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Diagnosing and treating frailty and sarcopenia in middle-aged and older adults

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Diagnosing and treating frailty and sarcopenia in middle-aged and older adults

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Table of contents

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Editorial: Diagnosing and treating frailty and sarcopenia in middle-aged and older adults

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Editorial on the Research Topic
Diagnosing and treating frailty and sarcopenia in middle-aged and older adults

In light of the global population's increasing age, it is essential to thoroughly explore the challenges this presents, especially within healthcare systems. As individuals age, various physiological and structural changes can affect their ability to generate force, often leading to a decline in functional capacity. Consequently, geriatric syndromes such as frailty and sarcopenia are becoming increasingly prevalent (1, 2). These conditions are interconnected and linked to numerous adverse outcomes, including an increased risk of falls, hospitalization, and even death. These outcomes significantly affect the quality of life for older adults (3, 4).

In this Research Topic, we have collected 10 research articles that examine the use of valid testing protocols for accurate diagnosis of frailty and sarcopenia and the application of effective interventions to treat or reverse these conditions. These geriatric research articles offer valuable insights into systems and cutoff values for various populations and age groups, along with the development of more effective, individualized exercise programs. Consequently, these advancements allow for the identification of optimal strategies to preserve functional capacity in older populations.

In this context, the study by Setiati et al. provided valuable normative data, establishing crucial cutoff values for calf circumference, muscle strength, and physical performance indicators for diagnosing sarcopenia in Indonesian and Asian populations. Their multicenter, cross-sectional study involved 905 healthy Indonesian adults aged 20–39 years in urban regions. The authors used a 2-standard-deviation cut-off from the mean of a healthy young adult population to define normality. The following cut-off points were proposed: low calf circumference <29.92 cm and <26.70 cm; low handgrip strength <21.15 kg and <14.34 kg for men and women, respectively. Moreover, low physical performance was indicated by a walking pace of <0.51 $m \cdot s^{-1}$.

Wei et al. explored the relationship between chronic diseases, lifestyle factors, and the risk of sarcopenia among older Chinese individuals. Their research used data from the

China Health and Retirement Longitudinal Study (CHARLS) on participants aged 60 years and older ($n = 7{,}841$). The researchers found a non-linear relationship between physical activity and the risk of sarcopenia, and that the primary risk factors for sarcopenia include advancing age, chronic health conditions, lifestyle habits, and levels of social participation.

In a similar vein, but focusing only on a rural Chinese population aged 60–94 years ($n = 291$), Guo and Shi sought to identify risk factors for physical frailty by developing a predictive model, discovering that family income, physical activity, depressive symptoms, and fear of falling are significant risk factors for physical frailty in rural older adults, underscoring the importance of identifying high-risk environments to prevent frailty.

Given that machine learning (ML) is a powerful tool for predictive disease modeling, three studies were conducted to explore its applications. First, Du et al. also used CHARLS data to identify risk factors for sarcopenia ($n = 2{,}717$). ML allowed for the identification of time-dependent risk factors. The XGB algorithm was used, with an area under the receiver operating characteristic curve (ROC-AUC) of 0.70. These cohort study findings showed that living conditions, health status, and behavioral habits significantly influenced the model's predictive performance.

In another ML exploration using the CHARLS dataset, Peil Yu et al. examined community-dwelling older adults with cardiovascular disease (CVD). A sarcopenia prevalence of 18.61% was identified. The XGB algorithm was used, with an ROC-AUC of 0.87. The authors' findings indicated that, in older adults with CVD, lower BMI was a predictor of sarcopenia; conversely, regular weekly contact with children was found to act as an important protective factor.

Yu et al. investigated the relationship between grip strength and frailty using the CHARLS dataset ($n = 10{,}834$). The LightGBM model was used, with an ROC-AUC of 0.77. The researchers identified a significant negative correlation between grip strength and frailty risk, with variation based on gender (especially above 29.00 kg for men and 19.00 kg for women).

Given that insulin resistance and sarcopenia are prevalent among older adults, Li et al. conducted a study to investigate the correlations between the triglyceride-glucose (TyG) index, the TyG-body mass index (TyG-BMI), and sarcopenia in Chinese non-diabetic middle-aged and older women. Their cross-sectional study included a sample of 460 postmenopausal women and revealed a significant association between a higher TyG index and TyG-BMI index and a reduced risk of sarcopenia. This finding underscores the value of considering the TyG-BMI index as an effective biomarker for predicting sarcopenia risk in this population.

Supporting the idea that resistance training programs are a vital intervention to combat frailty in older adults living in daycare centers, Abreu et al. investigated, in a 12-week interventional study, the effects of a low-volume, remotely supervised resistance training (RT) program in four Portuguese daycare centers ($n = 44$). The prevalence of all frailty criteria decreased during the intervention period (from 48.4% to 25.8%), with the most significant reductions observed in low physical activity and exhaustion. This approach demonstrated that a low-volume, remotely supervised RT program can provide substantial benefits in the management of frailty.

In line with the importance of analyzing exercise approaches to counteract age-related muscle weakness, Desachy et al. conducted a comprehensive analysis comparing cortical activity during concentric and eccentric quadriceps contractions in both young and older healthy participants ($n = 38$). The authors found that eccentric movements elicited greater cortical activity than concentric movements in both age groups. This finding is particularly valuable for effectively addressing age-related issues, as it targets both muscle atrophy and brain changes.

Finally, within a patient-centered framework, Uchmanowicz et al. emphasized the significance of a multidisciplinary, multi-specialty, and holistic approach to frailty interventions. This framework encourages collaboration among professionals from different fields to enhance patients' overall quality of life. The authors point out that dietary, exercise, and cognitive interventions must be personalized for everyone, while simultaneously promoting opportunities for social engagement.

The collection of articles in this Research Topic aims to contribute to the advancement of research in geriatrics by encouraging the development of practical interventions and strategies for the early diagnosis and treatment of frailty and sarcopenia in middle-aged and older adults.

Author contributions

DLM: Writing – original draft, Conceptualization, Writing – review & editing. HN: Validation, Writing – review & editing. DAM: Validation, Writing – review & editing. MI: Validation, Writing – review & editing. MM: Validation, Conceptualization, Writing – review & editing.

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Predicting grip strength-related frailty in middle-aged and older Chinese adults using interpretable machine learning models: a prospective cohort study

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Introduction: Frailty is an emerging global health burden, and there is no consensus on the precise prediction of frailty. We aimed to explore the association between grip strength and frailty and interpret the optimal machine learning (ML) model using the SHapley Additive exPlanation (SHAP) to predict the risk of frailty.

Methods: Data for the study were extracted from the China Health and Retirement Longitudinal Study (CHARLS) database. Socio-demographic, medical history, anthropometric, psychological, and sleep parameters were analyzed in this study. We used the least absolute shrinkage and selection operator (LASSO) regression to filter the model for the best predictor variables and constructed six ML models for predicting frailty. The feature performance of six ML models was compared based on the area under the receiver operating characteristic curve (AUROC) and the light gradient boosting machine (LightGBM) model was selected as the best predictive frailty model. We used SHAP to interpret the LightGBM model and to reveal the decision-making process by which the model predicts frailty.

Results: A total of 10,834 eligible participants were included in the study. Using the lowest quartile of grip strength as a reference, grip strength was negatively associated with the risk of frailty when grip strength was >29.00 kg for males or >19.00 kg for females ($p < 0.001$). The LightGBM model predicted frailty with optimal performance with an AUROC of 0.768 (95% CI 0.741 ~ 0.795). The SHAP summary plot showed that all features predicted frailty in order of importance, with cognitive function being considered the most important predictive feature. The poorer the cognitive function, nighttime sleep duration, body mass index (BMI), and grip strength, the higher the risk of frailty in middle-aged and older adults. The SHAP individual force plot clearly shows that the LightGBM model predicts frailty in the individual decision-making process.

Conclusion: The grip strength-related LightGBM prediction model based on SHAP has high accuracy and robustness in predicting the risk of frailty. Increasing grip strength, cognitive function, nighttime sleep duration, and BMI reduce the risk of frailty and may provide strategies for individualized management of frailty.

KEYWORDS
frailty, grip strength, machine learning, SHapley Additive exPlanation, CHARLS

1 Introduction

Frailty is a complex, multidimensional biopsychosocial syndrome associated with aging, encompassing the activity, physiological, cognitive, social, and psychological domains, and characterized by a decline in the physiological capacity of multiple organ systems leading to increased sensitivity to stressors (1). Epidemiologic surveys of people aged 50 years and older in 15 countries showed an average prevalence of frailty of 17.4% (ranging from 3.9 to 51.4%), with a higher prevalence of frailty among older persons in upper-middle-income countries than in high-income countries (2). A prospective study of people over 85 years of age found that frail patients had more than twice the risk of death as non-frail patients at 7 years, and that frailty led to a 54 to 101% increase in healthcare expenditures (3). Therefore, early recognition and treatment of frailty have important public health and clinical implications.

Currently, several well-established methods are available to assess frailty, each offering distinct strengths and limitations. The frailty phenotype model, introduced by Fried LP et al., characterizes frailty based on five physical criteria: unintentional weight loss, exhaustion, low physical activity, slow walking speed, and weak grip strength (4). This model is widely adopted due to its simplicity and emphasis on physical attributes. In contrast, the cumulative deficit model, developed by Rockwood et al., evaluates frailty by tallying health deficits across multiple domains—including physical, cognitive, and social factors—to calculate a frailty index (5). Additionally, tools such as the Tilburg Frailty Indicator (TFI) and the Edmonton Frail Scale (EFS) provide multidimensional assessments that encompass psychological and social domains (6).

Among these methods, grip strength has been extensively validated as a simple, objective, and reliable biomarker for assessing physical frailty. Its use is particularly advantageous in large-scale cohort studies due to its ease of measurement and established association with overall health status (7). Studies have shown grip strength to be generally consistent with the assessment of overall body strength, upper extremity function, fractures, bone density, falls, aging, malnutrition, cognitive dysfunction, depression, sleep disorders, diabetes mellitus, and co-morbidities, and to be associated with all-cause mortality and disease-specific mortality (8). A Mendelian randomization study showed that grip strength was positively and causally related to lumbar spine bone density at the best incidence of osteoporotic fracture, but not to heel forearm or femoral neck bone density (9). A review of the relationship between grip strength and diabetes mellitus by Hamasaki H et al. suggests that grip strength is a reliable indicator for identifying the risk of diabetes mellitus, cardiovascular disease, and mortality, as well as for assessing skeletal muscle mass and strength (10). In addition, Hadzibegovic S et al. concluded that grip strength can also be used to assess the strength and functional status of cancer patients, especially those with cancer cachexia, and is a widely used functional test (11).

Machine learning (ML) represents a powerful tool in predictive disease modeling, offering significant advantages over traditional statistical methods, especially in handling complex, high-dimensional datasets (12). There are many different algorithms for ML, each with different characteristics for analyzing data. Various ML methods have been widely applied in health research, including Support Vector Machine (SVM) known for its classification precision in high-dimensional spaces, Random Forest (RF) for its robustness in variable selection, and Gradient Boosting methods like Light Gradient Boosting Machine (LightGBM) and Extreme Gradient Boosting (XGBoost) for their superior performance in imbalanced datasets. Interpretable ML overcomes the shortcomings of the black-box nature of ML, which allows users to better understand the underlying logic of the predictive model, increases the credibility of the predictive model, and enables the timely detection of possible biases in the model, as well as the diagnosis and repair of the model (13). To the best of our knowledge, no studies have explored grip strength as a predictor of frailty in middle-aged and older Chinese using interpretable ML methods and explored the relationship between grip strength and frailty. To fill this gap, we hypothesized that grip strength could be used as an independent predictor of frailty in middle-aged and older Chinese adults. Based on the data from the China Health and Retirement Longitudinal Study (CHARLS), we tested whether grip strength is an independent predictor of frailty in a representative national population and confirmed their relationship.

The purpose of the study is to explore the relationship between grip strength and frailty in middle-aged and older Chinese adults using the CHARLS dataset and to select the optimal interpretable ML model to predict frailty in middle-aged and older adults. The SHapley Additive exPlanation (SHAP) tool was used to explain the optimal model for predicting frailty in middle-aged and older adults, to explore independent risk factors for frailty, and to provide individualized strategies for the management and prevention of frailty in middle-aged and older adults.

2 Materials and methods

2.1 Study design and population

Our study data were extracted from the CHARLS wave 2 (2013) dataset, which is openly available at http://charls.pku.edu.cn/. CHARLS is a nationally representative longitudinal research cohort in China that collects high-quality data on households and individuals of middle-aged and older adults aged 45 years and above to analyze population aging. As described by Liu Y et al. CHARLS began in 2011–2012 with a baseline survey in 28 provinces, 150 counties, 450 villages, and 10,257 households across the country. Respondents were assessed every 2 years with face-to-face personal interviews, sociodemographics, lifestyle, anthropometric measurements, and laboratory analysis (14).

Since the CHARLS study in wave 2 (2013) has more complete information on the variables, we chose this survey cycle as the data source for our study. A total of 18,605 people were collected in the initial survey, and 10,834 participants were eventually included in the study after gradual screening. The inclusion criteria were as follows: (1) the age ≥ 45 years; (2) completed grip strength tests in both hands; and (3) obtained informed consent. Exclusion criteria were (1) the

age < 45 years; (2) missing age, gender, grip strength, and frailty data; and (3) the history of wrist or hand surgery or pain in the last 3 months. The screening process for study participants and the study design are shown in Figure 1.

2.2 Ethics statement

The study procedures followed the Declaration of Helsinki, and the CHARLS study was approved by the Ethics Committee of Peking University (Approval No. IRB00001052-11015), and all participants signed the written informed consent. We followed the CHARLS guidelines for data use for study analysis only. All participants' protected personal information is anonymized during our use of CHARLS data.

2.3 Feature extraction

Based on previous studies (15–17) and expert opinions (three independent geriatricians from the Second Affiliated Hospital of Wenzhou Medical University), we selected 31 variables including demographics, anthropometric measurements, lifestyles, medical histories, laboratory analyses, socioeconomic information, and psychiatric interview data (Supplementary material 1) as the original candidates for the prediction of frailty model. We excluded candidate variables with more than 15% missing values, including tobacco use and activities of daily living (ADL) score. To avoid overfitting and multicollinearity, we used the least absolute shrinkage and selection operator (LASSO) regression to screen candidate predictor variables for predicting the frailty model (18, 19). We used 10-fold cross-validation to confirm the appropriate tuning parameter (λ) of the LASSO regression analysis to screen the optimal predictor frailty model variables and the predictor variables with a p-value less than 0.05 were used as the final predictor frailty model variables (Figure 2). For this reason, we removed marital status, hypertension, diabetes, cancer, heart disease, stroke, dyslipidemia, liver disease, kidney disease, asthma, alcohol consumption, tobacco use, insurance, social activities, depression, ADL score, orientation, and pain. After variable screening, inclusion in the final predictive frailty model consisted of 13 features and 1 label, with 5 categorical and 8 continuous variables.

2.4 Definition of features and the label

Diagnostic components of frailty based on the description of Bu F et al. include fatigue, weakness, decreased physical activity, weight loss, and slow movement, and frailty is defined as meeting 3 or more of the 5 indicators (20). Whereas those who meet 1 or 2 indicators are pre-frail, those who meet 0 are non-frail (21). Nighttime sleep duration was obtained by asking the question "During the past month, how many hours of actual sleep did you get at night (average hours for one night)?." Poor sleep quality was assessed based on "my sleep was restless" and was categorized into 4 groups. Chronic diseases (hypertension, diabetes, cancer, chronic lung disease, heart disease, stroke, mental disease, arthritis or rheumatism, dyslipidemia, liver disease, kidney disease, digestive disease, and asthma) and pain were defined by self-report. The Katz Activities of Daily Living (ADL) score was used to assess the ability to perform activities of daily living, which are included in the CHARLS questionnaire: eating, dressing, transferring, toileting, bathing, and continence (22). Cognitive functioning was assessed through visuospatial skills, memory, orientation, and attention (23). The specific methods were as follows: (1) visuospatial skills were assessed by redrawing two overlapping

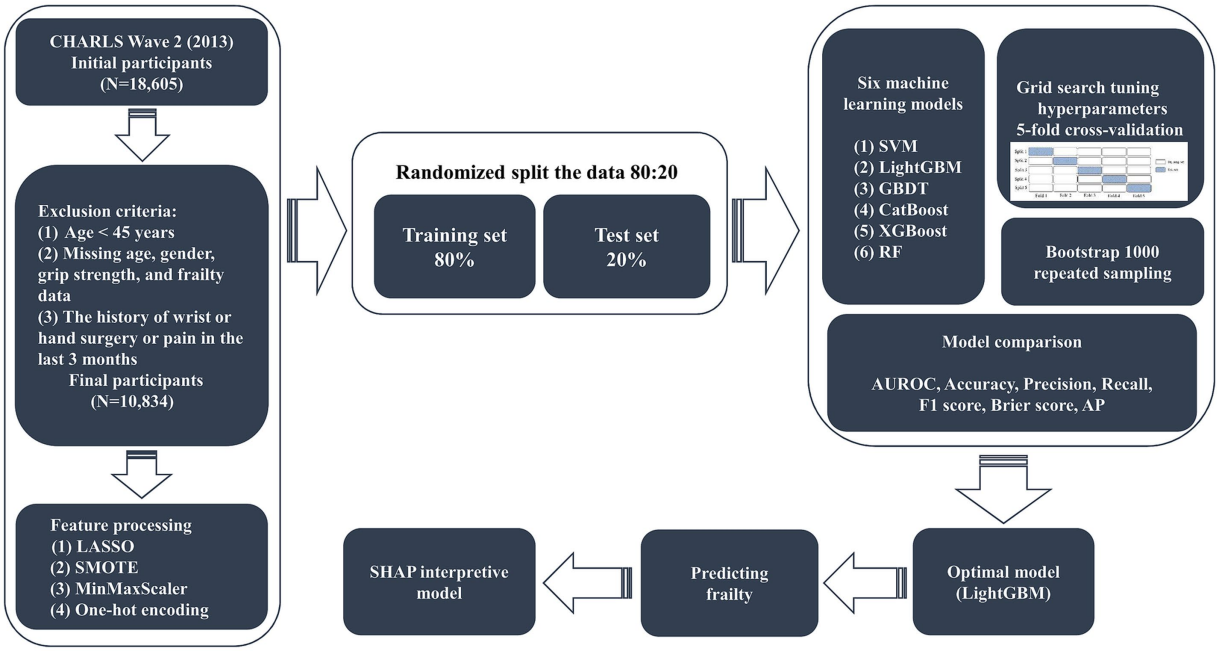

FIGURE 1
Study participants' selection and design flowchart.

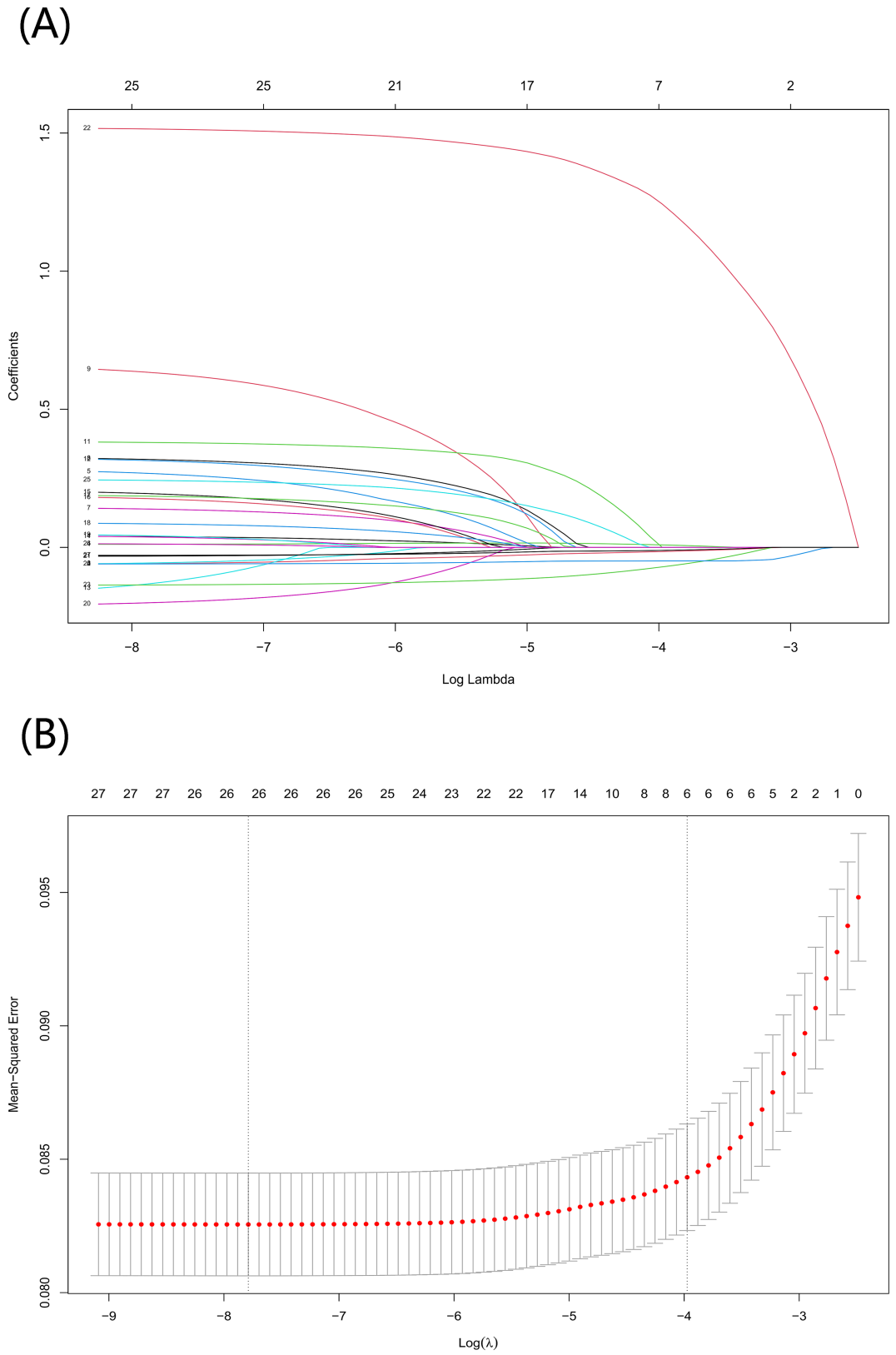

FIGURE 2
Screening for optimal model variables using the LASSO regression model. **(A)** To generate coefficient curves based on log(λ) sequences and to create nonzero coefficients by optimal λ. **(B)** The best λ in the LASSO model was selected by 10-fold cross-validation and using a minimum value criterion. The binomial deviation curves relative to the log(λ) are plotted and a virtual vertical line is drawn at the optimal value using one SE of the minimum criterion.

pentagons; (2) memory was measured by the average score of immediate and delayed recall of 10 Chinese words; (3) orientation and attention were measured by cognitive status telephone interview, which was calculated based on responses to questions about the year, month, day, week, and season. The sum of the above items is the total cognitive functioning score, and the score ranges from 0 to 21, the higher the score the better the cognitive functioning (24). Mental health status was assessed using the Center for Epidemiologic Studies Depression Scale (CES-D) as described by Bergenfeld I et al. with a total score of 30 and depression defined as 10 and above (25).

2.5 Handling of missing values

We observed that the presence of missing data for some variables is common in the CHARLS dataset, and that direct deletion of information about individuals with missing data can lead to wasted medical information and participant selection bias. To optimally preserve participant information and biological characteristics of the original dataset, we performed an algorithm based on the K Nearest Neighbors (KNN) for missing value interpolation using the DMwR2 (version0.0.2) R package for variables with less than 15% missing data. To validate the effectiveness of the KNN interpolation method, we compared it with the average interpolation and multiple interpolation methods on the missing dataset using the Root Mean Square Error (RMSE) and Mean Absolute Error (MAE) as the evaluation metrics. The KNN interpolation method performs well in preserving data integrity and minimizing the prediction error.

2.6 Predictive modeling strategy

We randomly split the original dataset into 80:20 to better evaluate the performance and generalization ability of the frailty prediction model on unknown data, where 80% of the data is used as the model training set ($N = 8{,}667$) and 20% of the data is used as the model testing set ($N = 2{,}167$). We trained the predictive frailty model using the training set data, tested the predictive frailty model on the test set data, and tuned the hyperparameters using grid search to improve the generalization performance of the predictive frailty model (26). To better represent the generalization ability of the predictive frailty model, we used 5-fold cross-validation to evaluate each hyperparameter combination of the predictive frailty model as a way to identify and select the optimal hyperparameter combination (27). Since the prevalence of frailty in the participants of this study was only 10.61%, the data had class-imbalanced characteristics, which tends to bias the accuracy towards more classes when predicting frailty using ML models. To overcome such problems, we processed the class-imbalanced data for predicting frailty using the Synthetic Minority Oversampling Technique (SMOTE) to achieve class balance in the data (28). To eliminate the differences in the data magnitude of different features of the predictive frailty model and convert the data to a uniform scale, we normalized the continuous features using MinMaxScaler and converted the categorical features to a numerical form that can be used for the training of the predictive frailty model using one-hot coding (29, 30).

Different ML algorithms have different applicability properties and performance to the original dataset, so we used six ML models including SVM, Gradient Boosting Decision Tree (GBDT), LightGBM, Category Boosting (CatBoost), XGBoost, and RF to predict the grip strength-related frailty in middle age and older adults. The optimal prediction frailty model is identified based on the area under the receiver operating characteristic curve (AUROC) metrics of different prediction frailty models, and the optimal prediction frailty model is interpreted using the SHAP tool.

2.7 Interpretability tool for SHAP-based predictive frailty modeling

We used SHAP as an interpretable tool for optimal prediction of frailty models in middle-aged and older adults. Traditional variable importance only ranks the importance of the variables in predicting the frailty model and cannot explain how the variables affect the final frailty prediction of the model (31). SHAP is based on cooperative game theory, where the magnitude of the SHAP value accurately assesses the value of each feature's contribution to the frailty prediction, and the positivity or negativity of the SHAP value suggests the directionality of the contribution (32).

2.8 Statistical analysis

Depending on whether the data conformed to a normal distribution, continuous variables were expressed as mean (standard deviation) or median (quartiles 1–3), and categorical variables were expressed as frequency (percentage). We divided all participants into two groups according to whether they were frail or non-frail. We compared each continuous variable between the two groups of patients using the Mann–Whitney U test, and compared differences in categorical variables using either the χ^2 test or Fisher's precision probability test. The relationship between grip strength and frailty was analyzed using multivariate logistic regression, trend tests, and interactions. We used Python (version 3.11.5) to analyze the ML models and evaluated the performance of each ML model using metrics such as AUROC, Accuracy, Precision, Recall, F1 Score, Brier Score, and Area under the Precise Recall (P-R) curve (AP). Comparisons between groups and logistic regression analysis of variables were statistically analyzed using R (version 4.3.1). The R packages we used include haven, gtsummary, DMwR2, dplyr, plyr, interactions, tidyverse, caret, arsenal, glmnet, and ggplot2. We used the Python libraries Scikit-learn (version 1.2.2) and imblearn library (version 0.10.1). The difference was considered statistically significant with a two-sided p value <0.05.

3 Results

3.1 Baseline characteristics of the participants

Based on the inclusion and exclusion criteria, the final study cohort included a total of 10,834 study participants, of which females: 5,749, and males: 5,085 were included in the baseline frailty status analysis, and the baseline characteristics of these participants are shown in Table 1. The prevalence of frailty in the present study

TABLE 1 Baseline characteristics of study participants.

