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Development of a Practical Screening Tool to Predict Sarcopenia in Patients on Maintenance Hemodialysis

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Data Collection B
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Manuscript Preparation E
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Conflict of interest:

None declared

Background:

Sarcopenia is a common complication in maintenance hemodialysis (MHD) and can increase patient hospitalization and mortality. No simple and reliable tools to identify sarcopenia exist. We aimed to develop a screening tool to predict MHD patients at high risk for sarcopenia.

Material/Methods:

This cross-sectional study included 589 and 216 MHD patients for training and validation sets, respectively. We used diagnostic criteria developed by the Asian Working Group on Sarcopenia to screen for sarcopenia. The risk prediction model was established by univariate and multivariate logistic regression analyses. We used the area under the receiver operating characteristic curve (AUROC), calibration curve, Hosmer-Lemeshow test, and decision curve analysis (DCA) to evaluate the model's discrimination ability, calibration ability, and clinical utility.

Results:

The incidence of sarcopenia was 17.1% in the training set and 18.1% in the validation set. We constructed prediction models applying age, body mass index, calf circumference, and serum creatinine and plotted a nomogram. The training set model had an AUROC of 0.922, sensitivity of 85.1%, specificity of 85.9%, and chi-square value (Hosmer-Lemeshow test) of 5.603 ($P>0.05$); the DCA diagram showed that when the threshold probability was 0 to 0.95, the model predicted a net benefit for sarcopenia in MHD patients. The validation set model had an AUROC of 0.913, sensitivity of 94.3%, specificity of 82.9%, and chi-square value (Hosmer-Lemeshow test) of 9.822 ($P>0.05$).

Conclusions:


The screening tool has good discrimination ability, calibration ability, and clinical utility. It could help to identify MHD patients at a high risk for sarcopenia.

Keywords:

Continuous Renal Replacement Therapy • Sarcopenia • Risk Factors

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Background

Sarcopenia is a degenerative syndrome characterized by decreased skeletal muscle mass and either low muscle strength or function and is now officially recognized as a muscle disease (diagnosis code, ICD-10-MC) [1]. Maintenance hemodialysis (MHD) is one of the main renal replacement therapies for patients with end-stage renal disease. The loss of amino acids during dialysis, the increase of inflammatory factors, metabolic acidosis, mitochondrial dysfunction, and the reduction of protein intake increase the risk of sarcopenia in patients undergoing MHD [2-4]. Some studies have shown that the prevalence of sarcopenia in MHD patients is 3.9% to 63.3% [5-7]. Sarcopenia increases the risk of frailty, falls, fractures, cardiovascular complications, and death in patients on MHD, thus changing their lifestyle and reducing their quality of life [7,8]. Patients actively seeking effective interventions, such as exercise training and nutritional support, as well as their combination, seems promising [9,10]. In 2018, the European Working Group on Sarcopenia in Older People (EWGSOP) emphasized that early screening of patients at a high risk for sarcopenia and providing early interventions have important clinical significance [1]. Therefore, intervention in the early stages of sarcopenia may be a valuable opportunity to delay its progression.

The diagnosis of sarcopenia requires not only a decrease in muscle mass but also a decrease in muscle strength and/or physical performance [11]. Muscle strength is commonly assessed by hand grip strength (HGS), whereas physical performance is assessed by usual gait speed [1,11]. The measurement of muscle mass is the first and necessary step for diagnosing sarcopenia, and sarcopenia in patients on MHD is also mainly determined by muscle mass [12]. Muscle quantity or mass is generally diagnosed using techniques such as dual-energy X-ray absorptiometry, bioelectrical impedance analysis, magnetic resonance imaging, and computed tomography [1,11]. Unfortunately, the recommended diagnostic procedure for sarcopenia is complex and requires special equipment. Recently, researchers have developed simple sarcopenia screening tools in the general population based on general demographic data and anthropometric indicators [13].

Currently, there are no studies on screening tools for sarcopenia in patients on MHD. Therefore, we designed and conducted an analysis using easily obtained parameters to develop a practical screening tool for sarcopenia in patients on MHD. The model we constructed can be used clinically, and the sarcopenia status of patients on MHD can be preliminarily judged through routine examination indicators, demographic data, or some simple questionnaires.

Material and Methods

Study Population

This study was conducted in the blood purification centers of 2 tertiary hospitals, and 589 patients on MHD who underwent hemodialysis between May and September 2020 were selected as the training set. The inclusion criteria were age ≥ 18 years, meeting the diagnostic criteria for chronic kidney disease stage 5 (eGFR < 15 mL/min), steady dialysis time ≥ 3 months, hemodialysis 3 times a week, clear awareness and no communication barriers, and voluntary participation in this study. The exclusion criteria were pregnancy, record of 1 month of bleeding or infection, critical illnesses (such as severe cardiopulmonary disease or advanced cancer), inability to undergo a bioelectrical impedance analysis test owing to pacemaker installation, cardiovascular stent implantation, artificial joint replacement, or amputation surgery, and patients with incomplete clinical data. This study was approved by the ethics committee of our institution, and all patients provided informed consent and voluntarily participated in this study. Data collection was performed on patients' second and third weekly dialysis sessions.

