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Development and Validation of a Risk Prediction Model for Sarcopenia in Chinese Older Patients with Type 2 Diabetes Mellitus

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Purpose: Sarcopenia is a common prevalent age-related disorder among older patients with type 2 diabetes mellitus (T2DM). This study aimed to develop and validate a nomogram model to assess the risk of incident sarcopenia among older patients with T2DM.

Patients and methods: A total of 1434 older patients (≥ 60 years) diagnosed with T2DM between May 2020 and November 2023 were recruited. The study cohort was randomly divided into a training set (n = 1006) and a validation set (n = 428) at the ratio of 7:3. The best-matching predictors of sarcopenia were incorporated into the nomogram model. The accuracy and applicability of the nomogram model were measured by using the area under the receiver operating characteristic curve (AUC), calibration curve, Hosmer-Lemeshow test, and decision curve analysis (DCA).

Results: 571 out of 1434 participants (39.8%) had sarcopenia. Nine best-matching factors, including age, body mass index (BMI), diabetic duration, glycated hemoglobin A1c (HbA1c), 25 (OH)Vitamin D, nephropathy, neuropathy, nutrition status, and osteoporosis were selected to construct the nomogram prediction model. The AUC values for training and validation sets were 0.800 (95% CI = 0.773–0.828) and 0.796 (95% CI = 0.755–0.838), respectively. Furthermore, the agreement between predicted and actual clinical probability of sarcopenia was demonstrated by calibration curves, the Hosmer-Lemeshow test ($P > 0.05$), and DCA.

Conclusion: Sarcopenia was prevalent among older patients with T2DM. A visual nomogram prediction model was verified effectively to evaluate incident sarcopenia in older patients with T2DM, allowing targeted interventions to be implemented timely to combat sarcopenia in geriatric population with T2DM.

Keywords: sarcopenia, type 2 diabetes mellitus, older adults, nomogram, prediction model

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic, non-communicable metabolic disorder that requires long-term medical support and care. Recent evidence suggests that approximately 10.5% of the global population has been diagnosed with T2DM, and it is estimated to reach nearly 12.2% worldwide by 2045.[1] The increasing rate of an aging population and poor diabetic management in China has led to a rapid growth in the prevalence of T2DM and its comorbidities among older Chinese individuals. Accordingly, the substantial medical expenditures related to diabetes and its complications impose a significant financial burden on families and national healthcare systems.[2] Notably, older patients with T2DM exhibit reduced muscle mass and diminished muscle strength in their extremities compared to those without T2DM, accelerating age-related sarcopenia.[3] Therefore, the Asian Working Group for Sarcopenia (AWGS) emphasizes the importance of screening for sarcopenia in healthcare for older patients with T2DM.[4]

Sarcopenia is defined as a geriatric syndrome characterized by age-related loss of skeletal muscle mass and reduced muscle strength. It is closely associated with physical disability, falls, unfavorable metabolism, frailty, impaired cardiopulmonary performance, as well as multimorbidity in older adults.[5] Prior reports indicate that the

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prevalence of sarcopenia ranges from 10% to 40% among older Chinese individuals aged 60 years and older, this is largely due to the rapidly aging population in China.[6,7] Growing evidence demonstrates the coexistence of diabetes and sarcopenia, although the underlying mechanisms remain incompletely understood. Sarcopenia is strongly associated with decreased daily activity, worsened physical functioning, and reduced quality of life among patients with T2DM.[8] Furthermore, previous studies have revealed that T2DM pathophysiological characteristics such as chronic hyperglycemia and insulin resistance, promote declines in muscle mass and physical performance in the older population, suggesting that diabetes may be a potential risk factor for inducing sarcopenia.[9]

Nomograms have increasingly become vital graphical tools for efficient disease diagnosis and prognostic assessment in clinical settings due to their practicality.[10] Older patients with T2DM necessitate prolonged therapy and supervision, posing challenges for healthcare providers in continuous condition monitoring and management.[11] Therefore, to implement tailored management strategies, it is imperative to develop an accurate nomogram model to identify older patients with T2DM at an elevated risk of sarcopenia. Nevertheless, clinically diagnosing sarcopenia in older patients with T2DM remains challenging due to insufficient attention from healthcare professionals, hindering early identification and timely therapeutic intervention.[12] Furthermore, despite existing diagnostic standards for sarcopenia, tools such as dual-energy X-ray absorptiometry and bioelectrical impedance analysis are not widely available in most local hospitals, particularly in rural areas.[13] Consequently, these barriers hinder the aging population from receiving proper T2DM management and improving their quality of life. Thus, it is imperative to effectively identify and assess older patients with T2DM who are at high risk for sarcopenia.

In this study, we sought to develop and validate a clinical model for effectively predicting the occurrence of sarcopenia among geriatric individuals with T2DM in China. Our objective was to provide clinicians with a practical and efficient tool for early sarcopenia detection among older T2DM individuals during routine examinations, thereby facilitating timely clinical decision-making and enhancing long-term health outcomes.

Methods

Participants and Study Design

This study utilized a cross-sectional design. Data were collected from three tertiary hospitals affiliated with China Medical University (Shenyang, China) between May 2020 and November 2023. A total of 1434 eligible participants were recruited through a convenience sampling method. The inclusion criteria were: (1) age ≥ 60 years; (2) diagnosis of T2DM for at least one year; (3) voluntary participation in this study and provision of written informed consent; (4) physical ability to independently complete the sarcopenia test; (5) complete clinical data. The exclusion criteria were: (1) physical disabilities such as carpal tunnel syndrome, history of stroke, severe hip or knee osteoarthritis, and Parkinson's disease that hindered the performance of sarcopenia assessment; (2) impairments in speaking, hearing, vision, and cognition that prevented cooperation; (3) acute complications such as diabetic ketoacidosis and hyperosmotic nonketotic coma; (4) acute comorbidities, such as acute myocardial infarction, acute pancreatitis, and acute inflammation; (5) severe life-threatening diseases (such as malignancy in later stage) and endocrine disorders, including thyroid gland dysfunction and Cushing's syndrome; (6) receiving hormonal treatment (such as diuretics, sex hormones, and glucocorticoids) that affected muscle metabolism or nutritional supplements (such as protein powder and vitamin D) within the past three months; (7) experiencing a weight loss greater than 5% of body weight in the preceding three months.

Sample Size

For the sample size calculation, a minimum of ten events per variable (EPV) was required to fit the predictive model via logistic regression.[14] Considering the 38 evaluated variables in the logistic regression model, an approximate 36% predicted prevalence of sarcopenia among older Chinese adults with T2DM,[15] and a 10% anticipated dropout rate, the estimated sample size was a minimum of 1174. Of the 1670 patients with T2DM initially recruited, 236 were excluded (the data screening process was depicted in Figure 1). Finally, 1434 eligible participants completed the entire study. Written informed consent was obtained from all participants, ensuring that the collected data were used anonymously and confidentially for scientific purposes. This study was approved by the Ethics Committee of the First Affiliated Hospital of China Medical University (No. 2020-HS-102) and adhered to the Declaration of Helsinki.