Characteristic	Non-frail (*N* = 9,684)	Frail (*N* = 1,150)	*p*-value
Height (cm)	158 (152, 164)	155 (149, 161)	<0.001
Weight (kg)	59 (52, 67)	52 (45, 61)	<0.001
BMI (kg/m^2)	23.7 (21.4, 26.2)	21.9 (18.5, 24.8)	<0.001
Age (years)	60 (53, 66)	64 (58, 73)	<0.001
Age group			<0.001
<55	2,812 (29.04%)	194 (16.87%)	
55–64	3,834 (39.59%)	406 (35.30%)	
65–74	2,205 (22.77%)	296 (25.74%)	
≥75	833 (8.60%)	254 (22.09%)	
Gender			<0.001
Female	5,036 (52.00%)	713 (62.00%)	
Male	4,648 (48.00%)	437 (38.00%)	
Marital status			<0.001
Unmarried	1,214 (12.54%)	261 (22.70%)	
Married	8,470 (87.46%)	889 (77.30%)	
Self-perceived health status			<0.001
Fair	5,017 (51.88%)	364 (32.36%)	
Good	2,335 (24.14%)	95 (8.44%)	
Poor	2,319 (23.98%)	666 (59.20%)	
Hypertension			<0.001
No	7,142 (73.75%)	777 (67.57%)	
Yes	2,542 (26.25%)	373 (32.43%)	
Diabetes			<0.001
No	8,985 (92.78%)	1,031 (89.65%)	
Yes	699 (7.22%)	119 (10.35%)	
Cancer			<0.001
No	9,616 (99.30%)	1,130 (98.26%)	
Yes	68 (0.70%)	20 (1.74%)	
Chronic lung disease			<0.001
No	8,817 (91.05%)	985 (85.65%)	
Yes	867 (8.95%)	165 (14.35%)	
Heart disease			<0.001
No	8,599 (88.80%)	926 (80.52%)	
Yes	1,085 (11.20%)	224 (19.48%)	
Stroke			<0.001
No	9,497 (98.07%)	1,103 (95.91%)	
Yes	187 (1.93%)	47 (4.09%)	
Mental disease			0.010
No	9,594 (99.07%)	1,130 (98.26%)	
Yes	90 (0.93%)	20 (1.74%)	
Arthritis or rheumatism			<0.001
No	6,831 (70.54%)	687 (59.74%)	
Yes	2,853 (29.46%)	463 (40.26%)	

(Continued)

TABLE 1 (Continued)

Characteristic	Non-frail (*N* = 9,684)	Frail (*N* = 1,150)	*p*-value
Dyslipidemia			0.400
No	8,698 (89.82%)	1,023 (88.96%)	
Yes	986 (10.18%)	127 (11.04%)	
Liver disease			0.010
No	9,370 (96.76%)	1,096 (95.30%)	
Yes	314 (3.24%)	54 (4.70%)	
Kidney disease			<0.001
No	9,159 (94.58%)	1,048 (91.13%)	
Yes	525 (5.42%)	102 (8.87%)	
Digestive disease			<0.001
No	7,652 (79.02%)	811 (70.52%)	
Yes	2,032 (20.98%)	339 (29.48%)	
Asthma			<0.001
No	9,430 (97.38%)	1,096 (95.30%)	
Yes	254 (2.62%)	54 (4.70%)	
Alcohol consumption			<0.001
No	6,319 (65.30%)	871 (77.49%)	
Yes	3,358 (34.70%)	253 (22.51%)	
Tobacco use			0.500
No	5,522 (93.70%)	665 (93.01%)	
Yes	371 (6.30%)	50 (6.99%)	
Insurance			0.002
No	9,373 (96.79%)	1,093 (95.04%)	
Yes	311 (3.21%)	57 (4.96%)	
Social activities			<0.001
No	3,853 (39.79%)	564 (49.04%)	
Yes	5,831 (60.21%)	586 (50.96%)	
Poor sleep quality			<0.001
Rarely or none of the time	4,922 (52.28%)	287 (29.41%)	
Some or a little of the time	1,534 (16.29%)	144 (14.75%)	
Occasionally or a moderate amount of the time	1,298 (13.79%)	198 (20.29%)	
Most or all of the time	1,661 (17.64%)	347 (35.55%)	
Nighttime sleep duration (h)	6.00 (5.00, 7.50)	5.50 (4.00, 7.00)	<0.001
Depression			<0.001
No	6,419 (72.26%)	208 (25.09%)	
Yes	2,464 (27.74%)	621 (74.91%)	
ADL score	6 (6, 6)	6 (6, 6)	<0.001
Orientation	4 (3, 5)	3 (1, 4)	<0.001
Cognitive function	11.5 (8.0, 14.0)	8.0 (4.5, 11.5)	<0.001
Life satisfaction			<0.001
Fair	6,821 (70.44%)	719 (62.52%)	
Good	2,386 (24.64%)	165 (14.35%)	
Poor	477 (4.93%)	266 (23.13%)	

(Continued)

TABLE 1 (Continued)

Characteristic	Non-frail (*N* = 9,684)	Frail (*N* = 1,150)	*p*-value
Hearing			<0.001
Fair	4,488 (47.27%)	461 (45.24%)	
Good	3,747 (39.47%)	266 (26.10%)	
Poor	1,259 (13.26%)	292 (28.66%)	
Vision			<0.001
Fair	2,965 (31.22%)	345 (33.82%)	
Good	4,540 (47.81%)	332 (32.55%)	
Poor	1,991 (20.97%)	343 (33.63%)	
Pain			<0.001
Yes	3,209 (33.14%)	608 (52.87%)	
No	6,475 (66.86%)	542 (47.13%)	
Waistline (cm)	87 (80, 94)	84 (76, 91)	<0.001
Grip strength (kg)	29 (22, 36)	22 (16, 30)	<0.001

TABLE 2 Multivariate logistic regression analysis of grip strength and the risk of frailty in males.

Exposure	Model I		Model II		Model III	
	OR (95%CI)	*p*-value	OR (95%CI)	*p*-value	OR (95%CI)	*p*-value
Grip strength (continuous)	0.932 (0.923, 0.942)	<0.001	0.939 (0.929, 0.950)	<0.001	0.943 (0.931, 0.954)	<0.001
Grip strength (quartiles)						
Q1 (≤29.00)	Reference		Reference		Reference	
Q2 (>29.00, ≤35.25)	0.446 (0.345, 0.572)	<0.001	0.497 (0.382, 0.642)	<0.001	0.518 (0.398, 0.671)	<0.001
Q3 (>35.25, ≤41.25)	0.367 (0.279, 0.479)	<0.001	0.453 (0.338, 0.602)	<0.001	0.494 (0.368, 0.657)	<0.001
Q4 (>41.25, ≤67.63)	0.225 (0.162, 0.307)	<0.001	0.305 (0.214, 0.429)	<0.001	0.361 (0.252, 0.509)	<0.001
p for trend	<0.001		<0.001		<0.001	
Grip strength	Cognitive function		Nighttime sleep duration		BMI	
p for interaction	<0.001		0.231		0.980	

OR, odds ratio; CI, confidence intervals; Model I: no covariate adjustment; Model II: Adjusted for age; Model III: adjusted for age, chronic lung disease, mental disease, arthritis or rheumatism, digestive disease, nighttime sleep duration, and waistline.

was 10.61% (1,150/10,834) and the patients with frailty were older, with 22.09% being ≥75 years of age. Frail patients were more often unmarried (22.70%) and more often in poor self-perceived health (59.00%). The incidence of frailty was 62.00% in females and 38.00% in males, which is a significant difference. In the frail group, height, weight, body mass index (BMI), alcohol consumption, social activities, nighttime sleep duration, ADL score, orientation, cognitive function, waistline, and grip strength were significantly lower than that of the non-frail group, and the difference was statistically significant ($p < 0.01$). Hypertension, diabetes, cancer, chronic lung disease, heart disease, stroke, mental disease, arthritis or rheumatism, liver disease, kidney disease, disability, insurance, poor sleep quality, depression, poor life satisfaction, poor hearing, poor vision, and pain were significantly higher in the frail group than in the non-frail group. Disease, digestive disease, asthma, insurance, poor sleep quality, depression, poor life satisfaction, poor hearing, poor vision, and pain were significantly higher than those of the non-frail group, and the difference was statistically significant ($p < 0.01$).

3.2 Multivariate logistic regression analysis of grip strength and the risk of frailty

To ensure that a wide range of variations in different grip strength levels could be captured while avoiding bias due to the subjective setting of thresholds, we explored thresholds and dose–response relationships for grip strength and risk of frailty by stratifying grip strength by quartiles (33). Table 2 presents the results of a multivariate logistic regression analysis examining the association between grip strength and the risk of frailty in males. In Model I, a negative association was observed between grip strength and frailty risk, with higher grip strength associated with a reduced risk (OR = 0.932, 95% CI: 0.923–0.942, $p < 0.001$). This association remained statistically significant in Model II after adjusting for age (OR = 0.939, 95% CI: 0.929–0.950, $p < 0.001$). In Model III, which included full adjustment for covariates, the association persisted, with each unit increase in grip strength corresponding to a 5.7% decrease in frailty risk (OR = 0.943, 95% CI: 0.931–0.954, $p < 0.001$). Moreover, in the fully adjusted Model III, males in the highest quartile of grip strength demonstrated a

TABLE 3 Multivariate logistic regression analysis of grip strength and the risk of frailty in females.

Exposure	Model I		Model II		Model III	
	OR (95%CI)	*p*-value	OR (95%CI)	*p*-value	OR (95%CI)	*p*-value
Grip strength (continuous)	0.928 (0.917, 0.939)	<0.001	0.947 (0.935, 0.958)	<0.001	0.951 (0.939, 0.963)	<0.001
Grip strength (quartiles)						
Q1 (≤19.00)	Reference		Reference		Reference	
Q2 (>19.00, ≤23.50)	0.461 (0.376, 0.564)	<0.001	0.556 (0.450, 0.685)	<0.001	0.565 (0.456, 0.698)	<0.001
Q3 (>23.50, ≤28.25)	0.306 (0.243, 0.382)	<0.001	0.409 (0.321, 0.519)	<0.001	0.426 (0.334, 0.542)	<0.001
Q4 (>28.25, ≤61.38)	0.279 (0.220, 0.352)	<0.001	0.405 (0.313, 0.521)	<0.001	0.457 (0.351, 0.590)	<0.001
p for trend	<0.001		<0.001		<0.001	
Grip strength	Cognitive function		Nighttime sleep duration		BMI	
p for interaction	<0.001		<0.010		0.825	

OR, odds ratio; CI, confidence intervals; Model I: no covariate adjustment; Model II: Adjusted for age; Model III: adjusted for age, chronic lung disease, mental disease, arthritis or rheumatism, digestive disease, nighttime sleep duration, and waistline.

63.9% lower risk of frailty compared to those in the lowest quartile (OR = 0.361, 95% CI: 0.252–0.509, $p < 0.001$). In addition, to explore whether grip strength interacted with other important variables, we analyzed the interaction of grip strength with the top three important variables of the SHAP summary plot of the optimal model, respectively. The results showed that there was an interaction effect between grip strength and cognitive function ($p < 0.01$). Table 3 presents the analysis of the association between female grip strength and the risk of frailty. In Model I, a negative association was identified, with higher grip strength associated with a reduced risk of frailty (OR = 0.928, 95% CI: 0.917–0.939, $p < 0.001$). This association remained statistically significant in Model II after adjusting for age (OR = 0.947, 95% CI: 0.935–0.958, $p < 0.001$). In Model III, after full adjustment for covariates, a consistent 4.9% reduction in frailty risk was observed for each unit increase in grip strength (OR = 0.951, 95% CI: 0.939–0.963, $p < 0.001$). Furthermore, in the fully adjusted Model III, individuals in the highest quartile of grip strength exhibited a 54.3% lower risk of frailty compared to those in the lowest quartile (OR = 0.457, 95% CI: 0.351–0.590, $p < 0.001$).

3.3 Performance evaluation and comparison of six ML models

Figure 3 listed seven performance discriminators for SVM, LightGBM, GBDT, CatBoost, XGBoost, and RF models used to predict frailty. We trained six predictive frailty ML models on the training set data and tested each predictive frailty model on the test set data for seven performance discriminators, including AUROC, accuracy, precision, recall, F1 score, Brier score, and AP. In addition, we performed 1,000 resamplings using Bootstrap to calculate the AUROC 95% CI for each predicted frailty model. Based on AUROC, the LightGBM model had the best predictive frailty performance compared to the other five models with an AUROC of 0.768 and 95% CI of 0.741–0.795 (Figure 4). According to the confusion matrix, the LightGBM model predicts frailty with high accuracy and robustness with accuracy, precision, recall, F1 score, Brier score, and AP of 96.9, 76.9, 100%, 0.869, 0.111, and 0.322, respectively, (Figure 5; Figure 6). Ultimately, we use the LightGBM model as the optimal model for predicting frailty and further interpret the model using the SHAP.

3.4 Interpreting the LightGBM model for predicting frailty using SHAP summary plot

The SHAP summary plot listed the SHAP values of each feature, which was used to obtain the magnitude of each feature's contribution to the LightGBM model's prediction of frailty, and ordered the importance of each feature from highest to lowest (Figure 7). Cognitive function was the most important feature of the LightGBM model for predicting frailty, followed by nighttime sleep duration and BMI. Higher feature values in the SHAP summary plot are indicated by a reddish color, and a bluish color indicates lower feature values and the horizontal direction represents whether the SHAP value of the feature has a positive or negative effect on the prediction of frailty by the LightGBM model. We observed from the SHAP summary plots that a decreased value of the cognitive function feature has a positive effect on the model predicting frailty, while an increased value of the nighttime sleep duration feature has a negative effect on the model predicting frailty.

3.5 The SHAP individual force plot for the predicted frailty LightGBM model

Figure 8 shows the individual force plots for (A) non-frailty and (B) frailty. The SHAP value for each feature is labeled below the arrows, indicating the contribution of each feature to the model's frailty prediction, and the number on the horizontal axis is the probabilistic prediction value f(x). The red arrows on the left side represent features that positively influence the model's frailty prediction, the blue arrows on the right side represent features that negatively influence the model's frailty prediction, and the length of the arrows indicates the magnitude of the feature's contribution value to the model's frailty prediction. Figure 8A demonstrates that the LightGBM model predicted a frail individual, and Figure 8B indicates that the LightGBM model predicted a non-frail individual.

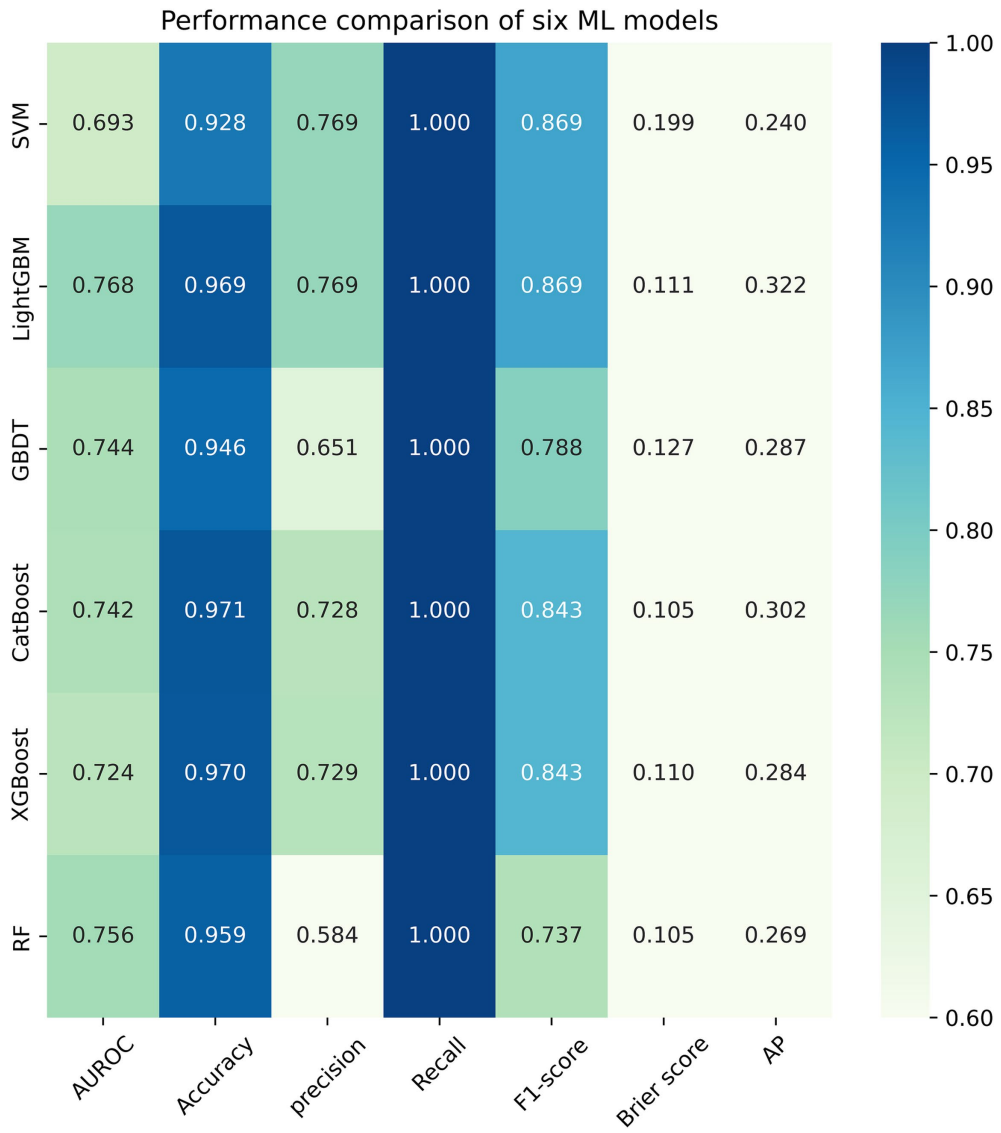

FIGURE 3
Heatmap comparing the performance of six ML models.

4 Discussion

This study is the first to explore the relationship between grip strength and frailty in middle-aged and older adults using the interpretable ML method, which showed a prevalence of frailty of 10.61%, which is consistent with the previously reported prevalence of frailty of 4.6% ~ 17.1% (34). Studies have shown that frailty is closely associated with hospitalizations, falls, fractures, and death, so accurately identifying those at risk for frailty is important for preventing frailty and related adverse outcomes (35). Our analysis revealed a negative association between grip strength and the risk of frailty, with this relationship becoming evident when grip strength exceeded 29.00 kg in males and 19.00 kg in females. This finding suggests the presence of a grip strength threshold for assessing frailty, which varies by gender. Specifically, grip strength is negatively correlated with frailty risk and can serve as an indicator of frailty only when it exceeds 29.00 kg in males and 19.00 kg in females. We constructed the SHAP-based interpretable lightGBM model to predict grip strength-related frailty in the middle-aged and older adults. In addition, we trained five other ML models, among which the LightGBM model has the optimal performance. The performance metrics of the LightGBM model, including AUROC, accuracy, precision, recall, F1 score, Brier score, and AP, were 0.768 (95% CI, 0.741–0.795), 96.9, 76.9, 100%, 0.869, 0.111, and 0.322, respectively. These results demonstrate the model's high reliability, robustness, and accuracy in predicting frailty. The model demonstrated moderate to good discriminatory ability in predicting frailty, as an AUROC between 0.7 and 0.8 is generally regarded as acceptable in medical prediction tasks (36).

The LightGBM model's superior performance is rooted in its efficient computational design and advanced feature handling capabilities. By using histogram-based learning, LightGBM significantly reduces computational overhead, making it faster and more memory-efficient than other gradient-boosting frameworks

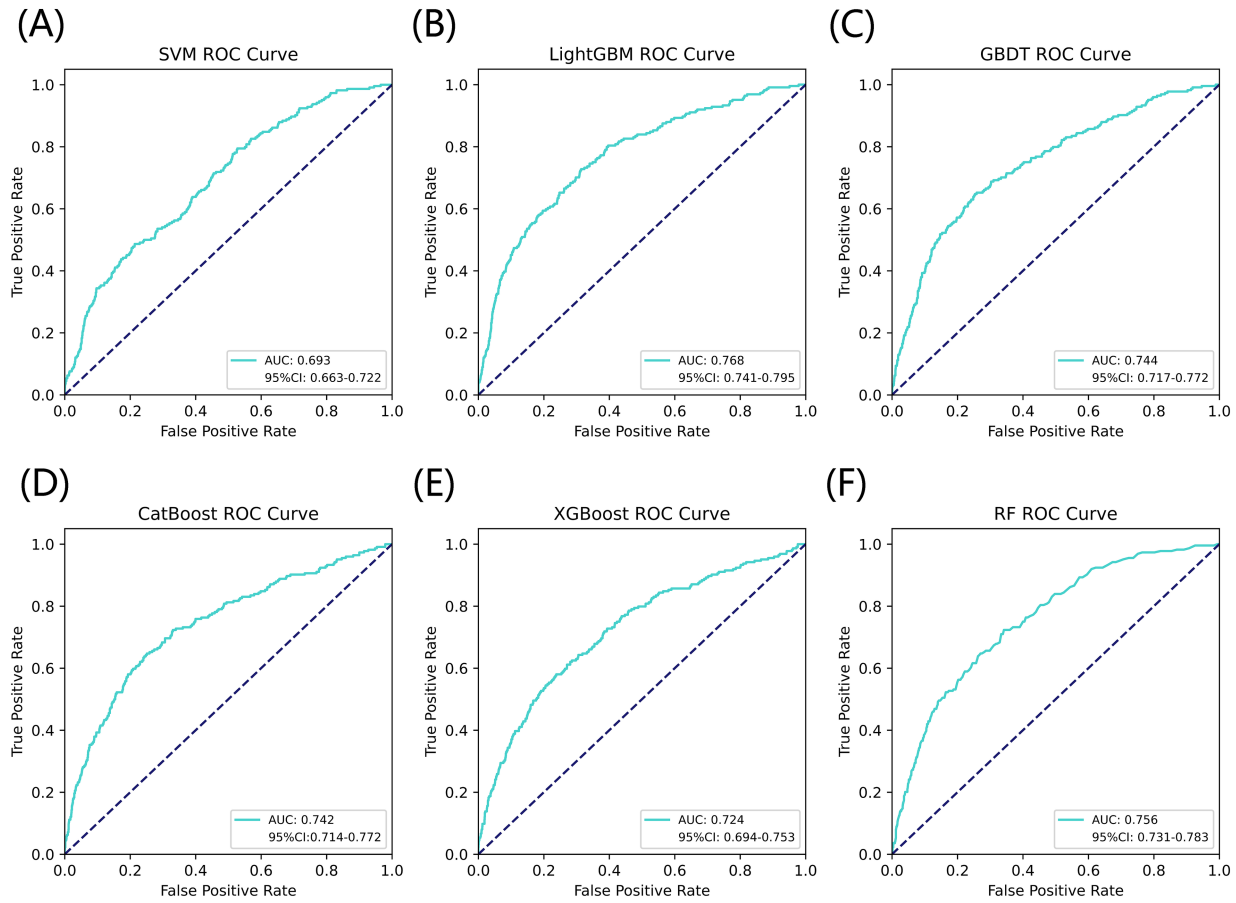

FIGURE 4
AUROC comparison of six ML models for predicting frailty. **(A)** SVM, **(B)** LightGBM, **(C)** GBDT, **(D)** CatBoost, **(E)** XGBoost, and **(F)** RF.

like XGBoost. Its leaf-wise tree growth strategy enhances the model's ability to identify complex interactions between variables, leading to higher predictive accuracy. Moreover, the integrated regularization mechanisms effectively prevent overfitting, a critical advantage when working with imbalanced datasets like ours. These factors collectively contribute to the model's robustness and reliability, underscoring its suitability for predicting frailty in middle-aged and older populations. Using SHAP individual force plots to interpret the LightGBM model allows for a better understanding of the decision-making process for model prediction frailty. Using the SHAP global summary plot, we also identified and ranked the importance of significant risk factors that predict frailty in the middle-aged and older adults. Cognitive function is the most important predictor variable for the LightGBM model, followed by nighttime sleep duration, BMI, and grip strength. Ma W et al. also confirmed the existence of a significant association between frailty and cognitive function and found that depression partially mediated the link between frailty and cognitive function (37).

Using the interpretable LightGBM model to predict frailty, we found that lower grip strength, cognitive function, BMI, and nighttime sleep duration were associated with a higher risk of frailty in middle-aged and older adults. Older age and female gender were also associated with a higher risk of frailty. A cross-sectional study of the relationship between frailty and muscle response by Suzuki Y et al. showed that grip reaction speed decreases with frailty, and that measuring grip strength in both hands can help to study the relationship between frailty and grip strength (38). A review by Vaishya R et al. stated that hand grip strength is a basic indicator for assessing muscle function and overall body function, is particularly relevant to old age, identifies a variety of health problems, and is an important biomarker of health (39). A cross-sectional observational study by Choe et al. found that muscle mass did not directly affect frailty and that grip strength mediated the relationship between muscle mass and frailty in older Korean adults (40). A systematic review and meta-analysis by Robinson TL et al. noted that frailty has a significant and negative impact on cognitive function, and their combined effect may increase the risk of adverse health outcomes in older adults (41). Jayanama K et al. examined the relationship between high BMI and frailty and mortality and found that being overweight or obese was associated with a higher risk of frailty and that the relationship between BMI and frailty was partly due to body fat (42). Arias-Fernández L et al. studied the relationship between sleep disorders and impaired physical functioning in older adults and suggested that self-reported poor sleep quality was associated with frailty and muscle weakness (43). These points confirmed our findings, and we hypothesized that grip strength, cognitive function, BMI, and nighttime sleep duration could serve as independent predictors of frailty.

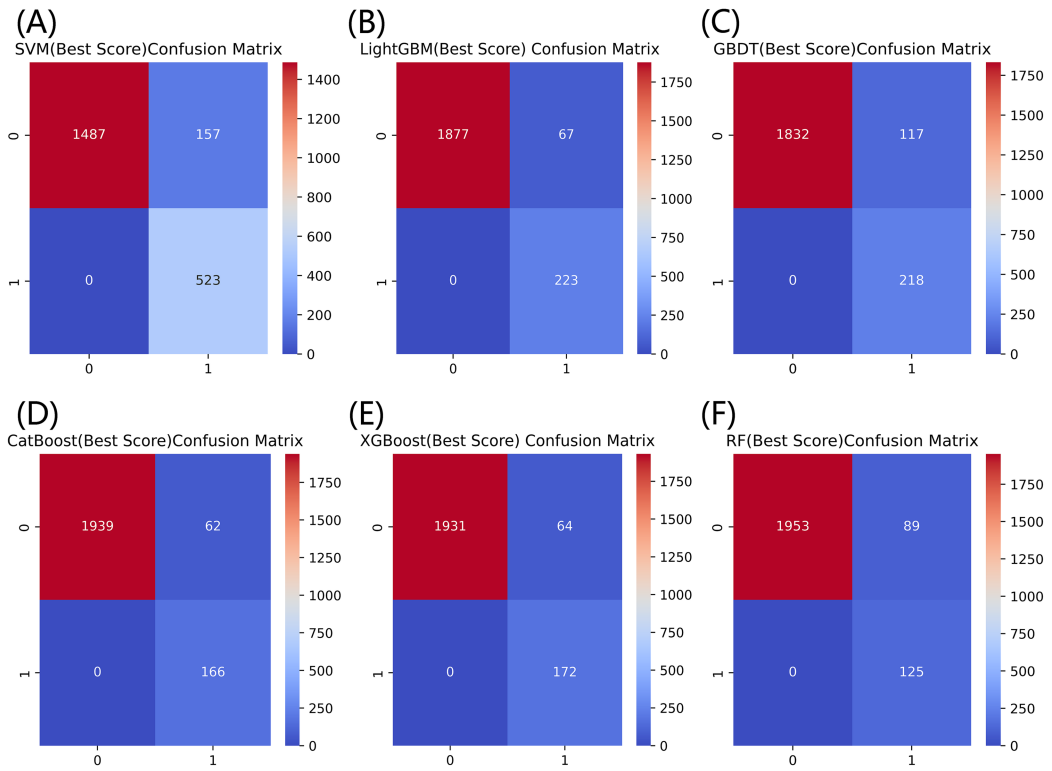

FIGURE 5
Comparison of confusion matrices for six models for predicting frailty. **(A)** SVM, **(B)** LightGBM, **(C)** GBDT, **(D)** CatBoost, **(E)** XGBoost, and **(F)** RF.

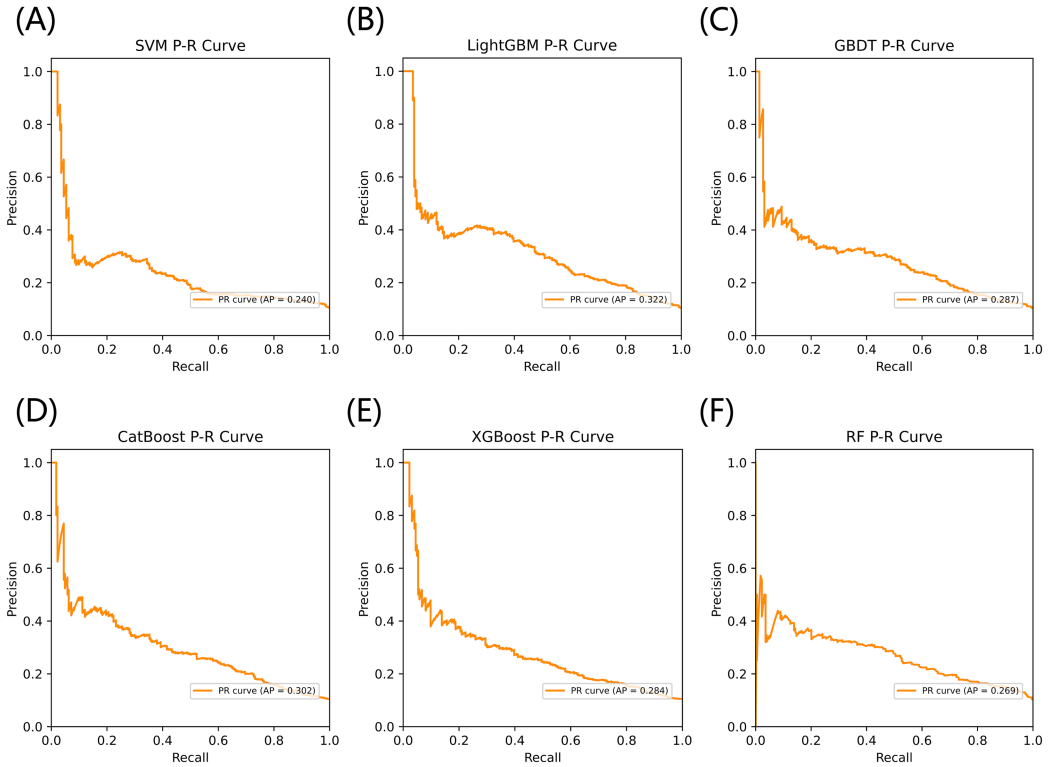

FIGURE 6
The AP comparison of six models for predicting frailty. **(A)** SVM, **(B)** LightGBM, **(C)** GBDT, **(D)** CatBoost, **(E)** XGBoost, and **(F)** RF.

