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Construction and evaluation of sarcopenia risk prediction model for patients with diabetes: a study based on the China health and retirement longitudinal study (CHARLS)

Mingrui Zou[1,2,3] and Zhenxing Shao[1,2*]

Abstract

Purpose Sarcopenia is a common complication of diabetes. Nevertheless, precise evaluation of sarcopenia risk among patients with diabetes is still a big challenge. The objective of this study was to develop a nomogram model which could serve as a practical tool to diagnose sarcopenia in patients with diabetes.

Methods A total of 783 participants with diabetes from China Health and Retirement Longitudinal Study (CHARLS) 2015 were included in this study. After oversampling process, 1,000 samples were randomly divided into the training set and internal validation set. To mitigate the overfitting effect caused by oversampling, data of CHARLS 2011 were utilized as the external validation set. Least absolute shrinkage and selection operator (LASSO) regression analysis and multivariate logistic regression analysis were employed to explore predictors. Subsequently, a nomogram was developed based on the 9 selected predictors. The model was assessed by area under receiver operating characteristic (ROC) curves (AUC) for discrimination, calibration curves for calibration, and decision curve analysis (DCA) for clinical efficacy. In addition, machine learning models were constructed to enhance the robustness of our findings and evaluate the importance of the predictors.

Results 9 factors were selected as predictors of sarcopenia for patients with diabetes. The nomogram model exhibited good discrimination in training, internal validation and external validation sets, with AUC of 0.808, 0.811 and 0.794. machine learning models revealed that age and hemoglobin were the most significant predictors. Calibration curves and DCA illustrated excellent calibration and clinical applicability of this model.

Conclusion This comprehensive nomogram presented high clinical predictability, which was a promising tool to evaluate the risk of sarcopenia in patients with diabetes.

Keywords Prediction model, Sarcopenia, Diabetes, Nomogram, CHARLS

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Introduction

Diabetes mellitus (DM) is a chronic metabolic disease, which is mainly characterized by hyperglycemia and hyperglycemia-induced complications [1]. According to the latest statistics provided by the International Diabetes Federation (IDF), the global diabetic population amounted to an estimated 537 million individuals in 2021, a figure expected to escalate 643 million by 2030 and 783 million by 2045 [2]. In China, approximately 11% of the population are affected by diabetes, with a large proportion remaining undiagnosed [3]. Moreover, the complications of diabetes also inflict considerable distress on patients, predominantly in the forms of microvascular complications and macrovascular complications [4]. Among these complications are certain geriatric syndromes, such as sarcopenia [5]. Many studies have demonstrated that poor glucose control, prolonged diabetic progression and the existence of other complications may increase the risk of sarcopenia among diabetic patients, especially those with heart failure with reduced ejection fraction (HFrEF) [6–9].

Sarcopenia, characterized by progressive loss of skeletal muscle mass and function, is increasingly acknowledged as a significant health issue, particularly among the elderly [10]. The European Working Group on Sarcopenia in Older People (EWGSOP) defines "sarcopenia" as diminished skeletal muscle strength with reduced skeletal muscle mass or decreased physical function [11]. It is well-established that this condition amplifies the risk of falls, fractures and physical disabilities, leading to a decline in quality of life [12, 13]. It is estimated that sarcopenia affects 10 -16% of elderly worldwide. Compared to general population, patients are at a higher risk of developing sarcopenia [14]. Moreover, previous studies have demonstrated that the prevalence of sarcopenia in patients with diabetes is much higher, ranging from 7–29.3% [15, 16]. Research shows that the pathogenesis of sarcopenia in patients with diabetes is intricate, influenced by many factors such as insulin resistance, systemic inflammatory responses, unhealthy lifestyle, malnutrition and dysfunction of gut microbiota [17–20]. Xia et al. revealed that T2DM patients with sarcopenia exhibited a higher 10-year risk of atherosclerotic cardiovascular disease (ASCVD) compared to those without sarcopenia, and sarcopenia might serve as an independent risk factor for patients with diabetes [21]. Without prompt diagnosis and timely interventions, the condition of diabetic patients with sarcopenia is likely to deteriorate, escalating the mortality rate. Hence, the establishment of a practical model for assessing the risk of sarcopenia in patients with diabetes holds great significance.

At present, the diagnosis of sarcopenia primarily focuses on measuring muscle mass, which usually necessitates professional equipment and techniques such as Bio-impedance analysis (BIA), dual-energy X-ray absorptiometry (DXA), muscle ultrasound, X-ray computed tomography (CT) and magnetic resonance imaging (MRI) [22]. However, in regions with limited medical resources, such as rural areas, the diagnosis of sarcopenia poses a significant challenge. In addition, conventional diagnostic approaches for sarcopenia provide limited assistance for individuals with diabetes. Therefore, it is urgent to develop a novel diagnostic tool to evaluate the risk of sarcopenia for patients with diabetes, facilitating the early screening and diagnosis of this condition.

In this study, we utilized data from China Health and Retirement Longitudinal Study (CHARLS) to establish a nomogram model based on easily accessible demographic, clinical or laboratory factors. As a result, it can serve as a practical tool to help evaluate the risk of sarcopenia in patients with diabetes.

Materials and methods

Study design and data source

This study was a cross-sectional study in the general population of China Health and Retirement Longitudinal Study (CHARLS). CHARLS is a longitudinal survey conducted in China, aiming at investigating the health, economic and retirement status of the elderly people in China. Data from CHARLS 2011 and 2015 were collected for analysis in this study, which were publicly available at http://charls.pku.edu.cn. The CHARLS protocol obtained approval from the Ethical Review Committee of Peking University (Approval number: IRB00001052-11015), and the written informed consents were received from each participant [23].

Participants

In this study, individuals with diabetes were included, which can be classified based on anyone of the following criteria: (1) Fasting blood glucose levels≥126 mg/dl (7mmol/L); (2) Random blood glucose levels≥200 mg/dl (11.1mmol/L); (3) Glycohemoglobin (HbA1c) levels≥6.5%; (4) Self- reported diagnosed of diabetes [1].

Outcomes

The assessment of sarcopenia was conducted based on the 2019 consensus of the Asian Working Group for Sarcopenia (AWGS), with muscle strength, appendicular skeletal muscle mass (ASM) and physical performance being regarded as three parameters for the diagnosis of sarcopenia [24]. According to AWGS 2019, low muscle strength was defined as hand grip strength≤28 kg for men and ≤18 kg for women. To assess muscle mass, ASM and skeletal muscle mass index (SMI) were calculated using the following physical measurement formulas: ASM=0.193 × weight (kg)+0.107 × height (cm) − 4.157 × gender − 0.037 × age (years) − 2.631 (Male was

encoded as 1 and female as 2); SMI = (ASM/height^2). Previous studies have demonstrated that ASM calculated by the aforementioned formula presented good consistency with the dual energy X-ray absorptiometry (DXA) [25, 26]. The cut-off for low muscle mass was set as the sex-specific lowest 20% of SMI among the population, with 7.28 kg/m^2 in male and 5.55 kg/m^2 in female. In addition, low physical performance was defined as the gait speed < 1.0 m/s or the 5-time chair stand test ≥ 12s. People with low muscle mass plus low muscle strength or low physical performance were classified as sarcopenia patients [24].