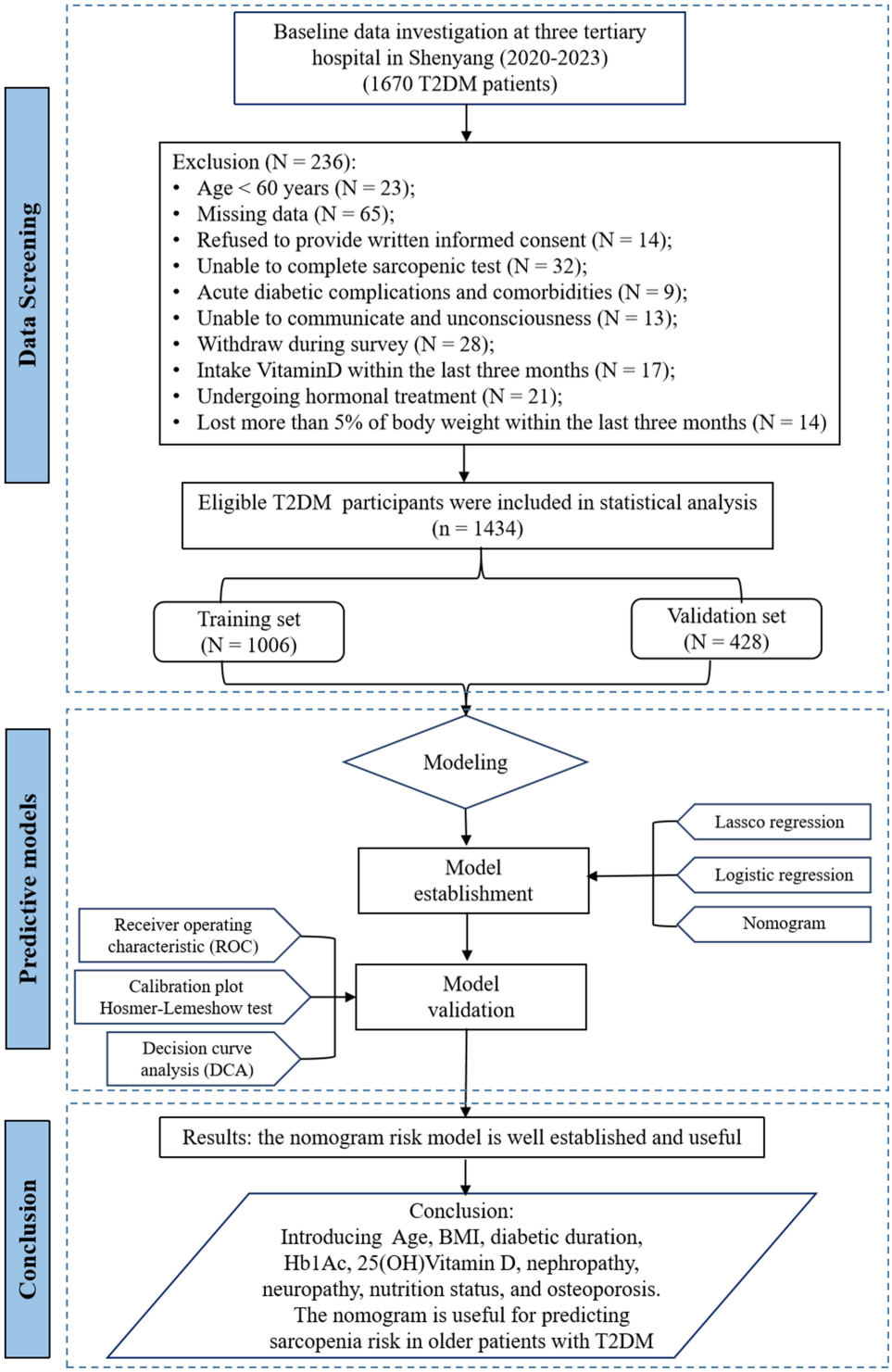

Figure 1 Flow diagram of study design.
Abbreviations: BMI, Body Mass Index; T2DM, type 2 diabetes mellitus, HbA1c glycated hemoglobin A1c.

Data Collection

Basic Information Collection

Demographic characteristics, including age (years), Body Mass Index (BMI, kg/m^2), gender (female/male), residence (rural/urban), marital status (single/married), education (primary school and below/middle school and above), current

smoking status (yes/no), current alcohol consumption (yes/no), and living arrangements (whether participants lived alone) were collected through a self-reported survey. Additionally, disease-related variables such as T2DM duration (years), treatment methods for T2DM (diet control alone/oral agents/insulin/oral agents + insulin), and chronic diseases (hypertension, dyslipidemia, cancer, anemia, cardiovascular disease, diabetic retinopathy, diabetic nephropathy, diabetic peripheral neuropathy, osteoporosis) were collected from medical records and self-reported surveys. Furthermore, routine blood analyses and biochemical indices, including fasting blood glucose (FBG), blood urea nitrogen (BUN), serum creatinine (Scr), triglycerides (TG), cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), C-reactive protein (CRP), uric acid (UA), glycated hemoglobin A1c (HbA1c), Cystatin C (Cysc), and 25-OH-Vitamin D (VitD) levels were extracted from the most recent medical records within the last three months. Diastolic blood pressure (DBP) and systolic blood pressure (SBP) were measured during recruitment.

Diagnosis of Sarcopenia

According to the criteria recommended by the AWGS 2019, sarcopenia is defined as having low muscle mass in combination with either low muscle strength or low physical performance.[16] 1) **Muscle mass measurement**: The Inbody120 Body Composition Analyzer was utilized to accurately measure the participants' muscle mass. The appendicular skeletal muscle mass index (ASMI) was calculated as the ratio of limb skeletal muscle mass to the square of height (kg/m^2). The ASMI thresholds for reduced muscle mass are < 7.0 kg/m^2 for men and < 5.7 kg/m^2 for women; 2) **Muscle strength evaluation**: Muscle strength is evaluated using the Xiangshan Electronic Grip Strength Meter. The maximum value is recorded for further analysis following two measurements for each hand. The diagnostic cutoff values for low muscle strength are < 28.0 kg for men and < 18.0 kg for women; 3) **Physical performance**: A 6-meter walking test is conducted to evaluate the participants' muscle function. The walking test is performed on an indoor flat surface with a measuring scale. The time taken by the subjects to walk a distance of six meters at their usual speed is recorded with a manual timer. The diagnostic threshold for physical decline is set at < 1.0 m/s.

Measurement

Nutrition Assessment

The nutrition status of the participants was assessed using the Mini Nutritional Assessment Short-form (MNA-SF),[17] which has demonstrated satisfactory sensitivity and specificity in the Chinese geriatric population.[18] The MNA-SF consists of six items, with total scores ranging from 0 to 14 points. The higher the score, the better the nutrition status of the subject: 0–11 points indicates "Malnourished/Malnutrition Risk" and 12–14 points indicates "Normal Nutrition".

Physical Activity Measurement

The physical activity (PA) level was measured using the Chinese version of the Short International Physical Activity Questionnaire (IPAQ-S-C), which has demonstrated good validity and reliability among Chinese adults.[19] This scale contains seven items to evaluate the sitting time, vigorous intensity, moderate intensity, and walking activities sustained for at least 10 minutes during the last week. The total weekly metabolic equivalent (MET) for each task is calculated by the duration and frequency of engaging in each intensity of activity with the following formula: Total MET-min/week = Low PA (3.3 METs × min × days) + Moderate PA (4.0 METs × min × days) + Vigorous PA (8.0 METs × min × days). The PA is then categorized into "High", "Moderate", and "Low" levels based on the total weekly MET-min.[20]

Sleep Quality Evaluation

Participants' sleep quality was assessed by the Chinese version of the Pittsburgh Sleep Quality Index (PSQI), which demonstrated good validity and reliability in the Chinese population.[21] This scale includes seven components, with each component scoring between 0 and 3. The total score ranges from 0 to 21 points, with higher scores indicating poorer sleep quality. The PSQI score at 8–21 points represented "Poor" sleep quality and 0–7 points represented "Good" sleep quality.