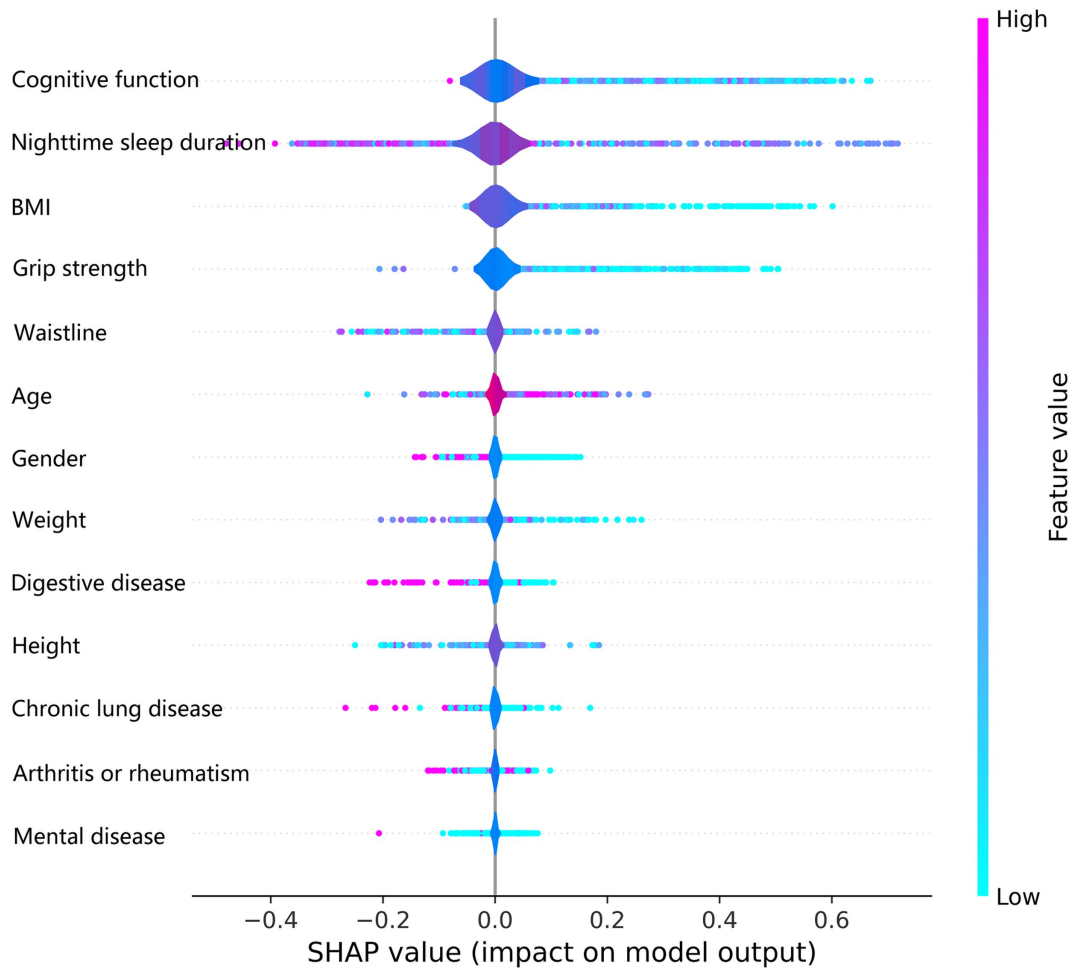

FIGURE 7
The SHAP global summary plot for the LightGBM model.

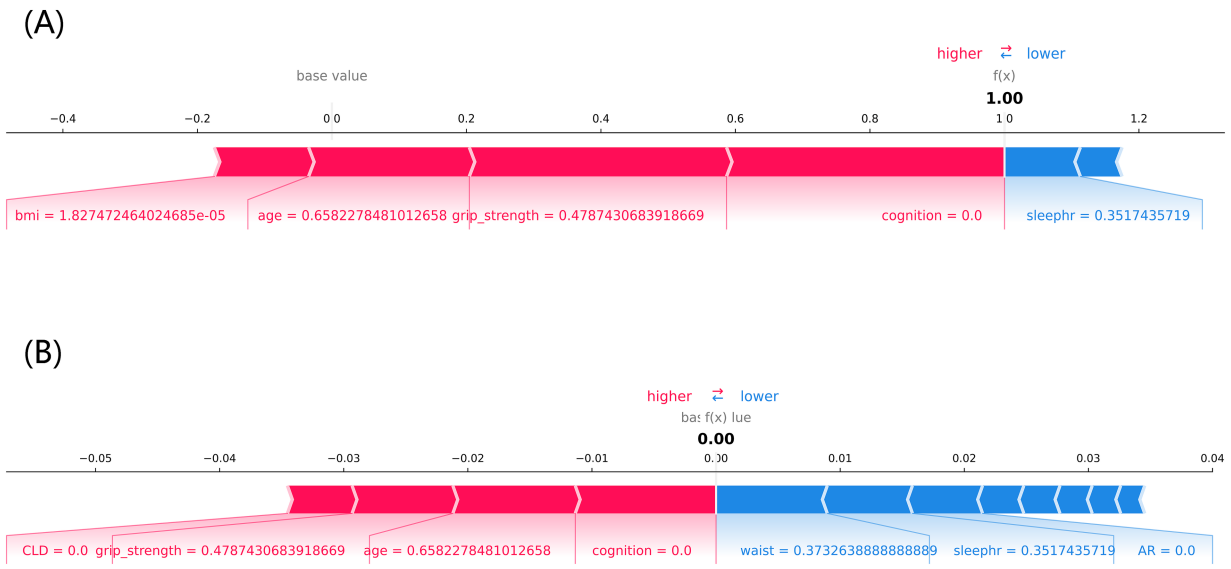

FIGURE 8
The SHAP force plot of individuals with different frailty prediction outcomes. **(A)** frailty, **(B)** non-frailty, cognition: cognitive function, sleephr: nighttime sleep duration, CLD: chronic lung disease, waist: waistline.

Gordon EH et al. suggested that aging is a major risk factor for most chronic diseases and that frailty is associated with many factors over the life course, particularly smoking, chronic disease, obesity, and economic deprivation (44). Bellelli F et al. showed that frailty increases with age and is associated with shorter years of education and that there is an exponential interaction between education and age in influencing frailty (45). Park C et al. and Zeidan RS et al. found that frailty is a manifestation of age-related decline in physiologic reserve and increased vulnerability and that there is a significant gender difference in the prevalence of frailty, with frailty being more common and severe in females, but with a relatively lower risk of death in females (3, 46). A cross-sectional study of frailty and gender differences in Europe found that females in Europe were more frail and had more comorbidities than males (47). These points are consistent with our findings and also suggest that age and gender may serve as independent predictors of frailty.

The interpretable LightGBM predictive model developed in this study demonstrates significant clinical utility in the management of frailty. For middle-aged and older adults, grip strength can be enhanced through strength training and nutritional interventions as part of personalized frailty management strategies. Given the observed relationship between nocturnal sleep duration and frailty risk, measures such as behavioral therapies, reduction in the use of central nervous system depressants, and optimization of the sleep environment may help improve sleep quality. Cognitive function, identified as a critical predictor of frailty, can be targeted through interventions like cognitive training and social engagement activities. For patients with excessively low body weight and muscle mass, maintaining a healthy BMI through dietary modifications and moderate exercise can mitigate the risk of frailty. The SHAP force plot offers a valuable tool for visualizing the contribution of individual features to a patient's frailty risk. For instance, patients with low grip strength but high BMI may benefit from prioritized interventions focused on strength training and weight management. Furthermore, the SHAP global feature importance map highlights key predictors, such as cognitive function and sleep duration, which can be incorporated into clinical screening protocols to guide early intervention efforts. By leveraging SHAP values, specific frailty management pathways can be designed to identify high-risk individuals. These patients can then be allocated to tailored intervention programs, such as grip strength training or cognitive function rehabilitation. The interpretability of the model provides clinicians with actionable decision support, particularly when managing a large cohort of patients with limited resources. Through feature prioritization, the model facilitates the efficient allocation of intervention resources, ensuring that high-impact strategies are applied where they are most needed.

This study has some strengths and limitations regarding the prediction of frailty. First, this study is based on the CHARLS data, which is nationally representative and high-quality data. It also uses the big data analytic power of ML to predict frailty in China's middle-aged and older adults. Second, the SHAP-based interpretable LightGBM model makes it easy for users to understand how it predicts frailty in middle-aged and older adults. Third, since the CHARLS data was a prospective study, it was possible to infer the existence of a causal relationship between the variables and the outcome, making the LightGBM model highly reliable in predicting frailty. The potential underrepresentation of rural populations in the CHARLS dataset introduces a limitation to our study. Rural communities often experience unique sociodemographic and health-related challenges, including lower socioeconomic status, limited healthcare access, and higher prevalence of malnutrition, which may influence the relationship between grip strength and frailty. Future studies should aim to validate our findings using datasets with a more balanced representation of rural and urban populations, or by employing stratified sampling techniques to minimize bias.

5 Conclusion

The grip strength-related LightGBM prediction model, constructed and tested based on SHAP, has high accuracy, robustness, and reliability in predicting the risk of frailty in middle-aged and older Chinese adults. The interpretable LightGBM predictive model we created accurately explores risk factors for frailty in middle-aged and older adults and has important clinical applications. Reducing grip strength, cognitive function, nighttime sleep duration, and BMI increases the risk of frailty and may provide strategies for individualized management of frailty in middle-aged and older adults.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the ethics committee of Peking University, Approval No. IRB00001052-11015. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

LY: Investigation, Methodology, Resources, Software, Writing – review & editing. SC: Conceptualization, Data curation, Formal analysis, Funding acquisition, Project administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. BS: Methodology, Resources, Validation, Visualization, Writing – review & editing. YH: Conceptualization, Funding acquisition, Investigation, Methodology, Resources, Software, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1489848/full#supplementary-material

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Higher triglyceride-glucose index and triglyceride glucose-body mass index protect against sarcopenia in Chinese middle-aged and older non-diabetic women: a cross-sectional study

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Purpose: Sarcopenia, an age-related complication, constitutes a major public health problem given the aging of the population. However, it is frequently overlooked and undertreated in mainstream practice. The study aimed to investigate the correlations between triglyceride-glucose (TyG) index and TyG-body mass index (BMI) and sarcopenia in non-diabetic middle-aged and older women and whether they would be helpful indicators of sarcopenia.

Patients and methods: This cross-sectional study was conducted in the Department of Endocrinology, Hebei Medical University Third Hospital. This study prospectively enrolled 460 non-diabetic postmenopausal women aged ≥50 years.

Results: As TyG and TyG-BMI increased, the prevalence of sarcopenia decreased. In multivariate analysis, the TyG index and TyG-BMI index were inversely associated with sarcopenia (OR: 0.492; 95% CI: 0.256–0.944 and OR: 0.948; 95% CI: 0.934–0.962). Women in the fourth TyG-BMI quartiles showed decreased OR of 0.009 (95% CI: 0.001–0.072) for sarcopenia with respect to first quartiles after adjusting confounding factors. The area under the curve (AUC) for TyG index in the diagnosis of sarcopenia was 0.598 (95% CI: 0.529–0.666), while the AUC for TyG-BMI index was 0.858 (95% CI: 0.816–0.899).

Conclusion: Higher TyG index and TyG-BMI index protected against sarcopenia in non-diabetic middle-aged and older females. Moreover, the TyG-BMI index was a reliable and cost-efficient biomarker to predict sarcopenia.

KEYWORDS

sarcopenia, triglyceride-glucose index, triglyceride glucose-body mass index, insulin resistance, middle-aged and older non-diabetic women

Introduction

Sarcopenia is recognized as an important nutritional problem accompanying age-related loss of muscle mass and function that reduces mobility, diminishes quality of life, and can lead to death (1). Estrogen contributes to skeletal muscle health by promoting muscle stem cell proliferation, differentiation, and regeneration (2). Owing to aging and estrogen deficiency, sarcopenia is found to be more prevalent in postmenopausal middle-aged and older women (2). In a population of postmenopausal women, the prevalence of sarcopenia ranges from 10 to 40% (3), undoubtedly increasing the health burden and socioeconomic costs. Sarcopenia has been overlooked in mainstream practice, due to the complexity of determining what variables to measure. Hence, it is critically significant to detect postmenopausal individuals with sarcopenia in advance by a reliable, inexpensive and convenient marker, thus implementing early intervention strategies to lower risk of sarcopenia.

The sarcopenia phenotype has many contributing causes beyond aging. Previous studies reported that insulin resistance (IR) may be contribute to the decline in muscle mass (4), progressively giving rise to sarcopenia. Skeletal muscle is a primary organ for insulin disposal. Insulin plays a major role in boosting muscle protein gain and muscle growth through increasing muscle protein synthesis coupled with inhibiting proteolysis (5). Due to a defect in the insulin signal transduction pathway, the anabolic action of insulin is afflicted, which could result in skeletal muscle loss (5). Moreover, development of IR may induce mitochondrial alterations leading to a reduction in energy production required for muscle contraction (5). Menopause is a natural event for women during their lifespan caused by the cessation of spontaneous menses or ovariectomy with estrogen decreasing and androgen increasing in circulation (6). Several researches have revealed that endogenous estrogens can protect against IR (7, 8). Lower incidence of IR diminishes severely when women reach the postmenopausal situation (9).

Traditional methods for evaluating IR, including hyperinsulinemic-euglycemic clamp and the homeostasis model assessment—estimated insulin resistance (HOMA-IR), are invasive and unavailable in most developing countries, and they may be interfered with by exogenous insulin levels, which limits their applications in clinical practice. The triglyceride-glucose (TyG) index—which formulated by fasting triglycerides and plasm glucose—can accurately assess IR (10) and has been shown to be superior to the HOMA-IR for the identification of several IR related conditions like type 2 diabetes mellitus (T2DM) (11). Obesity, identified by body mass index (BMI), is another principal factor linked to IR. Recently, a combination of TyG and BMI (TyG-BMI) index has been proposed as a reliable and highly sensitive and specific alternative marker of IR (12). Several studies have reported that higher TyG-BMI index is proportionally related to cardiac and cerebrovascular events in the older or female patients (13) and non-alcoholic fatty liver disease incidents in a healthy population (14).

Considering the relationship between IR and low muscle mass, the elevated TyG index and TyG-BMI index may be risk predictors for sarcopenia. However, recent clinical studies reached contradictory results due to different participants. A research based on Korean populations aged ≥ 40 showed that increased TyG index is associated with the risk of low muscle mass (15). A Chinese investigation reported that TyG index was positively correlated with muscle mass in female subjects with T2DM when TyG index was <9 (16). These outcomes suggested that the degree of IR may have different effects on muscle mass. Besides, T2DM is a disorder of glucose metabolism on the basis of severe IR, which may lead to muscle damage beyond IR itself. Moreover, TyG index and TyG-BMI index are not only IR markers, but also indicators of the body's nutritional status. Hence, further study on the effect of TyG index and TyG-BMI index on muscle mass in the population without significant IR will be helpful for the prevention and management of sarcopenia in clinical practice. To the best of our knowledge, no relevant studies have investigated the association between the TyG index and TyG-BMI index and sarcopenia in non-diabetic Chinese postmenopausal women. Given the important existing gap in this field and its clinical implications, the purpose of the present study was to investigate whether the TyG index and TyG-BMI index are related to sarcopenia and whether they would be suitable for use as indicators of sarcopenia in Chinese non-diabetic postmenopausal women.

Methods

Study design and participants

This cross-sectional study was conducted in the Department of Endocrinology, Hebei Medical University Third Hospital from 21th August 2021 to 21th September 2023. The minimum sample size of 378 was calculated using t-tests in G*Power statistical analysis software version 3.1.9.7 considering an effect size of 0.5, alpha error probability of 0.05, power of 0.95, and allocation ratio of N2/N1 of 5, having a sample of 63 sarcopenia and 315 non-sarcopenia. A total of 520 subjects were included based on the following criteria: (1) age more than 50 years old and (2) no menstruation for at least 1 year by self-reporting or at least 6 months after bilateral oophorectomy. We excluded 60 participants who could meet the following criteria: (1) diagnosis of diabetes mellitus by doctors ($n = 15$); (2) chronic liver disease ($n = 4$) or kidney disease ($n = 4$) or cancer ($n = 2$); (3) thyroid disease ($n = 10$) or taking steroid ($n = 5$) that could affect muscle metabolism; (4) cognitive impairment or physical dysfunction ($n = 2$); (5) lack of complete data ($n = 18$) (Figure 1). Finally, there were total 460 postmenopausal women enrolled in the analysis, of which 73 participants were diagnosed with sarcopenia. None of the study participants used hormone therapy or specific supplements for menopause. The study was carried out in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Hebei Medical University Third Hospital (No. ke2023-080-1 and ke2021-045-1). Written informed consents were signed by all individuals prior to participation.

Data collection

Baseline data including date of birth, menopausal age, height and weight of patients were collected. Total 5 mL fasting blood samples were collected. Levels of fasting plasma glucose (FPG), triglycerides (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), uric acid (UA), creatinine (Cr), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and albumin (ALB) were measured enzymatically by an auto-analyzer (Olympus AU 2700, Japan) in the biochemical laboratory. The TyG index was calculated as ln

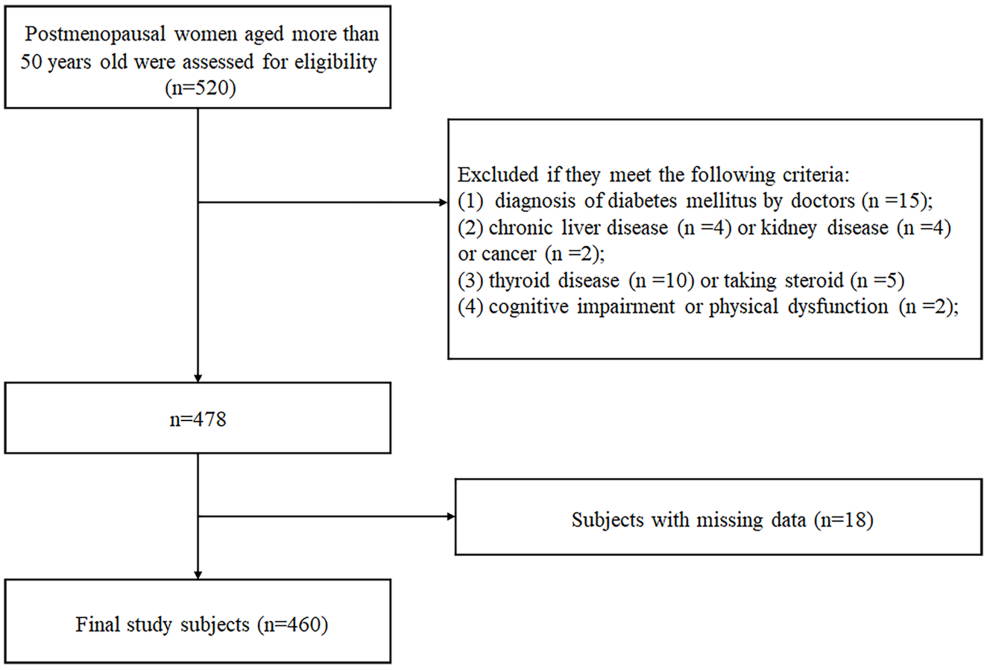

FIGURE 1
Flow diagram of participant enrollment.

[triglyceride (mg/dL) × fasting plasma glucose (mg/dL)/2]. BMI was calculated as weight (kg)/height in meters squared (m^2). The TyG-BMI index was calculated as TyG × BMI.

Diagnosis of sarcopenia

Appendicular skeletal muscle mass (ASM) was measured using the Dual-energy X-ray absorptiometry (DXA: Lunar IDXAGE, GE, United States). Relative ASM index (RSMI, ASM/height^2) was calculated. Handgrip strength (HS) was determined by a dynamometer (Jamar, United States). Measurements were taken twice and the mean values were calculated. Six meter walking test was completed by measuring the time taken to walk 6-meter at a normal pace from a moving start, without deceleration, and taking the average result of at least 2 trials as the recorded gait speed (GS). Based on the updated consensus by the Asian Working Group for Sarcopenia 2019 (AWGS, 2019) (17), sarcopenia was defined as (1) low muscle mass (RSMI, women: <5.4 kg/m^2) plus (2) low muscle strength (HS, women: <18 kg) and/or low physical performance (6 m walking test <1 m/s).

Statistical analysis

Statistical analysis was performed using SPSS software (version 24) and graphs were performed using GraphPad Prism 8.0 software. The Shapiro–Wilk test was performed to assess the distribution of continuous data. Normally distributed data were presented as mean ± standard deviation (mean ± SD) and compared using independent sample *t*-test. Non-normally distributed data were expressed as median and inter-quartile range (IQR) and compared using Mann–Whitney *U* tests to check the differences between groups. Categorical variables were expressed as numbers and percentages and compared using the chi-square test. The participants were divided into four groups based on their TyG and TyG-BMI quartiles in order to assess the independent impact factors of sarcopenia. Univariate and adjusted multivariate logistic regression analyses were performed to investigate the associations between the TyG index and TyG-BMI index and the risk of sarcopenia according to their quartiles, respectively. Receiver operating characteristic (ROC) curve analysis was done to evaluate the diagnostic value of TyG index and TyG-BMI index for sarcopenia. The best cut-off values were calculated using the Youden index, which were calculated according to the corresponding sensitivity, specificity for each index. A two-sided *p*-value <0.05 was considered statistically significant.

Results

Clinical characteristics of the study participants

Among the 460 participants, 73 individuals had sarcopenia, whereas other participants did not have sarcopenia. Table 1 shows the baseline characteristics of participants and the differences between the two groups. Compared with non-sarcopenia women, women with sarcopenia were significantly older, had significantly lower level of BMI, RSMI, HS, GS, ALB, UA, FPG, ALT, and higher level of HDL-C (all $p < 0.05$). Meanwhile, there were no differences in other biochemical parameters including Cr, TC, TG, LDL-C and AST between the two groups (all $p > 0.05$). Compared with women without sarcopenia, both TyG index and TyG-BMI index were significantly decreased in women with sarcopenia (all $p < 0.05$).

TABLE 1 Characteristics of the study participants and differences between women with sarcopenia and non-sarcopenia.

	All patients	Non-sarcopenia	Sarcopenia	*P*-value
Number	460	387	73	
Age (year)	64 (58,68)	63 (56,67.5)	68 (65.5,71)	<0.001
BMI (kg/m^2)	23.95 (21.76,26.00)	24.44 (22.45,26.36)	20.37 (19.42,22.15)	<0.001
RSMI (kg/m^2)	6.05 (5.63,6.52)	6.18 (5.84,6.61)	5.20 (5.01,5.32)	<0.001
HS (kg)	22.21 ± 6.05	22.68 ± 6.04	19.74 ± 5.48	<0.001
GS (m/s)	1.07 ± 0.22	1.09 ± 0.22	0.98 ± 0.21	<0.001
ALB (g/L)	45.63 (44.01,47.82)	45.96 (44.30,47.97)	44.24 (41.05,44.61)	<0.001
Cr (μmmol/L)	67.47 (59.46,76.92)	66.99 (59.67,76.46)	69.43 (57.83,80.97)	0.451
UA (ummol/L)	325.21 ± 90.17	330.30 ± 89.77	298.62 ± 88.16	0.006
FBG (mmol/L)	5.47 (5.08,6.05)	5.59 (5.15,6.14)	5.15 (4.75,5.48)	<0.001
TG (mmol/L)	1.51 ± 0.99	1.54 ± 1.04	1.34 ± 0.72	0.127
TC (mmol/L)	5.12 ± 1.14	5.12 ± 1.17	5.13 ± 0.95	0.939
LDL-C (mmol/L)	2.92 ± 0.69	2.92 ± 0.70	2.93 ± 0.67	0.891
HDL-C (mmol/L)	1.41 ± 0.29	1.39 ± 0.28	1.49 ± 0.33	0.012
ALT (U/L)	22.98 ± 13.69	23.55 ± 14.22	19.99 ± 9.93	0.042
AST (U/L)	21.45 ± 7.96	21.73 ± 8.35	19.95 ± 5.25	0.079
TyG	8.63 (8.29,8.98)	8.65 (8.30,9.01)	8.48 (8.15,8.78)	0.008
TyG-BMI	206.68 (184.81,228.10)	212.31 (192.39,231.34)	173.30 (161.68,189.18)	<0.001

Data presented as mean ± standard deviation or median (inter-quartile range). BMI, body mass index; RSMI, relative skeletal muscle mass index; HS, handgrip strength; GS, 6-meter gait speed; FPG, fasting plasma glucose; TG, triglycerides; TC, total cholesterol; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; UA, uric acid; Cr, creatinine; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; TyG, triglyceride-glucose; TyG-BMI, triglyceride glucose–body mass index. Statistically significant ($p < 0.05$) (non-sarcopenia vs. sarcopenia).

Prevalence of sarcopenia according to quartiles of the TyG index and TyG-BMI index

The TyG index and TyG-BMI index were divided into four groups according to quartiles, respectively. As shown in Figure 2, the prevalence of sarcopenia was 20, 17.4, 17.4, and 8.7% in the first, second, third, and fourth quartile of the TyG index, respectively. Meanwhile, the prevalence of sarcopenia was 44.3, 14.8, 3.5, and 0.9% in the first, second, third, and fourth quartile of the TyG-BMI index, respectively. The prevalence of sarcopenia decreased precipitously with increasing quartiles of the TyG-BMI index ($p < 0.05$).

Associations between TyG index and TyG-BMI index and sarcopenia

Binary logistic regression analysis was done to assess the associations between TyG and TyG-BMI and sarcopenia. As shown in Table 2, in the univariate analysis, the TyG and TyG-BMI index were significantly inversely associated with sarcopenia (odds ratio [OR]: 0.486; 95% confidence interval [CI]: 0.290–0.815; $p = 0.006$) and (OR: 0.948; 95% CI: 0.935–0.961; $p < 0.001$) respectively. In multivariate analysis, the TyG and TyG-BMI index were inversely associated with sarcopenia (OR: 0.492; 95% CI: 0.256–0.944; $p = 0.033$) and (OR: 0.948; 95% CI: 0.934–0.962; $p < 0.001$) respectively after adjusting for confounding variables including age, ALB, Cr, UA, TC, ALT, and AST. As shown in Table 3, in the unadjusted and fully adjusted models, fourth quartile of TyG-BMI showed significantly decreased OR of 0.011 (95% CI: 0.001–0.082; $p < 0.001$) and 0.009 (95% CI: 0.001–0.072, $p < 0.001$) respectively for sarcopenia with respect to its first quartile value. However, there was no significant difference between the quartile 1–4 of TyG index and sarcopenia after rectifying the covariates.

The ROC curves for the TyG index and TyG-BMI index

The ROC curves were performed to check the diagnostic value of TyG index and TyG-BMI index for sarcopenia. The area under the curve (AUC) for TyG index in the diagnosis of sarcopenia was 0.598 (95% CI: 0.529–0.666; $p = 0.008$), and at a cut-off point set at 8.88, the sensitivity was 84.9% and specificity was 35.9%. The AUC for TyG-BMI index was 0.858 (95% CI: 0.816–0.899; $p < 0.001$), and at a cut-off point set at 192.92, the sensitivity was 82.2% and specificity was 74.2% (Figure 3).

Discussion

The current study revealed that sarcopenic women had lower levels of ALB, ALT and UA but higher level of HDL-C, which was consistent with some previous results (18–20). Recent studies have suggested that excessively high HDL-C levels may negatively affect the survival of older adults (21, 22). This negative effect may be stronger than the protective effect of normal HDL-C levels (22, 23). UA, an important antioxidant, was positively associated with muscle mass (24), muscle strength (25) and nutrition score (26). ALT, a transaminase enzyme found in the liver and muscle tissue, has been revealed to be positively associated with muscle mass (27) and

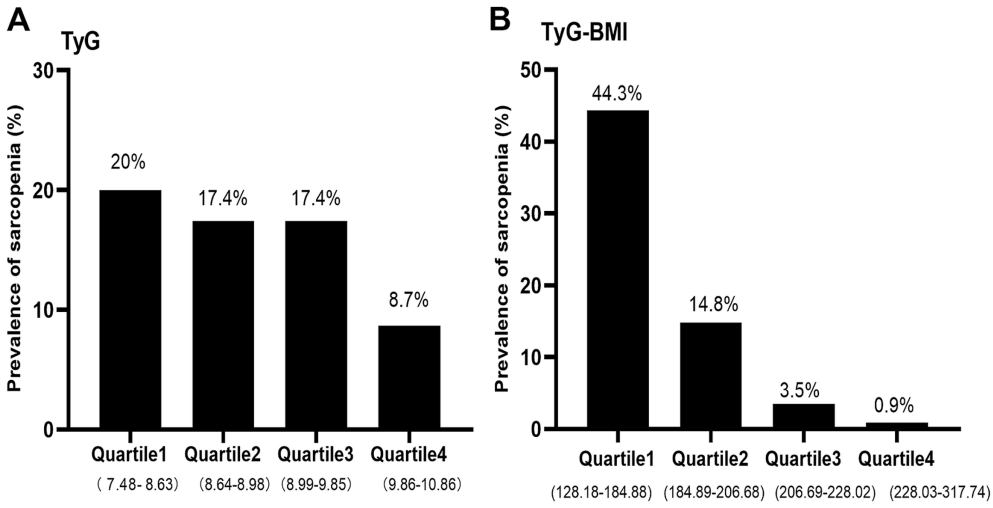

FIGURE 2
The prevalence of sarcopenia by quartiles of TyG **(A)** and TyG-BMI **(B)** index in non-diabetic, postmenopausal women. TyG, triglyceride-glucose; TyG-BMI, triglyceride glucose–body mass index.

TABLE 2 Binary logistic regression analysis of the independent factors for sarcopenia (TyG and TyG-BMI as continuous variables).