Diagnosis of Sarcopenia

Similar to a previous study on sarcopenia in patients on MHD [14], we used the diagnostic criteria recommended by the Asian Sarcopenia Working Group (AWGS) [11]. The diagnosis of sarcopenia requires not only a decrease in muscle mass but also a decrease in muscle strength and/or physical performance.

The skeletal muscle index was measured by a multi-frequency bioelectrical impedance analysis device (InBody S10; InBody, Seoul, Korea) and was measured 30 min after a hemodialysis session [15]. All the patients were in a lying position, their arms were not in contact with the torso, and their feet were not in contact with each other. They were silent during the measurement and did not move their bodies. Decreased skeletal muscle mass was diagnosed when the skeletal muscle index was < 7.0 kg/m² in men and 5.7 kg/m² in women [11].

The HGS was used to indicate muscle strength. On the day of dialysis, HGS was measured using an electronic dynamometer (EH101; Xiangshan, Guangdong, China) before the initiation of dialysis. Before the measurement, the patients were familiarized with the use of the dynamometer. The distance between the grips of the dynamometer was adjusted according to the size of the patients' hands. With their bodies upright and their arms drooping naturally, the patients used the dominant hand to grasp the dynamometer as hard as possible, without bending their arms or waist (patients with an arteriovenous fistula used their hand without the fistula). The measurements were repeated thrice, and the maximum HGS

value was recorded. Male and female patients with HGS <28 and <18 kg, respectively, were diagnosed as having decreased muscle strength [15]. Before the initiation of dialysis, the patients' physical performance was assessed with the 6-m walk test, which involved walking a distance of 6 m at a normal speed from the beginning of the movement, without deceleration; the average speed of 2 trials was recorded. Low physical performance was defined as a 6-m walk speed <1.0 m/s [11]. HGS and walk speed were measured separately by 2 study members. Measurements were taken while the patients were waiting in the dialysis treatment waiting room for the start of dialysis, approximately 30 min before the start of dialysis treatment. After a 5-min rest period at the end of the grip strength measurement, the stride speed was measured.

Demographic, Comorbidities, and Biochemical Measurements

Demographic and clinical data (age, sex, marital status, education level, monthly income, duration of dialysis, and primary renal disease) were collected. The Charlson comorbidity index (CCI) was used to score the patients' comorbidities. The CCI includes 19 comorbidities, which are weighted according to the severity of the corresponding chronic disease [16]. Lin et al [17] found that the CCI is a strong predictor of outcomes in patients on MHD and correlates with hospitalization. Fasting blood samples before dialysis and biochemistry data (albumin [Alb], hemoglobin, blood urea nitrogen, serum creatinine [Scr], calcium, phosphorus, intact parathyroid hormone, total cholesterol, and triglycerides) were analyzed using an automatic chemistry analyzer (Beckman Coulter, Brea, CA, USA).

Anthropometric Measurements

After dialysis, anthropometric measurements were performed by the same trained observers. All patients used a fixed-height meter and electronic weight scale to measure their height and weight. The formula $\text{weight (kg)}/\text{height}^2 (\text{m}^2)$ was used to calculate the patients' body mass index (BMI). With the patients standing, a flexible, non-stretchable measuring tape was used to measure the mid-arm circumference (MAC) and calf circumference (CC) to the nearest 0.1 cm. The MAC measurement was performed on the arm without an arteriovenous fistula. The CC was measured at the largest circumference of the calf without edema. We determined whether there was edema in the patient's calf by observing and pressing the local skin of the calf. If there was no edema in both lower limbs, the CC of both lower limbs was measured and the average value was taken.

Physical Activity Level

We used the International Physical Activity Questionnaire-Short Form to assess the physical activity (PA) level of patients. The

patients were asked to report the frequency and cumulative daily duration of walking, moderate PA, and high-intensity PA for at least 10 min at a time during the past week. The metabolic equivalent values for walking, moderate PA, and high-intensity PA were 3.3, 4.0, and 8.0, respectively. According to the scoring protocol, the patients' total PA energy was calculated. The patients' PA levels were categorized into low, moderate, and high according to the questionnaire's manual [18].