Statistical Analysis

Data were analyzed using SPSS software version 26.0. Continuous variables with a normal distribution were presented as mean ± standard deviation (SD) and compared using the Student's *t*-test. Furthermore, continuous variables with a non-

normal distribution were represented as median (P25, P75) and compared using the Mann–Whitney *U*-test. Categorical variables were described as frequencies (percentages) and compared using the Chi-square test.

Additionally, a predictive model was established using R software (version 4.3.0). Random resampling was performed at a 7:3 ratio to create the training set (n = 1006) and validation set (n= 428). A nomogram model was developed using the Least Absolute Shrinkage and Selection Operator (LASSO) regression analysis to assess the risk of sarcopenia in older patients with T2DM.[22] Initially, the training set data underwent LASSO regression to identify potential risk factors associated with sarcopenia in older patients with T2DM. Subsequently, a tenfold cross-validation was conducted to determine the appropriate penalty parameter (λ) for the LASSO regression analysis. The best matching variables with non-zero coefficients were screened using the LASSO algorithm with the "glmnet" function. These identified factors were then integrated into a multivariate logistic regression model by using the "lrm" function. Finally, the best matching predictors ($p < 0.05$) were included in the nomogram model with the help of the "rms" package.

Furthermore, discrimination, accuracy, and clinical validity were employed to validate the prediction model. The model's discrimination ability was assessed by calculating the area under the receiver operating characteristic (ROC) curve (AUC) using the "pROC" package. Calibration curves and the Hosmer-Lemeshow test were utilized to evaluate the accuracy of the nomogram model with the "calibrate" package. The clinical practicability of the nomogram model was measured through decision curve analysis (DCA) using the "rmda" package. A two-tailed test with a *P*-value of < 0.05 was considered statistically significant.

Results

Baseline Characteristics

Among the 1434 participants with T2DM, the prevalence of sarcopenia was found to be 39.8% (571/1434). The cohort consisted of 752 females (52.4%) and 682 males (47.6%), with an average age of 68.23 ± 6.44 years, ranging from 60 to 91. Detailed demographic and clinical information were summarized in Table 1. Several variables, including age ($P < 0.001$), BMI ($P < 0.001$), gender ($P < 0.001$), physical activity ($P = 0.018$), nutrition status ($P = 0.001$), sleep quality ($P = 0.004$), T2DM duration ($P < 0.001$), anemia ($P = 0.003$), osteoporosis ($P < 0.001$), diabetic retinopathy ($P = 0.031$), neuropathy ($P < 0.001$), nephropathy ($P < 0.001$), angiopathy ($P = 0.008$), TC ($P = 0.012$), HbA1c ($P < 0.001$), Cys-C ($P = 0.020$), VitD ($P < 0.001$), and DBP ($P = 0.005$), showed statistically significant differences between T2DM patients with or without sarcopenia

Table 1 Comparison of Clinical Data Between Participants with or without Sarcopenia (N = 1434)

Variable	Total (N = 1434)	No sarcopenia (N = 863)	Sarcopenia (N = 571)	Statistics	*P*-value
Age (Years)					
60–69	929 (64.8)	632 (73.3)	297 (52.0)	92.723	< 0.001***
70–79	410 (28.6)	209 (24.2)	201 (35.2)		
≥ 80	95 (6.6)	22 (2.5)	73 (12.8)		
BMI (kg/m^2)					
<18.5	60 (4.2)	7 (0.8)	53 (9.3)	69.288	< 0.001***
18.5–23.9	547 (38.1)	316 (36.6)	231 (40.4)		
≥ 24	827 (57.7)	540 (62.6)	287 (50.3)		
Gender					
Female	752 (52.4)	486 (56.3)	266 (46.6)	13.045	< 0.001***
Male	682 (47.6)	377 (43.7)	305 (53.4)		
Marital status					
Single	351 (24.5)	208 (24.1)	143 (25.0)	0.165	0.707
Married	1083 (75.5)	655 (75.9)	428 (75.0)		
Residence					
Rural	685 (47.8)	424 (49.1)	261 (45.7)	0.204	0.214
Urban	749 (52.2)	439 (50.9)	310 (54.3)		

(*Continued*)

Table 1 (Continued).

Variable	Total (N = 1434)	No sarcopenia (N = 863)	Sarcopenia (N = 571)	Statistics	*P*-value
Education					
Primary school or below	709 (49.4)	417 (48.3)	292 (51.1)	1.092	0.296
Middle school or above	725 (50.6)	446 (51.7)	279 (48.9)		
Living alone (%)	133 (9.3)	88 (10.2)	45 (7.9)	2.191	0.139
Current smoking (%)	348 (24.3)	194 (22.5)	154 (27.0)	3.770	0.052
Current drinking (%)	433 (30.2)	248 (28.7)	185 (32.4)	2.187	0.142
Physical activity					
Low	629 (43.9)	390 (45.2)	239 (41.9)	7.999	0.018*
Moderate	616 (43.0)	347 (40.2)	269 (47.1)		
High	189 (13.1)	126 (14.6)	63 (11.0)		
Nutrition status					
Normal nutrition	622 (43.4)	405 (46.9)	217 (38.0)	11.147	0.001**
Malnourished/Malnutrition risk	812 (56.6)	458 (53.1)	354 (62.0)		
Sleep quality					
Good	804 (56.1)	510 (59.1)	294 (51.5)	8.074	0.004**
Poor	630 (43.9)	353 (40.9)	277 (48.5)		
T2DM duration	10.09 [5.68, 14.43]	9.32 [5.21, 13.73]	11.35 [6.10, 15.47]	4.457	< 0.001***
Treatment of diabetes					
Diet control alone	375 (26.2)	212 (24.6)	163 (28.5)	3.365	0.339
Oral agents	341 (23.8)	215 (24.9)	126 (22.1)		
Insulin	359 (25.0)	219 (25.4)	140 (24.5)		
Oral agents + insulin	359 (25.0)	217 (25.1)	142 (24.9)		
Comorbidities and complications					
Hypertension (%)	398 (27.8)	241 (27.9)	157 (27.5)	0.032	0.859
Dyslipidemia (%)	581 (40.5)	362 (41.9)	219 (38.4)	1.841	0.175
Cancer (%)	28 (2.0)	17 (2.0)	11 (1.9)	0.003	0.954
Anemia (%)	319 (22.2)	169 (19.6)	150 (26.3)	8.883	0.003**
Osteoporosis (%)	449 (31.3)	226 (26.2)	223 (39.1)	26.451	< 0.001***
Cardiovascular disease (%)	399 (27.8)	233 (27.0)	166 (29.1)	0.735	0.391
Diabetic retinopathy (%)	164 (11.4)	86 (10.0)	78 (13.7)	4.632	0.031*
Diabetic nephropathy (%)	373 (26.0)	180 (20.9)	193 (33.8)	29.911	< 0.001***
Diabetic neuropathy (%)	144 (10.0)	51 (5.9)	93 (16.3)	40.967	< 0.001***
Diabetic angiopathy (%)	40 (2.8)	16 (1.9)	24 (4.2)	6.994	0.008**
Laboratory values					
FBG (mmol/L)	7.38 [6.70, 8.90]	7.30 [6.70, 8.90]	7.40 [6.70, 9.04]	0.509	0.611
BUN (mmol/L)	5.50 [4.60, 6.70]	5.40 [4.50, 6.70]	5.50 [4.60, 6.70]	0.354	0.723
Scr (μmol/L)	67.60 [57.60, 81.70]	67.30 [57.80, 80.80]	68.00 [57.20, 84.20]	0.725	0.469
TC (mmol/L)	4.91 ± 1.03	4.97 ± 1.00	4.83 ± 1.07	2.526	0.012*
TG (mmol/L)	2.01 [1.51, 2.52]	2.02 [1.56, 2.53]	2.00 [1.44, 2.51]	1.398	0.162
HDL-C (mmol/L)	1.23 [1.07, 1.43]	1.24 [1.07, 1.41]	1.22 [1.07, 1.45]	0.280	0.779
LDL-C (mmol/L)	2.71 [2.20, 3.20]	2.71 [2.24, 3.21]	2.69 [2.17, 3.20]	1.232	0.218
CRP (mg/L)	1.90 [1.10, 3.50]	1.90 [1.10, 3.30]	1.90 [1.00, 3.80]	0.539	0.590
UA (μmol/L)	297.40 [243.67, 356.88]	297.40 [249.82, 356.88]	297.40 [243.87, 362.83]	0.195	0.846
HbA1c (%)	8.94 [8.27, 9.51]	8.78 [7.89, 9.37]	9.10 [8.58, 9.83]	9.378	< 0.001***
Cys-C (mg/L)	0.94 ± 0.25	0.93 ± 0.24	0.96 ± 0.25	1.215	0.020*
25-OH-Vitamin D (ng/mL)	25.57 [17.76, 36.58]	27.03 [18.94, 39.49]	23.79 [16.50, 32.37]	5.134	< 0.001***
SBP (mmHg)	134.73 ± 20.39	134.81 ± 19.38	134.62 ± 21.85	0.172	0.864
DBP (mmHg)	75.00 ± 11.00	75.66 ± 10.89	74.00 ± 11.12	2.798	0.005**

