No	1.0		1.0	
Light	2.0 (1.2, 3.2)	0.007	2.7 (1.5, 4.8)	<0.001
Moderate	1.4 (0.7, 2.8)	0.411	1.8 (0.7, 4.2)	0.198
Heavy	1.6 (0.3, 8.1)	0.587	1.4 (0.2, 9.4)	0.699
Smoking				
Non-smoker	1.0		1.0	
Ex-smoker	0.6 (0.3, 1.1)	0.082	0.5 (0.3, 1.0)	0.040
Current smoker	2.3 (1.3, 3.9)	0.003	1.3 (0.7, 2.7)	0.386
Insomnia				
No	1.0		1.0	
Yes	3.5 (2.2, 5.5)	<0.001	2.5 (1.5, 4.2)	<0.001
Exercise				
0	1.0		1.0	
>0,≤3	0.2 (0.1, 0.5)	<0.001	0.4 (0.2, 1.0)	0.038
>3	0.4 (0.2, 0.9)	0.019	0.8 (0.3, 1.8)	0.570
Hypertension				
No	1.0			
Yes	0.9 (0.5, 1.4)	0.560		
Gender				
Male	1.0			
Female	1.4 (0.9, 2.1)	0.152		

OR, Odds ratio; CI, confidence interval; BMI, body mass index; PIR, poverty to income ratio.

minimum criteria, and the 1 standard error of the minimum criteria. As shown in Figure 2B, a coefficient profile plot was produced against the log (lambda) sequence. The optimal tuning parameter (lambda) selection in the LASSO model used 10-fold cross-validation and the 1 standard error of the minimum criterion. At the optimal lambda value was 0.0497, the four optimal predictive variables with non-zero coefficients, including age, smoking, PIR, and insomnia were selected from the LASSO regression model, and then a simple nomogram model was constructed (Figure 1B).

The ROC analysis of the full and simplified model was shown in Figure 3. In the development group, the C statistic was 0.799 (95% CI: 0.763–0.835) for the full model and 0.772 (95% CI: 0.732–0.812) for the simplified model (Figure 3A). In addition, in the validation group, the C statistic was 0.731 (95% CI: 0.685–0.779) in the full model and 0.711 (95% CI: 0.662–0.761) in the simplified model (Figure 3B), indicating that our model has good stability and predictive accuracy. As shown in Figure 4, the calibration curves of the full model in the development and validation groups were plotted: the x-axis represents the predicted depression risk, and the y-axis represents the actual diagnosed depression; the diagonal dotted line represents a perfect prediction by an ideal model; the solid line represents the performance of the nomogram, of which a closer fit to the diagonal dotted line represents a better prediction. The Hosmer–Lemeshow goodness of fit test showed a *p*-value of