Modified Quantitative Subjective Global Assessment

The Modified Quantitative Subjective Global Assessment (MQSGA) evaluated the patients' nutritional status based on 7 items: weight change, diet intake change, gastrointestinal symptoms, physiological function status, dialysis complications, decreased subcutaneous fat, and muscle loss. Each part was scored from 1 (normal) to 5 (severe), with a total score of 7 (normal) to 35 (severe malnutrition). The higher the score, the more severe the patients' malnutrition and inflammation [19].

Hospital Anxiety and Depression Scale

We used the Hospital Anxiety and Depression Scale (HADS) to assess the psychological status of patients on MHD. The HADS is mainly applied to the screening of anxiety and depression among patients in general hospitals and consists of 14 items, of which 7 items assess depression and 7 items assess anxiety. The scores of the 2 subscales range from 0 to 21 points, and a score ≥ 8 indicates the presence of anxiety or depression symptoms. The scores indicate the severity of the patient's anxiety or depression state. The HADS has good reliability, and the Cronbach's α coefficients of the overall scale, anxiety subscale, and depression subscale were 0.879, 0.806, and 0.806, respectively [20].

Statistical Analysis

Continuous variables conforming to a normal distribution are presented as mean \pm standard deviation. Non-normally distributed continuous variables are presented as median and interquartile ranges. Categorical variables are presented as numbers and percentages. Differences between groups were compared using the chi-square test, Mann-Whitney U test, or *t* test. We developed a predictive risk model using binary logistic regression (with forward stepwise regression). The area under the receiver operating characteristic curve (AUROC), sensitivity, specificity, and Youden index were used to evaluate the discrimination of the model. The calibration curve and Hosmer-Lemeshow test were used to evaluate the calibration of the model. The DCA curve was used to evaluate the clinical utility of the model. SPSS version 25.0 (IBM Corp., Armonk, NY, USA) and R version 4.2.0 (The R Foundation, Vienna, Austria) were used for the statistical analysis. A *P* value <0.05 was considered statistically significant.

Establishment Predictive Model

The variables that were statistically significant in the univariate analysis were included in the multivariate logistic regression analysis. The independent variables finally screened out through multi-factor logistic regression analysis establishment the predictive model, that is, a mathematical expression constructed from the independent variables in the regression model and their corresponding regression coefficients: $R_A = \beta_1 X_1 + \beta_2 X_2 + \dots + \beta_m X_m$, $\beta_1, \beta_2, \dots, \beta_m$ are regression coefficients, X_1, X_2, \dots, X_m are independent variables.

Results

Characteristics of the MHD Patients

Of the 589 patients on MHD (male, 385, 65.4%; female, 204, 34.6%) in the training set, 101 (17.1%) received a diagnosis of sarcopenia. The mean patient age was 53.8 ± 13.7 years (range, 22-88 years). A total of 331 (56.2%) patients had a dialysis duration ≥ 36 months; 148 (25.1%) patients had hypertension as the primary disease, 160 (27.2%) patients had diabetes, 144 (24.4%) patients had chronic glomerulonephritis, 30 (5.1%) patients had polycystic kidney disease, and 107 (18.2%) patients had other diseases. Other patient characteristics are presented in **Table 1**.

Screening of Predictive Model Variables

The results of the univariate analysis (**Table 1**) showed that age, CCI score, MQSGA score, and depression score of patients with sarcopenia were higher than those of patients without sarcopenia, and the Alb, Scr, BMI, MAC, CC, and PA levels of patients with sarcopenia were lower than those of patients without sarcopenia, and the differences were statistically significant ($P < 0.05$). The variables that were statistically significant in the univariate analysis ($P < 0.05$; **Table 1**) were included in the multivariate logistic regression analysis, which revealed that age (odds ratio [OR], 1.085; $P < 0.001$), BMI (OR, 0.841; $P = 0.010$), CC (OR, 0.658; $P < 0.001$), and SCr (OR, 0.998; $P = 0.029$) were independent predictors of sarcopenia (**Table 2**).

Construction of the Predictive Model

Based on the results of logistic regression analysis, the 4 variables obtained were included in the equation, and the formula of the obtained prediction model was:
 $\text{Logit}(P) = 0.082 \times \text{age} - 0.173 \times \text{BMI} - 0.419 \times \text{CC} - 0.002 \times \text{Scr}$.
 The optimal cut-off value of the equation obtained from the receiver operating characteristic curve was -13.455 points, with a score ≤ -13.455 indicating a low-risk population and a score > -13.455 indicating a high-risk population. In addition,

we plotted a predictive nomogram for the risk of the development of sarcopenia in patients on MHD (**Figure 1**).