Predictors

Variable screening was conducted based on clinical significance and knowledge established in previous studies [16, 27–29], which could be classified into socio-demographic factors, behaviors factors, mental factors and health factors.

Socio-demographic factors

Socio-demographic factors included age, gender, education, marital status and permanent address. Education was classified into "Below Middle school", "Middle school", "High school" and "College and above". Marital status was divided into "married" and "unmarried" based on whether the participant was current married and living with a spouse. Permanent address was categorized as either "Urban" or "Rural".

Behavioral factors and mental factors

Drinking status and Smoking status were selected as behavioral factors, which reflected whether the participants were still smoking or drinking alcohol. Mental factors included Center for Epidemiologic Studies Depression 10 (CESD10) Scale, life satisfaction, episodic memory and mental status. CESD10 is a widely used scale to assess the mental health status and the risk of depression. The total score of the CESD10 scale is 30 points, with a score of 10 or more indicating a high risk of depression [30]. Life satisfaction was classified into "Completely satisfied", "Very satisfied", "Somewhat satisfied", "Not very satisfied" and "Not at all satisfied". The episodic memory ability was evaluated by reading 10 words to participants and asking them to recall as much as possible. 1 point was assigned if recalling 1 word, with a maximum of 10 points. Mental status of participants was assessed based on their basic cognition, computational ability and drawing ability, with a total score of 11 points. Firstly, participants were required to answer the year, month, day, season and week of the interview day, and 1 correct answer counted 1 point. Furthermore, participants needed to perform 5 calculations, with each correct calculation counting 1 point. Finally, participants were asked to illustrate a graph according to the interview's requirement, and if it was corrected, 1 point was assigned.

Health factors

Health factors were divided into the following 5 categories: (1) Body index (BMI, waist, height and weight); (2) Self-perceived health status; (3) Activities of daily living (Activity of daily living (ADL) score, Instrumental activities of daily living (IADL) score and disability status); (4) Chronic diseases (Hypertension, chronic lung disease, heart disease, stroke, arthritis or rheumatism, dyslipidemia, liver disease, digestive disease and asthma); (5) Levels of common laboratory test indicators (Systolic pressure, diastolic pressure, total cholesterol (TC), Triglyceride (TG), High-density lipoprotein cholesterol (HDL-C), Low-density lipoprotein cholesterol (LDL-C), uric acid, hematocrit, hemoglobin, white blood cell (WBC), mean corpuscular volume (MCV) and platelet). Self-perceived health status was classified into "Excellent", "Very good", "Good", "Fair" and "Poor". ADL and IADL scale were used to assess the activities of daily living of participants. Six items of ADL (Dressing, bathing, feeding, transferring, going to the toilet, continence) and five items of IADL (Doing chores, cooking, shopping, managing money, taking medicine) were included in CHARLS questionnaire. For each item, 1 point was assigned if the participant had difficulty doing it. The ADL scale ranged from 0 to 6 points, while the IADL scale ranged from 0 to 5 points, representing the degree of dependency of participants [31, 32]. Disability and the 9 chronic diseases were defined based on self-reported diagnoses. Besides, hypertension was also considered if the participant had a systolic pressure ≥ 140 mmHg or a diastolic pressure ≥ 90 mmHg.

Model development and validation

In our study, samples containing missing values of the variables were excluded. Finally, data of 783 participants of CHARLS 2015 were left for analysis. Among them, 72 patients were diagnosed with sarcopenia, accounting for 9.2% of all participants. Due to the imbalance of data between the sarcopenia and non-sarcopenia groups, we employed the oversampling process utilizing the "ROSE" package (V.0.0–4). Random Over-Sampling Examples (ROSE) process produces a sample of synthetic data by enlarging the features space of minority and majority class examples [33].

Continuous variables with normal distribution were presented as mean ± standard deviation (SD), and comparison between groups were performed using *t*-test. While continuous variables with abnormal distribution were expressed by median (Interquartile range (IQR)), and group comparisons were made using the

Mann-Whitney U test. Categorical variables were presented as frequency (percentage), and comparison between groups were conducted using chi-square test.

To establish and validate the nomogram, the oversampled CHARLS 2015 data was randomly split into training set (Containing 70% of the dataset) and internal validation set (Containing 30% of the dataset). In addition, to mitigate the overfitting effect caused by oversampling, we employed CHARLS 2011 data as the external validation set. In the training set, the least absolute shrinkage and selection operator (LASSO) regression analysis was applied to identify predictors of sarcopenia in patients with diabetes. Subsequently, selected predictors were included in multivariate logistic regression analysis to validate the independent predictors with p-value < 0.05, and the nomogram was developed based on these independent predictors. In addition, 5 machine learning (ML) models, including Gradient Boosting Machine (GBM), k-Nearest Neighbor (KNN), regularized discriminant analysis (RDA), Random Forest (RF) and Support Vector Machine (SVM), were constructed to further evaluate the predictive performance and importance of the predictors used to develop the nomogram. We used grid search and 5-fold cross validation to find the optimal parameters [34].

Model performance evaluation

The area under receiver operating characteristic (ROC) curve (AUC) was used to evaluate the discrimination ability of the model. The consistency between actual result and predicted probability was assessed by calibration curves and Hosmer–Lemeshow goodness-of-fit test. Decision curve analysis (DCA) was used to assess the clinical efficacy of the nomogram.

Data analysis

All the data analyses were performed using R software (4.3.1), with p-value < 0.05 considered statistically significant.

Results

Baseline characteristics

The detailed sampling process is shown in Fig. 1. A total of 783 participants with diabetes in CHARLS 2015 were included in this study, and 72 were identified as sarcopenia patients. The demographic and clinical characteristics of participants are listed in Table S1. After the oversampling process, 1,000 samples (289 with sarcopenia and 711 without sarcopenia) were left, and the incidence of sarcopenia reached 28.9%. The demographic and clinical characteristics of samples used to develop models are listed in Table 1. Many factors including age, marital status, permanent address and ADL score differed significantly (p < 0.05).

The 1000 samples were randomly split into training set (70%) and internal validation set (30%), and we performed comparisons to confirm the dividing rationality of the dataset (Table S2). The results in Table S2 suggested that no statistically significant difference was detected between the two groups (p > 0.05).

To mitigate the overfitting effect caused by oversampling, CHARLS 2011 data was used as the external validation set. Finally, the external validation set included 945 participants, and 74 were defined as sarcopenia patients.