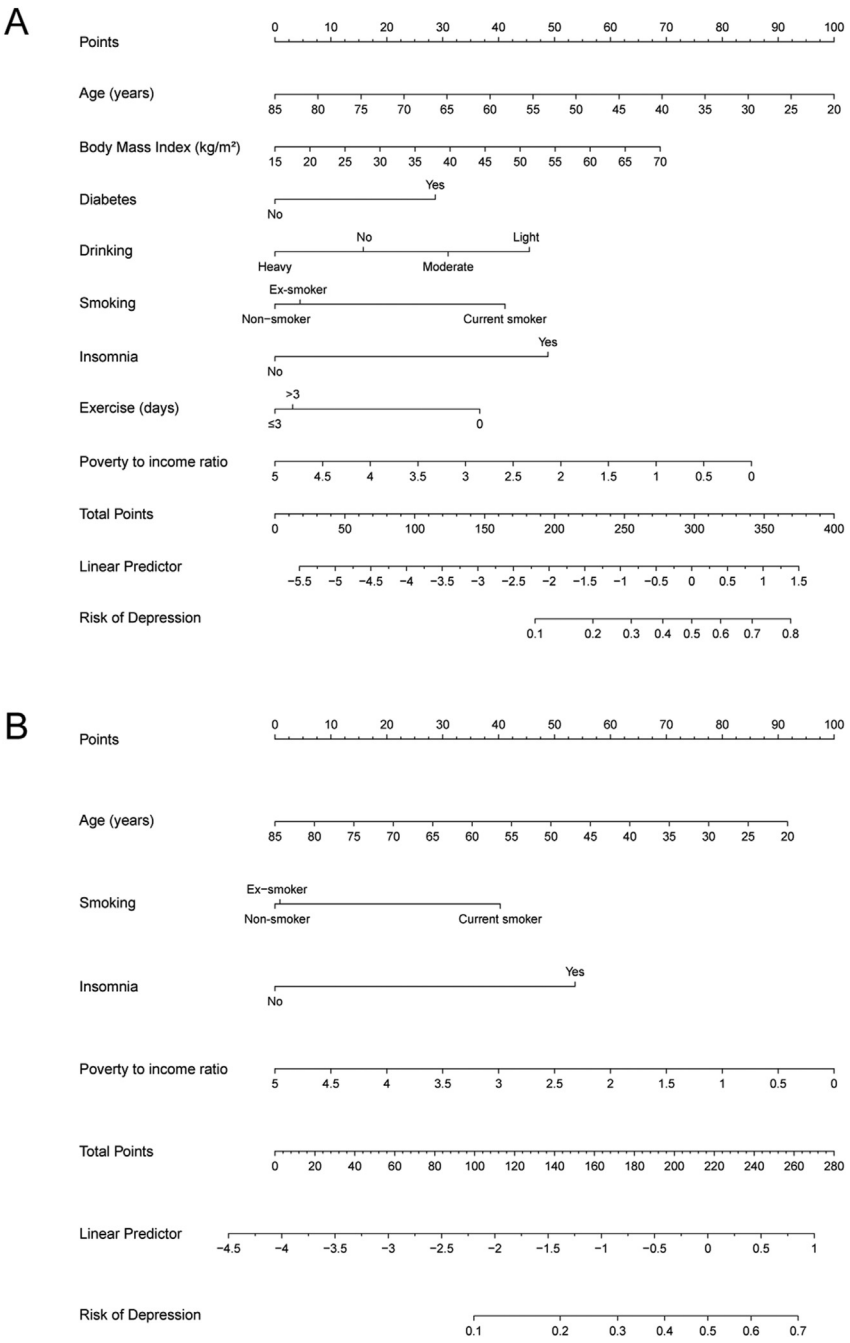

Figure 1. Nomogram predicting the probability of depression in the development group. (A) full model, (B) simplified model.

0.449 for the development group and of 0.765 for the validation group, indicating that the model was well calibrated.

4. Discussion

Currently, there are no practical predictive tools to identify individuals in MI survivors who may develop depression. Therefore, we used data from 1615 patients with MI to develop and validate a nomogram-based risk score to predict the risk of depression after MI.

Unlike previous depression scales, the predictors we included are all objective depression-related variables that can evaluate patients' depression well in terms of objectivity. The full nomogram model included 8 items: age, BMI, smoking, drinking, diabetes, exercise, insomnia, and PIR. Similar to the results of previous studies, we found that diabetes [9], insomnia [12], and BMI [7] were significantly associated with depression, while age [26] was inversely associated with depression. In addition, ex-smokers [27] and subjects who participated in moderate-intensity physical activity [13] had the lowest risk of depression. PIR is a measure of household income after adjusting for inflation and household size [28]. In our study, PIR was inversely associated with depression, suggesting that lower levels of household income are associated with higher likelihood of depression [29, 30]. Interestingly, we found that light and moderate drinkers had a significantly higher risk of depression than non-drinkers, with light drinkers having the highest risk. This is contrary to the findings of a study based on older Irish adults who found that light and moderate drinkers had a lower risk of depression than non-drinkers [31]. However, Churchill et al. found that alcohol consumption may increase a person's risk of depression [10]. These dissimilarities may be related to differences in study populations and classifications of drinking levels.