Notes: Data were depicted as Mean ± standard deviation, Median (P25, P75), or N (%). *$P < 0.05$, **$P < 0.01$, *** $P < 0.001$, statistically significant.

Abbreviations: BMI, Body Mass Index; BUN, blood urea nitrogen; CRP, C-reactive protein; UA, uric acid; Cysc, Cystatin C; DBP, diastolic blood pressure; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; HbA1c, glycated hemoglobin A1c; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; TC, total cholesterol; T2DM, type 2 diabetes mellitus; SBP, systolic blood pressure; Scr, serum creatinine.

(Table 1). After randomly splitting the data into the training (n = 1006) and validation (n = 428) sets, comparisons between the two sets were presented in Supplementary Table 1. No statistically significant differences were found between the two sets (all $P > 0.05$).

Best Predictor of Sarcopenia Screening

A LASSO regression model was constructed to identify the best predictors of sarcopenia and the characteristics of these screened variables were depicted in Figure 2A. The best matching factors were screened using the ten-fold cross-validation method. 18 variables with non-zero coefficients were identified when λ value was at its minimum (λ.min = 0.00969, Log[λ.min] = −4.636), potentially rendering the model more redundant and complex. Subsequently, the λ value within one standard error (1-SE) was selected as the optimal λ (λ.1-SE = 0.02961, Log[λ.1-SE] = −3.520) (Figure 2B). Nine candidate variables of non-zero coefficients, including age, BMI, T2DM duration, nutrition status, osteoporosis, neuropathy, nephropathy, HbA1c, and VitD, were identified as best matching factors.

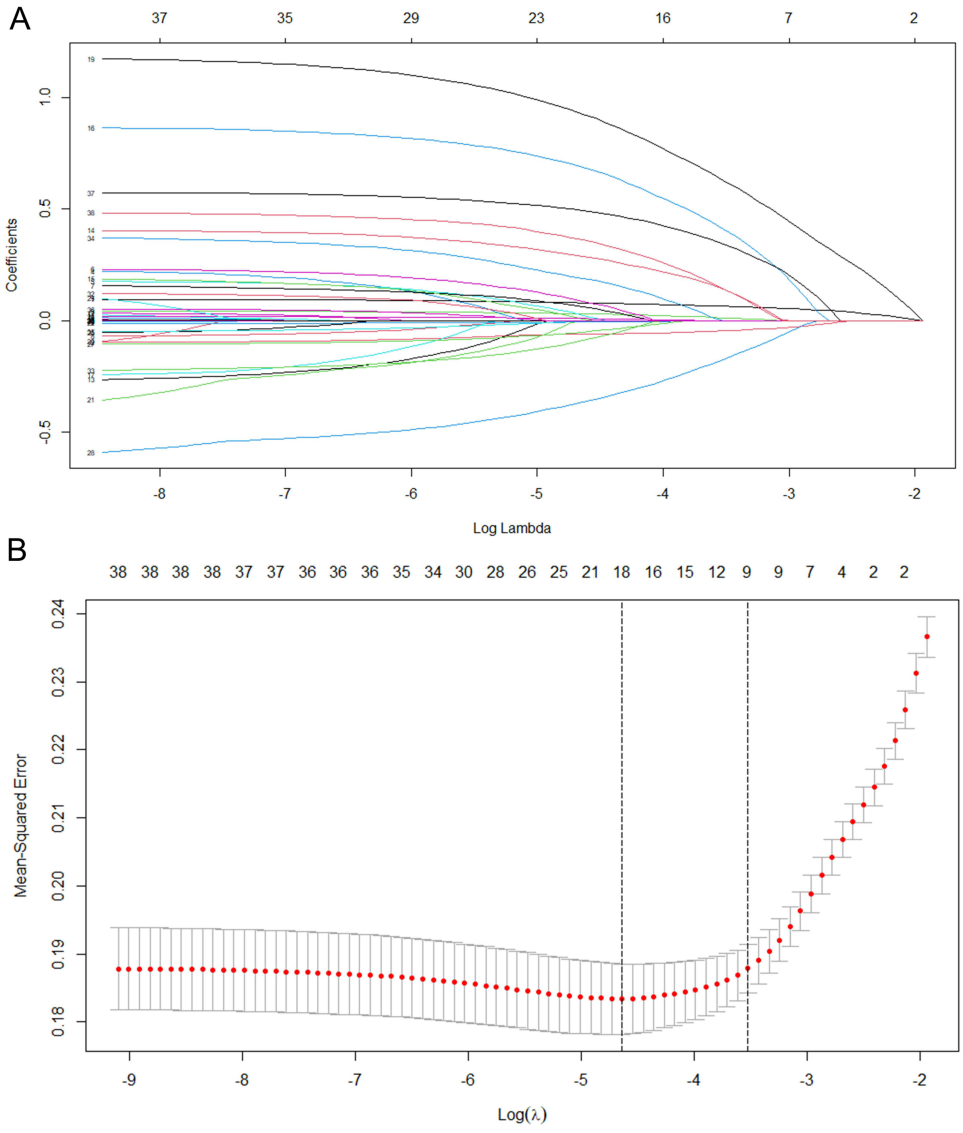

Figure 2 Best-matching factor screening using the LASSO regression analysis. (**A**) Coefficient path of the LASSO regression model. (**B**) Cross-validation curve for LASSO regression. The best-matching factors with non-zero coefficients were selected using ten-fold cross-validation, employing both the λ.minimum criterion (left dotted line) and the λ.1-SE criterion (right dotted line). For this study, the best-matching factors were selected based on the λ.1-SE criterion.
Abbreviations: LASSO, Least Absolute Shrinkage and Selection Operator; SE, standard error.