Predictor screening and construction of the nomogram model

LASSO regression analysis was conducted to identify non-zero coefficients as potential indicators of sarcopenia (Fig. 2A and B). Subsequently, multivariate logistic regression analysis revealed that age (OR: 1.16, 95%CI: 1.13–1.20), marital status (OR: 0.57, 95%CI: 0.38–0.85), ADL (OR: 1.45, 95%CI: 1.26–1.68), permanent address (OR: 2.08, 95%CI: 1.49–2.93), CESD10 (OR: 1.03, 95%CI: 1.01–1.06), smoking status (OR: 1.77, 95%CI: 1.22–2.56), WBC (OR: 0.87, 95%CI: 0.79–0.96), Hemoglobin (OR: 0.86, 95%CI: 0.77–0.95) and MCV (OR: 1.04, 95%CI: 1.02–1.06) were independent predictors of sarcopenia with statistical significance (p < 0.05).

Based on the selected 9 predictors (Age, marital status, ADL, permanent address, CESD10, smoking status, WBC, hemoglobin and MCV), the predictive model was constructed, and was presented as a nomogram (Fig. 3). The nomogram could be used to quantitatively predict the risk of sarcopenia in patients with diabetes. The scores of characteristics were calculated by the scale on the top, and the risk of sarcopenia for patients with diabetes could be estimated by a perpendicular line from the total point axis to the axis corresponding to risk.

Assessment of the performance of the nomogram model

The discrimination of the nomogram model was assessed by the ROC curves and AUC values in the three sets. As shown in Fig. 4A, B and C, the training set yielded an AUC of 0.808 (95%CI: 0.772–0.843), with a specificity of 0.787 and sensitivity of 0.703. In the internal validation set, the AUC was 0.811(95%CI: 759-0.862), with a specificity of 0.709 and sensitivity of 0.782. For the external validation set, the AUC was 0.794 (95%CI: 0.739–0.850), with a specificity of 0.691 and sensitivity of 0.811.

We constructed 5 ML models to further evaluate the predictive performance and importance of the predictors used to develop the nomogram. As Fig. 5A, B and C presented, GBM, RF and SVM models had the highest AUC in both the training set and internal validation set. In the external validation set, these three models still exhibited good discriminatory ability and predictive values. In both

Table 1 Baseline characteristics of samples after oversampling

Variables	Total ($n=1000$)	Non-sarcopenia ($n=711$)	Sarcopenia ($n=289$)	*P*-value
Age	67.00 [63.00, 73.00]	66.00 [62.00, 70.00]	73.00 [69.00, 76.00]	< 0.001
Gender (%)				0.039
Female	513 (51.2)	380 (53.4)	133 (46.0)	
male	487 (48.7)	331 (46.6)	156 (54.0)	
Education (%)				0.009
Below Middle school	473 (47.3)	319 (44.9)	154 (53.3)	
Middle school	272 (27.2)	195 (27.4)	77 (26.6)	
High school	155 (15.5)	113 (15.9)	42 (14.5)	
College and above	100 (10.0)	84 (11.8)	16 (5.5)	
Marital status (%)				< 0.001
Married	811 (81.1)	605 (85.1)	206 (71.3)	
Unmarried	189 (18.9)	106 (14.9)	83 (28.7)	
Permanent address (%)				< 0.001
Urban	428 (42.8)	332 (46.7)	96 (33.2)	
Rural	572 (57.2)	379 (53.3)	193 (66.8)	
Drinking status (%)				0.754
No	694 (69.4)	496 (69.8)	198 (68.5)	
Yes	306 (30.6)	215 (30.2)	91 (31.5)	
Smoking status (%)				0.001
No	722 (72.2)	535 (75.2)	187 (64.7)	
Yes	278 (27.8)	176 (24.8)	102 (35.3)	
CESD10	7.00 [3.00, 12.00]	6.00 [3.00, 12.00]	8.00 [5.00, 14.00]	< 0.001
Life satisfaction (%)				0.397
Completely satisfied	17 (1.7)	11 (1.5)	6 (2.1)	
Very satisfied	58 (5.8)	44 (6.2)	14 (4.8)	
Somewhat satisfied	510 (51.0)	350 (49.2)	160 (55.4)	
Not very satisfied	348 (34.8)	258 (36.3)	90 (31.1)	
Not at all satisfied	67 (6.7)	48 (6.8)	19 (6.6)	
Episodic memory	3.00 [1.50, 4.00]	3.00 [2.00, 4.00]	2.50 [1.00, 3.00]	< 0.001
Mental status	8.00 [6.00, 10.00]	9.00 [6.00, 10.00]	7.00 [5.00, 9.00]	< 0.001
BMI	23.79 [21.22, 26.42]	25.18 [23.14, 27.63]	20.83 [19.52, 21.57]	< 0.001
Waist	88.00 [80.40, 95.72]	91.80 [84.60, 98.25]	80.40 [74.70, 84.60]	< 0.001
Height	1.57 [1.51, 1.63]	1.58 [1.52, 1.64]	1.53 [1.50, 1.60]	< 0.001
Weight	58.25 [51.20, 67.20]	63.20 [55.50, 70.60]	50.10 [44.90, 52.90]	< 0.001
Self-perceived health status (%)				< 0.001
Excellent	64 (6.4)	51 (7.2)	13 (4.5)	
Very good	247 (24.7)	136 (19.1)	111 (38.4)	
Good	534 (53.4)	416 (58.5)	118 (40.8)	
Fair	66 (6.6)	55 (7.7)	11 (3.8)	
Poor	89 (8.9)	53 (7.5)	36 (12.5)	
ADL score	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 2.00]	< 0.001
IADL score	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.010
Disability				0.254
No	917 (91.7)	657 (92.4)	260 (90.0)	
Yes	83 (8.3)	54 (7.6)	29 (10.0)	
Hypertension				< 0.001
No	532 (53.2)	332 (46.7)	200 (69.2)	
Yes	468 (46.8)	379 (53.3)	89 (30.8)	
Chronic lung disease				0.001
No	840 (84.0)	615 (86.5)	225 (77.9)	
Yes	160 (16.0)	96 (13.5)	64 (22.1)	
Heart disease				0.002
No	741 (74.1)	507 (71.3)	234 (81.0)	

Table 1 (continued)