Effect Analysis of Prediction Model

The AUROC of the model was 0.922 (95% confidence interval, 0.899-0.946) (**Figure 2A**), with a sensitivity of 85.1%, specificity of 85.9%, and Youden index of 0.710, indicating that the prediction model had good discrimination; the chi-square value of the Hosmer-Lemeshow test was 5.325 ($P = 0.722$); in addition, the calibration curve (**Figure 3A**) showed that the model had good calibration.

Clinical Application of Predictive Models

The DCA diagram of the prediction model (**Figure 4**) shows that when the threshold probability of a patient was 0 to 0.95, the model predicted a net benefit for sarcopenia in MHD patients. In addition, we selected 216 patients who underwent MHD treatment in a tertiary hospital from May to July 2021 for the external validation set of the model. According to the model established in this study, 66 cases of sarcopenia were predicted to occur, of which 35 cases actually occurred; meanwhile, 150 patients were predicted not to develop sarcopenia, and, of these, 146 cases did not occur, with an accuracy of $(35+146)/216 = 83.8\%$. The AUROC of the external validation of this risk prediction model was 0.913 (95% CI, 0.870-0.956) (**Figure 2B**), with a sensitivity of 94.3%, specificity of 82.9%, Youden index of 0.772, chi-square value (Hosmer-Lemeshow test) of 9.822 ($P = 0.278$), and a calibration curve near the ideal curve (**Figure 3B**). These results suggest that predictive models have high potential for clinical application and can predict sarcopenia in patients on MHD.

Discussion

Sarcopenia seriously affects the clinical outcome of patients undergoing MHD [5,7,8,21]. Early identification and effective intervention measures have important clinical significance [1,10,11]. The diagnostic procedures for sarcopenia are complex and require expensive equipment. Previous studies have mostly focused on the risk factors of sarcopenia; however, there are many risk factors, and some controversies remain [5,21,22]. This prevents medical staff from quickly and accurately identifying high-risk patients, which limits prevention and treatment efforts.

To estimate the risk of sarcopenia in patients on MHD, we screened easily accessible clinical risk factors based on previous studies in the literature and removed confounders by multivariate analysis. We obtained a simple formula, measured its cutoff value, and constructed a visual nomogram for clinical

Table 1. Univariate analysis of associated factors with sarcopenia in patients on maintenance dialysis (MHD).

Variable	MHD (N=589)	Without sarcopenia (n=488)	With sarcopenia (n=101)	P
Age (years)	54 (44, 64) ^a	66 (61, 73) ^a	52 (42, 59) ^a	<0.001*
Sex				0.356**
Male	385 (65.4) ^b	323 (66.2) ^b	62 (61.4) ^b	
Female	204 (34.6) ^b	165 (33.8) ^b	39 (38.6) ^b	
Marital status				0.772**
Married	479 (81.3) ^b	398 (81.6) ^b	81 (80.2) ^b	
Unmarried	51 (8.7) ^b	43 (8.8) ^b	8 (7.9) ^b	
Divorced or other	59 (10.0) ^b	47 (9.6) ^b	12 (11.9) ^b	
Education level (years)				0.065*
≤6	281 (33.0) ^b	93 (42.7) ^b	72 (59.0) ^b	
6-9	335 (39.3) ^b	82 (37.6) ^b	37 (30.3) ^b	
≥9	236 (27.7) ^b	43 (19.7) ^b	13 (10.7) ^b	
Monthly income (yuan)				0.351**
≤3000	553 (64.9) ^b	137 (62.8) ^b	82 (67.2) ^b	
>3000	299 (35.1) ^b	81 (37.2) ^b	40 (32.8) ^b	
Primary renal disease				0.374**
Hypertensive	193 (22.7) ^b	51 (23.4) ^b	23 (18.9) ^b	
Diabetes	259 (30.4) ^b	79 (36.2) ^b	56 (45.9) ^b	
Glomerulonephritis	210 (24.6) ^b	24 (11.0) ^b	12 (9.8) ^b	
Polycystic kidney				
Others	190 (22.3) ^b	64 (29.4) ^b	31 (25.4) ^b	
Duration of dialysis (months)				0.878**
<36	375 (44.0) ^b	93 (42.7) ^b	51 (41.8) ^b	
≥36	477 (56.0) ^b	125 (57.3) ^b	71 (58.2) ^b	
CCI score	3 (0, 5) ^a	3 (2, 5) ^a	4 (3, 5) ^a	<0.001*
Alb (g/L)	39.90 (36.9, 42.90) ^a	40.10 (37.40, 43.20) ^a	38.00 (34.70, 42.00) ^a	<0.001*
Hb (g/L)	99.09±19.22 ^c	99.25±18.77 ^c	98.29±21.38 ^c	0.674 [#]
BUN (mmol/L)	26.17±7.78 ^c	26.43±7.58 ^c	24.88±8.61 ^c	0.067 [#]
SCr (umol/L)	896.78±261.53 ^c	936.62±252.13 ^c	704.30±217.76 ^c	<0.001 [#]
Ca (mmol/L)	2.13 (1.99, 2.28) ^a	2.13 (1.99, 2.29) ^a	2.12 (1.99, 2.25) ^a	0.156*
P (mmol/L)	1.96±0.59 ^c	1.98±0.59 ^c	1.89±0.62 ^c	0.157 [#]
iPTH (pg/mL)	321.50 (175.20, 539.40) ^a	320.87 (177.40, 547.50) ^a	322.20 (160.70, 502.30) ^a	0.615*
TC (mmol/L)	3.70 (3.19, 4.35) ^a	3.70 (3.18, 4.32) ^a	3.71 (3.24, 4.63) ^a	0.445*
TG (mmol/L)	1.26 (0.88, 1.80) ^a	1.27 (0.88, 1.85) ^a	1.23 (0.84, 1.56) ^a	0.150*