Variable	Model 1		Model 2		Model 3	
	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value
TyG	0.486 (0.290–0.815)	0.006	0.470 (0.269–0.822)	0.008	0.492 (0.256–0.944)	0.033
TyG-BMI	0.948 (0.935–0.961)	<0.001	0.947 (0.934–0.961)	<0.001	0.948 (0.934–0.962)	<0.001

TyG, triglyceride-glucose; TyG-BMI, triglyceride glucose–body mass index; OR, odds ratio; 95% CI, 95% confidence interval; ALB, albumin; Cr, creatinine; UA, uric acid; TC, total cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase. Model 1: not adjusted for any variable; Model 2: adjusted for age; Model 3: adjusted for age, ALB, Cr, UA, TC, ALT, and AST. Statistically significant ($p < 0.05$).

TABLE 3 Binary logistic regression analysis of the independent factors for sarcopenia (TyG and TyG-BMI as categorical variables).

Variable	Model 1		Model 2		Model 3	
	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value
TyG						
Quartile 1	Reference		Reference		Reference	
Quartile 2	0.842 (0.433–1.636)	0.612	0.785 (0.389–1.584)	0.499	0.784 (0.374–1.646)	0.520
Quartile 3	0.842 (0.433–1.636)	0.612	0.721 (0.357–1.455)	0.361	0.711 (0.328–1.540)	0.387
Quartile 4	0.381 (0.172–0.842)	0.017	0.411 (0.180–0.935)	0.034	0.461 (0.181–1.169)	0.103
p for trend		0.027		0.039		0.113
TyG-BMI						
Quartile 1	Reference		Reference		Reference	
Quartile 2	0.218 (0.116–0.410)	<0.001	0.197 (0.098–0.394)	<0.001	0.218 (0.105–0.454)	<0.001
Quartile 3	0.045 (0.016–0.131)	<0.001	0.037 (0.012–0.113)	<0.001	0.035 (0.011–0.114)	<0.001
Quartile 4	0.011 (0.001–0.082)	<0.001	0.009 (0.001–0.069)	<0.001	0.009 (0.001–0.072)	<0.001
p for trend		<0.001		<0.001		<0.001

TyG, triglyceride-glucose; TyG-BMI, triglyceride glucose–body mass index; OR, odds ratio; 95% CI, 95% confidence interval; ALB, albumin; Cr: creatinine; UA, uric acid; TC, total cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase. Model 1: not adjusted for any variable; Model 2: adjusted for age; Model 3: adjusted for age, ALB, Cr, UA, TC, ALT, and AST. Statistically significant ($p < 0.05$).

negatively with sarcopenia (28) and mortality risk (27). ALB is an indicator of protein metabolic balance and nutrient status. In a meta-analysis, low ALB levels were found to be associated with sarcopenia among older individuals (29).

The BMI is a composite index that reflects body composition, including fat, muscle, and bone tissue. The relationship between BMI and skeletal muscle mass has been intensively studied in different populations but results have been inconsistent. Some studies concluded that higher

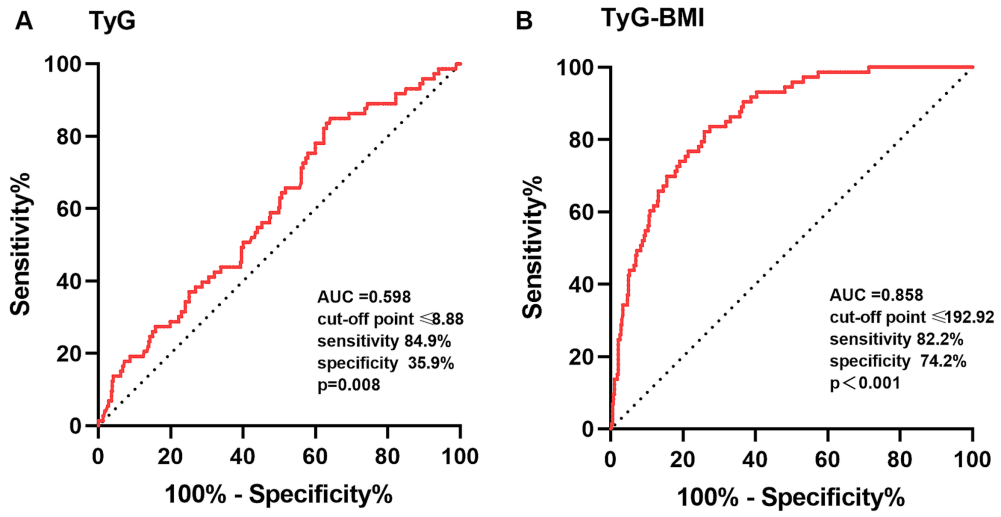

FIGURE 3
The ROC curves of TyG **(A)** and TyG-BMI **(B)** index for the diagnosis of sarcopenia. TyG, triglyceride-glucose; TyG-BMI, triglyceride glucose–body mass index; ROC, receiver operating characteristic; AUC, area under the curve. The comparison of the AUC was performed by a *p*-value<0.05.

BMI were significantly related to loss of skeletal muscle and sarcopenia (30, 31) due to systemic inflammation and insulin resistance (32). Quite the reverse, other studies showed that higher BMI protected against sarcopenia in older adults (33, 34) and patients with diabetes (35). Zhang et al. (36) conducted a 4 years of follow-up study in older Chinese populations (females with a mean age of 67 ± 6 in baseline) and found that BMI was positively associated with muscle mass and negatively associated with sarcopenia. In agreement with these studies, our study (females with a mean age of 64 ± 7 years) also showed that BMI is remarkably lower in non-diabetic postmenopausal individuals with sarcopenia with respect to non-sarcopenia group. Overweight may be more beneficial than lower level of normal weight in older-old and vulnerable older people (37). Possible mechanism by which obesity protected muscle mass was as follows. Firstly, skeletal muscle stimulation was increased as a higher level of muscle mass was observed in the obese group (33). Over time, there is less loss of muscle mass owing to the greater load required for exercise (33). Secondly, as hormone levels change with aging, the proportion of fat increases in older individuals (33). Adipose tissue is an essential endocrine organ that regulates hormonal levels like estrogen (34), and abdominal fat in women stores high levels of sex hormones and positively affects skeletal muscle mass (33, 34).

The IR was regarded as a prominent risk factor for sarcopenia or low muscle mass (4, 38). The TyG index is determined as a convenient, cost-effective and reliable indicator for identifying individuals with IR and metabolic syndrome (MetS) in the general population. Higher TyG index has been recently revealed as a potential marker with sarcopenia and low muscle mass in particular individuals (15, 39). TyG-BMI index, which combines serum triglycerides, fasting plasma glucose, and obesity status, is considered more reliable than TyG index for the identification of IR (12). We conducted the study to investigate the association of TyG and TyG-BMI index with muscle mass and sarcopenia in non-diabetic, postmenopausal individuals. Contrary to some previous studies, the present study demonstrated that the TyG index and TyG-BMI index were positively associated with RSMI, and negatively associated with risk of sarcopenia. Similar findings have also been described by Kim et al. (11), in which increased TyG index and BMI were inversely correlated with the incidence of sarcopenia. Nevertheless, the AUCs of TyG index yielded by the ROC curve analysis were only 0.598 for females, which limits its value for early detection of sarcopenia in clinical applications. TyG-BMI index, which incorporates TyG and BMI, appear to be a more useful predictor of sarcopenia than single TyG index for postmenopausal women, with AUC of 0.858.

One explanation was that there was a threshold or saturation effect for TyG index or TyG-BMI index as an indicator of IR. Currently, it was thought that the TyG index ≥8.7 may indicate the presence of IR, regardless of age and sex. Lee et al. reported that non-diabetic and normal weight Korea women with the TyG index ≥8.73 was at a higher risk of metabolic syndrome (40). Similarly, Li et al. (41) reported that the TyG index ≥8.7 was associated with metabolic syndrome in middle-aged and older Chinese, which implied that values above this range were connected with IR. Zhu et al. (42) reported that the TyG index >8.73 and the TyG-BMI index >222.45, respectively, was associated with poor glycemic control in Chinese older individuals with T2DM, which also suggested that it might be related to the development of IR. In our study, the major values of TyG index and TyG-BMI index were less than 8.7 and 222 respectively, which did not meet the threshold for IR. Consist with our results, Hu et al. (16) found that TyG index was positively correlated with SMI in female subjects when the TyG index was <9.

TyG-BMI index—which incorporates fasting blood glucose, serum triglyceride levels and BMI—is also a nutritional indicator within a certain threshold in addition to indicating IR. Nutritional supplementation is required to maintain or improve muscle quality and muscle strength. The present study found that women with sarcopenia showed lower TG than women with non-sarcopenia, however, the difference was not statistically significant. Similar result was found by Yin et al. (19) and Hu et al. (16). Several follow-up studies in Chinese older adults found decreased TG level seem to be associated with increased all-cause mortality risk, which suggests the clinical importance of revisiting the concept of "the lower the better" for the oldest old (23, 43). Lower TG values may be a consequence of poor health status associated with sarcopenia (18). In addition, our

investigation also revealed that women with sarcopenia showed dramatically decreased FPG level compared with non-sarcopenia group. Previous study reported that higher glycemic values (glycosylated hemoglobin Alc, HbA1c ≥ 8.5%) in older patients with diabetes were associated with lower muscle mass and muscle quality (44). However, no correlation was found between hyperglycemia and muscle loss in diabetic patients with a mean HbA1c value of 7.0% (45). This discrepancy may be owing to different TG and glycemic concentrations in the study population. Hyperlipidemia and hyperglycemia are widely recognized as risk factors for sarcopenia, nonetheless, the levels of lipid and glucose in our study population are in the normal range. There were no glucotoxic or lipotoxic effects exist but the nutritive supportive effects on muscle synthesis by proper glucose and lipid control.

A relatively higher TyG index is usually accompanied by higher insulin level. Insulin has anabolic effects on muscle mass and protein metabolism in non-insulin resistant men and women (46). In situations where amino acids (AAs) delivery is unchanged, supraphysiological concentrations of insulin are needed to achieve skeletal muscle anabolism (47). Meanwhile, insulin also plays a clear role in reducing muscle protein breakdown independent of AA availability (47). In a cross-sectional study of older Chinese females aged over 50 years, lower-insulin was associated with sarcopenia and risk factors for low muscle mass (19). Sugimoto et al. (48) and Bouchi et al. (49) have also reported that the insulin treatment could improve muscle mass and gait speed and attenuate the progression of sarcopenia in T2DM. All of these results suggested that insulin at the upper limit of the normal range was necessary to maintain muscle mass and function.

In brief, our findings suggested that reasonable weight management should be promoted to guard against muscle damage caused by low body weight in non-diabetic postmenopausal women without apparent IR. Moreover, the risk of sarcopenia caused by hypolipidemia should be considered in patients who require long-term use of lipid-lowering agents. This study provided evidence to support the prevention and treatment of sarcopenia in non-diabetic postmenopausal women.

Strengths and limitations

There were both strengths and limitations to the current study. To our knowledge, this is the first study to investigate the relationship between TyG index and TyG-BMI index and sarcopenia in Chinese non-diabetic, postmenopausal women. However, this study had some limitations. First, it was a cross-sectional design, which need future longitudinal studies to conclude the cause-and-effect relationship. Second, as a one-center study with a relatively small sample size conducted in Chinese middle-aged and older females, it is unclear whether the findings are applicable to individuals of other ethnicities or in other countries. Therefore, multi-center and multi-ethnic studies with larger sample sizes should be performed to validate conclusions' reproducibility. Third, some potential covariates, such as dietary intake and supplements, were not examined. The influence of potential unmeasured confounders on the effect of the study indicators on sarcopenia risk needs to be investigated in future studies.

Conclusion

This cross-sectional study confirmed that there seemed no obvious IR existed in non-diabetic Chinese postmenopausal women. As nutritional indicators, higher TyG index and TyG-BMI index protected against sarcopenia in non-diabetic middle-aged and older females without IR status. Moreover, the TyG-BMI index, with both sensitivity and specificity, was a simple, robust surrogate and cost-efficient biomarker to predict the risk of sarcopenia in non-diabetic Chinese middle-aged and older women. In addition, the current study revealed that sarcopenic individuals had lower values of BMI, ALB, TG, FPG, ALT, and UA, that is to say, individuals with sarcopenia had relative malnutrition. Given this, it may be pertinent to clinically assess nutritional status in older individuals who are at risk for sarcopenia, so as to provide adequate nutritional profile to preserve muscle mass and physical function.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by The Ethics Committee of Hebei Medical University Third Hospital (No. ke2023-080-1 and ke2021-045-1). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

ML: Conceptualization, Formal analysis, Investigation, Methodology, Writing – original draft. YL: Investigation, Writing – original draft. LG: Investigation, Methodology, Writing – original draft. YZ: Formal analysis, Writing – original draft. LC: Formal analysis, Writing – original draft. YW: Conceptualization, Methodology, Writing – review & editing. WZ: Conceptualization, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Integrating frailty interventions into existing care models: a comprehensive approach to enhancing patient outcomes in chronic disease management

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Frailty syndrome (FS) is a complex and multifaceted condition commonly observed in old adults patients with chronic diseases, often accompanied by cognitive impairments. This review explores the integration of frailty interventions into existing care models to improve patient outcomes, focusing on four key areas. First, it emphasizes the importance of comprehensive assessment tools to identify frailty and cognitive impairments early, facilitating targeted care planning. Second, it highlights the value of personalized interventions, such as dietary modifications, exercise programs, and cognitive training, tailored to individual patient needs and preferences. Third, the review underscores the critical role of multidisciplinary care teams in providing holistic and coordinated care, leveraging the expertise of diverse healthcare professionals. Finally, it examines the potential of technological innovations and caregiver support systems in enhancing frailty management and addressing the challenges posed by cognitive impairments. By integrating these approaches, this review presents a patient-centered framework aimed at mitigating the impact of frailty and improving long-term outcomes. The findings emphasize the need for a unified strategy that combines personalized care, interdisciplinary collaboration, and technological advancements to address the multifaceted challenges of frailty in chronic disease management.

KEYWORDS

frailty syndrome, chronic disease management, cognitive impairment, personalized interventions, multidisciplinary care, polypharmacy, caregiver support, telemedicine

1 Introduction

As healthcare systems face the growing burden of chronic diseases, particularly in aging populations, the need for innovative approaches to enhance patient outcomes becomes increasingly urgent (1). Frailty syndrome (FS) is a clinical condition characterized by diminished strength, endurance, and physiological function, resulting in increased vulnerability to adverse health outcomes, particularly in older adults (2). It is a multidimensional concept encompassing physical, cognitive, social, psychological, and nutritional domains, each of which contributes to the complexity of frailty (3). Physical frailty, commonly linked to sarcopenia, manifests as reduced muscle strength and mobility (4). Cognitive frailty combines physical decline with impairments such as memory deficits or diminished executive function (5). Social frailty stems from limited networks and support systems, exacerbating isolation and its associated health risks (6). Psychological frailty includes conditions such as depression or anxiety, which further compound physical and cognitive challenges, while nutritional frailty is characterized by malnutrition or vitamin deficiencies, undermining overall resilience and recovery (7).

FS is closely associated with chronic diseases, such as cardiovascular disease, diabetes, chronic obstructive pulmonary disease (COPD), and osteoporosis (8, 9). Evidence indicates that frailty exacerbates the progression and outcomes of these conditions. For instance, patients with heart failure and frailty experience higher rates of hospitalization and mortality, while individuals with diabetes and frailty often face complications linked to poor glycemic control and comorbidities (7, 10, 11). Epidemiological studies show that frailty affects approximately range between 4.0 and 59.1% of community-dwelling older adults (12), with prevalence increasing to around 50% in those with chronic illnesses (8, 13). Furthermore, the burden of frailty is particularly pronounced in regions with limited access to healthcare and higher rates of multimorbidity (14). Due to global population aging, the prevalence of frailty is projected to rise significantly in the coming decades, posing substantial challenges for healthcare systems worldwide.

Frailty not only diminishes the quality of life for patients but also contributes to increased healthcare utilization and costs due to frequent hospitalizations, prolonged recovery periods, and higher rates of morbidity (15).

Integrating frailty interventions into existing care models offers a promising pathway to address these challenges. Frailty interventions, including targeted assessments, physical rehabilitation, nutritional support, and coordinated care strategies, have the potential to improve patient resilience, reduce the progression of chronic conditions, and enhance overall health outcomes. By embedding these interventions into the fabric of current healthcare delivery systems, it is possible to create a more holistic, patient-centered approach that proactively manages both chronic diseases and their associated risks (16). This paper aims to explore the comprehensive integration of frailty interventions into established care models, examining the evidence supporting their efficacy, the challenges of implementation, and the potential benefits for patients with chronic diseases. In doing so, it highlights the importance of a multidisciplinary approach, where clinicians, caregivers, and healthcare systems work in concert to deliver personalized, preventative care that enhances patient quality of life and reduces the strain on healthcare resources.

2 Methods

The search database was PubMed. The retrieval time node ranged from January 2014 to December 2024. The retrieval strategy was optimized with the use of Boolean logical operators. The search terms included a combination of MeSH terms and keywords, such as: "old adults frailty," "frailty in older adults," "frail old adults populations," "frailty and heart failure," "frailty and multimorbidity," "multimorbidity and heart failure," "frailty and cardiovascular diseases," "frailty and diabetes," and "frailty and cognitive impairment." This comprehensive search strategy ensured that the review covered both historical and recent studies, offering a full spectrum of evidence on frailty and its patients with chronic diseases.

All retrieved citations were imported into Zotero for reference management and deduplication. The inclusion criteria were defined as follows: (1) papers covered a population of adults; (2) the paper's main topic was frailty and frality in the context of chronic diseases (e.g., multimorbidity, heart failure, diabetes, or cognitive impairment); (3) the full text was accessible; and (4) the paper was published in English.

2.1 Challenges in interventions for patients with cognitive impairments

2.1.1 Understanding and communication

Interventions designed to mitigate the effects of FS include surgical options (e.g., ventricular assist devices, heart transplantation) and non-surgical options (e.g., exercise and nutritional interventions) (17). Non-surgical interventions can be complex, however. As people with HF and FS often have co-occurring cognitive impairment, non-surgical interventions may be challenging (18, 19). For example, exercise interventions include a multitude of activities designed to improve balance, strength and mobility (1, 4). Clients with HF and FS may have difficulty recalling the exercises and the frequency at which they should be performed due to memory deficits (18, 20). Dietary restrictions focus on increased intake of macronutrients such as proteins and micronutrients such as vitamin D and iron (17, 21). Clients with cognitive impairment may fail to recall nutritional recommendations or understand the association between the nutritional recommendations and improved management of HF and FS (18, 20). Furthermore, as comorbid illness is common in HF, people might have to balance several nutritional recommendations simultaneously (e.g., low-salt and diabetic diet) (17, 18, 20). People with cognitive impairment may have difficulty coordinating multiple nutritional recommendations. Clinicians must be vigilant with frail HF clients that demonstrate cognitive impairment to ensure maximum benefit from non-surgical interventions.

2.1.2 Self-management and monitoring challenges

Cognitive impairments range from mild cognitive decline to severe dementia, and can be classified into subjective cognitive decline (SCD), mild cognitive impairment (MCI), and dementia (22). SCD involves perceived memory issues without measurable deficits, while MCI presents detectable cognitive impairment but allows for some level of independence. In dementia, self-care abilities are typically lost entirely, and patients become dependent on external support for basic

daily activities. Cognitive impairments are linked to various negative health outcomes, including poor disease management, increased hospitalization rates, a higher risk of adverse events, and reduced quality of life (23).

Cognitive impairment often accompanies chronic conditions, and act as a "hidden disability" which complicates treatment and patient care (24). Certain chronic illnesses such as cerebrovascular disorders, malignancies, metabolic diseases like diabetes are linked to higher risks of cognitive decline (25). Elderly individuals are at greater risk for cognitive impairments, which frequently coexist with chronic conditions, further complicating the management of their illnesses (26). For example, in heart failure patients, cognitive decline increases the risk of hospitalization and adverse events, while in cases of chronic pain, adherence to pain management regimens becomes more challenging (27, 28).

Self-care plays a pivotal role in managing chronic conditions and maintain overall health. It refers to the actions individuals take to maintain health, monitor illness, and manage ongoing medical conditions Effective self-care leads to better outcomes, fewer hospitalizations, and improved quality of life (29). However, cognitive impairments significantly reduce self-care capacity, particularly in dementia, where memory lapses, symptom misrecognition, and difficulty following health regimens lead to worsened outcomes (30, 31). Self-care requires intact cognitive functions, such as the ability to learn, perceive, and interpret symptoms—skills that are often compromised in patients with cognitive impairments. Without these abilities, patients struggle to recognize symptoms, follow treatment plans, or make timely health decisions (32).

Patients with cognitive impairments face distinct challenges in self-care based on the severity of their condition. For example, in individuals with type 2 diabetes, cognitive impairment increases the risk of non-adherence to prescribed therapies, leading to poor disease control and preventable complications (33). Although patients outwardly struggle with managing their chronic illnesses, the underlying cognitive impairment often goes unnoticed (34). This hidden aspect complicates treatment, as patients may fail to adhere to medication schedules, manage dietary restrictions, or attend follow-up appointments, not due to a lack of effort, but because of unrecognized cognitive limitations (35). Even in early-stage dementia, self-care challenges such as medication adherence and hygiene management remain significant (36). Moreover, cognitive impairments undermine critical aspects of self-care, including the ability to learn new information and interpret symptoms, thereby complicating the management of complex chronic conditions (37).

Addressing the challenges of self-care in cognitively impaired patients is complex due to overlapping factors. Traditional assessment tools, such as neuroimaging and cognitive tests, measure cognitive decline but do not effectively capture self-care capacity. Self-report tools are often unreliable due to memory deficits. Digital tools, including online cognitive training programs, offer a valuable complement to traditional methods, providing real-time, more accurate assessments of cognitive function and self-care abilities (36).

Several interventions have been found effective in improving self-care in cognitively impaired patients. Cognitive training programs, for instance, have been shown to help patients with MCI maintain self-care abilities. More severe impairments, such as dementia, necessitate caregiver-supported care to ensure that daily tasks and health decisions are effectively managed (38). Despite progress, there is still a gap in fully understanding self-care behaviors in patients with cognitive impairments, which highlights the need for further research. Technologies, such as mobile apps and wearables, offer potential support for patients by assisting with medication reminders and other self-management tasks (38).

Self-efficacy, or the belief in one's ability to manage health, plays a critical role as a mediator of self-care behaviors. Patients with higher self-efficacy are more likely to engage in effective self-care practice (39, 40). Programs focusing on memory and attention exercises have been shown to improve self-care behaviors in patients with mild cognitive impairment (41). In this regard, caregiver-supported interventions are particularly valuable, as caregivers can provide the structure needed to improve adherence to treatment regimens (42). Additionally, patients with strong social support networks tend to experience better self-care outcomes, while those living alone are at higher risk for poor disease management and faster cognitive decline (26).

As cognitive impairment progresses, patients require increasing levels of supervision (43). Caregivers, whether family members or professional healthcare workers, play a crucial role in ensuring that these patients receive appropriate care, from administering medications to assisting with daily tasks (44). Constant supervision improves safety and helps prevent dangerous situations such as falls, medication errors, or malnutrition. However, the burden on caregivers can be significant, often resulting in caregiver burnout, which affects the quality of care and the overall health of both the patient and caregiver (45). Increased support from healthcare providers is crucial to help alleviate this burden and ensure the safety and well-being of both parties (46).

Denial of cognitive decline poses a significant barrier to timely intervention, particularly in early dementia (47). This denial delays diagnosis and reduces the effectiveness of interventions that could slow disease progression and deteriorate quality of life (48). Furthermore, social isolation can exacerbate both cognitive decline and physical health issues. The absence of regular social interaction often accelerates the progression of conditions like dementia, while also increasing depression and reducing physical activity levels (49, 50). This cycle of social withdrawal and declining health highlights the importance of integrated interventions that address both the social and cognitive needs of patients, as well as early detection and ongoing support from healthcare providers. Cognitive impairment greatly hinders effective self-care in chronic conditions, often leading to poor health outcomes. Early detection, tailored interventions, and constant caregiver support are essential for improving patient care and quality of life.

Memory and Task Execution Problem. The prevalence of cognitive decline, particularly dementia, increases exponentially with advancing age. Cognitive impairment occurs in over 40% of older people (51). FS is very common in people with dementia (50.8 to 91.8%). People with FS use polypharmacy much more often (52). Older people often have chronic diseases that require a strict therapeutic regimen (e.g., arterial hypertension). The level of adherence to antihypertensive treatment, depending on age, takes the shape of a U curve. The most adherent to the therapy are patients around 65 years of age, while the lowest level of adherence to therapeutic recommendations is observed in patients aged 30 and > 80 years (53). Cognitive impairment significantly affects adherence to therapeutic recommendations. A study of 436 older people showed that 48.6% of them had poor medication compliance. The presence of cognitive impairment increased the risk of medication non-adherence by almost 3-fold

(OR = 3.95; 95% CI: 2.63–5.92, $p < 0.001$) (54). High medication concerns among frail older patients inhibit their medication adherence (52). In older people using polypharmacy, a number of adverse situations related to treatment may occur: (1) neglecting to fill a prescription for a recommended medicine; (2) skipping at least one dose; (3) taking the wrong medication; (4) taking an excessive amount of a prescribed medication; (5) stopping a medication too soon; (6) incorrect use of medical equipment like inhalers and syringes, and (7) taking damaged, expired, or improperly stored medicines. All of this makes older people require more detailed instructions for using medications and educational and behavioral interventions that improve adherence to treatment (55). Self-management interventions and electronic health interventions might be effective in improving medication adherence for older people with multimorbidity (56). Cognitive-based behavior change techniques are effective interventions eliciting improvements in medication adherence that are likely to be greater than the behavioral and educational interventions largely used in current practice (57). Whenever possible, combined treatment should be recommended, e.g., in patients with hypertension and lipid disorders (one tablet containing two antihypertensive drugs and one tablet containing a statin and ezetimibe - this allows for a 50% reduction in the number of tablets). The use of combined treatment improves adherence and is associated with a lower risk of adverse effects (58). In people with cognitive disorders and FS, cognitive training is very beneficial. It has been shown that cognitive training significantly benefits overall cognitive function, delayed memory, orientation, attention, and language skills in aged patients with cognitive impairment (59). This may significantly translate into a greater likelihood of compliance with medical recommendations regarding the treatment of chronic diseases. Increasing the level of adherence is very important because it has been shown that good adherence was associated with a 21% reduction in long-term mortality risk in comparison to medication non-adherence (adjusted hazard ratio 0.79, 95% CI 0.63, 0.98) (54). In old adults patients with polypharmacy, the medications used should be assessed as well as the patient. It is recommended that in the context of the medications used: (1) assess drug–drug, drug-disease interactions; (2) identify non-beneficial therapy and simplify; and (3) identify high risk therapy and reconsider, while in the context of the patient assessment, it is recommended to: (1) medication reconciliation (are all medications indicated?); (2) assess adherence and each barrier; (3) adjust for elimination avoiding toxicity (clearance, metabolism); (4) identify functional status, deficits and readdress medication resources; and (5) identify goals of care and adjust for medications that are consistent (60).

2.2 Selected chronic diseases and frailty

Hafızoğlu et al. recently presented the results of an interesting study in which they analyzed which indicator related to the measure of multimorbidity is most appropriate in the context of frailty. The relationships between four multimorbidity indices (CIRS-G, ACCI, GIC, ICED) and three scales related to the severity of frailty (FRAIL, CFS, TFI) were analyzed. CIRS-G was found to be the most appropriate indicator (61). The CIRS-G scale includes an assessment of the following systems or organs for chronic diseases: cardiovascular system, circulatory system, respiratory system, vision, hearing, pharynx and larynx, digestive system, excretory system, musculoskeletal system, nervous system and endocrine system (62). It is therefore worth paying attention to the relationship between selected most common chronic diseases from the above-mentioned areas and frailty syndrome.

Recently, results from a study were presented that evaluated the impact of a 12-week nursing intervention based on the integration theory of health behavior change in frail older adults with type 2 diabetes mellitus. Among other things, significant improvement was observed in frailty level ($p = 0.006$) and quality of life (all $p < 0.001$) (63). Similarly, according to a recently published systematic review, the exercise, diet, and education programs were shown to reduce the risk of frailty or progression to more advanced stages in patients with type 2 diabetes and frailty (64).

The relationship between frailty syndrome and arterial hypertension is worse. Both hypertension increases the risk of frailty and frailty syndrome has a negative impact on hypertension management (65). Nevertheless, it remains questionable to what extent antihypertensive treatment has a beneficial effect on frailty status in this population (66).

According to recently published results, not only overt cardiovascular disease, but even signs of subclinical dysfunction or damage, such as increased levels of natriuretic peptides or cardiac troponin, translate into a significant increase in the risk of frailty syndrome (67). According to a study by Zhong et al., different cardiovascular therapeutic interventions may have different effects depending on frailty status (68). Ijaz et al. drew attention to the multitude of interventions to improve the frailty status in patients with cardiovascular diseases (classified into physical, pharmacological, cognitive, nutritional, and psychosocial interventions) and the need to individualize the management depending on the needs of a specific patient (69).

Pulmonary rehabilitation has been shown to have a positive effect on handgrip strength in patients with COPD. Interestingly, positive handgrip strength delta was associated with higher baseline quality of life scores (70). Importantly, exercise intervention may also have a positive impact in frail patients hospitalized due to COPD exacerbation as an adjunct to standard treatment (71).

In a study by Yamashita et al., it was found that proactive foot care can be of significant importance in reducing the risk of fractures in frail older individuals (72). This is particularly important for patients at increased risk of fractures, such as those with osteoporosis.