Variables	Total ($n=1000$)	Non-sarcopenia ($n=711$)	Sarcopenia ($n=289$)	*P*-value
Yes	259 (25.9)	204 (28.7)	55 (19.0)	
Stroke				0.104
No	929 (92.9)	667 (93.8)	262 (90.7)	
Yes	71 (7.1)	44 (6.2)	27 (9.3)	
Arthritis or rheumatism				0.995
No	514 (51.4)	366 (51.5)	148 (51.2)	
Yes	486 (48.6)	345 (48.5)	141 (48.8)	
Dyslipidemia				< 0.001
No	671 (67.1)	439 (61.7)	232 (80.3)	
Yes	329 (32.9)	272 (38.3)	57 (19.7)	
Liver disease				0.019
No	922 (92.2)	646 (90.9)	276 (95.5)	
Yes	78 (7.8)	65 (9.1)	13 (4.5)	
Digestive disease				0.063
No	668 (66.8)	488 (68.6)	180 (62.3)	
Yes	332 (33.2)	223 (31.4)	109 (37.7)	
Asthma				0.326
No	923 (92.3)	652 (91.7)	271 (93.8)	
Yes	77 (7.7)	59 (8.3)	18 (6.2)	
Systolic pressure	131.00 [118.00, 143.10]	131.50 [120.20, 145.50]	125.0 [114.50, 140.00]	< 0.001
Diastolic pressure	73.00 [65.50, 81.00]	74.50 [67.50, 82.50]	68.50 [62.50, 78.00]	< 0.001
TC	189.58 [164.48, 210.42]	189.58 [164.86, 211.58]	193.82 [163.71, 207.72]	0.538
TG	135.40 [93.81, 188.50]	143.36 [102.65, 207.52]	103.54 [84.96, 150.44]	< 0.001
HDL-C	48.65 [41.70, 56.37]	47.49 [40.93, 55.21]	50.19 [44.79, 60.62]	0.001
LDL-C	103.47 [83.78, 123.17]	104.63 [84.94, 123.55]	100.00 [81.85, 123.17]	0.885
Uric acid	4.90 [4.10, 5.80]	5.00 [4.30, 6.00]	4.70 [3.90, 5.70]	0.001
Hematocrit	41.30 [38.50, 44.62]	41.50 [38.65, 44.50]	40.80 [38.20, 45.00]	0.362
Hemoglobin	13.60 [12.50, 14.60]	13.70 [12.70, 14.70]	12.90 [12.20, 14.10]	< 0.001
White blood cell	5.96 [5.00, 7.30]	6.12 [5.16, 7.40]	5.70 [4.73, 7.18]	< 0.001
MCV	92.10 [88.70, 96.10]	92.00 [88.40, 95.35]	93.40 [89.10, 97.40]	< 0.001
Platelet	195.00 [157.00, 237.00]	197.00 [158.00, 240.00]	191.00 [157.00, 233.00]	0.055

Data are expressed as mean ± standard deviation and numbers (percentage) as appropriate.

SD, Standard Deviation; CESD10 Center for epidemiologic studies depression scale 10; ADL, Activity of daily living; IADL; Instrumental activities of daily living; TC Total cholesterol; TG Triglyceride; HDL-C High-density lipoprotein cholesterol; LDL-C Low-density lipoprotein cholesterol; MCV mean corpuscular volume.

GBM and RF models, age, white blood cell, hemoglobin and mean corpuscular volume were the top 4 important predictors (Fig. S1 and S3). While in the SVM model, age, ADL, hemoglobin, CESD10 were the most important (Fig. S2). It was probable that age and hemoglobin might play important roles in predicting the risk of sarcopenia for patients with diabetes.

Calibration curves and Hosmer–Lemeshow goodness-of-fit test were employed to evaluate the consistency between actual result and predicted probability. The calibration curves of the nomogram model in three sets presented good fit between the actual observed values and the predicted values, suggesting good consistency (Fig. 6A, B and C). *P*-values of Hosmer–Lemeshow goodness-of-fit test were all greater than 0.05, indicating that the nomogram model had a good fit for the training set ($\chi^2=10.571$, df=8, $p=0.2272$), internal validation set ($\chi^2=15.186$, df=8, $p=0.0556$) and external validation set ($\chi^2=6.355$, df=8, $p=0.6075$).

DCA was applied to evaluate the clinical validity of the nomogram (Fig. 7A, B and C). The results indicated that the nomogram model yielded significant net benefit in the training set, internal validation set and external validation set, which meant the nomogram exhibited robust predictive accuracy and clinical efficacy in predicting the risk of sarcopenia.

Discussion

Diabetes and sarcopenia are prevalent disorders, which profoundly affects the quality of life of patients. Studies have shown that the prevalence of sarcopenia in patients with diabetes is much higher, ranging from 7–29.3% [15, 16].In some areas, the prevalence of sarcopenia among diabetic patients over 70 can reach 50% [22]. Despite the introduction of novel indicators like axial thoracic

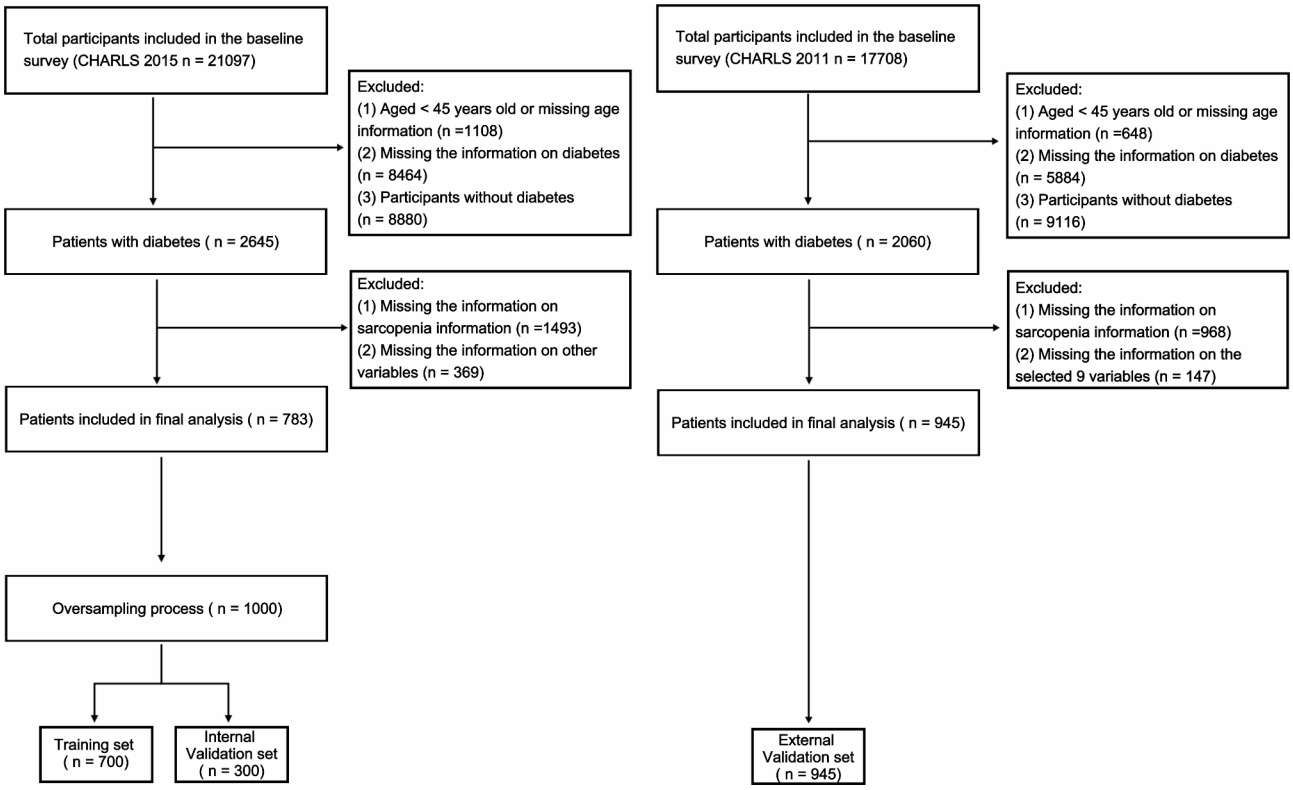

Fig. 1 Flowchart of participant selection. CHARLS, China Health and Retirement Longitudinal Study