Table 1 continued. Univariate analysis of associated factors with sarcopenia in patients on maintenance dialysis (MHD).

Variable	MHD (N=589)	Without sarcopenia (n=488)	With sarcopenia (n=101)	P
BMI (kg/m ²)	22.7 (20.4, 25.1) ^a	23.4 (20.9, 25.7) ^a	20.4 (18.6, 22.5) ^a	<0.001*
MAC (cm)	28.0 (25.5, 30.5) ^a	29.0 (26.0, 31.0) ^a	26.0 (24.0, 27.5) ^a	<0.001*
CC (cm)	33.2 (30.7, 35.2) ^a	33.7 (31.5, 35.7) ^a	29.5 (27.7, 30.7) ^a	<0.001*
PA level				<0.001*
Low	315 (53.5) ^b	241 (49.4) ^b	74 (73.3) ^b	
Moderate	258 (43.8) ^b	232 (47.5) ^b	26 (25.7) ^b	
High	16 (2.7) ^b	15 (3.1) ^b	1 (1.0) ^b	
MQSGA Score	10 (10, 13) ^a	10 (10, 13) ^a	13 (10, 15) ^a	<0.001*
HADS Score				
Anxiety	2 (1, 5) ^a	2 (1, 5) ^a	3 (1, 5) ^a	0.334*
Depression	6 (2, 9) ^a	5 (2, 9) ^a	7 (4, 11) ^a	0.001*

^a Median (inter-quartile range); ^b n (%); ^c mean±standard deviation; * Mann-Whitney U test; ** Chi-squared test; # t test. Alb – albumin; BMI – body mass index; Ca – calcium; BUN – blood urea nitrogen; CC – calf circumference; CCI – Charlson comorbidity index; HADS – Hospital Anxiety and Depression Scale; Hb – hemoglobin; iPTH – intact parathyroid hormone; MAC – middle-arm circumference; MQSGA – modified quantitative subjective global assessment; P – phosphorus; PA – physical activity; SCr – serum creatinine; TC – total cholesterol; TG – triglycerides.

Table 2. Multivariate analysis of associated factors with sarcopenia in patients on maintenance hemodialysis (n=589).

Variable	Regression coefficient	OR	95% CI	p
Age (years)	0.082	1.085	1.057-1.114	<0.001
BMI (kg/m ²)	-0.173	0.841	0.737-0.959	0.010
CC (cm)	-0.419	0.658	0.570-0.760	<0.001
Scr (umol/L)	-0.002	0.998	0.997-1.000	0.029

BMI – body mass index; CC – calf circumference; CI – confidence interval; OR – odds ratio; Scr – serum creatinine.