These potential factors were subsequently included in the multivariate logistic regression model (Figure 3). It was found that older age (OR = 1.092, 95% CI = 1.071–1.115, $P < 0.001$), longer T2DM duration (OR = 1.043, 95% CI = 1.019–1.069, $P = 0.001$), osteoporosis (OR = 1.749, 95% CI = 1.339–2.283, $P < 0.001$), neuropathy (OR = 2.796, 95% CI = 1.841–4.248, $P < 0.001$), nephropathy (OR = 1.686, 95% CI = 1.272–2.234, $P < 0.001$), higher HbA1c (OR = 3.131, 95% CI = 2.566–3.820, $P < 0.001$), and malnourished/malnutrition risk (OR = 1.471, 95% CI = 1.144−1.892, $P = 0.003$) were identified as independent risk factors for sarcopenia in older patients with T2DM (Figure 3). Conversely, larger BMI (OR = 0.921, 95% CI = 0.890–0.953, $P < 0.001$), and higher VitD levels (OR = 0.967, 95% CI = 0.957–0.976, $P < 0.001$) were identified as protective predictors against sarcopenia in older adults with T2DM (Figure 3).

Nomogram Model Development for Sarcopenia

A visual nomogram model was developed to quantitatively predict the risk of sarcopenia in older adults with T2DM (Figure 4A). The patient's sarcopenia risk could be evaluated by summing the corresponding points of age, BMI, T2DM duration, nutrition status, osteoporosis, neuropathy, nephropathy, FBG, and TG on the nomogram. A higher total score indicated a greater probability of sarcopenia in older adults with T2DM. For example, an 87-year-old individual with a BMI of 18.34 kg/m^2, a T2DM duration of 19 years, at risk of malnutrition, with neuropathy, an HbA1c level of 7.68 mmol/L, and a VitD level of 9.55 ng/mL, would have an estimated sarcopenic probability of 0.868 (Figure 4B).

Predictive Model Validation

Discrimination

Initially, the discriminative ability of the predictive model to distinguish the occurrence of sarcopenia in older patients with T2DM was assessed by calculating the AUC value in both the training and validation sets. As shown in Figure 5A, the AUC value of the predictive model in the training set was 0.800 (95% CI = 0.773–0.828), while in the validation set (Figure 5B), the predictive model yielded an AUC value of 0.796 (95% CI = 0.755–0.838). The nomogram demonstrated good discriminatory ability and predictive value in effectively identifying nonsarcopenic and sarcopenic older populations with T2DM.

Correction of the Predictive Model

Calibration curves and the Hosmer-Lemeshow test were performed to measure the goodness-of-fit of the nomogram. The calibration plots for the nomogram revealed high concordance between the predicted and actual probabilities of sarcopenia in both the training (Figure 6A) and validation (Figure 6B) sets. Furthermore, the Hosmer-Lemeshow test indicated that the model fit well in both the training set ($R^2 = 7.745$, $P = 0.560 > 0.05$) and validation set ($R^2 = 12.897$, P

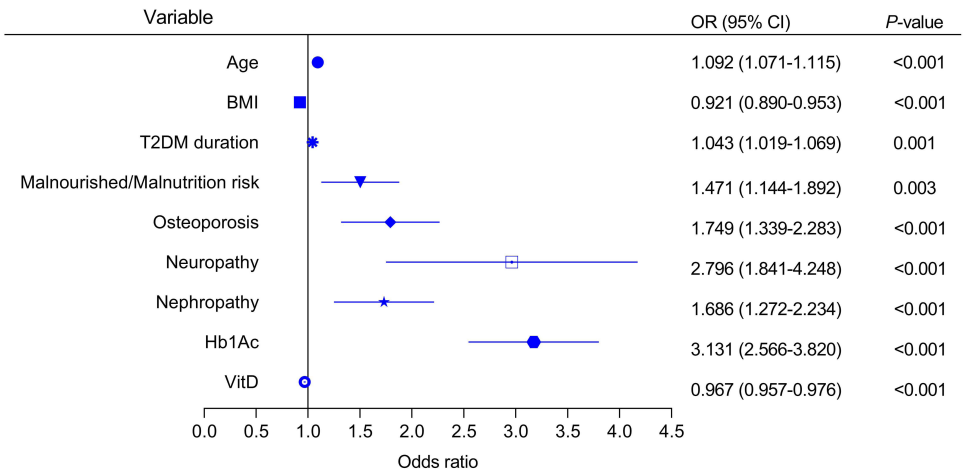

Figure 3 Forest plots of risk factors for sarcopenia by multivariate logistic analysis. $P < 0.05$, statistically significant.
Abbreviations: BMI, Body Mass Index; T2DM, type 2 diabetes mellitus; HbA1c, glycated hemoglobin A1c; VitD, 25-OH-Vitamin D; OR, odds ratio; CI, confidence interval.