skeletal muscle size for assessing sarcopenia risk, the diagnosis of sarcopenia continues to encounter significant challenges in regions with limited medical resources [9]. Hence, it is of great importance to promptly evaluate the risk of sarcopenia in patients with diabetes and implement timely intervention. In our study, we used data from CHARLS to construct a nomogram model, which could help clinicians evaluate the risk of developing sarcopenia in patients with diabetes. In the nomogram, the scores of characteristics were calculated by the scale on the top, and the risk of sarcopenia for patients with diabetes could be estimated by a perpendicular line from the total point axis to the axis corresponding to risk. The nomogram model consisted of 9 predictors, encompassing age, marital status, ADL, permanent address, CESD10, smoking status, white blood cell, hemoglobin and mean corpuscular volume. Specifically, increasing age, being unmarried, higher ADL and CESD10 scores, residing in rural areas, smoking, lower levels of white blood cells and hemoglobin, and higher levels of MCV were risk factors for developing sarcopenia in diabetic patients. In clinical practice, diabetic patients exhibiting these aforementioned traits should be closely monitored to prevent the onset of sarcopenia. Results of ROC curves, calibration curves and DCA revealed that this model exhibited excellent discrimination, calibration and clinical efficacy, underscoring its great potential as a practical tool for identifying sarcopenia.

For Socio-demographic factors, three factors (Age, marital status and permanent address) were identified as independent predictors of sarcopenia. We have observed a positive correlation between age and sarcopenia, indicating that as people grow older, the risk of sarcopenia increases. Previous studies have underscored age as one of the most significant risk factors for sarcopenia [35]. Starting from middle age, there is approximate 8% decline in muscle mass per decade, and after the age of 70, this rate may accelerate to a decrease of 15% per decade [36]. The potential mechanism by which senility increases the risk of sarcopenia is intricate. As people grow older, the regenerative capacity of muscle cells decreases, and the number of muscle fibers gradually decreases [37]. Furthermore, there will be significant changes in the levels of hormones and inflammatory cytokines, exacerbating the disequilibrium in muscle injury and repair processes [38, 39]. Besides, our research highlighted that unmarried participant exhibited higher risk of developing sarcopenia than married participants. Previous sociological studies have illustrated that married individuals typically have better health conditions and lower mortality rates [40]. Specifically, marriage may play a protective role by providing social support, improving lifestyle habits, and increasing economic resources [41]. Social support can

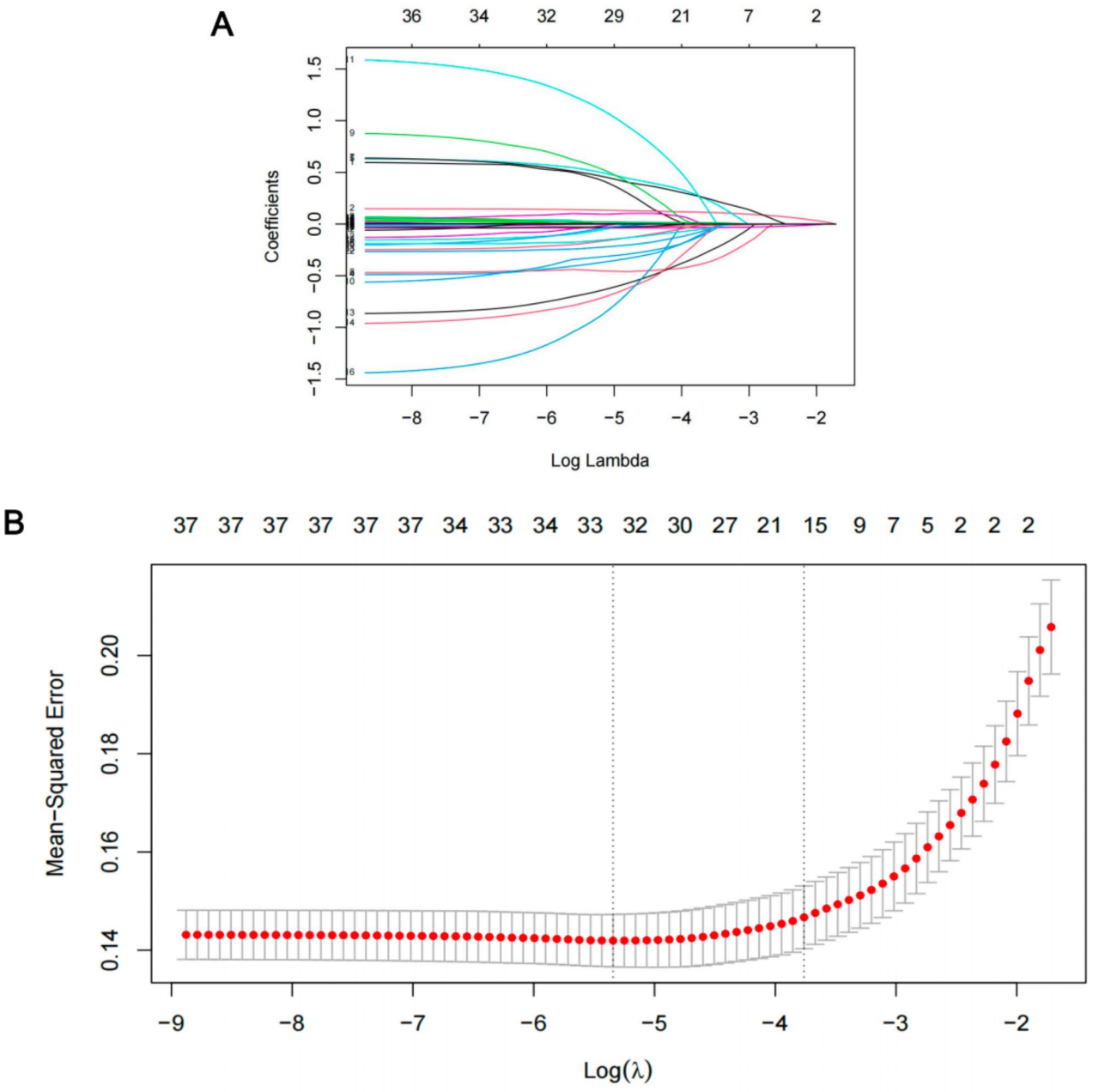

Fig. 2 Predictor screening through the LASSO regression model. (**A**) According to the logarithmic (lambda) sequence, a coefficient profile was generated, and non-zero coefficients were produced by the optimal lambda. (**B**) The optimal parameter (lambda) in the LASSO model was selected via 10-fold cross-validation using minimum criterion plus one standard error (right vertical line)

alleviate stress and depression, and these negative emotional states have been proven to be associated with sarcopenia [42]. In addition, the nomogram indicated that participants live in the rural areas have a higher sarcopenia risk than those live in urban areas. As is well known, urban residents may have easier access to medical resources and health information, while rural residents may encounter deficiencies in these areas [43]. However, higher levels of stress and unhealthy lifestyles in urban settings may also have a negative impact on muscle mass [44]. Therefore, the impact of residential location on the risk of sarcopenia is complex and multifaceted.