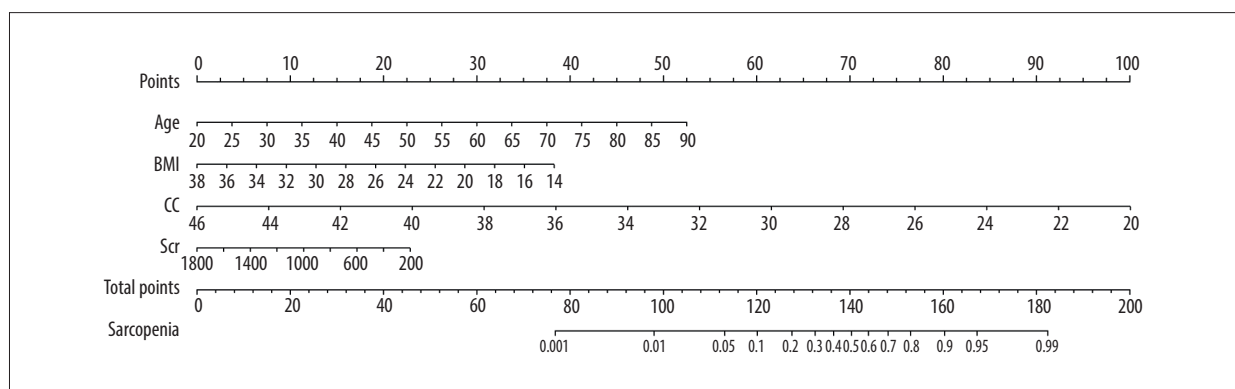


Figure 1. Predictive nomogram for the risk of sarcopenia in patients on maintenance dialysis (MHD). Each risk factor can obtain the corresponding score by referring to the score scale of the first row. The score of all existing risk factors is summed to obtain the total score. The total score is used to obtain the corresponding probability of sarcopenia in MHD patients.

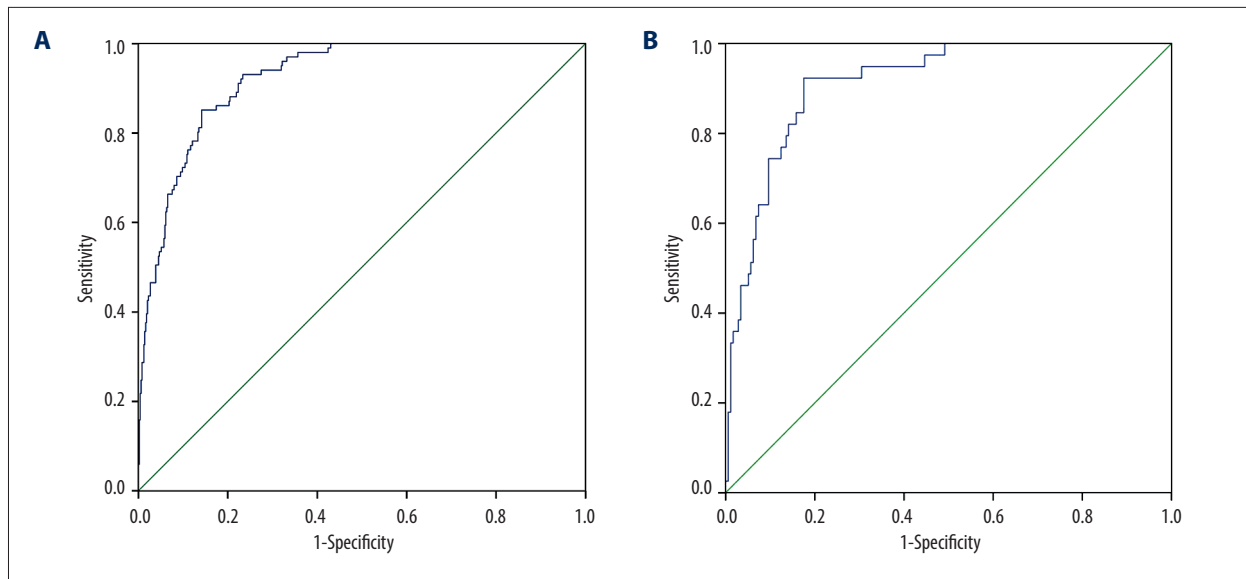


Figure 2. (A) Receiver operating characteristic (ROC) curve for the prediction of the risk of sarcopenia in patients on maintenance dialysis (MHD) in the training set. (B) ROC curve for the prediction of the risk of sarcopenia in MHD patients in the validation set.