2.3 Nutrition and physical activity

2.3.1 Nutritional status assessment

Poor nutritional status is regarded as one of the key, modifiable clinical markers of FS. Comprehensive nutritional assessment plays an essential role in the holistic approach to chronic disease management, aiming to improve patient outcomes and quality of life (73). Malnutrition is associated with FS, and screening and early identification of malnutrition can help prevent the progression of disability, particularly among older adults (74). Tools for assessing malnutrition include body mass index (BMI), anthropometric measures, biochemical markers, and nutritional risk assessment scales (75). While BMI is widely used, it may be unreliable due to confounding factors such as edema or lack of specificity regarding

body composition. Furthermore, when used as a single marker, BMI may fail to capture the phenotypic presentation of FS, often characterized by unintentional weight loss exceeding 4.5 kg or ≥ 5% (76).

For malnutrition risk assessment, tools like the Mini Nutritional Assessment (MNA) and Nutritional Risk Score 2002 (NRS-2002) are available. The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends the standardized criteria of the Global Leadership Initiative on Malnutrition (GLIM), involving a two-step procedure: initial screening with any validated tool, e.g., NRS-2002, SGA, or MNA, followed by comprehensive diagnostics including phenotypic and etiologic criteria along with the assessment of malnutrition severity (77). In comprehensive assessment, both quantitative and qualitative parameters should be considered. Many studies describe an inverse relationship between protein intake and the prevalence of FS, although evidence remains heterogeneous. Sarcopenia, associated with the loss of muscle mass and strength, is considered a critical component of frailty and appears linked to protein intake (78, 79). Not only daily protein intake but also its distribution throughout the day impacts the incidence of FS (74).

In a meta-analysis by Coelho et al., high dietary protein intake was inversely correlated with frailty status in older adults (80). In a subsequent study by the same author, although protein intake was not significantly associated with frailty in older adults, it was noted that protein sources could play a key role in the development of frailty, with higher intake associated with lower FS risk (80). Thus, assessing protein intake quality by a qualified dietitian, along with identifying potential deficiencies, can aid in identifying patients at risk. A 24-h dietary recall or a nutritional interview may assist in evaluating intake.

Individuals with FS generally exhibit lower intake of energy, protein, fiber, vitamin D, vitamin C, folate, and B vitamins compared to non-FS individuals. Thus, screening for potential deficiencies is a key component. Vitamin D deficiency, for example, is associated with poorer physical function and may predict physical disability in older adults (81). The relationship between vitamin D levels and frailty has been evaluated in numerous studies. Observational data from Hirani et al. indicated that low vitamin D levels are independently associated with frailty (82). Wang et al. confirmed that lower levels of vitamin D (RR: −3.22, 95% CI: −3.86 to 2.59, $p < 0.001$) may be associated with frailty. Notably, vitamin D is essential for maintaining calcium homeostasis and bone health, as low calcium levels may contribute to FS through mechanisms affecting muscle strength and bone density. Additionally, prevalent osteoporosis and sarcopenia in older adults increase susceptibility to frailty, disability, hospitalization, and decreased quality of life (83). Similar deficiencies may include other vitamins, such as vitamin B6 and folate, as well as trace elements and minerals (84, 85). A cross-sectional study among women aged 70–80 participating in the Women's Health and Aging Studies I and II demonstrated a higher likelihood of low trace element levels among FS patients (86). Therefore, conducting a thorough nutritional analysis and managing FS-specific nutrient deficiencies provide a multifaceted approach and should be implemented in this patient group.

2.3.2 Nutritional interventions

Multimodal interventions, including effective nutritional strategies, should aim to mitigate adverse health effects and reduce FS severity (87). Nutritional support should be personalized, with nutrient intake adjusted based on a thorough analysis of nutritional status, physical activity level, and patient condition.

A key component of nutritional intervention is meeting the patient's energy requirements. Low energy intake commonly affects older individuals, particularly between the fourth and seventh decades of life (84, 88). A study by Kim et al. demonstrated that protein-energy supplementation among old adults patients with low socioeconomic status slows functional decline (89). Therefore, exploring interventions to stimulate food intake is crucial. This could include strategies such as meal fortification, additional snacks, dietary fortification (particularly with oral nutritional supplements, ONS), enhancing palatability, ensuring high energy density, and providing suitable meal forms (88). ONS can be beneficial for improving nutritional status, especially when combined with multifactorial interventions (89, 90). Proper identification and treatment of unintentional weight loss and malnutrition are recommended among FS patients (91).

Among older adults, protein intake may be insufficient, leading to reduced physical performance and poorer clinical outcomes. Evidence supports the effect of protein supplementation on clinical outcomes. Although the optimal protein intake for older adults remains undefined, a study by Vellas et al. found that women consuming over 1.2 g/kg body weight/day of protein experienced fewer health issues compared to those consuming 0.8 g/kg/day (84, 92). In research by Bonnefoy et al., protein-energy supplementation did not significantly increase lean body mass but improved muscle strength in older FS patients (93). Protein intake for older adults should be tailored to nutritional status, physical activity level, health condition, and tolerance, ranging from 1.0–1.2 g/kg body weight in healthy individuals to up to 2 g/kg in severely malnourished or acutely ill patients (94, 95). Another potential intervention includes even distribution of protein across meals. Loenneke et al. demonstrated that consuming meals with 30–45 g of protein per meal was associated with greater strength and leg lean mass (96). Though further research is needed, even protein distribution throughout the day may enhance not only patient outcomes but also total daily protein intake. Additional studies on the quantity, quality, and types of protein intake, as well as new strategies addressing impaired muscle protein synthesis related to the inflammatory state in FS, are needed (84).

There is a significant gap in the literature on the effects of mineral and vitamin supplementation in FS patients, and results from current studies remain inconclusive (97). Some evidence suggests that micronutrient supplementation may improve nutritional status and functional capacity, though its impact on frailty is unclear, as highlighted by a recent systematic review (98). While vitamin D intake is critical, particularly among older adults due to its association with bone health, muscle strength, and function, the impact of supplementation on FS remains uncertain (91). A meta-analysis by Muir et al. found that daily vitamin D supplementation (20–25 μg) was associated with improved gait speed and muscle strength in older adults (99). Furthermore, old adults individuals living with FS may have reduced sun exposure, indicating a need for vitamin D supplementation (100).

A critical element in the personalization of dietary intervention is recognizing that a patient's diet may not meet basic nutrient needs, including minerals and vitamins, and deficiencies may indirectly affect clinical outcomes. Consulting a qualified dietitian and conducting a detailed nutritional assessment may help identify issues and provide appropriate nutritional support. Selecting the right dietary model and

nutritional intervention should involve a thorough dietary and health history and be tailored individually to the patient's condition. The nutrition plan should consider patient preferences, cultural aspects, potential allergies, and the need to address any nutrient deficiencies. Figure 1 provides a summary of dietary interventions used in FS.

2.3.3 Physical exercise programs

Low levels of physical activity are much more common in people with FS (101). It is worth emphasizing that people with higher levels of physical activity are characterized by a 37% lower risk of developing FS (ES 0.63, 95% CI: 0.52–0.77) (102). Physical activity/exercise is considered one of the main strategies to counteract frailty-related physical impairment in the old adults (103). There are various physical exercise programs available to improve the condition of patients with FS. One of them is the VIVIFRAIL Multicomponent Physical Exercise Program to Prevent Frailty and the Risk of Falls, which includes seven different exercises: (1) walking (when muscle strength allows, otherwise it should be improved first; walking time should be gradually extended depending on individual capabilities); (2) squeeze a ball (12 repetitions, 3 sets); (3) lift a bottle (12 repetitions, 3 sets); (4) extend legs using a ballested ankle brace (12 repetitions, 3 sets); (5) standing up from a chair with the help of a

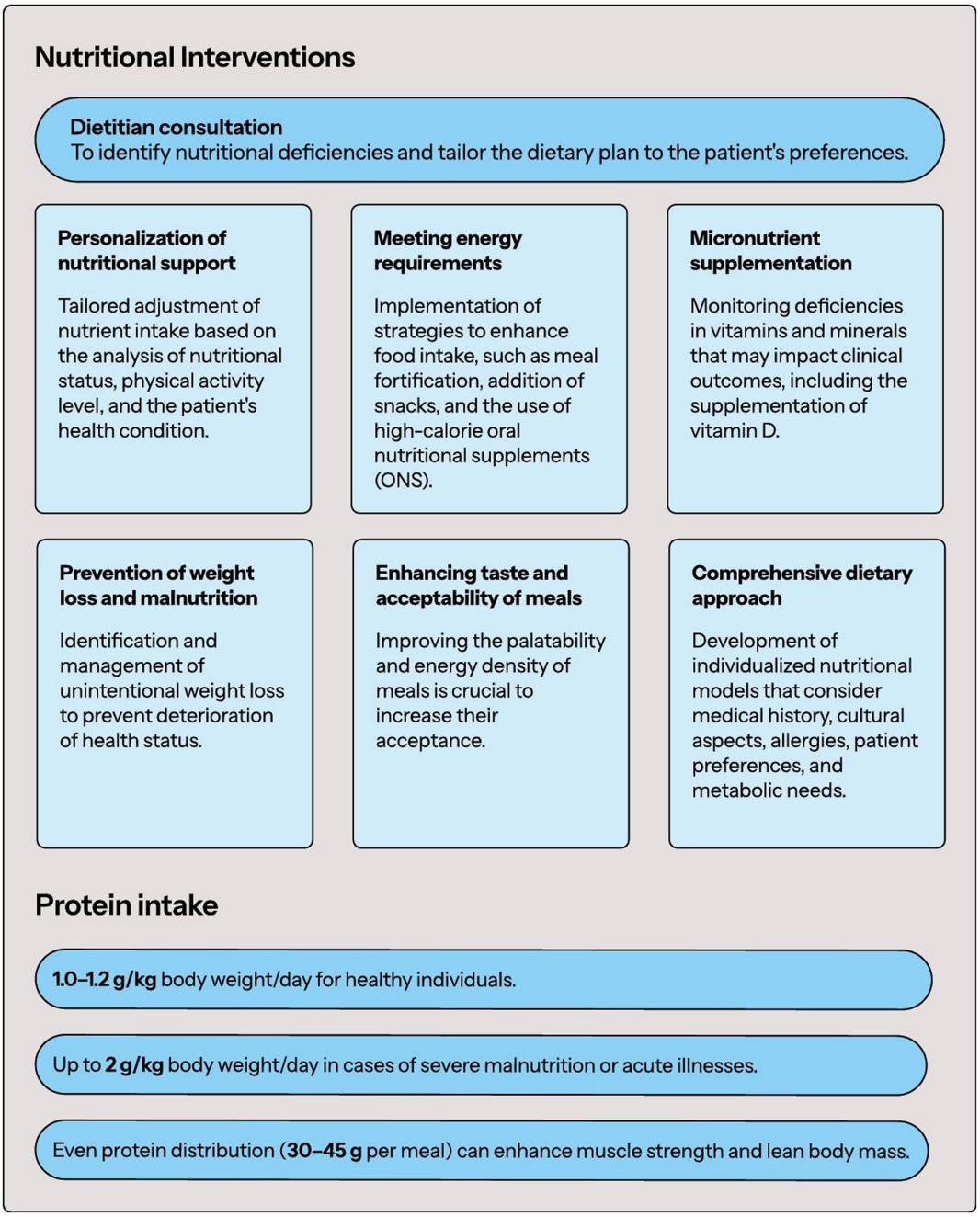

FIGURE 1
Nutritional interventions in FS.

companion (12 repetitions, 3 sets); walking with feet on a line (15 paces, 3 sets); and (6) strange arms (3 repetitions, 3 sets; maintain 10 s). Example of exercise wheels for each functional level that include the exercises, series and repetitions that should be done every week (104). It should be emphasized that the progressive decrease in intrinsic capacity and functional reserve (ultimately leading to disability) can be significantly slowed down at the pre-frailty and frailty stages if appropriate therapeutic intervention is undertaken (a program of appropriate physical exercises is implemented). At the disability stage, the reversibility of the lost intrinsic capacity and functional reserve is much more difficult to achieve (103). The extraordinary importance of physical activity in people with FS is emphasized by the fact that physical activity might partly compensate for the greater mortality risk associated with frailty in old age (105). In the context of implementing a program of appropriate physical exercises, special attention should be paid to people who were less physically active earlier in life. The risk of FS in such people is significantly higher, therefore such people require special education and physical activity programs to reduce this risk (105). Maintaining an appropriate level of physical activity in people with FS is also associated with a significant improvement in global cognition and mental flexibility (106). FS is one of the most important factors increasing the risk of falls in the old adults (107). Physical activity, in addition to its beneficial effect on longevity and cognitive functions, contributes to reducing the risk of falls in frailty patients (risk ratio 0.66; 95% CI: 0.52–0.84) (108). It should be emphasized that physical activity, in order to be as beneficial as possible in people with FS, should be regular, involve different parts of the body and should be adapted to the individual capabilities of the patient. The problem of sarcopenia in patients with FS cannot be forgotten. Sarcopenia and frailty co-occurred in 12.1% of the patients. The co-occurrence of FS and sarcopenia worsens the prognosis of patients (109). It has been shown that physical activity contributes to reducing the risk of both FS and sarcopenia in the old adults (110, 111). Physical activity reduces the risk of sarcopenia in the old adults by up to 50% (110). First-line therapy for the management of frailty should include a multi-component physical activity program with a resistance-based training component (strong recommendation) (112). Of course, it is best if the health intervention in a person with FS includes not only physical activity, but also cognitive exercises, improving eating habits (including proper hydration and supplementation of possible deficiencies) (113). Figure 2 provides a Physical Exercise Programs in FS.

3 Role of caregivers and multidisciplinary team

3.1 Role of caregivers: caregiver burden and support: challenges associated with caring for patients, and the need for education and support for caregivers

Informal caregivers play a pivotal role in supporting patients with chronic illnesses, ensuring that these individuals adhere to treatment plans and prevent complications (114). Their contribution is particularly important when patients must adhere to complex treatment regimens and require assistance with daily care (29). Involving caregivers in daily self-care tasks is critical to preventing poor health outcomes and improving the patient's overall well-being. Active caregiver involvement has been shown to significantly reduce symptom burden and enhance chronic illness management (115).

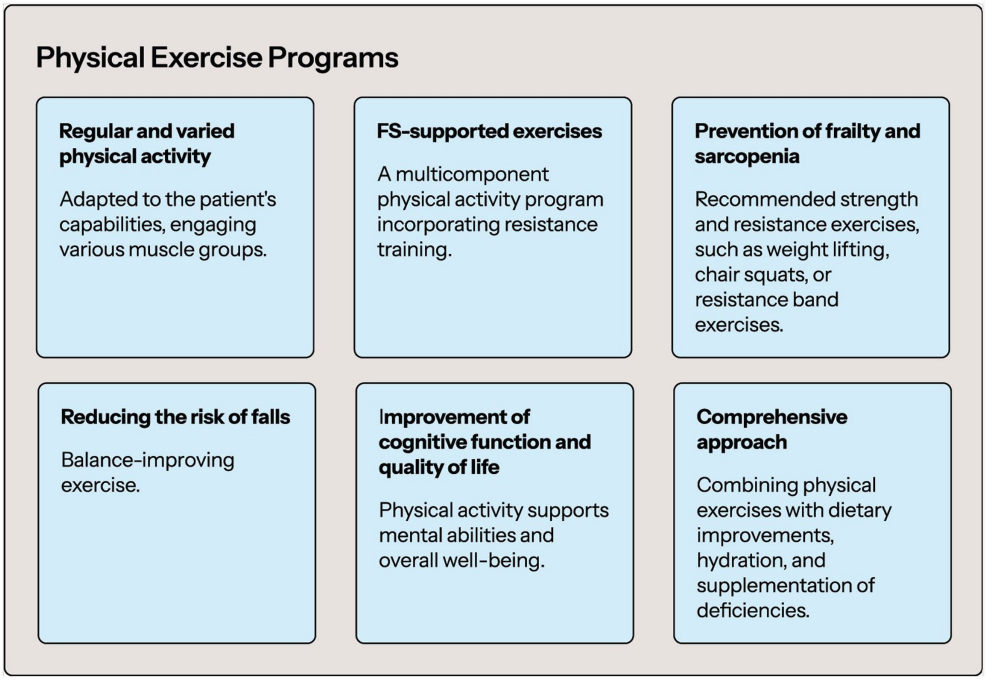

FIGURE 2
Physical exercise programs summary.

The role of caregivers becomes even more important when cognitive impairment, such as dementia, coexist with the chronic illness. In these cases, caregivers must deal not only with the physical demands of care, but also with the difficulties determined by cognitive dysfunctions, such as memory lapses, and confusion, which create, above others, significant challenges in adhering to the treatment plan (116). There is evidence that caregivers of patients with dementia are often more stressed than those caring for other illnesses and face greater emotional and mental distress, which can lead to higher rates of depression and anxiety (117).

Caregiving preparedness is another key factor in ensuring effective care. Preparedness refers to the caregiver's perceived ability to handle the emotional and physical responsibilities of caregiving. Studies have shown that caregivers who are better prepared for their roles suffer less from anxiety and depression, which enhances their ability to provide consistent, high-quality care (118). In addition, caregiver confidence, the belief in their own ability to provide effective care, is critical. Confident caregivers are more likely to contribute positively to patient self-care, maintain patient stability, and respond appropriately to health deterioration (118). Therefore, promoting caregiver preparedness and confidence is critical to improving both patient and caregiver outcomes.

Despite the positive aspects the caregiving experience entails (e.g., personal growth and role satisfaction) (119), caregivers face numerous challenges, particularly when caring for patients with both chronic illnesses and cognitive impairment (120). Physical strain is common, as tasks such as assisting with mobility and personal care can lead to chronic pain and fatigue (121). Emotionally, caregivers experience increased stress due to the psychological and behavioral symptoms associated with conditions such as dementia (122). Over time, these stressors can lead to burnout, which not only affects the well-being of the caregiver but also diminishes the quality of care provided to the patient (45).

Other factors that hinder the caregiving process include social isolation, loneliness, and financial burden. Due to the demanding nature of their responsibilities and tasks, caregivers often become isolated and without social support (123). This lack of connection exacerbates emotional fatigue and contributes to a decline in mental health. Additionally, financial burden is common, as many caregivers reduce their working hours or quit their job entirely to provide care (124). These cumulative challenges highlight the need for comprehensive support systems to reduce caregiver burden.

To improve the health outcomes of both members of the dyad, enhancing caregiver contribution and preparedness is essential, particularly for patients with cognitive impairment. Educational programs (i.e., courses on medication management, emotional support initiatives, and digital platforms such as mobile apps and virtual reality) have proven effective in improving caregiver outcomes (125), especially those that equip caregivers with the skills needed to manage medical tasks and symptoms. Respite care is another strategy that could be implemented because it offers temporary relief from their duties and reduces the risk of burnout (126). Access to mental health services and support groups is equally important, providing emotional validation and helping caregivers cope with the stresses of their role (127, 128). For caregivers who are alone, tailored interventions, such as mindful meditation, computer-based applications, and music therapy, are essential to help reduce feelings of isolation and loneliness. These interventions not only provide emotional relief but also enhance caregivers' ability to cope with the stress (128). Caregivers are essential for managing chronic illnesses, particularly when cognitive impairment is present. Improving caregiver preparedness and providing comprehensive support systems are essential to ensuring high-quality care for patients while safeguarding the caregiver well-being.

3.2 Multidisciplinary team

An old adults person with FS is characterized by very complex problems that significantly worsen their quality of life. A meta-analysis covering over 54 thousand old adults people showed that frailty and pre-frailty, according to a multidimensional definition, are common in older people affecting, respectively, one person over four and one over three (129). Frailty, geriatric syndromes, disability and multimorbidity often overlap and increase the risk of mortality and poorer quality of life (130). It is worth emphasizing that the prevalence of multimorbidity in frail individuals was 72% (131). FS covers several domains of human functioning: (1) Physical condition: sarcopenia, physical insufficiency, oral dysfunction, malnutrition; (2) Mental condition: cognitive impairment, dementia, depression; (3) Social condition: social isolation, living alone, lack of social support, economic deprivation (132). This indicates the need for comprehensive, multi-specialist and holistic care for these patients. Optimal care for a patient with FS should be multidirectional and include: (1) improving eating habits, supplementing deficiencies, proper hydration (an important role for a clinical dietitian); (2) broad education regarding, among others, the need to follow therapeutic recommendations (an important role for a nurse); (3) improving physical condition and implementing a program of individually adapted physical exercises (an important role for a physiotherapist-rehabilitator); (4) assessing the need for and monitoring the medications used (an important role for a doctor and pharmacist); (5) controlling comorbidities (an important role for doctors of various specialties); (6) assessing health needs (an important role for a geriatrician) and (7) psychological support (an important role for a psychologist) (133). The following scales are extremely helpful in assessing the severity of the FS and specifying individual needs: (1) Multidimentional frailty assessment: Frailty Index of Cumulative Deficits; Edmonton Frail Scale; Tilburg Frailty Indicator; Groningen Frailty Indicator; Kihon Checlist; (2) Cognitive impairment assessment: Mini-Mental State Examination; Montreal Cognitive Assessment; Mini-Cog; Short Portable Mental Status Questionnaire; (3) Physical Frailty Assessment: Fried's Frailty Phenotype; FRAIL Scale; Frailty Screening Index; Clinical Frailty Scale; Short Physical Performance Battery; (4) Social frailty assessment: Makizako's Questionnaire; Garre-Olmo's Questionnaire; Teo's Questionnaire; Lubben Social Network (132). An extremely important aspect is to increase the awareness of medical personnel and families of older people with FS about their individual health needs. Table 1 presents a summary of comprehensive, multi-specialist, and holistic care for frail patients.

4 Medication management and safety

4.1 Medication management

Polypharmacy is one of the critical issues that is discussed in the context of FS, especially in the old adults. There is no one commonly

TABLE 1 Summary of comprehensive care for the frail patient (132).

Comprehensive, multi-specialist and holistic care for frailty patients	
Task	Key person
Improving eating habits, supplementing deficiencies, proper hydration	Clinical dietitian
Broad education regarding, among others, the need to follow therapeutic recommendations	Nurse
Improving physical condition and implementing a program of individually adapted physical exercises	Physiotherapist-rehabilitator
Assessing the need for and monitoring the medications used	Doctor and pharmacist
Controlling comorbidities	Doctors of various specialties
Assessing health needs	Geriatrician
Psychological support	Psychologist
Helpful tools for assessing patients with frailty syndrome	
1. Multidimentional frailty assessment: Frailty Index of Cumulative Deficits; Edmonton Frail Scale; Tilburg Frailty Indicator; Groningen Frailty Indicator; Kihon Checlist; 2. Cognitive impairment assessment: Mini-Mental State Examination; Montreal Cognitive Assessment; Mini-Cog; Short Portable Mental Status Questionnaire; 3. Physical Frailty Assessment: Fried's Frailty Phenotype; FRAIL Scale; Frailty Screening Index; Clinical Frailty Scale; Short Physical Performance Battery; 4. Social frailty assessment: Makizako's Questionnaire; Garre-Olmo's Questionnaire; Teo's Questionnaire; Lubben Social Network.	

accepted definition of polypharmacy. According to the report prepared by the World Health Organization, polypharmacy can be defined as "the concurrent use of multiple medications" and it is "often defined as the routine use of five or more medications" (134). Definitions available in the literature are differentiated. Some definitions include only a number of drugs, or in combination with the duration of therapy, or even in a health care setting (135). Although polypharmacy can be partially considered as a consequence of multimorbidity (136) and, therefore, difficult to avoid in order to treat simultaneously multiple chronic diseases in accordance with current medical knowledge, the literature discusses it as a significant problem, mainly in the old adults, and a risk factor that can lead to further decreases in health state (137, 138). There is no doubt that the list of medications used by a patient must be regularly verified to avoid inappropriate prescribing (139). The risk of iatrogenic complications increases especially in patients with FS (140), who are characterized by reduced physiological reserves and reduced resistance to stress factors (141).

Gutiérrez-Valencia presented the results of a systematic-review including 25 observational studies. Most publications included in the analysis (16 of 18 cross-sectional studies and five of seven longitudinal analyses) indicate a significant association between polypharmacy and frailty (142). It is worth noting that different conclusions from individual studies may result from different definitions of polypharmacy. Some studies indicate that the use of six or more medications may be considered a good predictor of an increased risk of developing FS (143, 144).

Polypharmacy was shown to increase risk of frailty in different populations.

A strong positive correlation was found between frailty status (assessed by Clinical Frailty Scale) and polypharmacy (defined as taking at least five drugs) in 298 primary care patients aged at least 65 years (145). Similarly, a significant association between polypharmacy and risk of frailty was shown on a group of 124 hospitalized patients (146). Hemodialysis patients taking more than 11 drugs has significantly higher risk for frailty occurrence at baseline than patients taking fewer than eight drugs (OR 1.54, 95% CI 1.05–2.26). Moreover, the risk for frailty development in two-year observation is significantly higher in patients taking more than 11 medications than patients taking fewer than eight drugs (sub-distribution HR 2.15, 95% CI 1.32–3.48) (147). Significant impact of number of medications on frailty occurrence was shown also in other study involving 388 Japanese hemodialysis patients (OR = 1.351, 95% CI 1.163–1.570) (148). In the group of patients with HIV infection, each additional chronic non-antiretroviral medication is associated with a 4% increase in risk of having an adapted frailty-related phenotype domain (OR 1.04; 95% CI 1.03, 1.05) (149). According to another study, in older patients with HIV infection analogous value of increase in the risk of frailty diagnosis was assessed at the level of 6% (adjusted OR 1.06, 95% CI 0.002–0.11, $p = 0.04$) (150). In a retrospective study including older critical care patients, the patient median Clinical Frailty Scale was shown to increase by 1 with polypharmacy classification increments ($p < 0.001$) (151). Taking at least eight medications was found to be significantly associated with frailty in patients with blood neoplasms (adjusted OR 2.82, 95% CI 1.92–4.17) (152). Pre-frailty and frailty was associated with increased risk of polypharmacy also in patients with history of cancer (OR 8.26, 95% CI 1.74–39.2) (153). Polypharmacy is associated not only with frailty but also pre-frailty. In an observational, cross-sectional study in which 201 patients participated, individuals with frailty and pre-frailty were shown to have increased risk for polypharmacy when compared to patients with no features of frailty (OR 2.36, CI 95% 1.05–5.37; $p = 0.04$) (154). In community dwelling older adults in Europe, a prevalence of polypharmacy was found to be three times more prevalent in frail patients and two times in pre-frail individuals, when compared with patients without features of FS (155).

According to a meta-analysis prepared by Wang et al., polypharmacy was shown to be a significant risk factor for FS development (RR 1.72, 95% CI 1.17–2.28, $p < 0.001$ in studies taking into consideration a precise number of drugs; RR 1.49, 95% CI 1.39–1.60, $p < 0.001$ in studies not taking into consideration a precise number of drugs). Interestingly, in the same meta-analysis such factors as age, stroke, and cardiac diseases, were not shown to be significantly associated with increased risk of frailty (156). In a meta-analysis of 13 studies it was found that patients with frailty and heart failure are characterized by a higher risk of polypharmacy (OR 1.87, 95% CI 1.72–2.04, $p < 0.01$) compared to patients without frailty

(157). Similarly, a meta-analysis of 12 studies shown polypharmacy to be a risk factor for frailty in patients with chronic obstructive pulmonary disease (158).

There are also data showing that polypharmacy may also be associated with worse outcomes. A large analysis conducted using the Korean National Health Insurance claims follow-up data from 2002 to 2017 on a group of 55,228 people found that polypharmacy was associated with increased risk for all-cause mortality, hospitalization, and emergency room visits among older colorectal cancer survivors (159). Similarly, polypharmacy is associated with worse prognosis in patients with severe aortic stenosis (160). Interestingly, de Breij et al. found polypharmacy to be an explanatory factor of the association between frailty and mortality in the old adults (161).

Taking into consideration significant impact of polypharmacy to frailty development, it can be expected that deprescribing could be beneficial in patients predisposed to FS. Deprescribing could be defined as the process of medication withdrawal or dose reduction to correct or prevent medication-related complications (162). Ibrahim et al. presented the results of a systematic review of studies aimed to assess the impact of deprescribing among old adults with frailty. Although the authors emphasized that there is a paucity of research in this area, included studies suggest that deprescribing can lead to important benefits (163). Dinarvand et al. described the critical role of the cooperation of geriatricians and pharmacists in deprescribing in the frail ageing population treated due to diabetes and hypertension. Moreover, necessity for further trials has been emphasized (164).

5 Patient safety

In the case of people with FS, ensuring the patient's safety by avoiding factors that may predispose to adverse events is particularly important. In the context of pharmacotherapy, it is crucial to avoid drugs that may contribute to reduced skeletal muscle tone and excessive sleepiness what is associated with increased risk of falls. Medicament with anticholinergic properties were shown to be independently associated with increased of falls in frail (adjusted OR = 3.84, 95% CI 1.48–9.93, $p = 0.006$) and pre-frail participants (OR = 2.71, 95% CI 1.25–5.89, $p = 0.012$), but not in robust subjects (165). According to the analysis based on data from the National Health Interview and Examination Survey for Adults 2008–2011, use of psychotropic drugs is independently associated with an increased risk of falls (OR 1.64, 95% CI 1.14–2.37), especially for selective serotonin reuptake inhibitors (OR 6.22, 95% CI 2.28–17.0) (166).