In our study, we observed positive associations between ADL and CESD10 with sarcopenia, which meant poor self-care ability (High ADL score) and higher levels of depression increased the risk of sarcopenia. A study conducted in the Netherlands suggested a bidirectional association between sarcopenia and ADL limitation. On the one hand, muscle loss led to a decline in functional capacity, while on the other hand, ADL limitation

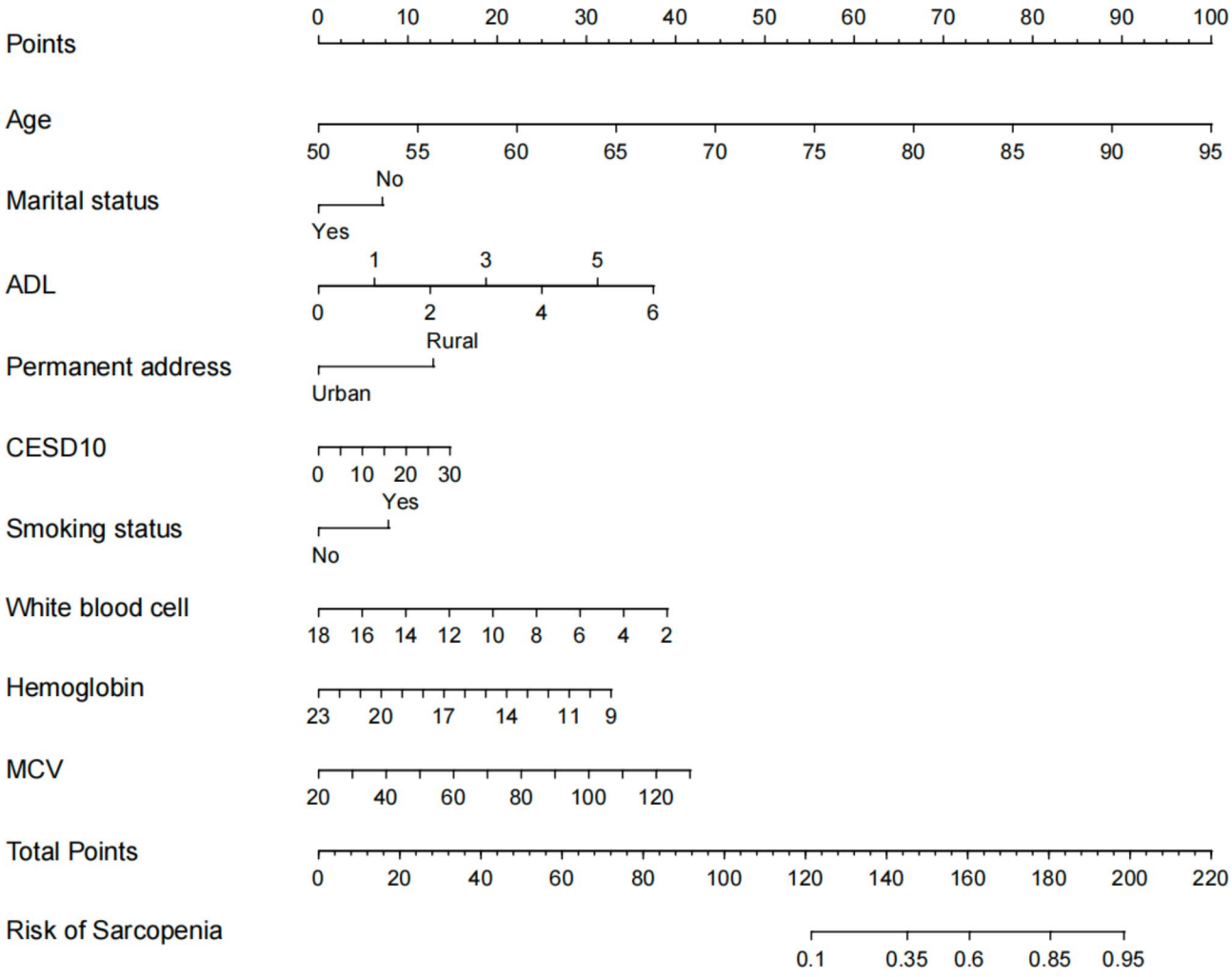

Fig. 3 Nomogram to evaluate the risk of sarcopenia in patients with diabetes. ADL, Activity of daily living; CESD10, Center for Epidemiologic Studies Depression Scale; MCV, mean corpuscular volume

Table 2 Multivariate logistic regression analysis of the risk factors of Sarcopenia in the prediction model

Variable	Multivariate analysis OR (95% CI)	*P*-value
Age	1.16 (1.13–1.20)	< 0.001
Marital status		
No	Reference	
Yes	0.57 (0.38–0.85)	0.006
ADL	1.45 (1.26–1.68)	< 0.001
Permanent address		
Urban	Reference	
Rural	2.08 (1.49–2.93)	< 0.001
CESD10	1.03 (1.01–1.06)	0.028
Smoking status		
No	Reference	
Yes	1.77 (1.22–2.56)	0.002
White blood cell	0.87 (0.79–0.96)	0.007
Hemoglobin	0.86 (0.77–0.95)	0.003
Mean corpuscular volume	1.04 (1.02–1.06)	< 0.001

OR, Odds ratio; CI, Confidence interval.

might lead to a more sedentary lifestyle, further exacerbating muscle loss [45]. Furthermore, a decline in muscle mass increases the risk of falls and fractures, consequently further limits patients' mobility and quality of life [46]. For depression, a cohort study based on CHARLS found that depression was associated with an increased risk of sarcopenia, which could be mitigated by maintaining a healthy lifestyle [47]. In addition, a Mendelian randomization study indicated a causal association between depression and sarcopenia [48]. The mechanism by which depression increases the risk of sarcopenia is complex and remains unclear. Studies have unveiled that patients with depression often experience a reduction in physical activity levels, which might potentially lead to a decline in muscle mass and function [49]. In addition, depression may affect muscle metabolism by influencing the endocrine system, particularly by promoting inflammation response and cortisol secretion [50, 51]. In terms of nutritional intake, depressed patients may reduce their