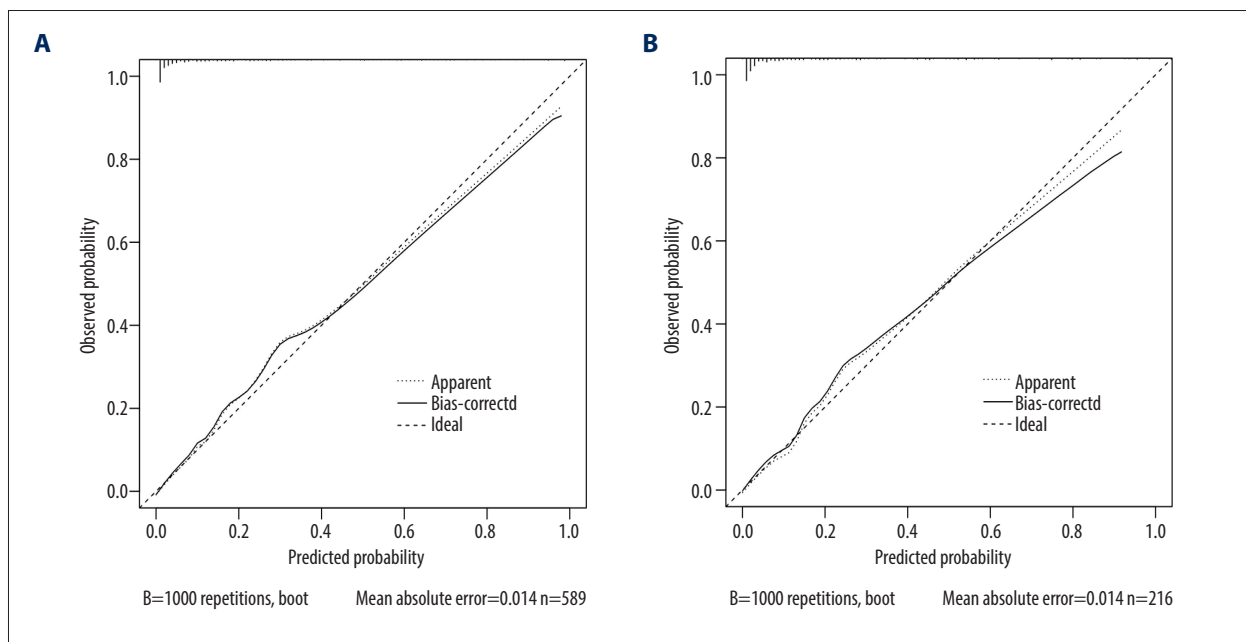


Figure 3. (A) Calibration curve for risk of sarcopenia in patients on maintenance dialysis (MHD) in the training set. The X-axis represents the predicted probability, and the Y-axis represents the actual probability. The degree of fit of the curve and diagonal reflects the calibration of the model. (B) Calibration curve for risk of sarcopenia in MHD patients in the validation set. The X-axis represents the predicted probability, and the Y-axis represents the actual probability. The degree of fit of the curve and diagonal reflects the calibration of the model.

application. To the best of our knowledge, no prior study, except for a study in older adults [13], has used regression methods to predict the risk for sarcopenia in patients on MHD. The 4 predictors in the model of this study were not opportunity-based, and they were strongly associated with sarcopenia in MHD patients.

Our study found that advanced age was a risk factor for sarcopenia in patients undergoing MHD ($P<0.001$), which was consistent with the findings of Yang et al [23]. Sarcopenia is defined as age-related sarcopenia, with normal adults losing 1% to 2% of their muscle mass per year from the age of 30

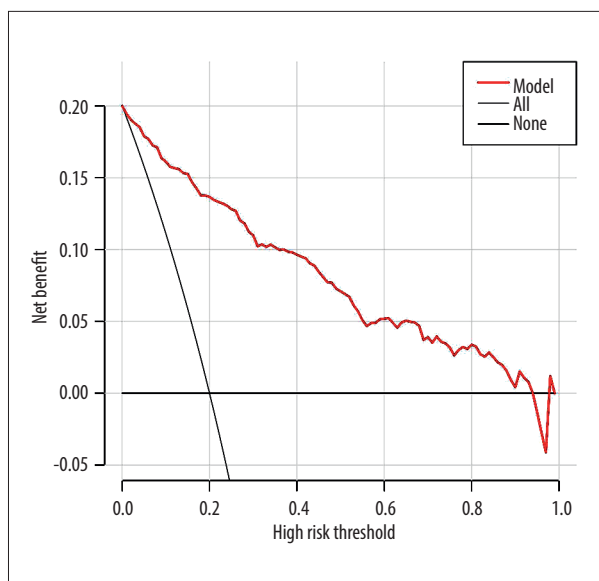


Figure 4. The decision curve analysis (DCA) curve of prediction model for predicting the risk of sarcopenia in patients on maintenance hemodialysis (MHD). The X-axis represents the threshold probability, and the Y-axis represents the net benefit rate. Horizontal lines indicate that all samples were negative and untreated, with a net benefit of 0. The slope line indicates that all samples were positive and all received intervention, and the slope of the net benefit is the reverse slope line of the negative value.

years and up to 30% at the age of 80 years [24]. With increasing age, the decomposition and synthesis of muscle proteins in patients gradually become imbalanced, muscle fibers are transformed from type II to type I, and the quality of skeletal muscle is significantly reduced. In addition, mitochondrial dysfunction, motor neuron degeneration, and abnormal hormone metabolism caused by aging will damage muscle function, which leads to sarcopenia [25].

Our findings showed that a low BMI was strongly associated with sarcopenia in patients on MHD ($P=0.010$), consistent with the findings of Macedo et al [26]. A low BMI often indicates the presence of malnutrition, inadequate energy and protein intake in malnourished patients, gastrointestinal dysfunction, poor digestion and absorption, decreased plasma amino acid concentration, and decreased muscle protein synthesis rate, which, in turn, lead to impaired skeletal muscle quality, strength, and function [27]. In addition, malnutrition is associated with the phenotype of sarcopenia, and the Global Initiative for Leadership in Malnutrition proposes that low skeletal muscle mass is also part of the diagnosis of malnutrition [28].