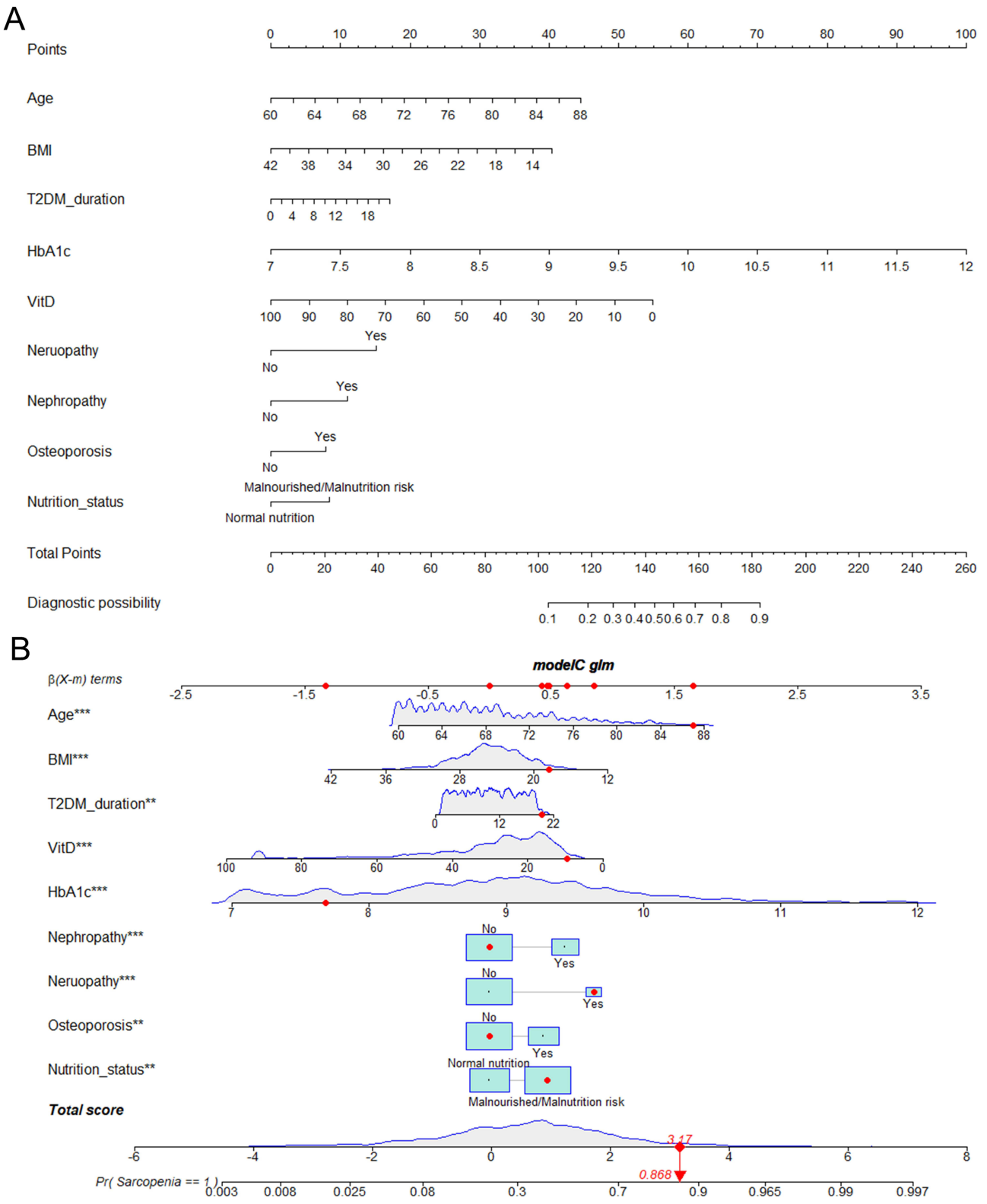

Figure 4 Nomogram model. (**A**) Nomogram for predicting sarcopenia in older adults with T2DM. (**B**) An example of dynamic nomogram. The red dots located on each variable indicated the score calculated for that variable. The red dot on the total Points axis represented the total scores (3.17) of the aforementioned variables, and the red arrows pointing downward to the bottom axis indicated the probability of incident sarcopenia (0.868) in an 87-year-old patient with T2DM.
Abbreviations: BMI, Body Mass Index; T2DM, type 2 diabetes mellitus; HbA1c, glycated hemoglobin A1c; VitD, 25-OH-Vitamin D.

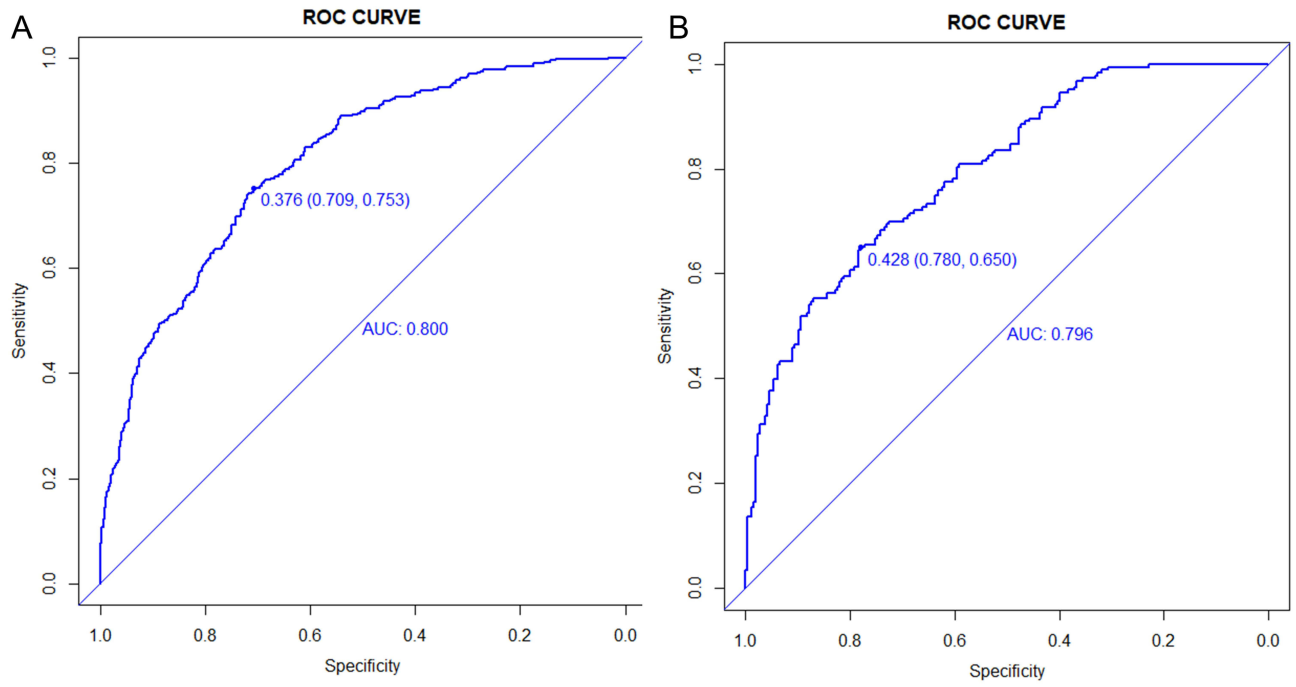

Figure 5 ROC curves of the nomogram model for predicting sarcopenia. (**A**) ROC curve of the nomogram model for the training set. (**B**) ROC curve of the nomogram model for the validation set.
Abbreviation: ROC, receiver operating characteristic.

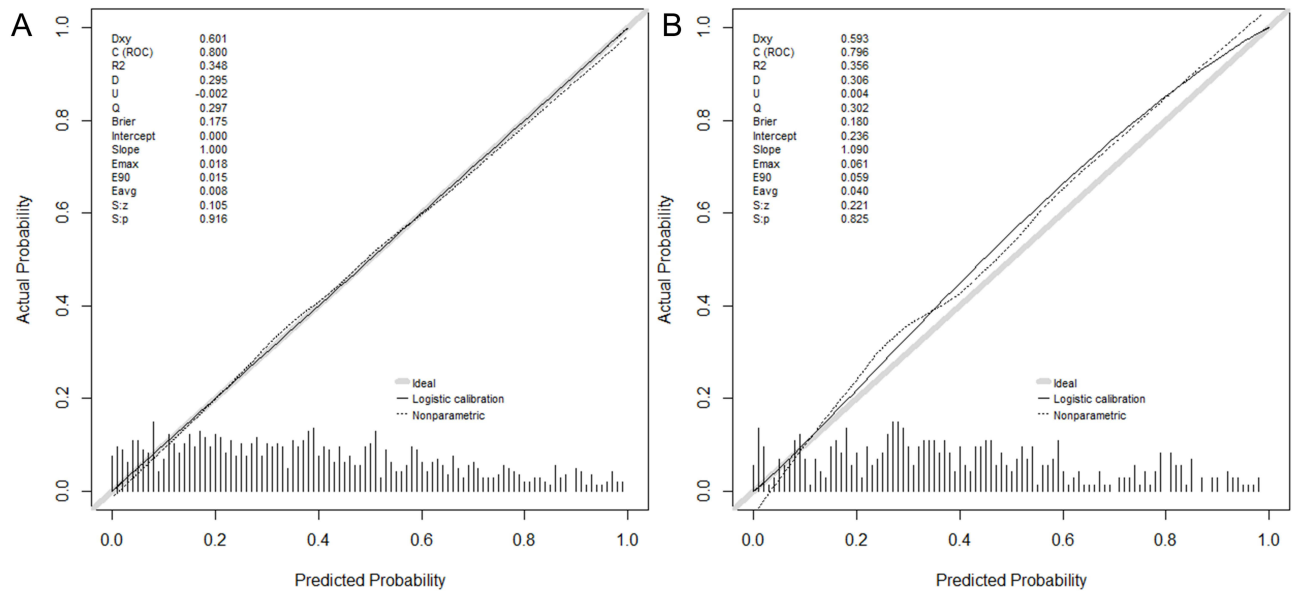

Figure 6 Calibration curves of the nomogram model for predicting sarcopenia. (**A**) Calibration curves of the nomogram model for the training set. (**B**) Calibration curves of the nomogram model for the validation set.