In the case of old adults people with frailty, it may be necessary to modify the pharmacological treatment of chronic diseases, especially in the field of drugs affecting blood pressure and antidiabetic drugs. The proportion between the expected benefits of excellent control of chronic diseases and the risk associated with pharmacotherapy should be considered in the context of life expectancy. In many cases, it is beneficial to adopt less restrictive therapeutic goals for the control of chronic diseases to avoid complications of possible hypotension and hypoglycemia what also can lead to increased risk of falls as well as decline in cognitive function (167). Therefore, in the case of old adults people with severe FS (at least 5 points on the Clinical Frailty Scale), a satisfactory level of diabetes control can be considered as HbA1c < 8.5%. If it is necessary to reduce the amount of medication used, it is worth considering first discontinuing insulin and sulfonylurea derivatives, i.e., drugs that can lead to hypoglycemia (168). In a large study by Nguyen et al. (11,400 participants, including 25.7% frail), it was confirmed that intensive glucose-lowering and antihypertensive treatments may be less beneficial in patients with frailty (169). However, it should be emphasized that the research results regarding the relationship between chronic disease control and the risk–benefit balance in frail patients are not fully unambiguous. O'Donoghue et al. emphasized that different frailty classifications may be associated with different prognostic implications for the purpose of the application of hypertension management guidelines (170). On the other hand, according to Wang et al. patients with frailty should be treated similarly to other patients, because there is no significant difference in benefits from intensive blood pressure control without an increased risk of serious adverse events (171).

6 Tailoring interventions to individual needs

6.1 Personalization of interventions

Personalization of interventions is now universally recognized as a key aspect in the treatment of frailty (172). These come primarily through personalized care planning (PCP), which is considered in effect an intervention with which known positive outcomes are associated (173). In fact, PCP is associated to a greater control of the own health and to an improvement of physical and mental health (173) and, in particular, to an increased willingness to adhere to healthy behaviors (174). As described above, frailty has a multidimensional nature. In this perspective, a multi-domain assessment, leaded by a multidisciplinary team, is mandatory and should be the first step in order to counteract frailty (175). In addition to the pharmacological approach, it is well known in the literature that exercise, nutritional interventions and cognitive support represent effective approaches in treating frailty, even being able to reverse its course toward healthy and active aging (176). The following chapters will elaborate on these types of interventions.

6.2 Tailored exercise programs: adapting exercise programs to the individual capabilities of the patient

Recent systematic reviews with meta-analysis agree that exercise brings benefits in counteracting frailty (102, 177). It remains unclear what type of exercise is optimal for the frail old adults, although variation of interventions seems to bring benefits (177). However, the first step should be an in-depth assessment of the persons' abilities and capabilities. This assessment should include, but should not be limited to: skeletal muscle, respiratory system, cardiovascular system and endocrine system (103). This assessment will allow the person to be framed in order to identify the types of physical activity that can be done safely. It is important to remember how, in addition to these fundamental considerations that are a guarantee of safety for the person, the choice of intervention should also be made respecting the

person's preferences, so as to have his or her greater involvement in the course of treatment and, consequently, greater adherence (173). However, with full respect for the person's abilities and preferences, group physical activity should be the first choice. In fact, there is evidence that group physical activity leads to benefits not only in the physical domain, but also in the social domain, with a decrease in loneliness' levels and social isolation (178). Exercise should embrace all the facets, with a part dedicated to muscle strengthening, a resistance training and an aerobic component (177); nevertheless, also programs based on flexibility activities, such as yoga (179) and Tai Chi (102) brings benefits. Individual physical activity should follow the same principles, with the advantage of a wider possibility of customizing the intervention, and with the opportunity to be home-based.

6.3 Customized nutritional interventions: personalized nutritional interventions that address individual needs

In order to optimize exercise-related outcomes, a careful assessment of nutritional status is essential (180). In fact, it is well-documented that in older adults both energy and protein intakes are lower than required (181), thereby hindering the benefits of exercise. In this perspective, this type of assessment should be carried out in conjunction with exercise assessment. It is recommended that healthy individuals consume protein at a level of 1.0–1.2 g/kg of body weight (182). In the case of older adults who are malnourished or diagnosed with a chronic disease that may increase the risk of malnutrition, the intake should range from 1.2 to 1.5 g of protein/kg of body weight. Patients suffering from acute illness or severe malnutrition may require a protein intake of up to 2 g/kg of body weight. The amount should be individually adjusted based on nutritional status, physical activity levels, disease condition, and tolerance (94, 95). The recommended daily energy intake for older adults is 30 kcal per kilogram of body weight; however, this value should be individually adjusted based on nutritional status, physical activity level, and health condition (94, 183).

6.4 Cognitive and mental health support: cognitive and psychological support tailored to the patient

Physical activity shows benefits also in cognitive functioning (184). Additionally, supplementing physical activity with cognitive stimuli, such as dual-task exercises, showed important improvements in cognitive outcomes (185). However, more specific and focused interventions are needed. Cognitive stimulation, defined as an intervention designed to encourage participation in tasks aimed at improving social and cognitive functioning, is reported to be effective (186). These interventions are also based on activities of daily living (ADLs), in order to enhance the applicability of the trained abilities in the context of everyday life (186). Regarding well-being and anxiety, animal-assisted activities (especially dogs) are very effective, with perceived improvement in quality of life, emotional state and positive emotions (186). Finally, virtual and augmented reality are a promising intervention in counteracting frailty (187, 188).

6.5 Monitoring and feedback

As it turns out, interventions to counter frailty are complex. Especially in the early stages, adherence to the individualized intervention program can be challenged by the many difficulties encountered by the person (189). Nevertheless, following the Stages of Change Theory (190), even after passing the initial stages of the new behavior (in this case, the individualized intervention program), the so-called "maintenance" stage is threatened by the absence of tangible and immediate results, unlike the initial stage, where these are present (191). In this perspective, monitoring (included self-monitoring) and feedback are fundamental.

6.6 Real-time monitoring and adjustments

During exercise, real-time monitoring is critical. It is first and foremost a safety issue, especially in people with advanced frailty. For this reason, it is important that the activity be carried out in the presence of personnel trained to intervene in case of sudden health problems. However, this is not possible when the exercise is carried out independently by the person at his or her home. While educating people and their caregivers in early recognition of signs and symptoms of exercise-related health issues is still crucial (192), Information and communication technologies (ICTs) are very useful. In particular, physical activity seems to particularly benefits of an ICT component in the intervention, both in the monitoring (180) and in its conduction (193), which allows a more immediate capacity of adjustments when needed. The adoption of ICTs allows the monitoring of progress with a great accuracy, also with the possibility to collect data useful to tailor the intervention to the person. Nevertheless, these data can also represent a "biofeedback" for the person, allowing to adapt in real-time the activities.

6.7 Education and support: patient education and empowerment

Education is fundamental when dealing with frailty, and it should be included in the training programs of the involved health personnel (194). There is evidence that lifestyle is strictly related to FS (195), thus often requiring it to be modified. The changes to behavior required are often numerous and complex for the person, and this aspect should be considered in advanced care planning (196). However, although patient education is an integral and fundamental part of advance care planning, there is evidence that it is still underestimated (197). In particular, patient empowerment is very effective, since it can enhance patient understanding, deal with alleged obstacles, and develop patient confidence and communication abilities (198).

6.8 Educating patients to better manage FS

As we can see, education still plays a pivotal role in the management of FS. In this context, there is evidence that it is fundamental in building a body of knowledge on the topic, and it contributes in gathering confidence, skills and abilities that lead to the adoption of a healthy lifestyle (199). A recent systematic review showed that the educational

areas of intervention mainly concern empowerment, self-care, and health promotion (199). Nevertheless, self-management behaviors, especially those related to physical activity, such as body weight maintaining and increasing frequent physical exercise, are associated with an improvement of the frailty condition (200).

6.9 Empowerment through technology: using technology to support patient autonomy

First of all, there is undoubtedly a role for computer-based and online versions of frailty education interventions, given current advancements in digital technology (199). ICTs give not only the ability to monitor the person at home, but also to communicate with them in real time and in a timely manner. In this perspective, it is possible to schedule and perform telemedicine and telenursing visits; to collect relevant information on the frailty status through home automation and sensors (e.g., weight loss, gait speed); and to monitor exercise (including providing live feedback) (201). Figure 3 figure synthesizes the key elements of dietary, exercise, and cognitive strategies, along with their assessment, modifications, and follow-up processes, offering practical guidance for implementation in clinical practice.

7 Conclusion and future trends

Integrating personalized interventions into the management of FS in patients with chronic diseases, especially those with cognitive impairments, is essential for improving patient outcomes. However, current strategies face significant limitations. First, a frequent underdiagnosis of cognitive impairments remains, resulting in inadequate care planning. Nevertheless, the lack of standardized protocols, insufficient resources such as specialized personnel and technological tools, and inadequate support for overburdened caregivers further hinder the widespread adoption of individualized care. Additionally, challenges arise from addressing the diverse cultural, social, and socioeconomic backgrounds of patients, limited training among healthcare professionals in recognizing and managing FS and cognitive impairments, ethical and legal considerations related to patient autonomy and consent, financial constraints, and technological barriers among patients and caregivers.

To address these challenges, future research should focus on several key areas. Enhancing the diagnosis of cognitive impairments through more effective screening and assessment tools will enable more accurate care planning. Development of standardized guidelines for more tailored interventions is essential to unify practices across different settings. Improving resource accessibility, including specialized personnel and technological tools, and providing comprehensive support programs for caregivers will help alleviate their burden. Additionally, ensuring that

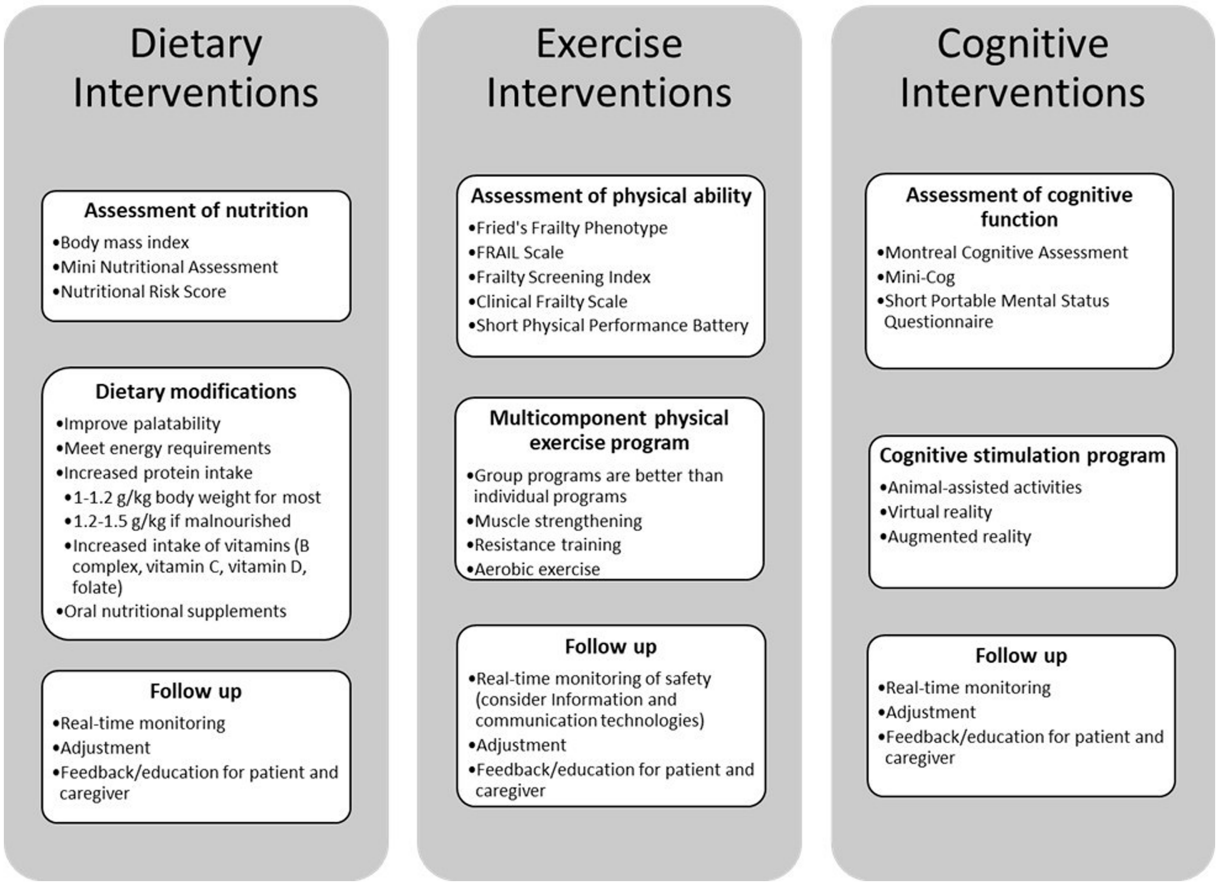

FIGURE 3
Comprehensive roadmap for integrating frailty interventions into existing care models.

interventions are culturally competent and adaptable will better serve patients from diverse backgrounds. Validating technological innovations, such as AI-based monitoring systems and wearable devices, can offer new opportunities for patient care. Promoting interdisciplinary collaboration among healthcare professionals will foster holistic approaches in patient management. Actively involving patients in their own care through education and shared decision-making improves medication adherence and related clinical outcomes, especially in patients treated with polypharmacotherapy. Integrating community resources can provide additional support, while advocating for healthcare policy reforms can address systemic issues such as funding and resource allocation. Empowering patients through education and self-management strategies can significantly improve their quality of life and promote autonomy in this vulnerable population. Therefore, ongoing research and innovation are pivotal for developing effective, scalable, and adaptable strategies that meet the needs of diverse patient populations.

Author contributions

IU: Conceptualization, Funding acquisition, Methodology, Supervision, Writing – original draft, Writing – review & editing. KF: Writing – original draft, Writing – review & editing. PI: Writing – original draft, Writing – review & editing. AK: Writing – original draft, Writing – review & editing. SS: Writing – original draft, Writing – review & editing. CM: Writing – original draft, Writing – review & editing. GJ: Writing – original draft, Writing – review & editing. YL: Writing – original draft, Writing – review & editing. DJ: Writing – original draft, Writing – review & editing. AR-P: Writing – original draft, Writing – review & editing. MC: Conceptualization, Supervision, Writing – original draft, Writing – review & editing. BU: Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that Gen AI was used in the creation of this manuscript. Generative AI was used specifically to assist in translating the manuscript into English, utilizing OpenAI's ChatGPT. The authors take full responsibility for this use.

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The impact of chronic diseases and lifestyle on sarcopenia risk in older adults: a population-based longitudinal study

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Background: Sarcopenia, characterized by the gradual decline of muscle mass and strength, seriously affects the health and mobility of older adults. The purpose of this study is to investigate the risk factors for sarcopenia, particularly the relationship between chronic diseases and lifestyle factors in individuals aged 60 and over.

Methods: This study used data from the Longitudinal Study on Health and Retirement in China (CHARLS) collected in 2011 and 2015. All eligible participants were classified according to the standards established by the Asian Sarcopenia Working Group in 2019. The evaluation of sarcopenia was based on a comprehensive score across five dimensions: strength, assistance in walking, rise from a chair, climb stairs, and falls. A multivariate logistic regression model was employed to explore the risk factors for sarcopenia.

Results: The risk of sarcopenia is significantly influenced by multiple factors. Key findings include the association between past drinking and an increased risk of sarcopenia (HR = 2.198, 95% CI: 1.072–4.560, $p < 0.05$), indicating that individuals with a history of drinking have more than twice the risk of sarcopenia compared to non-drinkers. Chronic diseases such as stroke were also associated with a significantly elevated risk (HR = 3.137, 95% CI: 1.128–8.721, $p < 0.05$). Conversely, participation in social activities significantly reduced the risk of sarcopenia (HR = 0.482, 95% CI: 0.265–0.876, $p < 0.05$). A three-piece spline regression model revealed a nonlinear relationship between physical activity and the risk of sarcopenia, characterized by an initial decline in risk followed by an increase as physical activity levels rose. Moderate-intensity physical activity reduced the risk of sarcopenia by approximately 35% (HR ≈ 0.65). However, high-intensity physical activity led to a rebound in risk, increasing the likelihood of sarcopenia relative to moderate activity. Similarly, adequate sleep duration was associated with a reduced risk of sarcopenia, whereas excessive sleep counteracted this benefit.

Conclusion: The findings underscore the critical role of lifestyle modifications and balanced physical activity in mitigating the risk of sarcopenia among older adults. Implementing targeted interventions for high-risk groups is essential to reduce the incidence of sarcopenia.

KEYWORDS

sarcopenia, chronic diseases, lifestyle, CHARLS, national longitudinal study

1 Introduction

Sarcopenia is a progressive and pervasive skeletal muscle disease, which is associated with an increased risk of physical disability, decreased quality of life, and mortality in older adults (1). It is marked by declines in muscle mass, strength, and physical function, with its prevalence increasing significantly with age (2). This condition has become a major public health problem due to its direct impact on the functional independence of older adults (3).

Recently, various risk factors for sarcopenia have been identified, including age, gender, lifestyle, and the presence of comorbidities (4–6). Demographic and social factors, such as age, gender, education level, lifestyle, and health status, have also been found to affect the risk of sarcopenia (7–10). Habits such as smoking, drinking, and participation in social activities, for example, have been shown to play a role in altering muscle strength and physical function in older adults (11, 12). The risk is further exacerbated by chronic diseases, including heart and Pulmonary diseases (13, 14). In China, where the population is rapidly aging, sarcopenia has emerged as a major health issue (15, 16).

In recent years, significant progress has been made in sarcopenia research, particularly in regions such as Europe. These studies have explored the prevalence trends, risk factors, and intervention strategies for sarcopenia, guided by standardized diagnostic criteria (1). However, their findings are challenging to directly apply to China, a country characterized by a vast population, rapid aging, and notable differences in socioeconomic structures, lifestyles, nutritional patterns, and chronic disease burdens. The unique context of the Chinese older adult population profoundly influences sarcopenia risk and mechanisms. For instance, older adults in rural areas may face higher risks of sarcopenia due to lower economic levels and insufficient nutritional intake, while urban older adult individuals may be more vulnerable to sedentary behavior and social isolation (17–19). Moreover, the high prevalence of chronic diseases such as diabetes, cardiovascular diseases, and liver diseases in China may involve complex interactions with sarcopenia, which remain underexplored in current research (20–25).

To address these gaps, this study utilizes data from the China Health and Retirement Longitudinal Study (CHARLS) to systematically examine the prevalence of sarcopenia and its major influencing factors among the Chinese older adult population. CHARLS is a nationally representative longitudinal survey that includes a diverse sample of urban and rural residents across China, with detailed data on socioeconomic status, chronic disease profiles, physical activity, and social participation. By leveraging these data, this study investigates how chronic diseases, lifestyle factors, and social engagement influence sarcopenia risk. The findings aim to provide a robust scientific foundation for developing prevention and intervention strategies tailored to the specific socioeconomic and demographic context of China, thereby addressing the global knowledge gaps on sarcopenia in Chinese populations.

2 Methods

2.1 Study design and data source

The purpose of this study is to investigate the relationship between chronic diseases, lifestyle factors, and the risk of sarcopenia in the older adult population. To ensure data quality and the reliability of the research results, data from the CHARLS were used. The CHARLS project is designed to collect high-quality microdata from Chinese households and individuals aged 45 and above, with the aim of exploring issues related to population aging in China and promoting interdisciplinary research (16). The national baseline survey of CHARLS was launched in 2011, based on a multi-stage probability sampling method using proportional probability (PPS) sampling. The sample included 450 villages, 150 counties, and 28 provinces, involving more than 17,000 individuals and approximately 10,000 families. Thereafter, CHARLS conducted follow-up surveys every 2 to 3 years. To date, four rounds of national baseline survey data have been released, including the baseline survey in 2011 (the first wave), the first follow-up survey in 2013 (the second wave), the second follow-up survey in 2015 (the third wave), and the third follow-up survey in 2018 (the fourth wave). In this study, respondents aged 60 and above were selected to investigate the relationship between sarcopenia and cognitive function in the older adult. The CHARLS project was approved by the Peking University Biomedical Ethics Review Committee, and all participants were required to sign informed consent forms. Relevant data can be accessed through the website.[1]

This study utilized data from the 2011 and 2015 waves of the CHARLS. The inclusion criteria were as follows: (1) individuals aged 60 years or older in the 2011 and 2015 datasets; and (2) availability of data necessary for sarcopenia assessment. Exclusion criteria included: (1) missing data on sarcopenia status; (2) missing information on physical activity; (3) missing data on sleeptime; (4) age below 60 years; and (5) missing data on covariates. The 2011 dataset comprised 13,562 respondents, and the 2015 dataset included 5,610 respondents. After excluding individuals younger than 60 years and those with missing data, a final sample of 7,841 participants was retained for analysis. Figure 1 illustrates the detailed sample selection process.

2.2 Measurement of sarcopenia

The assessment of sarcopenia was based on a comprehensive scoring system covering five dimensions: strength, assistance in walking, rise from a chair, climb stairs, and falls. Strength (2 points): Difficulty in lifting/carrying approximately 4.5 kg. 0 points = no difficulty, 1 point = some difficulty (attempted but unable to complete the task), 2 points = great difficulty, unable to complete (unable to measure due to health reasons). Assistance in walking (2 points): Difficulty in walking across a room. 0 points = no difficulty, 1 point = some difficulty (uses a walking aid or cane), 2 points = great difficulty, requires assistance, unable to complete (uses a manual or electric wheelchair). Rise from a chair (2 points): Difficulty in standing up from a bed or chair. 0 points = no difficulty, 1 point = some difficulty (unable to stand up five times), 2 points = great difficulty, unable to complete without assistance (unable to stand up). Climb stairs (2 points): Difficulty in climbing 10 steps. 0 points = no difficulty, 1 point = some difficulty, 2 points = great difficulty, unable to complete. Falls (2 points): Number of falls in the past year. 0 points = 0 falls, 1 point = 1–3 falls, 2 points = 4 or more falls. Each

1 http://charls.pku.edu.cn/index.htm

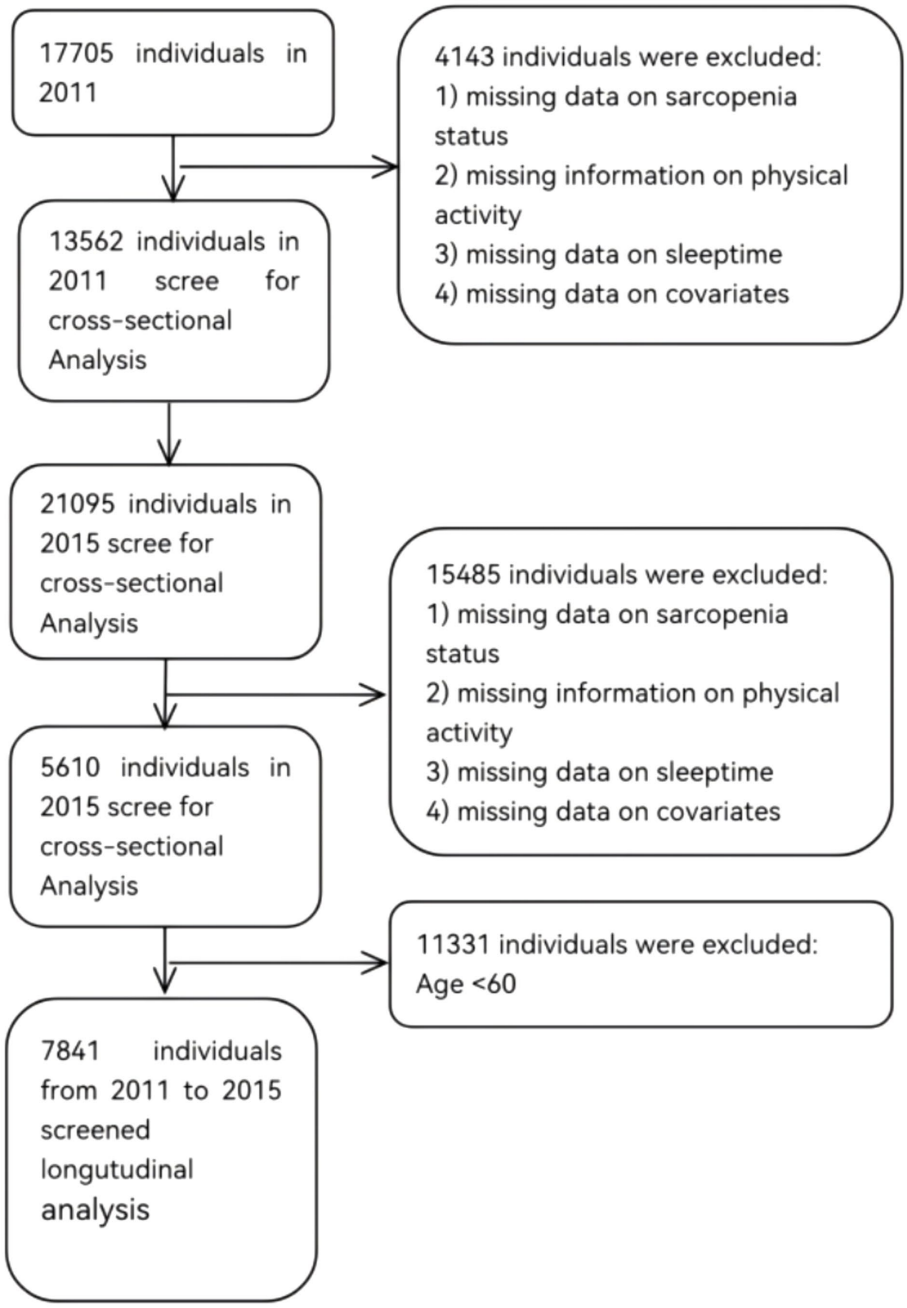

FIGURE 1
Flowchart of the sample selection process.

dimension was scored from 0 to 2, with a total score ranging from 0 to 10. According to the SARC-F scale, individuals with a total score ≥ 4 were defined as sarcopenia cases (1, 26).

2.3 Potential covariates

We considered socio-demographic characteristics and health-related factors based on existing knowledge. Socio-demographic characteristics included age, family size, family expenditure, family income, gender, education level (primary school and below, junior high school, senior high school and above), marital status (married, divorced, widowed, separated, and unmarried), region (eastern region, Central region, and western region), residence area (rural and urban), and medical insurance. The health-related factors included smoking, drinking, health status, social activities, dyslipidemia, and chronic diseases (Pulmonary disease, liver disease, heart disease, stroke, kidney disease, arthritis, and asthma).

2.4 Measurement of physical activity

Participants were asked to recall and report the time spent on various types of physical activities (METs) during the past week. Based

on the standards of the International Physical Activity Questionnaire-Short Form (IPAQ-SF), daily physical activity duration of the respondents was divided into five levels: 0 min, 10–29 min, 30–119 min, 120–239 min, and ≥ 240 min, and the median of each category was used for calculation. Second, physical activity types were classified into high-intensity (e.g., hiking, running, farming), moderate-intensity (e.g., brisk walking, tai chi), and low-intensity (e.g., casual walking). The assigned metabolic equivalent values for high, moderate, and low intensity were 8.0, 4.0, and 3.3, respectively. The METs score was calculated as the product of the intensity coefficient, the number of days, and the duration (in minutes) of each physical activity.

2.5 Measurement of sleeptime

Sleeptime was defined based on the response to the CHARLS: "On average, how many hours of actual sleep do you get at night during the past month?" The data collected from this question were used to determine the participants' self-reported average nightly sleeptime.

2.6 Statistical analysis

First of all, descriptive statistical analysis was carried out to check the basic characteristics of the samples, and sarcopenia cases were compared with non-sarcopenia cases in terms of age, gender, education level, marital status, residence, family income, smoking and drinking habits, chronic diseases, and other variables. Then, multivariate regression analysis was used to evaluate the relationship between different factors and the risk of sarcopenia. The results were expressed as hazard ratios (HR) with 95% confidence intervals (CI), showing the relative risk of sarcopenia associated with various factors. Furthermore, the dose–response relationship between sarcopenia and physical activity or sleep duration was analyzed using a cubic spline model, revealing the nonlinear relationship between these behavioral factors and the risk of sarcopenia. All statistical analyses were conducted using stata 16.0, with the significance level set at 0.05.

3 Results

3.1 Basic characteristics analysis

From the analysis in Tables 1, 2, significant differences in several key variables were observed between sarcopenia cases and non-sarcopenia cases. In terms of age, the average age of sarcopenia cases was 72.66 years, significantly higher than the 67.81 years for non-sarcopenia cases ($p < 0.001$). Regarding gender, the proportion of women in the sarcopenia group was higher (67.57%) than in the non-sarcopenia group (48.54%) ($p < 0.001$). Compared to women, the risk of sarcopenia in men was significantly lower (HR = 0.597, 95% CI: 0.336–1.061). In terms of education level, 87.26% of sarcopenia cases had a primary school education and below, significantly higher than the 79.06% in non-sarcopenia cases ($p = 0.005$). With regard to lifestyle, 65.64% of sarcopenia patients had never smoking, compared with 55.88% of non-sarcopenia patients ($p < 0.001$). The risk of sarcopenia was significantly increased among past drinking (HR = 2.198, 95% CI: 1.072–4.560), while no significant change in risk was observed among current drinking (HR = 1.160, 95% CI: 0.605–2.223). The results were consistent with the harmful effects of excessive drinking and the potential benefits of moderate drinking. Regarding health status, 70.66% of sarcopenia cases reported poor health, much higher than the 32.27% of non-sarcopenia cases ($p < 0.001$). Additionally, the proportions of individuals with Pulmonary disease, heart disease, and arthritis were significantly higher in the sarcopenia group than in the non-sarcopenia group, at 21.62% ($p < 0.001$), 21.62% ($p = 0.004$), and 48.65% ($p < 0.001$), respectively. In terms of social activities, 71.81% of sarcopenia cases did not participate in social activities, significantly higher than the 49.75% in non-sarcopenia cases ($p < 0.001$).