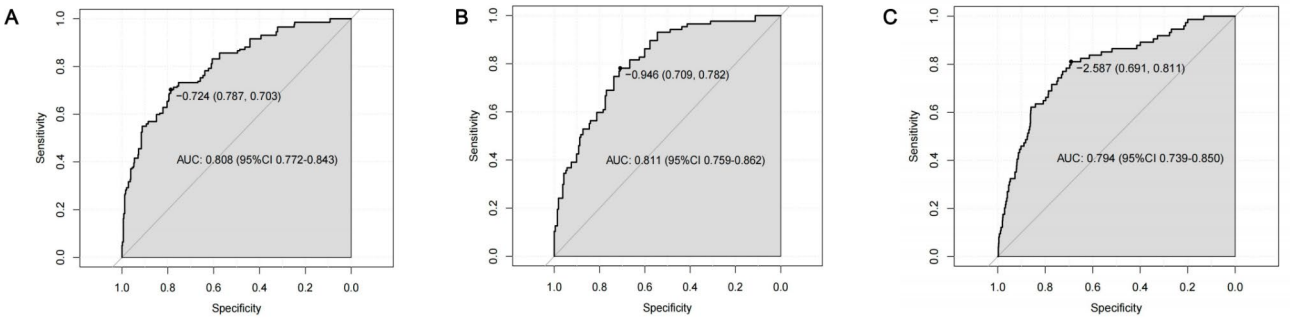

Fig. 4 Nomogram ROC curves and AUC for the training set (**A**), internal validation set (**B**) and external validation set (**C**)

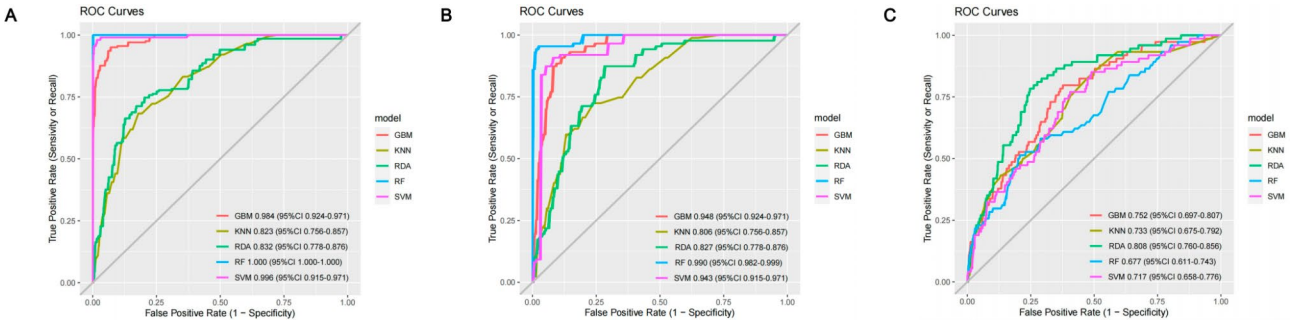

Fig. 5 ROC curves and AUC of the machine learning models for the training set (**A**), internal validation set (**B**) and external validation set (**C**)

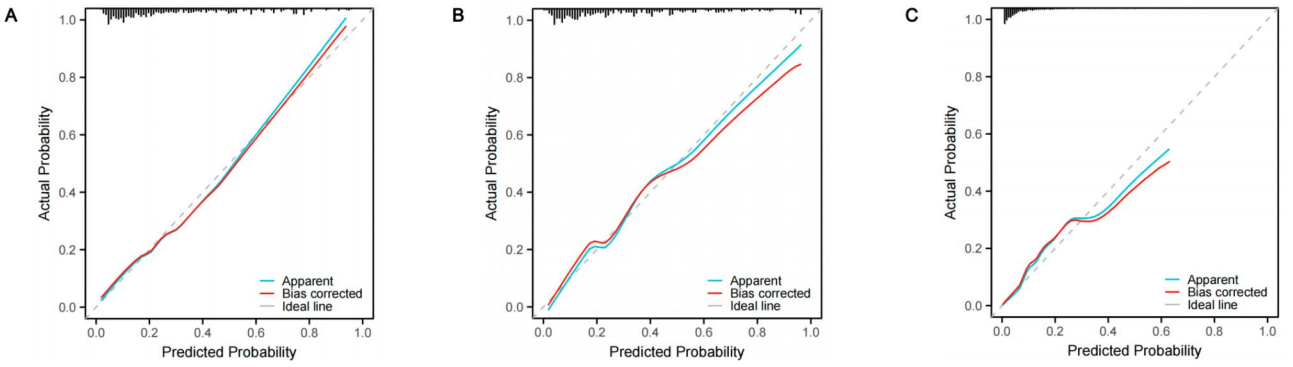

Fig. 6 Calibration curves of the nomogram prediction for the training set (**A**), internal validation set (**B**) and external validation set (**C**)

intake of protein and other important nutrients due to decreased appetite, thereby increasing the risk of sarcopenia [52]. In addition, our study revealed that participants who were still smoking exhibited higher risk of sarcopenia. Three cohort studies indicated that smoking was an important risk factor for sarcopenia [53–55]. The potential mechanism lies in smoking's capacity to induce oxidative stress and chronic inflammatory response, which are factors that promote muscle protein degradation and inhibit synthesis. In addition, smoking has been demonstrated to impact blood circulation and the transportation of essential nutrients to muscle tissue [56, 57].

Three laboratory test indicators, including hemoglobin, MCV, and WBC, have also been identified as independent predictors for sarcopenia. We observed a negative correlation between hemoglobin and sarcopenia. The association between reduced hemoglobin levels and increased risk of sarcopenia has been extensively studied. A meta-analysis revealed a negative correlation between hemoglobin levels and the risk of sarcopenia in elderly individuals [58]. In another study, diabetic patients with sarcopenia showed lower hemoglobin levels than other groups [59]. In terms of mechanisms, hemoglobin functions as a protein within red blood cells responsible for transporting oxygen to body tissues, and sufficient hemoglobin levels are crucial in guaranteeing the delivery of oxygen to muscle fibers [60]. Lower hemoglobin levels could cause hypoxia, leading to metabolic disorders and increased oxidative stress, affecting repair and regeneration processes of muscle fibers [61]. Our study also found