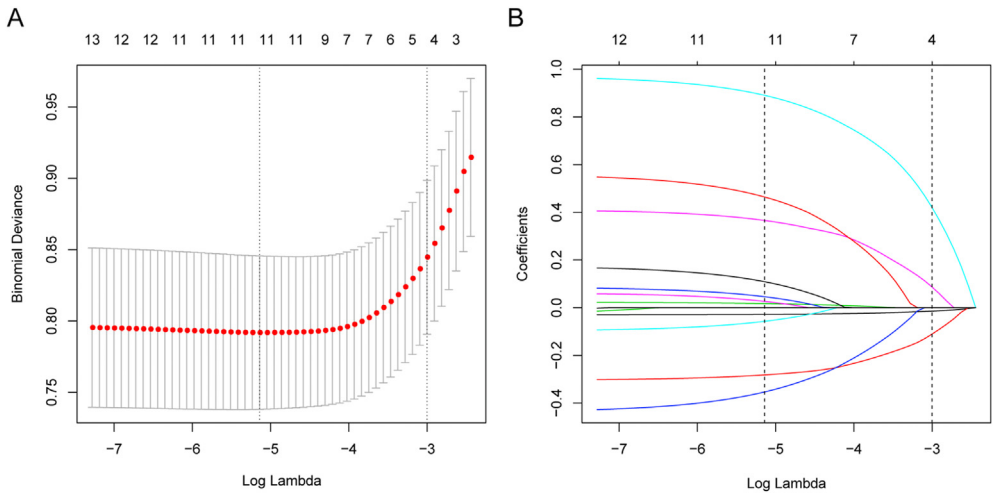

Figure 2. Features selection using the LASSO binomial regression model. (A) The partial likelihood deviance (binomial deviance) curve was plotted versus log (lambda). (B) LASSO coefficient profiles of the 13 features. LASSO, least absolute shrinkage and selection operator.

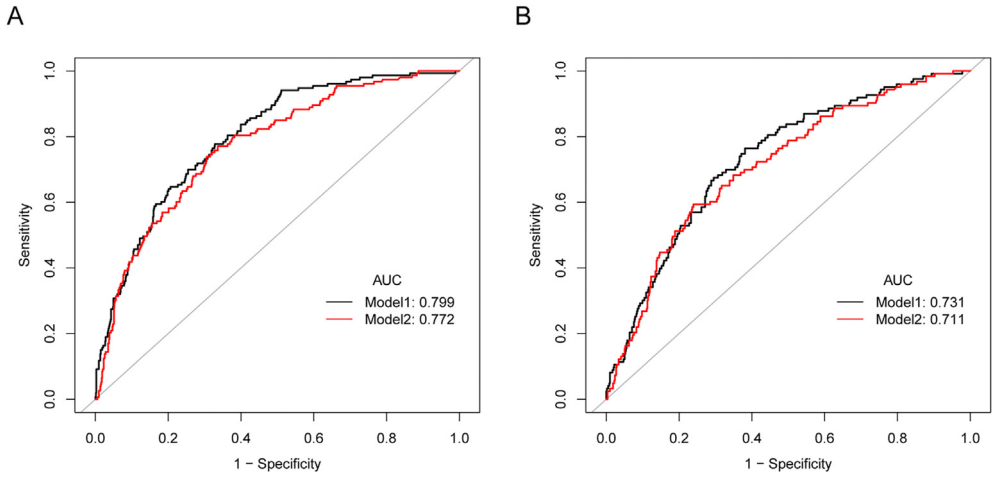

Figure 3. Receiver operating characteristic curve analyses. (A) development group, (B) validation group. AUC, area under the curve; model 1, full model; model 2, simplified model.