As shown in Supplementary Table 1, to assess potential multicollinearity among the explanatory and control variables, variance inflation factor (VIF) values were calculated. Supplementary Table 1 presents the VIF values for all variables. The maximum and average VIF values were 1.91 and 1.18, respectively, both of which are well below the commonly accepted threshold of 10. Therefore, it can be concluded that multicollinearity does not pose a concern in this study.

To address potential sample selection bias in this study, propensity score matching (PSM) was applied. Samples with chronic diseases were designated as the treatment group, while those without chronic diseases were assigned to the control group. Nearest-neighbor matching was performed to pair the treatment and control groups. As shown in Supplementary Table 2, the covariate balance tests before and after matching indicate that the absolute values of most covariate t-statistics significantly decreased post-matching, reflecting minimal differences in covariates between the two groups. Additionally, the post-matching bias rates further confirm that the differences between the treatment and control groups were substantially reduced.

3.2 Dose–response relationship (cubic spline model)

3.2.1 Sarcopenia and physical activity

From the Figure 2, the cubic spline model illustrating the association between physical activity and the risk of sarcopenia reveals a non-linear relationship, rather than a monotonic increase or decrease. When the metabolic equivalent of task ranges from 1 to 10, an increase in METs is associated with a decreasing risk of sarcopenia. However, when METs exceed 10, the risk of sarcopenia begins to increase with further increases in METs. The HR for sarcopenia demonstrates a trend of initially decreasing and then increasing as METs rise. Moderate-intensity physical activity reduced the risk of sarcopenia by approximately 35% (HR ≈ 0.65). However, high-intensity physical activity led to a rebound in risk, increasing the likelihood of sarcopenia relative to moderate activity. This finding suggests that engaging in moderate physical activity helps reduce the risk of sarcopenia among older adults, whereas excessive physical activity may elevate the risk.

3.2.2 Sarcopenia and sleeptime

As shown in Figure 3, sleep durations between 1 and 7 h are associated with a decreasing risk of sarcopenia as duration increases. However, when sleep duration exceeds 7 h, the risk of sarcopenia

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TABLE 1 Analysis of basic characteristics.

Category	Subcategory	Total (*n* = 7,841)	Non-sarcopenia (*n* = 7,582)	Sarcopenia (*n* = 259)	*p*-value
Age (years, M ± SD)	–	67.970 ± 6.602	67.809 ± 6.496	72.660 ± 7.861	<0.001
Family size M ± SD	–	3.084 ± 1.821	3.080 ± 1.818	3.201 ± 1.910	0.292
Family expenditure M ± SD	–	9.432 ± 1.387	9.439 ± 1.382	9.219 ± 1.502	0.012
Family income M ± SD	–	7.700 ± 3.353	7.719 ± 3.349	7.133 ± 3.433	0.006
Gender	Female	3,855 (49.16)	3,680 (48.54)	175 (67.57)	<0.001
	Male	3,986 (50.84)	3,902 (51.46)	84 (32.43)	
Education level	Primary school and below	6,220 (79.33)	5,994 (79.06)	226 (87.26)	0.005
	Junior high school	1,027 (13.10)	1,008 (13.29)	19 (7.34)	
	Senior high school and above	594 (7.58)	580 (7.65)	14 (5.41)	
Marital status	Divorced/widowed/separated/unmarried	1,603 (20.44)	1,521 (20.06)	82 (31.66)	<0.001
	Married	6,238 (79.56)	6,061 (79.94)	177 (68.34)	
Region	Eastern region	2,623 (33.45)	2,545 (33.57)	78 (30.12)	0.378
	Central region	2,883 (36.77)	2,788 (36.77)	95 (36.68)	
	Western region	2,335 (29.78)	2,249 (29.66)	86 (33.20)	
Residence area	Rural	4,713 (60.11)	4,538 (59.85)	175 (67.57)	0.013
	Urban	3,128 (39.89)	3,044 (40.15)	84 (32.43)	
Medical insurance	No	640 (8.16)	617 (8.14)	23 (8.88)	0.668
	Yes	7,201 (91.84)	6,965 (91.86)	236 (91.12)	
Smoking	Never	4,407 (56.20)	4,237 (55.88)	170 (65.64)	<0.001
	Past smoking	1,033 (13.17)	990 (13.06)	43 (16.60)	
	Current smoking	2,401 (30.62)	2,355 (31.06)	46 (17.76)	
Drinking	Never	4,432 (56.52)	4,267 (56.28)	165 (63.71)	<0.001
	Past drinking	966 (12.32)	921 (12.15)	45 (17.37)	
	Current drinking	2,443 (31.16)	2,394 (31.57)	49 (18.92)	
Health status	Poor	2,630 (33.54)	2,447 (32.27)	183 (70.66)	<0.001
	Fair	3,684 (46.98)	3,618 (47.72)	66 (25.48)	
	Good	1,032 (13.16)	1,027 (13.55)	5 (25.48)	
	Very good	475 (6.06)	470 (6.20)	5 (25.48)	
	Excellent	20 (0.26)	20 (0.26)	0 (0.00)	
Social activities	Not participated	3,958 (50.48)	3,772 (49.75)	186 (71.81)	<0.001
	Participated	3,883 (49.52)	3,810 (50.25)	73 (28.19)	
Dyslipidemia	No	7,039 (89.77)	6,814 (89.87)	225 (86.87)	0.117
	Yes	802 (10.23)	768 (10.13)	34 (13.13)	
Pulmonary disease	No	6,796 (86.67)	6,593 (86.96)	203 (78.38)	<0.001
	Yes	1,045 (13.33)	989 (13.04)	56 (21.62)	
Liver disease	No	7,517 (95.87)	7,272 (95.91)	245 (94.59)	0.295
	Yes	324 (4.13)	310 (4.09)	14 (5.41)	
Heart disease	No	6,638 (84.66)	6,435 (84.87)	203 (78.38)	0.004
	Yes	1,203 (15.34)	1,147 (15.13)	56 (21.62)	
Stroke	No	7,593 (96.84)	7,371 (97.22)	222 (85.71)	<0.001
	Yes	248 (3.16)	211 (2.78)	37 (14.29)	
Kidney disease	No	7,328 (93.46)	7,085 (93.45)	243 (93.82)	0.809
	Yes	513 (6.54)	497 (6.55)	16 (6.18)	

(Continued)

TABLE 1 (Continued)

Category	Subcategory	Total (*n* = 7,841)	Non-sarcopenia (*n* = 7,582)	Sarcopenia (*n* = 259)	*p*-value
Arthritis	No	5,005 (63.83)	4,872 (64.26)	133 (51.35)	<0.001
	Yes	2,836 (36.17)	2,710 (35.74)	126 (48.65)	
Asthma	No	7,455 (95.08)	7,218 (95.20)	237 (91.51)	0.007
	Yes	386 (4.92)	364 (4.80)	22 (8.49)	

TABLE 2 Risk of dermatomyositis incidence by different classifications.

Category	Subcategory	HR	95%CI
Gender	Female	1	Reference
	Male	0.597	0.336–1.061
Education level	Primary school and below	1	Reference
	Junior high school	1.286	0.599–2.762
	Senior high school and above	1.118	0.398–3.136
Marital status	Divorced/widowed/separated/unmarried	1	Reference
	Married	0.570	0.310–1.046
Region	Eastern region	1	Reference
	Central region	0.724	0.368–1.424
	Western region	0.894	0.454–1.759
Residence area	Rural	1	Reference
	Urban	0.726	0.400–1.320
Medical insurance	No	1	Reference
	Yes	0.535	0.240–1.191
Smoking	Never	1	Reference
	Past smoking	1.470	0.717–3.017
	Current smoking	0.621	0.303–1.275
Drinking	Never	1	Reference
	Past drinking	2.198	1.072–4.560
	Current drinking	1.160	0.605–2.223
Social activities	Not participated	1	Reference
	Participated	0.482	0.265–0.876
Dyslipidemia	No	1	Reference
	Yes	1.011	0.401–2.551
Pulmonary disease	No	1	Reference
	Yes	1.499	0.727–3.088
Liver disease	No	1	Reference
	Yes	2.631	1.043–6.635
Heart disease	No	1	Reference
	Yes	1.812	0.945–3.476
Stroke	No	1	Reference
	Yes	3.137	1.128–8.721
Arthritis	No	1	Reference
	Yes	1.722	0.983–3.014
Asthma	No	1	Reference
	Yes	1.286	0.400–4.135

begins to rise with further increases. The HR for sarcopenia exhibits a trend of initially decreasing and subsequently increasing with longer sleep durations. These findings suggest that adequate sleep duration benefits older adults by reducing the risk of sarcopenia, whereas excessive sleep duration may increase the risk.

4 Discussion

With increasing age, the incidence of sarcopenia shows a significant upward trend worldwide. There are considerable differences in the prevalence of sarcopenia across different countries and regions. According to European research data, the prevalence of sarcopenia is generally higher, which is related to the earlier aging of society in these regions. The prevalence of sarcopenia in individuals over 65 years old ranges from about 11 to 50%, and this variation is closely related to the study population, diagnostic criteria, and lifestyle habits. In North America, it is reported that the incidence of sarcopenia in similar age groups ranges from 13 to 24% (27). However, due to the rapid aging of the population, sarcopenia is a more serious problem in Asian countries. The prevalence of sarcopenia among older adults over 65 years old in Japan is 18.1% (6, 28). One study in South Korea showed that the prevalence rates among men and women were 15.4 and 22.1%, respectively (29). Research based on data from the CHARLS shows that the prevalence of sarcopenia among older adults aged 60 and over in China is 3.30%. The data indicate that the prevalence of sarcopenia in China is relatively low compared with Western countries. However, because of China's large population, the actual number of sarcopenia patients may far exceed that of other countries. This difference may be related to factors such as traditional Chinese diets, levels of physical activity, and healthy lifestyle habits (5).

As people age, muscle mass and strength gradually decline, which is one of the core characteristics of sarcopenia. Several studies show that muscle mass decreases by about 8% every ten years after the age of 40, and this rate accelerates to about 15% every ten years after the age of 60 (5). The underlying causes of this process include the decline in neuromuscular function, decreased muscle protein synthesis, and the accumulation of chronic inflammation (30). Among older adults, declining hormone levels, such as growth hormone and testosterone, are also considered major factors that accelerate muscle loss (31).

Chronic diseases are key factors that accelerate muscle loss, especially in patients with heart disease and chronic obstructive pulmonary disease (COPD). Chronic inflammatory states and metabolic disorders typically promote muscle tissue catabolism and further aggravate the onset of sarcopenia (13, 32, 33). In addition, individuals with liver disease and stroke have a

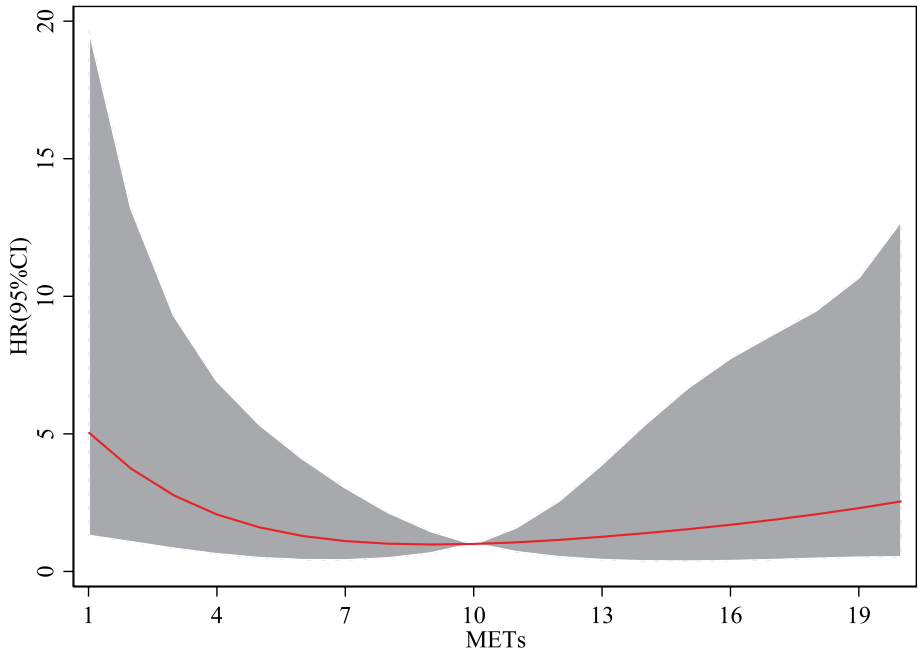

FIGURE 2
Trivariate spline model of the association between physical activity and dermatomyositis.

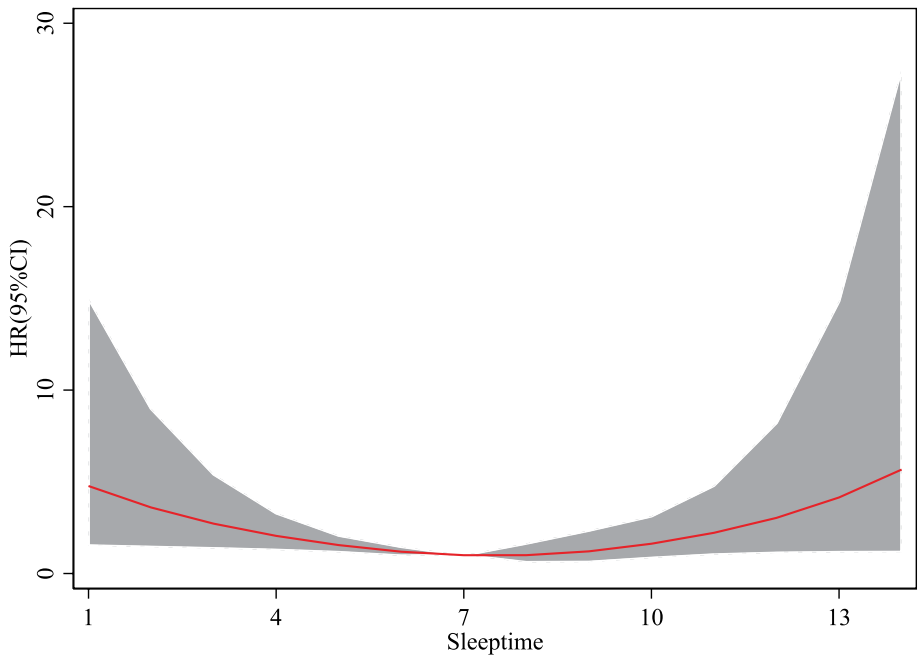

FIGURE 3
Trivariate spline model of the association between sleeptime and dermatomyositis.

significantly higher risk of sarcopenia than healthy individuals. The liver plays a key role in protein metabolism, detoxification, and energy storage, which makes liver disease closely related to sarcopenia. Liver disease leads to malnutrition, decreased protein synthesis, and chronic inflammation, all of which can contribute to sarcopenia (34–37). Nishikawa et al. conducted a study in Japan, demonstrating that systemic inflammation and impaired protein metabolism accelerate muscle wasting, leading to a high prevalence of sarcopenia in patients with liver disease (33). Similarly, Fülster et al. reported a significant prevalence of sarcopenia in patients with chronic heart failure, primarily driven by reduced physical activity and increased systemic catabolism

(38). These findings align with our study, further confirming that chronic diseases markedly increase the risk of developing sarcopenia.

Sarcopenia and chronic diseases have a bidirectional relationship, mutually influencing each other (39). Yu et al. demonstrated that sarcopenia significantly increases the risk of disease progression in patients with chronic liver disease, leading to worse clinical outcomes (23, 40). Furthermore, Sepúlveda-Loyola et al. reported that sarcopenia is strongly associated with a higher risk of chronic obstructive pulmonary disease (COPD), exacerbating patients' overall health status (32). Similarly, Damluji et al. highlighted that sarcopenia is closely linked to accelerated progression of cardiovascular diseases, increased mortality, higher fall incidence, and reduced quality of life, particularly in older adults (13). Collectively, these studies underscore the pivotal role of sarcopenia in driving the progression of chronic diseases.

Lifestyle factors play an important role in the pathogenesis and progression of sarcopenia. Proper physical activity helps maintain muscle mass, while both sedentary behavior and excessive activity increase the risk of sarcopenia. Studies have shown that moderate-intensity exercise, such as brisk walking or strength training, helps reduce the risk of sarcopenia, while excessive high-intensity exercise may lead to muscle injury, thereby increasing the risk (1, 5, 7, 41, 42). Additionally, the quality and duration of sleep are closely related to the occurrence of sarcopenia. Both insufficient and excessive sleep affect the endocrine system and inflammatory responses, accelerating muscle loss (9, 43–45). Furthermore, this study found that older adults who do not participate in social activities have a significantly higher risk of sarcopenia. Social isolation may exacerbate mental health problems, such as depression and anxiety, and further impact the physical activity levels and overall health of older adults (46, 47).

Although this study provides valuable insights into the prevalence and influencing factors of sarcopenia among older adults in China, it has some limitations. First, this study is based on samples of older adults primarily from specific areas, which may not fully reflect the situation of all older adults in the country, particularly those in remote or economically underdeveloped regions. Second, some lifestyle data (e.g., physical activity, smoking, and drinking) relied on self-reports from respondents, which carry the risk of recall bias and inaccurate reporting. This may lead to misclassification of some variables and affect the accuracy of the research. Third, some analyses are cross-sectional, making it difficult to determine causal relationships. The relationship among chronic diseases, lifestyle factors, and sarcopenia may be bidirectional, and this interaction cannot be fully captured by a cross-sectional design. Although this study adjusted for several potential confounders (e.g., age, gender, chronic diseases), other uncontrolled factors (such as genetic background and dietary patterns) may still influence the occurrence of sarcopenia. Moreover, this study used the SARC-F scale to evaluate sarcopenia. While this screening tool is highly practical, its sensitivity and specificity may be insufficient, potentially missing early or mild cases of sarcopenia.

5 Conclusion

This study identified the main risk factors for sarcopenia in older adults, including age, chronic diseases (such as lung and heart diseases), lifestyle factors (such as physical activity and sleep), and social participation. The results suggest that preventing sarcopenia should focus on lifestyle adjustments, particularly moderate exercise and the management of chronic diseases. Large-scale longitudinal research is needed in the future to explore the long-term impact of various risk factors and to formulate personalized intervention measures aimed at improving the quality of life for older adults and reducing the health risks associated with sarcopenia.

Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found at: https://charls.pku.edu.cn/en.

Ethics statement

The studies involving humans were approved by the Committee of Peking University. All participants provided written informed consent. All methods in this study adhered to relevant guidelines and regulations. Given the illiteracy of some participants, the investigator obtain informed consent by presenting and explaining its contents to them. Participants then provide their consent through handprints. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

W-xW: Writing – original draft, Writing – review & editing. Z-fM: Writing – original draft, Writing – review & editing. M-lC: Writing – review & editing. LM: Writing – original draft.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2025.1500915/full#supplementary-material

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Risk prediction model of physical frailty for a rural older population: a cross-sectional study in Hunan Province, China

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Introduction: Physical frailty is a common medical syndrome characterized by low muscle strength, low endurance, and reduced physiological function that leads to significantly negative health outcomes in older adults. This study investigated the risk variables among rural older adults in Hunan Province, China, and developed a physical frailty prediction model to inform policymaking to enhance their health and well-being.

Methods: This study was conducted from July 22 to September 3, 2022. A total of 291 participants were recruited using stratified cluster random sampling from five large villages in Hunan Province. Frailty screening was performed based on the Fatigue, Resistance, Ambulation, Illnesses, and Loss of Weight (FRAIL) scale, Geriatric Depression Scale 15-item version (GDS-15), Falls Efficacy Scale-International (FES-I), and Mini Nutrition Assessment-Short Form (MNA-SF). A logistic regression analysis was performed to identify the predictive factors for physical frailty and develop a physical frailty prediction model based on the area under the receiver operating characteristic (ROC) curve (AUC), sensitivity, specificity, and Youden index.

Results: The physical frailty prevalence among rural older adults in Hunan Province was 21.31% (n = 62). Household income and expenditure [odds ratio (OR): 1.826, 95% confidence interval (CI): 1.142–2.918], physical exercise frequency (OR: 1.669, 95% CI: 1.137–2.451), depressive symptoms (OR: 9.069, 95% CI: 3.497–23.516), and fear of falling (OR: 3.135, 95% CI: 1.689–5.818) were identified as significant predictors of physical frailty in rural older individuals. The AUC for the frailty predictive model was 0.860 (95% CI: 0.805, 0.914). The sensitivity and specificity at the optimal cutoff value were 80.6 and 76.0%, respectively, with a Youden index of 0.566.

Conclusion: The prediction model constructed in this study demonstrated promise as a potential tool for evaluating physical frailty risk in older adults, which can contribute to healthcare providers' screenings for high-risk populations. Further multidimensional and experimental intervention studies should be conducted to prevent the occurrence and delay the progression of physical frailty in older adults.

KEYWORDS

physical frailty, rural, older adults, FRAIL scale, predictive model

1 Introduction

Population aging has become a global challenge. Every country is experiencing the growing proportion of older adults in the population and China is no exception (1). An older adult is defined by the United Nations as a person who is over 60 years of age (2). Based on a China Bureau of Statistics report, people aged over 60 years has reached 296 million, accounting for 21.2% of the total population (3). Older people become frail due to physiological or psychological factors such as aging and illness (4). There are a number of older people in the Chinese rural regions, in rural areas the older population accounted for 17.72% of the total population, whereas in urban areas it accounted for 11.11%. Older population in rural area is a critical attention to achieve an objective of health care equity and healthy aging (5).

Frailty phenotype was initially defined by Fried et al. (6) and refers to an age-related medical syndrome increasing individual's excessive vulnerability for developing increased dependency and/or death. Physical frail older people are mainly manifested in the aspects of lower muscle strength, lower endurance, and decreased physiological function (7). A meta-analysis found that frailty prevalence in rural older residents was 18%, greater than the global estimate of 10.7% (8). Previous studies have compared the frailty prevalence between rural and urban regions (9–14), with a 1.5 times higher frailty prevalence (10). Physiological function frail leads to inadequate basic daily activities ability and is susceptible to chronic diseases or comorbidity (15). These health conditions induce a higher risk of negative health outcomes such as hospitalization or nursing home admission, premature death (16), and Medicare demand with increased costs for individuals and health systems (annual cost $3,781 healthy vs. $10,755 frail) (17). Many countries consider addressing physical frailty as a priority to reduce the medical burden (18, 19).

Early screening of high-risk populations is important for early intervention to delay the onset and progression of physical frailty (20). The risk levels of physical frailty older people were affected by a range of factors and conditions such as age (21, 22), educational level (23), depression, fear of falling, nutritional status (24), and loneliness (25). Previous studies have attempted to develop frailty prediction models for developing countries, particularly for use in rural areas. However, their use is context dependent. During the urbanization process in China, population migration has produced sociodemographic profiles for the rural older population that are influenced by various factors such as economic development (26), distribution of health resources, and individual lifestyles. Little attention has been paid to rural residents and risk identification models of physical frailty have not been applied in China. A predictive model enables the accurate calculation of risk and identification of high-risk rural residents. This study aims to identify risk variables and create a predictive model of physical frailty for rural older residents.

2 Materials and methods

2.1 Study design and participants

This cross-sectional observational study was conducted to develop a risk predictive model of physical frailty among rural populations in Hunan Province, central China. We report the results of this study in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist guidelines (Supplementary Appendix 1).

Stratified cluster random sampling was employed to recruit the participants. Specially, five large villages were randomly selected in this study from Yueyang City, Yongzhou City, Zhuzhou City, Chenzhou, City and Huaihua City. Participant inclusion criteria were: ① resided in the village at least 6 months; ② Age 60 years or older; ③ capable of communication; and ④ voluntarily agreed to participate in the study. Older adults with severe diseases, mental disorders, or serious audio-visual impairments were excluded so as to the accuracy of the study findings.

According to Kendall's sample size calculation method (27), the sample size should be 5–10 times the number of independent variables. Using three scales and 17 items, and assuming a 20% sample loss, the required sample size for this study was 120–240. Ultimately, 291 valid questionnaires were obtained to meet the sample size requirements.

2.2 Survey tools

The questionnaire employed in this study consisted of five parts: a general information questionnaire, the Fatigue, Resistance, Ambulation, Illnesses, & Loss of Weight (FRAIL) scale, Geriatric Depression Scale 15-item version (GDS-15), Falls Efficacy Scale-International (FES-I), and Mini Nutrition Assessment-Short Form (MNA-SF).

2.2.1 General information questionnaire

This section included 11 demographic items (age, sex, ethnicity, occupation, body mass index, education level, marital status, smoking status, alcohol consumption, family income, and living conditions) and 6 related factors (social activities, physical exercise, intellectual activities, falls in the past year, chronic diseases, and types of drugs administered).

2.2.2 FRAIL scale

The FRAIL scale was developed by the International Academy of Nutrition, Health, and Aging (28). It consists of five items: fatigue, resistance, ambulation, illnesses, and loss of weight. Each item is scored as 0 or 1, with the total score ranging from 0 to 5. According to the total scores are categorized as not-frailty (≤2 points), and frailty (≥ 3 points). In this study, the Cronbach's α coefficient of this scale was 0.605.

2.2.3 GDS-15

The GDS-15 was developed by Sheik and Yesavage (29) in the 1980s, and translated into Chinese by Tang et al. (30). The GDS-15 has 15 items, including 10 affirmative ("yes" is 1 point and "no" is "no") and 5 negative items ("yes" is 0 points and "no" is 1 point). The total GDS-15 score is 0–15 points, the cutoff point of ≥8 indicates the presence of depressive symptoms, and a higher score indicates more severe depressive symptoms. In this study, the Cronbach's α coefficient of this scale was 0.753.

2.2.4 FES-I

The FES-I was revised by Yardley et al. (31, 32) and translated into Chinese by the researcher Guo et al. (33). It consists two dimensions:

indoor physical activities (10 items) and outdoor physical activities (6 items). Items are scored using a Likert 4-point scale, ranging from "not at all worried" to "very worried," with scores from 1 to 4. The total score ranges from 16–64; higher scores indicate a higher degree of fear of falling. Specifically, scores of 16–31 indicate low, 32–47 indicate moderate, and 48–64 indicate high fear of falling. In this study, the Cronbach's α coefficient of this scale was 0.870.

2.2.5 MNA-SF

The MNA-SF was developed by Kaiser et al. (34) and then translated into the Chinese version by He et al. (35). The MNA-SF comprises six indicators: body mass index, decline in food, intake, stress, mobility, weight loss in the prior 3 months, and neuropsychiatric symptoms; a total score ranges from 0–14 points and scores are categorized as normal nutritional status (12–14 points), risk of malnutrition (8–11 points), and malnutrition (<8 points). The MNA-SF is an effective nutritional screening tool suitable for older adults because it demonstrates good sensitivity and specificity in identifying malnutrition among this population (36, 37). In this study, the Cronbach's α coefficient of this scale was 0.619.

2.3 Data collection

The questionnaires were collected face-to-face from July 22 to September 3, 2022. Before data collection, we recruited 12 sophomore nursing students as investigators who were divided into six groups (2 investigators in each group). The primary researcher taught them the nursing research curriculum and provided instructions for the questionnaire survey guidelines, quantitative research design, and data collection methods. The primary researcher printed written questionnaires and brought all groups of investigators to the five villages separately.

When collecting data, investigators used unified guidelines to ask participants about all items and filled in the questionnaires with their answers. If the older adults did not understand the meaning of the items or express their opinions accurately during the survey, their families or caregivers assisted in explaining them until they understood the meaning. After completing the questionnaire, each participant received a small gift (one toothbrush, one tube of toothpaste, and one bag of washing powder) to express gratitude. In this study, 306 questionnaires were collected; 15 invalid questionnaires that showed incomplete or incorrect information were excluded. Thus, 291 valid questionnaires were obtained with an effective rate of 95.10%.

2.4 Ethical considerations

This study was approved by the Institutional Review Board of the Medical Ethics Committee of Xiangnan University (registration number: 2022010). Before collecting data, all participants were informed about the purpose, process, and potential risks of the study and then were asked to provide written informed consent. They were allowed to withdraw from the study at any time without explanation. Their information was kept confidential and used only for research purposes. This study conformed to the guidelines of the 1995 Declaration of Helsinki (and its revised editions since 2000).

2.5 Data analysis

SPSS version 25.0 (IBM Corp., Armonk, NY, USA) was used to analyze data for all statistical analyses. A p-value <0.05 determined significance. The continuous data were statistically described by means and standard deviations, while the categorical data by frequency and percentage. For the univariate analysis, the $\chi 2$ test was employed. A binary multivariable logistic regression model was performed to estimate physical frailty risk and considered predictive factors as the significant factors obtained in the bivariate analysis. The discriminatory power of the risk model was evaluated based on the area under the receiver operating characteristic (ROC) curve (AUC), sensitivity, specificity, and Youden index. The Hosmer–Lemeshow test was used to analyze the model fit.

3 Results

3.1 Demographic characteristics and clinical characteristics

A total of 291 older people were investigated in this study. Figure 1 illustrates the recruitment process of participating rural older adults. Among them, there were 123 males (42.27%) and 168 females (57.73%); the age ranged from 60 to 94 years, with an average of (70.42 ± 7.09) years. 102 older adults (35.05%) had never attended school, 142 (48.80%) with primary school, and 47 (16.15%) with junior high school or above. In terms of family income, 143 older adults (49.14%) had income exceeding expenses, 96 (32.99%) with a balanced income and expenses, and 52 (17.87%) with expenses exceeding income. The prevalence of depressive symptoms was 12.37% (n = 36), and that of older adults at risk of malnutrition was 224 (76.97%). The fear of falling score was (29.69 ± 11.11), with an average score of (1.86 ± 0.69). The participant characteristics are listed in Table 1.