Our results showed that a larger CC was a protective factor in MHD patients with sarcopenia ($P<0.001$), which is compatible

with the findings of Bataille et al [12]. Compared with other parts of the body, the CC is less affected by local fat accumulation, which is highly correlated with skeletal muscle mass, and the influence of patient age and obesity, which is a sensitive indicator for predicting sarcopenia [29]. Both EWGSOP and AWGS recommend the use of CC to screen patients at high risk for sarcopenia [1,11]. The CC measurement is simple and easy to perform, but its accuracy is easily affected. Medical personnel need professional training to improve the accuracy of measurement results.

Our results also showed that a high level of Scr was a protective factor for sarcopenia in patients on MHD ($P=0.029$), consistent with the findings of Lin et al [30]. Mae et al [31] found that the Scr production rate can predict the occurrence of sarcopenia in MHD patients. Scr is a product of skeletal muscle metabolism in the human body, which is mainly excreted by glomerular filtration. In MHD patients without residual renal function, Scr is not only a marker of renal failure, but also a surrogate marker of muscle mass and lean body mass [32]. Patients on MHD need to reexamine the Scr level every 1 to 3 months to monitor the changes in the condition. The medical staff can collect various factors of this prediction model for sarcopenia assessment while reexamining the Scr of patients, without the need to increase the additional economic burden of patients.

The training set model had an AUROC of 0.922, sensitivity of 85.1%, specificity of 85.9%, and chi-square value (Hosmer-Lemeshow test) of 5.603 ($P=0.692$). The DCA curve showed that when the threshold probability of the patient was 0 to 0.95, the model predicted a net benefit for sarcopenia in MHD patients, with an accuracy of model prediction of 83.8%. Meanwhile, the validation set model had an AUROC of 0.913, sensitivity of 94.3%, specificity of 82.9%, and chi-square value (Hosmer-Lemeshow test) of 9.822 ($P=0.278$). These results showed that the prediction model constructed from age, BMI, CC, and Scr has good discrimination and calibration and also has some scientificity and practicability. This model can help healthcare providers make decisions related to the assessment and management of sarcopenia in MHD patients by providing personalized, highly accurate risk estimates. Clinical medical staff can use these indicators, which are easy to obtain in clinical practice, for evaluation and subsequently implement preventive and therapeutic measures as early as possible and change passive treatment into active prevention in order to reduce the occurrence of sarcopenia, improve the quality of life, and improve the prognosis of patients.

This study had some limitations. We developed and validated the prediction model in only 2 blood purification centers, and the sample size was small. Therefore, the findings cannot be generalized for all patients undergoing MHD. Moreover,

because acute comorbidities could quickly influence body fluid status and body composition [33], only clinically stable patients were included in the study. Our prediction models also cannot be applied to any patient who meets the exclusion criteria of this study. We still need to verify the model in a larger MHD population from multiple sources. In clinical work, the medical staff can use this prediction model and nomogram to regularly evaluate MHD patients, and when the model score is >-13.455 or the probability of nomogram is high, it indicates that the patient is very likely to have sarcopenia and suggests that they do further diagnostic tests. Appendicular skeletal muscle mass can be assessed by dual-energy X-ray absorptiometry, computed tomography, magnetic resonance imaging, and bioelectrical impedance analysis. Muscle strength can be assessed by measuring HGS and the chair-stand test. Physical performance can be assessed by methods including the Short Physical Performance Battery, 6-m walk test, stair-climb power test, timed-up-and-go test, and 5-time chair stand test [1,11]. At present, the main intervention measures for sarcopenia in MHD patients are exercise intervention, nutrition intervention, and drug intervention [34,35]. Exercise intervention includes exercise during non-dialysis period and exercise during dialysis. The main forms of intervention include aerobic exercise, resistance exercise, and aerobic combined with resistance exercise. Resistance exercise can better prevent and treat sarcopenia and is currently the most important intervention measure [36]. Martin-Alemañy et al found that the effect of exercise

combined with nutritional intervention was best [9]. In clinical practice, the medical staff should strengthen the attention to high-risk patients and patients close to high-risk, do a good job in health education for patients, develop a safe exercise prescription for them, actively supplement nutrition, and perform drug intervention when necessary.

Conclusions

The prediction model consisting of age, BMI, CC, and Scr is a simple, accurate, and reliable screening tool for predicting sarcopenia. Clinicians can use this prediction model to identify the risk of sarcopenia in patients on MHD earlier and more accurately. Healthcare providers can then offer early preventive intervention and thus improve clinical outcomes for patients on MHD.

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Declaration of Figures' Authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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