= 0.167 > 0.05). A higher degree of agreement between the predicted probabilities and actual outcomes (Hosmer-Lemeshow test: $P > 0.05$) indicated better reliability and accuracy of the predictive performance of the nomogram model.

Evaluation of Clinical Validity

The clinical practicability of the nomogram model was evaluated using the DCA method. The x-axis, ranging from 0 to 0.8, represented the high-risk threshold for sarcopenia; the y-axis represented the net benefit; the black line represented

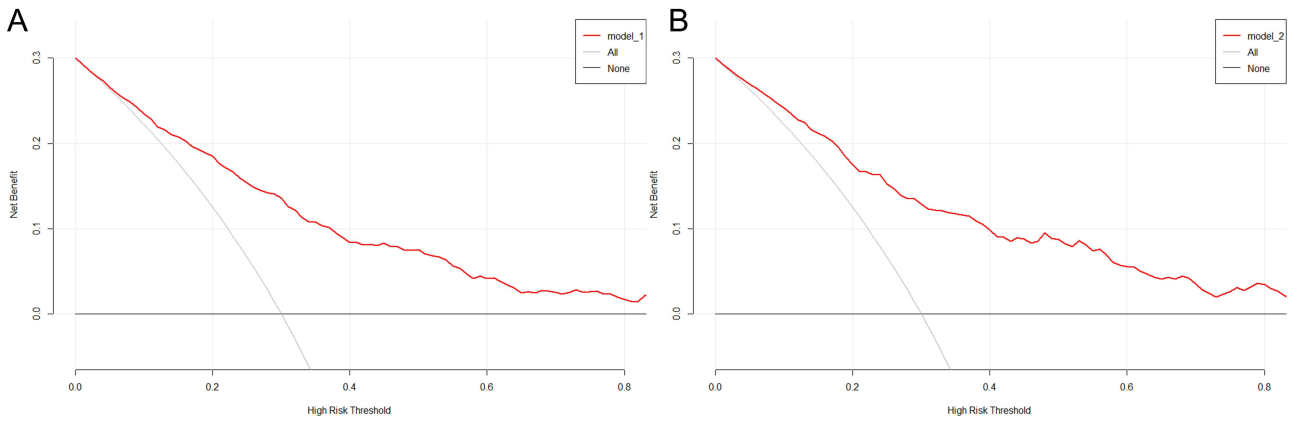

Figure 7 DCA for the nomogram model of sarcopenia. (**A**) DCA curve for the training set. (**B**) DCA curve for the validation set.
Abbreviation: DCA, Decision curve analysis.

that no patients suffered from sarcopenia; the gray dashed line represented that all patients suffered from sarcopenia; and the red line indicated the net benefit value of the nomogram model. The DCA curves showed that the net benefits of the nomogram model for both the training (Figure 7A) and validation (Figure 7B) sets consistently exceeded the black and gray lines, suggesting superior clinical applicability of this predictive model.

Discussion

Sarcopenia is characterized by the age-related decline in muscle mass and physical function. The prevalence of sarcopenia among T2DM patients has dramatically risen each year, primarily due to insulin resistance and endocrine dysfunction.[23] Therefore, developing a predictive model to identify potential factors influencing the occurrence of sarcopenia is essential for the clinical management of older patients with T2DM. Such a model enables the timely implementation of effective interventions and appropriate management strategies to mitigate the adverse impacts of sarcopenia. In this study, a nomogram-based model was developed and validated to predict the risk of sarcopenia in older patients with T2DM. This model identified several risk factors associated with sarcopenia detection in older patients with T2DM, including age, BMI, T2DM duration, HbA1c, VitD, nephropathy, neuropathy, nutrition status, and osteoporosis. This model demonstrated satisfactory accuracy, discriminative ability, and clinical applicability. It offers healthcare professionals a user-friendly tool for the prompt assessment of sarcopenia risk in geriatric patients with T2DM.

In recent years, epidemiologic studies have reported various parameters contributing to sarcopenia among diabetic patients in specific populations.[24,25] For instance, Yu et al,[24] developed a nomogram model to predict sarcopenia in 1131 Chinese T2DM patients, using factors such as age, gender, BMI, heart rate, and waist-to-hip ratio. Additionally, Li et al, created a nomogram model involving 3435 older Chinese adults, which included six factors: age, BMI, systolic and diastolic blood pressure, and pain.[26] In alignment with the previous findings, this study confirmed a significant relationship between advanced age and T2DM-related sarcopenia. As age is widely recognized as an independent risk factor for sarcopenia, the prevalence of sarcopenia in T2DM individuals increases with age, particularly in those over 70 years old.[27,28] Similarly, our study also found a gradual increase in the prevalence of sarcopenia with advancing age. This trend may stem from the accelerated loss of motor neurons in the brains of older populations compared to younger individuals,[29] leading to a noticeable decline in physical activity, bodily function, and muscle atrophy.[26]

Notably, osteoporosis has been identified as an independent risk factor for sarcopenia among older adults with T2DM according to the current nomogram model. Osteoporosis, a commonly geriatric comorbidity, is characterized by the microarchitectural degradation of bone tissue and low bone density, increasing bone fragility and fracture risk in older populations.[30] Given the closely related origins and pathophysiological bases of sarcopenia and osteoporosis, researchers have identified that both bone and muscle share similar secretion functions and signaling pathways, which are crucial for the simultaneous regulation of muscle and osteoclast formation.[31] Previous studies have confirmed the strong correlation between sarcopenia and osteoporosis. Ontan et al, reported a significant association between severe sarcopenia and

osteoporosis in 444 older adults in Turkey.[32] However, previous predictive models focusing on sarcopenia have paid less attention to osteoporosis. In this study, the nomogram model was the first to demonstrate that osteoporosis could serve as a potential risk factor for predicting sarcopenia among older adults with T2DM, encouraging clinicians to focus more on geriatric comorbidities alongside T2DM management.

Consistent with previous models,[24,26] our study also found that lower BMI was an independent risk factor for sarcopenia in older patients with T2DM, with lower BMI indicating a higher risk of sarcopenia. Since obesity or being overweight might be linked to a higher intake of nutrients necessary for healthy functioning, obesity has been suggested as a protective factor in older adults with sarcopenia.[33] However, in a recent cross-sectional study conducted in Brazil, which involved multiple predictive models of muscle strength, observed that patients with lower BMI were prone to increase muscle strength in older adults with T2DM, suggesting the controversial role of BMI as a risk factor in the development of pathological sarcopenia in T2DM.[34] This might be explained by the fact that the contributing elements differ among individuals from diverse cultural and biological backgrounds, resulting in heterogeneity in the observed relationships. Therefore, longitudinal data tracking changes in BMI and muscle function are needed to comprehensively investigate the causal relationship between BMI and sarcopenia in older adults with T2DM.