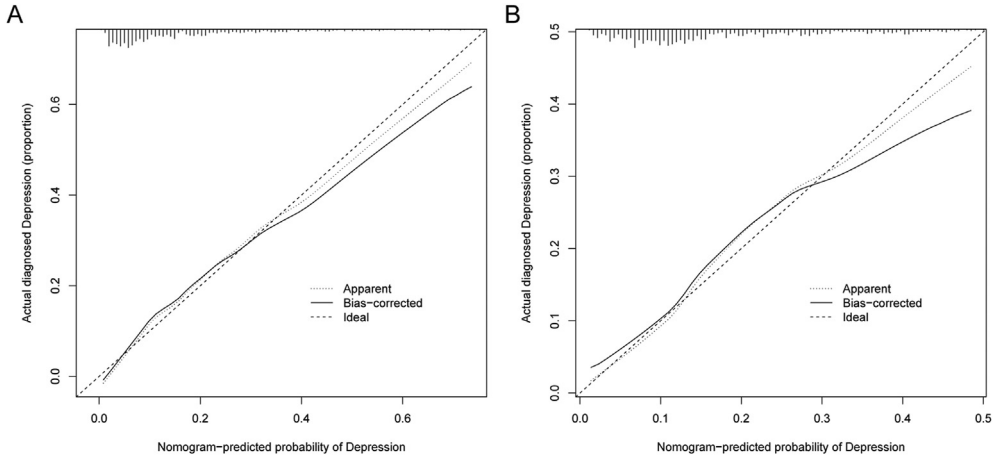

Figure 4. Calibration curve for the nomogram. (A) development group (B) validation group.

In the nomogram-based full model, the ROC analysis for the development group had an AUC of 0.799. We used data from other years for validation, and the AUC of the validation group was 0.731, indicating that our model has good predictive accuracy and stability. Additionally, the calibration curves showed good calibration results in the development and validation groups. To optimize the model, we used LASSO

regression to filter out the four optimal variables and constructed a simplified model. The AUC for the simplified model in the development and validation groups were 0.772 and 0.711, respectively. The prediction accuracy of the simplified model did not decrease significantly compared to the full model, but the number of predictive variables was smaller and therefore more convenient to use. Because the predictive variables of the model exclude mental, psychological, and emotional factors but are based on objective factors, such as the patient's existing demographic characteristics, lifestyle habits, and physical illness, the model is useful for identifying high-risk patients who have not yet developed depressive symptoms. In clinical use, the nomogram can be combined with existing depression scales to comprehensively evaluate individual patients. For example, patients who are not currently presenting with depression may have a score of zero on the depression screening scale, but that does not mean that the patient will not get depression later. At this point, our nomogram is able to obtain the individual's risk probability of developing depression and can be used as a supplement to existing depression screening scales to help clinicians make more patient-friendly treatment decisions. To our knowledge, this is the first study to build a predictive model based on the NHANES database to predict the risk of depression in MI survivors.

However, there were several limitations of our study. First, all our data were extracted from NHANES health examinations at the Home Interview and Mobile Examination Center, and data on some variables were based on self-report, such as exercise and alcohol consumption. Second, depression was determined using only one measure, the PHQ-9, and no depression severity stratification was performed. These limitations could have potentially reduced the accuracy and objectivity of our data. In addition, this model was established in the US population and may not apply directly to populations in other countries.

In conclusion, we developed a predictive model based on self-reported problems, simple demographics, lifestyle habits, physical illness, and other objective characteristics that predict the risk of depression in patients with MI. The model showed similarly good discrimination in data sets for different time periods. The nomogram helps to screen individuals who are vulnerable to depression after MI and can be used as a complement to existing depression screening scales to help physicians make better treatment decisions.

Declarations

Author contribution statement

Di Wang and Yongping Jia: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Siqi Jia and Shaoyi Yan: Contributed reagents, materials, analysis tools or data.

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Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

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