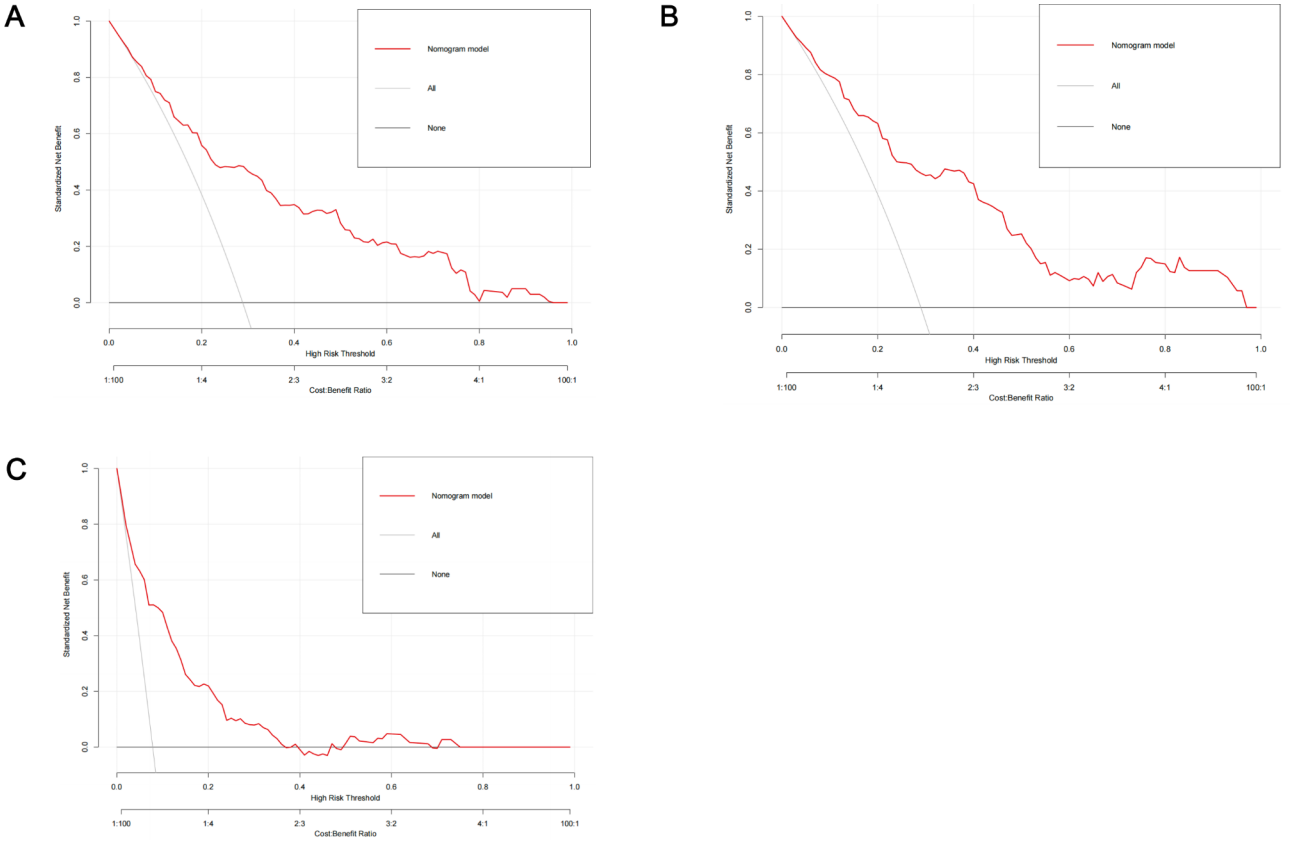

Fig. 7 DCA curves for the training set (**A**), internal validation set (**B**) and external validation set (**C**)

Declarations

that increased levels of MCV would increase the risk of sarcopenia. At present, few studies have focused on the association between MCV and sarcopenia. Elevated MCV may indicate a deficiency in folate or vitamin B12, which are crucial for DNA synthesis and the production of red blood cells [62]. Therefore, patients may be at high risk of sarcopenia due to increased MCV caused by malnutrition. Furthermore, we observed that lower levels of WBC were associated with increased risk of sarcopenia. However, two Korean studies have shown that higher levels of WBC increase the risk of sarcopenia [63, 64]. Generally, an increase in WBC count reflects the presence of chronic low-grade inflammation within the body, which is considered one of the key factors leading to disrupted muscle fiber damage and repair processes [65]. However, participants in our study are all Chinese diabetic patients, who may also have other diseases and are taking multiple medications. The levels of WBC are also closely related to the use of medications. In addition, this may be a unique physiological characteristic of Chinese patients with diabetes. In summary, the use of reduced WBC level as a predictor for sarcopenia needs to be treated with caution. In the future, additional cohort is needed to further validate our findings.

Strengths and limitations

This study has several strengths. Firstly, this is the first nomogram model to assess the risk of sarcopenia in patients with diabetes based on CHARLS, which serves as a practical tool for early screening of sarcopenia in this population. Furthermore, the nomogram model was constructed based on 9 easily accessible demographic, clinical or laboratory factors, which made the assessment of sarcopenia risk simpler. Lastly, in addition to the training set and internal validation set, we also used CHARLS 2011 data as the external validation set to mitigate the overfitting effect caused by oversampling.

Nevertheless, certain limitations warrant consideration. Firstly, this study is a cross-sectional study. Although the nomogram model constructed can quantitatively predict the risk of sarcopenia, it is still an exploration of association and cannot establish the causality between predictors and the outcome. Secondly, due to the exclusion of participants with missing data in CHARLS, our sample size is relatively limited. We still need data with larger sample size to validate our model in the future. Finally, all CHARLS data comes from the Chinese demographic, calling for further investigation to determine whether the model is applicable across other populations and races.

Conclusion

We have constructed a nomogram model utilizing data from CHARLS to evaluate the risk of sarcopenia in patients with diabetes. The nomogram model integrates age, marital status, ADL, permanent address, CESD10, smoking status, white blood cell, hemoglobin and mean corpuscular volume as 9 predictors, and exhibits excellent discrimination, calibration and clinical applicability. In the future, this model will be valuable in screening diabetic patients with high risk of sarcopenia and promote their quality of life.

Abbreviations

CHARLS	China Health and Retirement Longitudinal Study
LASSO	Least absolute shrinkage and selection operator
ROC	Receiver operating characteristic
AUC	Area under the curve
DCA	Decision curve analysis
ML	Machine learning
DM	Diabetes mellitus
IDF	International Diabetes Federation
EWGSOP	European Working Group on Sarcopenia in Older People
BIA	Bio-impedance analysis
CT	Computed tomography
MRI	Magnetic resonance imaging
AWGS	Asian Working Group for Sarcopenia
ASM	Appendicular skeletal muscle mass
SMI	Skeletal muscle mass index
DXA	Dual energy X-ray absorptiometry
CESD10	Center for Epidemiologic Studies Depression Scale
ADL	Activity of daily living
IADL	Instrumental activities of daily living
TC	Total cholesterol
TG	Triglyceride
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
WBC	White blood cell
MCV	Mean corpuscular volume
ROSE	Random Over-Sampling Examples
SD	standard deviation
IQR	Interquartile range
GBM	Gradient Boosting Machine
KNN	k-Nearest Neighbor
RDA	Regularized discriminant analysis
RF	Random Forest
SVM	Support Vector Machine

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13098-024-01467-w.

Supplementary Material 1

Acknowledgements

Not applicable.

Author contributions

MZ and ZS were responsible for the study conception and study design. MZ and ZS participated in data collection and study implementation. MZ analyzed the data and drafted the manuscript. MZ and ZS contributed to the interpretation and editing of the manuscript. All authors have read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Consent for publication

All authors have consented for publication.

Competing interests

The authors declare no competing interests.

Ethics approval

This is a study based on CHARLS database. The original CHARLS was approved by the Ethical Review Committee of Peking University (IRB00001052–11015).

Consent to participate

All participants signed the informed consent at the time of participation. This research followed the guidance of the Declaration of Helsinki.

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