Our model indicated that reduced nutritional scores and VitD levels heightened the risk of sarcopenia in older patients with T2DM. Accumulating evidence suggests that the deficient vitamin D levels and inadequate nutritional intake contribute to impaired skeletal muscle protein synthesis in older adults with diabetes.[35,36] Similarly, Lin et al, also incorporated malnutrition into a predictive model to identify older adults in Chinese communities at high risk of sarcopenia.[37] Furthermore, Zhang and Zhu developed a robust nomogram that incorporated nutrition status to predict sarcopenia in colorectal cancer patients.[38] Therefore, to prevent sarcopenia in older adults with T2DM, it is recommended to implement timely scientific and balanced dietary interventions to enhance neuromuscular function and improve diabetes management in high-risk patients, as indicated by their nomogram predictive score.[39]

Our findings also revealed that HbA1c was an independent risk factor for sarcopenia in older patients with T2DM. HbA1c, a crucial index of diabetes, is widely used to evaluate an individual's glucose metabolism over the past two to three months.[40] The relationship between HbA1c and low muscle mass remains controversial. On one hand, some scholars have found that low concentrations of HbA1c can predict malnutrition, potentially contributing to the decline in skeletal muscle mass and weight loss in older populations.[41] On the other hand, high HbA1c levels indicate insulin resistance, potentially leading to decreased muscle quality and poor glycemic control in older patients with diabetes.[42] For instance, a follow-up study conducted by Lin et al, found that increasing HbA1c levels in patients with T2DM were associated with a higher risk of developing sarcopenia.[43] Furthermore, Chang et al suggested that elevated HbA1c levels contributed to more severe albuminuria, which was associated with escalated sarcopenia among older patients with T2DM.[44] Thus, the laboratory test indicators should be given particular emphasis in clinical practice.

Additionally, our study found that participants with a longer duration of diabetes were more susceptible to sarcopenia. This phenomenon may be attributed to the accumulation of abnormal metabolites, such as advanced glycosylation end products, which are induced by chronic hyperglycemia and insulin resistance in patients with T2DM. These factors not only disrupt the delicate balance between muscle protein synthesis and degradation, but they also impair the skeletal muscle's ability to absorb and utilize glucose. This results in a reduced synthesis of whole-body proteins and inadequate energy generation, ultimately leading to muscle mass loss and diminished muscle function. Loss of muscle mass further exacerbates impaired insulin signaling, thereby initiating a vicious cycle in geriatric populations with T2DM.[45,46] Similarly, Takahashi et al, employing multivariable logistic regression models, confirmed that older age, lower BMI, and prolonged duration of diabetes were positively correlated with sarcopenia in patients with T2DM.[47] Accordingly, to prevent sarcopenia and improve health outcomes, older patients with a prolonged duration of T2DM should regularly participate in clinical examination programs.

Our study indicated that diabetic complications, such as diabetic nephropathy and neuropathy, were associated with a higher risk of sarcopenia in older patients with T2DM. Consistently, diabetic neuropathy, characterized by axonal degeneration and demyelination, has been confirmed to be significantly associated with diminished lower-extremity muscle strength in middle-aged and older patients with T2DM.[48] Studies have also reported that older patients with diabetic neuropathy exhibit increased ankle rigidity and slower walking speeds compared to non-diabetic controls.[49] A

recent logistic regression model by Fang et al further demonstrated the predictive role of diabetic neuropathy in sarcopenia among 196 patients with T2DM.[50] Additionally, our findings verified the causal relationship between diabetic nephropathy and sarcopenia in the aging population with T2DM.[51] Previous observational studies have uncovered that renal vascular endothelial dysfunction induced by insulin resistance in diabetic patients hinders dialysis procedures and triggers chronic inflammation. This inflammation promotes the causative mechanisms of muscle loss and sarcopenia in diabetic patients.[52,53] Likewise, a meta-analysis revealed that diabetic nephropathy possessed high diagnostic efficacy for screening sarcopenia in patients with diabetes.[46] Therefore, timely monitoring of diabetic complications such as diabetic neuropathy and nephropathy may be beneficial for early detection and prevention of sarcopenia in older adults with T2DM.

It is noteworthy that in our study, univariate analysis revealed that sleep quality and physical activity were significantly correlated with sarcopenia in older adults with T2DM. Evidence indicates that the high prevalence of sleep disorders in the older population contributes to insufficient physical activity levels.[34] Thus, both physical activity and sleep quality have been identified as crucial contributors to sarcopenia risk in older adults, according to previous predictive models.[54,55] Although the current study's LASSO analysis found no significant predictive effects of sleep quality and physical activity on sarcopenia, further investigations with more appropriate assessments might yield new insights. Therefore, for older patients with T2DM who suffer from sleep disorders and physical inactivity, it is advisable to evaluate the beneficial effects of improving sleep quality and physical activity levels on sarcopenia prevention.

Practical Implications

This research is the first to establish and validate a clinical predictive model for sarcopenia among older adults with T2DM. By thoroughly evaluating the predictive value of readily available clinical and laboratory variables, we identified age, BMI, T2DM duration, HbA1c, VitD, nephropathy, neuropathy, nutrition status, and osteoporosis as crucial factors predicting sarcopenia in older adults with T2DM. Specifically, our nomogram model, developed based on these nine factors, significantly predicted the risk of sarcopenia and demonstrated satisfactory discrimination and calibration. Using this nomogram model with easily accessible routine data reduces the difficulty of data collection and facilitates replication in extensive healthcare settings, particularly for older patients unsuitable for muscle mass measurement instruments or for those rural hospitals lacking muscle mass diagnostic techniques. This predictive model can be clinically applied to offer personalized risk evaluations for each patient by quantifying the total scores of the nine predictors. Therefore, this nomogram model serves as a highly efficient and accurate assessment tool to aid healthcare practitioners in screening the probability of sarcopenia occurrence in older patients with T2DM. Furthermore, early prevention and intervention strategies can be promptly implemented for patients at high risk of sarcopenia.

Limitations and Future Research Directions

The current study acknowledges several limitations. First, the data used for model construction in this study were collected from a single medical center in China, which lacks external validation in other older populations from different regions and countries, potentially limiting the generalizability of the findings. Therefore, larger cohorts from multiple centers with diverse ethnic and cultural backgrounds should be included to further validate and assess the applicability of the current nomogram model. Second, this study employed a cross-sectional design, making it difficult to determine a causal relationship between sarcopenia and the nine predictors. Therefore, longitudinal studies should be conducted to dynamically monitor the reciprocal relationships between these variables and sarcopenia in older patients with T2DM during a long-term follow-up to ensure a comprehensive understanding. Third, since this study was carried out during the COVID-19 pandemic, the low diagnostic efficacy of physical activity for detecting sarcopenia might be attributed to patients' restricted daily activity during the pandemic. Consequently, our results may underestimate the positive impact of physical activity in mitigating sarcopenia. Furthermore, participants with physical disabilities were excluded from the present study, which might affect the reported prevalence of sarcopenia in older patients with T2DM. Hence, further prospective investigations incorporating additional potential risk factors are necessary to update the prediction model in the future.

Conclusion

A predictive nomogram model for assessing the risk of sarcopenia in older adults with T2DM was constructed and validated in this study. This model highlights the significant diagnostic value of age, BMI, T2DM duration, HbA1c, VitD, nephropathy, neuropathy, nutrition status, and osteoporosis for sarcopenia in this vulnerable population. By integrating this advanced, user-friendly model into clinical practice, healthcare professionals can significantly enhance early sarcopenia screening and promptly provide therapeutic interventions for high-risk older adults with T2DM, thereby potentially improving diabetes management and the quality of life for these patients.

Data Sharing Statement

The data used to support the findings of this study are available from the corresponding author upon reasonable request.

Ethical Statement

This study was approved by the Ethics committee of the First Affiliated Hospital of China Medical University (No. 2020-HS-102) and was adhered to the Declaration of Helsinki. Written informed consent was obtained from all participants, ensuring that the collected data were used anonymously and confidentially for scientific purposes.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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