3.2 Prevalence of physical frailty and risk factors

The prevalence of physical frailty was 21.31% (n = 62) among the 291 rural older adults in Hunan Province. There were significant differences in the frailty of rural older people with age, marital status, smoking status, alcohol consumption, family income and expenditure, living conditions, frequency of participating in physical exercise, participating in intellectual activities, falling frequency within one year, number of comorbidities for chronic diseases, number of types of drugs administered, depressive symptoms, nutritional status, and fear of falling (all $p < 0.001$).

3.3 Predictive factors associated with physical frailty

Before the stepwise binary logistic regression, all independent variables were assigned points, as presented in Table 2. The results showed that family income, physical activity, depressive symptoms and the fear of falling were the main predictive factors affecting of older people ($p < 0.001$) (Table 3).

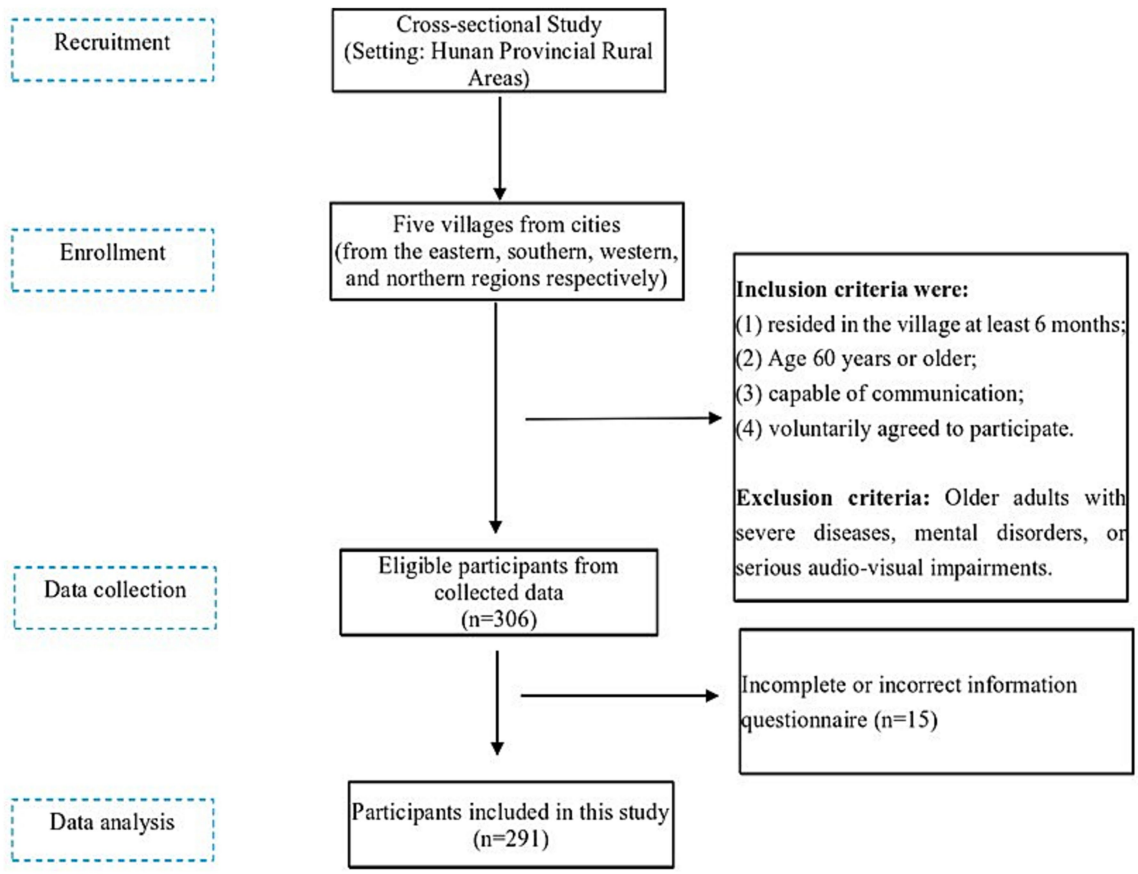

FIGURE 1
Flow diagram of recruitment procedure.

3.4 Effectiveness of risk prediction model of physical frailty

Based on the significant variables and assigned values, the final risk predictive model of physical frailty was Y = −9.076 + 0.623 family income +0.315 physical exercise +2.181 depression and + 1.165 fear of falling. The ROC curve was used to evaluate the effectiveness of the risk prediction model in the rural older population with physical frailty (Figure 2). The area under the ROC curve was 0.860 (95% CI: 0.805–0.914), which was greater than the theoretical acceptability of 0.700 (38), indicating satisfactory discriminatory performance for the risk model in identifying frail older adults in a rural setting. The optimal cutoff value of 0.201 was determined using the maximum Youden index value (0.566). The sensitivity and specificity of the optimal cutoff values were 80.6 and 76.0%, respectively. The Hosmer-Lemeshow test was used to assess goodness of fit of the predictive model; $\chi^2 = 7.5668$, $p = 0.363$ (>0.05) showed the model fitting degree is deal.

4 Discussion

This study established a risk prediction model for physical frailty among rural older residents, which is an essential tool in this era of an aging society. As the profile of rural older residents' changes, it is of utmost importance to provide a scientific model to identify residents in the early frailty stage.

The results indicated that frailty prevalence among the rural older people aged 60 years and older was 21.31%. The prevalence of rural frailty varies among countries. The prevalence rate in our study is similar to those in Vietnam (39) and Japan (40), higher than that of Malaysia (41) and Tanzania (42), and lower than those of Brazil (43) and the Republic of Korea (44). In addition, among the Chinese older people, physical frailty prevalence was much higher for those dwelling in rural areas of Hunan Province than those in Beijing (45) and Shanghai (10). The high prevalence of physical frailty in rural areas is prone to a wide range of adverse outcomes. Paying attention to frail older people was one of important measures to minimize adverse events (46). This finding calls for action to identify populations at high risk in order to prevent physical frailty at an early stage.

Several factors are associated with the prevalence and progression of physical frailty. Predictive factors are context dependent and vary. This study identified low income, physical activity, depression, and fear of falling as predictive factors for physical frailty among rural older residents.

Low income in rural regions, characterized by lower socioeconomic status and education levels. This is consistent with the findings of Ahmad et al. (41) and Huang et al. (14). The results of this study revealed that majority of rural older people had received a lower level of education, with 83.85% having no formal

TABLE 1 Socio-demographic characteristics and physical frailty prevalence among the rural older population in Hunan Province.

Variables		Frailty (%) (n = 62)	Non-frailty (%) (n = 229)	χ^2	p-value
Age in years	60–69	24 (16.67)	120 (83.33)	21.485	< 0.001*
	70–79	19 (17.43)	90 (82.57)		
	≥80	19 (50.00)	19 (50.00)		
Sex	Male	27 (21.95)	96 (78.05)	0.053	0.818
	Female	35 (20.83)	133 (79.17)		
Ethnicity	Han	59 (20.92)	223 (79.08)	0.720	0.396
	Minority	3 (33.33)	6 (66.67)		
Occupation	Farmer	55 (20.92)	192 (79.08)	0.900	0.343
	Non-farmer	7 (15.91)	37 (84.09)		
BMI (kg/m^2)	Low weight	11 (27.50)	29 (66.67)	1.938	0.379
	Normal	36 (18.95)	154 (79.08)		
	Overweight	15 (24.59)	46 (84.09)		
Educational level	No school	22 (21.57)	80 (78.43)	0.194	0.908
	Elementary school	29 (20.42)	113 (79.58)		
	Junior school or above	11 (23.40)	36 (76.60)		
Marital status	Married/Reconciled	35 (17.33)	167 (82.67)	6.237	0.013
	Unmarried/Divorced/ Widowed /Separated	27 (30.34)	62 (69.66)		
Smoking status	Never	41 (18.98)	175 (81.02)	6.677	0.035
	Current	15 (23.44)	49 (76.56)		
	Quit	6 (54.55)	5 (45.45)		
Alcohol consumption	Never	45 (22.06)	159 (77.94)	6.532	0.038
	Current	10 (14.08)	61 (85.92)		
	Quit	7 (43.75)	9 (56.25)		
Family income	Income more than expenditure	17 (11.89)	126 (88.11)	33.232	< 0.001
	Balance	19 (19.79)	77 (80.21)		
	Expenditure more than income	26 (50.00)	26 (50.00)		
Living conditions	Living with spouse	15 (14.85)	86 (85.15)	8.725	0.033
	Living with children	25 (32.05)	53 (67.95)		
	Living with spouse and children	16 (17.78)	74 (82.22)		
	Living alone	6 (27.27)	16 (72.73)		
Frequency of participating in social activities	≥ 1 time/week	17 (63.73)	59 (36.27)	0.069	0.792
	<1 time/week	45 (69.32)	170 (30.68)		
Frequency of participating in physical exercise	Everyday almost	1 (1.32)	75 (98.68)	37.015	< 0.001*
	3–5 times/week	11 (18.03)	50 (81.97)		
	1–8 times/week	15 (22.06)	53 (77.94)		
	<1 time/month	35 (40.70)	51 (59.30)		
Participation in intellectual activities	Yes	20 (15.04)	113 (84.96)	5.740	0.017
	No	42 (26.58)	116 (73.42)		

(Continued)

TABLE 1 (Continued)

Variables		Frailty (%) (n = 62)	Non-frailty (%) (n = 229)	χ^2	p-value
Falling occurred within 1 year	Yes	13 (34.21)	25 (65.79)	4.341	0.037
	No	49 (19.37)	204 (80.63)	1.099	0.295
Numbers of comorbidity of chronic disease	No	8 (8.42)	87 (91.58)	20.296	< 0.001*
	1	29 (22.31)	101 (77.69)		
	≥ 2	25 (37.88)	41 (62.12)		
Numbers and types of drugs administered	None	21 (12.96)	141 (87.04)	16.645	< 0.001*
	1	26 (35.62)	47 (64.38)		
	≥ 2	15 (26.79)	41 (73.21)		
Depression	Yes	26 (72.22)	10 (27.78)	63.523	< 0.001*
	No	36 (14.12)	219 (85.88)		
Nutritional status	Normal	6 (13.95)	37 (86.05)	10.196	0.006
	At risk of malnutrition	45 (20.09)	179 (79.91)		
	Malnutrition	11 (45.83)	13 (54.17)		
FOF level	Low	11 (7.38)	138 (92.62)	61.619	< 0.001*
	Middle	33 (27.97)	85 (72.03)		
	High	18 (75.00)	6 (25.00)		

BMI, body mass index; FOF, fear of falling.
*$p < 0.001$.

TABLE 2 Assigned points of variables in the logistic regression analysis model.

Variables	Assigned points
Age (years)	60–69 = 1; 70–79 = 2; ≥ 80 = 3
Marital status	Married/reconciled = 1; Unmarried/divorced/widowed/separated = 2
Smoking status	Never = 1; Current = 2; Quit = 3
Alcohol consumption	Never = 1; Current = 2; Quit = 3
Family income	Income more than expenditure = 1; balance = 2; expenditure more than income = 3
Living conditions	Living alone = 1; Living with spouse = 2; Living with children = 3; Living with spouse and children = 4
Frequency of participating in physical activities	Almost every day = 1; 3–5 times/week = 2; 5–8 times/month = 3; <1 time/month = 4
Participation in intellectual activities	No = 1; Yes = 2
Fall occurred within prior year	No = 1; Yes = 2
Number of chronic diseases	No = 1; 1 Type = 2; ≥ 2 Type = 3
Types of drugs administered	No = 1; 1 Type = 2; ≥ 2 Type = 3
Depression symptoms	No = 1; Yes = 2
Nutritional status	Normal = 1; Risk of malnutrition = 2; Malnutrition = 3
Fear of falling	Low = 1; Middle = 2; High = 3

schooling or only completed elementary school. This percentage was higher than educational level of nationwide older people, as reported in the 2021 Chinese General Social Survey (CGSS) (47, 48). Older adults with lower education exhibited higher rates of physical frailty compared to those with higher educational levels (49). Wongtrakulruang et al. (50) found that a lower education level, specifically primary school education or less, was associated with an increased risk of physical frailty. Low educational level in rural area may lead to lower family income for older people. Family income is the basic guarantee for better living. Older people with a high family income not only enjoy superior and comfortable living conditions but also have high quality nutritional intake, and high utilization rate of health services, which enables timely and effective treatment of diseases; 89% of rural older people suffer from one type of chronic disease or more (51). Worldwide, the prevalence rates appear to be higher in less developed environments and lower in more developed countries (52).

The findings of this study showed that depressive symptoms were another predictive factor of physical frailty in rural older individuals, which is consistent with the results of a study by Soysal

TABLE 3 Predictive risk factors associated with physical frailty for the rural older adults by the stepwise binary logistic regression.

Variables	β value	SE	Wald χ^2	OR (95% CI)	p-value
Constant	−8.477	1.000	71.829	-	< 0.001
Family income	0.602	0.239	6.332	1.826(1.142–2.918)	0.012
Frequency of participating in physical activities	0.512	0.196	6.833	1.669(1.137–2.451)	0.009
Depression symptoms	2.205	0.486	20.568	9.069(3.497–23.516)	< 0.001
Fear of falling level	1.143	0.316	13.113	3.135(1.689–5.818)	< 0.001

CI, confidence interval; OR, odds ratio; SE, standard error.

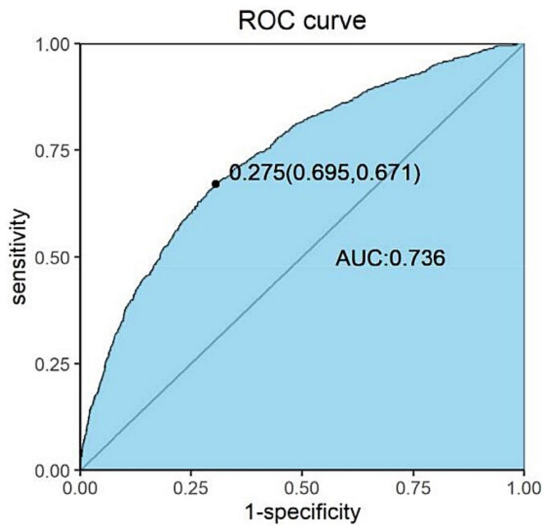

FIGURE 2
ROC curve for the physical frailty risk prediction model among older rural residents. The horizontal coordinate is 1-specificity, and the vertical coordinate is sensitivity. AUC, area under the curve; ROC, receiver operating characteristic.

et al. (53). Depression is a common cognitive factor. When depressive symptoms persist at high levels, they subsequently lead to cognitive decline as well as to the development or worsening of the physical frailty syndrome in older adults (54). The depression and physical frailty, in conjunction with environmental factors (e.g., low education, unhealthy dietary patterns, low physical activity) may negative influence on cognitive frailty (55), even brain aging. Ruan et al. (56) proposed that physical frailty contributed to cognitive impairment of cognitive frailty. Their interaction primarily rises from the fact that physical frailty and cognitive impairment share similar pathophysiological mechanism, which produces chronic inflammatory, oxidative stress, and mitochondrial dysfunction (53–56). Inflammatory cytokines play a crucial role in mediating cognitive frailty, meanwhile, high concentrations of inflammatory penetrate the blood–brain barrier and impact skeletal muscles, causing a reduction in muscle mass and strength, along with impaired functionality (57). This sequence of events ultimately gives rise to the onset of physical frailty. Additionally, individuals with depressive symptoms usually engage in less physical activity, have poor dietary intake (58), and are reluctant to participate socially, which increase the probability of physical frailty. In this study, 85% of older rural adults were at risk of or had malnutrition and social participation (74%) less than 1 time per week. Gaspar et al. (59) highlighted on the dimension of laser activities and free time as protective factors against cognitive impairment. It's necessary for the rural health government to provide a social platform to promote social and cultural activities for rural residents, which enriches their spiritual life to improve depressive symptoms.

Physical activity was correlated with physical frailty progression; the prevalence of physical frailty was lower in the moderate-intensity exercise group than in the sedentary or low-intensity exercise group, which is supported by the longitudinal cohort study of Rogers et al. (60). Regarding interventions based on physical activity, different kinds of exercises has been found to improve physical function and muscle strength, such as resistance exercise, Chinese traditional mind body exercise, exergaming-based exercise and Otago exercise program (61–63). It is possible that older rural people maintain their livelihoods through some form of labor, indirectly strengthening their physical health to reduce the occurrence of physical frailty. Accordingly, physical activity, the most effective non-pharmacological intervention, enhances cognition, physical function, and mental health in older persons with frailty, providing evidence to promote future exercise programs to prevent the onset and progression of physical frailty in older adults (18). It is suggested to encourage older people to actively participate in labor or physical activity when possible.

With their fear of falling, the likelihood of developing physical frailty in rural older adults increases (64, 65). This fear of falling may have an inhibitory effect on self-efficacy (66), making older people who were previously active less energetic. Increased risk of falling may lead to reduced physical activity, but also to reduced engagement in social activities and increased social isolation, which could lead to further cognitive and functional impairment (49). Therefore, it is important to psychologically counsel older people with frailty about their fear of falling and implement interventions to prevent falls and improve their health status.

The risk-predictive model in the present study indicated good discrimination and could identify high-risk physical frailty for rural older people. This identification provides scientific evidence for appropriate interventions of rural older adults with high frailty risk to avoid adverse outcomes.

The strength of this study lies in its focus on predictive factors for frail older individuals and good efficiency of the physical frailty predictive model in rural areas to expand our understanding of frailty in different specific rural regions given the uneven distribution of the population. However, several limitations should be acknowledged. Firstly, despite the methodologically and scientifically justified the sample size, the fact of participants

chosen from each village by cluster sampling within five municipalities of Hunan Province may limit the generalizability of the results to a broader rural population. Future studies should aim to expand the sample size and geographically diversify the participants to enhance external validity of the findings. Ideally, such studies could adopt a longitudinal research design to provide more robust evidence. Secondly, this study used a cross-sectional design, making it difficult to infer causality. Longitudinal studies are needed to track participants over time and provide more empirical evidence to support targeted interventions aimed at preventing or delaying the onset of physical frailty in rural older people. Thirdly, while this study has identified several important predictive factors for frailty, a wider range of potential factors should be incorporated to identify frailty to obtain more representative results in the future research. This would provide valuable evidence for physical frailty prevention programs in rural areas. Finally, the slightly insufficient Cronbach's alpha values were obtained for the Chinese-adapted MNA-SF instrument and the FRAIL scale (0.605), indicating potential room for improvement in the reliability of these measurement tools when applied to the Chinese population. Further research could be considered to explore methods for enhancing the reliability of these instruments in Chinese-contexts.

5 Conclusion

The study established a risk-predictive model that integrates factors such as low income, depressive symptoms, lack of physical activity, and fear of falling to identify physical frail older individuals in rural areas. Frailty is a multifaceted issue involving various factors. Collaboration among public health professionals, policymakers, and stakeholders is crucial for preventing frailty. Our model could provide a potential tool to identify rural older residents at risk of physical frailty and inform prevention programs.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

XG: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Visualization, Writing – original draft, Writing – review & editing. CS: Conceptualization, Funding acquisition, Investigation, Project administration, Resources, Supervision, Validation, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2025.1525580/full#supplementary-material

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Development of a visualized risk prediction system for sarcopenia in older adults using machine learning: a cohort study based on CHARLS

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Introduction: The older adult are at high risk of sarcopenia, making early identification and scientific intervention crucial for healthy aging.

Methods: This study utilized data from the China Health and Retirement Longitudinal Study (CHARLS), including a cohort of 2,717 middle-aged and older adult participants. Ten machine learning algorithms, such as CatBoost, XGBoost, and NGBoost, were used to construct predictive models.

Results: Among these algorithms, the XGBoost model performed the best, with an ROC-AUC of 0.7, and was selected as the final predictive model for sarcopenia risk. SHAP technology was used to visualize the prediction results, enhancing the interpretability of the model, and the system was built on a web platform.

Discussion: The system provides the probability of sarcopenia onset within 4 years based on input variables and identifies critical influencing factors. This facilitates understanding and use by medical professionals. The system supports early identification and scientific intervention for sarcopenia in the older adult, offering significant clinical value and application potential.

KEYWORDS

sarcopenia, risk prediction, visualized, machine learning, CHARLS

1 Introduction

Sarcopenia has become an important health concern for the older adult, characterized by reduced muscle mass, decreased muscle strength, and gradual physical function decline (1, 2). This degenerative condition severely limits mobility, increases the risk of falls and fractures, and may lead to a decline in quality of life and higher mortality rates (3). In China, with the rapid aging process, the prevalence of sarcopenia remains high, imposing significant burdens on healthcare systems and family care (4). Identifying high-risk individuals promptly and adopting scientific interventions, such as increased protein intake and enhanced physical activity, can help maintain healthy muscle conditions and reduce the risk of sarcopenia (5, 6).

With the rapid development of big data and artificial intelligence, machine learning models based on health data have shown great potential in disease risk assessment (7, 8).

These models can mine underlying patterns from large datasets, accurately identify high-risk populations, and analyze critical risk factors for diseases. For instance, Dong et al. developed a predictive model for diabetic nephropathy within 3 years among type 2 diabetes patients based on electronic health records, revealing that high homocysteine levels and poor blood glucose control were significant risk factors (9). Similarly, Wang et al. used six machine learning algorithms to predict all-cause mortality within 3 years for heart failure patients with coronary artery disease, identifying age, occupation, and nitrate use as key factors (10).

However, despite the significant achievements of machine learning in disease risk prediction, research on predicting sarcopenia in the older adult remains in its infancy. Most existing studies are based on cross-sectional data (11–13), limiting their ability to capture the dynamic process and time-dependent risk factors of sarcopenia development. Additionally, current studies primarily focus on model construction without in-depth analysis of the importance of risk indicators or features. The lack of interpretation hinders the comprehensive understanding of key influencing factors. Moreover, these studies have yet to translate their findings into practical tools, such as web-based or application-based sarcopenia assessment platforms, limiting their application in clinical practice and health management.

To address these gaps, this study utilized data from the 2011 and 2015 CHARLS databases to develop a visualized sarcopenia risk assessment system for the older adult. Various machine learning algorithms, including LightGBM, XGBoost, and AdaBoost, were employed to construct the models, with the best-performing model selected for predicting sarcopenia risk within 4 years. To enhance model interpretability, Shapley Additive Explanations (SHAP) were introduced to visualize the contribution of each feature to the prediction, increasing transparency and credibility. Finally, to further enhance the practical application value of this study, the trained model was deployed on a web platform, creating a risk prediction system for sarcopenia in older adults. This system enables medical professionals to quickly identify high-risk individuals and implement personalized prevention and intervention strategies effectively.

2 Results

2.1 Research subjects

This study initially included 17,708 participants. After excluding 14,991 participants based on exclusion criteria, 2,717 participants remained (Figure 1). Among them, 1,397 were male (51.42%), and 1,320 were female (48.58%), with an average age of 66.25 ± 5.37 years (Supplementary Table S1). After a 4-year follow-up, 222 participants were diagnosed with sarcopenia in 2015, yielding a prevalence of 8.17%.

2.2 Classification performance

In this study, we built older adult sarcopenia risk assessment models using 10 algorithms, including XGBoost (XGB), LightGBM (LGBM), AdaBoost (ADA), Random Forest (RF), Gradient Boosting Trees (GBT), CatBoost (CB), NGBoost (NGB), Logistic Regression (LR), Multi-Layer Perceptron (MLP), and Support Vector Machine (SVM). We used accuracy, precision, F1-score, and the area under the receiver operating characteristic curve (ROC-AUC) as evaluation metrics. As shown in Figure 2, the models constructed using XGB, RF, and GBT algorithms showed higher ROC-AUC, possibly because these algorithms enhance model generalization through ensemble learning methods, while also demonstrating strong robustness and interpretability (14). Additionally, the XGB model outperformed other models in terms of F1-score (Supplementary Table S2), and with a ROC-AUC of 0.7, demonstrated significant performance advantages (Supplementary Table S3). This success is due to its highly optimized gradient boosting framework and flexible regularization mechanisms, which effectively mitigate overfitting and enhance the model's ability to capture complex data patterns (15). Based on the above results, the XGB model demonstrated high classification stability and reliability. Therefore, we ultimately selected the model built using the XGB algorithm as the older adult sarcopenia risk prediction model (Supplementary Code S1).

We analyzed the sensitivity of the ROC curve for the XGB model across different gender subgroups using the Hanley-McNeil test (Supplementary Figure S1 and Supplementary Code S2). The results showed (Supplementary Table S4) that the differences in ROC-AUC between the Overall Data, Male Subgroup, and Female Subgroup were not statistically significant. This indicates that the XGB model performs consistently across different gender subgroups. We further evaluated the classification performance of the XGB model using the confusion matrix (Supplementary Figure S2). Among the 753 participants who did not develop sarcopenia after 4 years, 73.84% were correctly classified; among the 63 participants who developed sarcopenia, 60.32% were correctly classified. This demonstrates that the XGB model has some sensitivity in predicting whether individuals will develop sarcopenia in the future.

2.3 Feature importance

SHAP plots are intuitive tools for interpreting machine learning model outputs, measuring each feature's contribution to predictions (16, 17). SHAP values indicate the direction and magnitude of a feature's influence on predictions: positive values indicate a positive impact, while negative values indicate a negative effect. In the SHAP plot, features are ranked by importance on the vertical axis, and their specific effects on model output are shown on the horizontal axis. Each point represents a sample, with color indicating feature values (red for high values and blue for low values), providing a clear visualization of the relationship between features and prediction outcomes.

In the overall feature importance plot for sarcopenia (Figure 3), the household predictor "Does your residence have running water?" (F3) had the most significant impact, indicating a negative correlation between access to running water and future sarcopenia risk. Demographic predictors such as "Marital Status" (D2) and "Number of living children" (D5), and health predictors like "Have

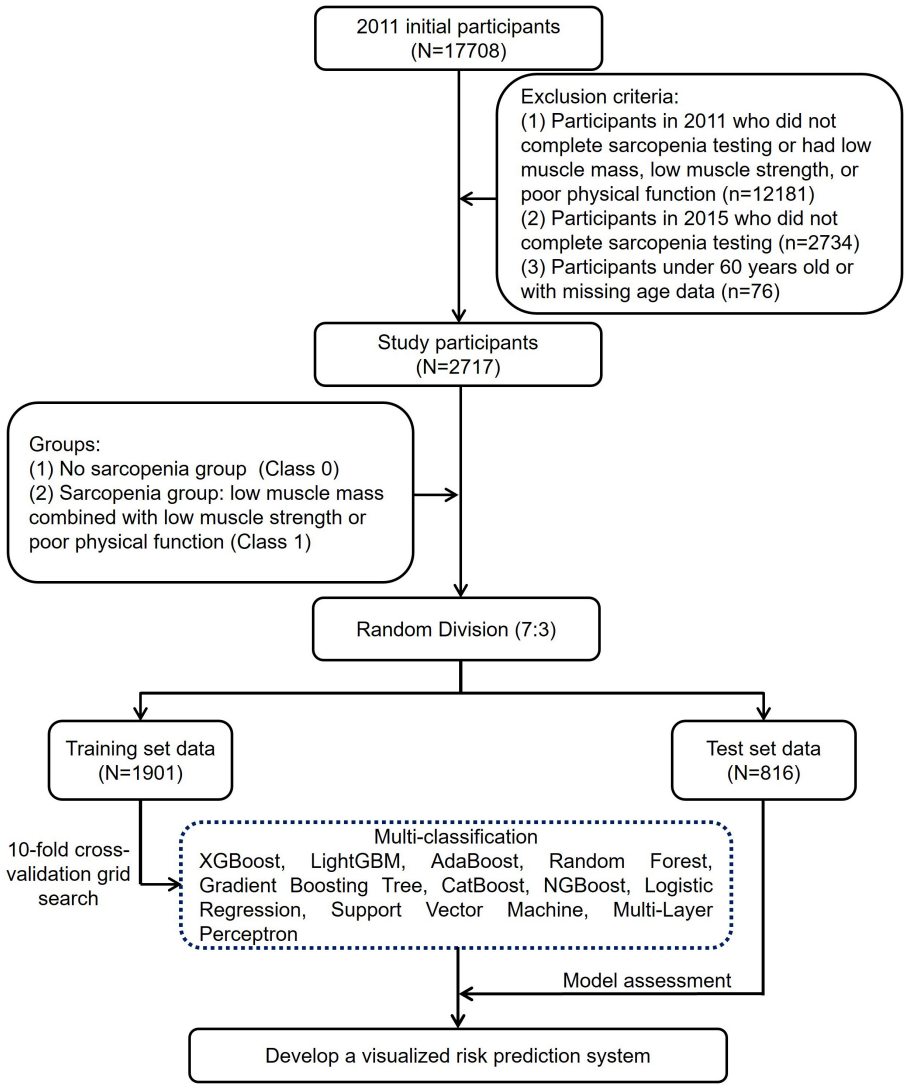

FIGURE 1
A flowchart describing the general framework of the study.

you lost all of your teeth?" (H47) and "The maximum value of the breathing test" (H24), also showed high importance. Participants with the following characteristics were at higher risk of developing sarcopenia: tooth loss (H47), poor self-rated health (H1), low breathing test values (H24), smoking (F2), lower systolic blood pressure (H21), and asthma (H14). These findings highlight the predictive value of living conditions, health status, and behavioral habits, providing a reference for targeted interventions and preventive strategies.

2.4 Risk prediction system

The visualized prediction system consists of an information input area on the left and a results display area on the right (Figure 4), shows that the input information is consistent with the features used in the training model (Supplementary Table S1). For continuous variables, input can be adjusted using sliders, while categorical variables (e.g., gender) can be selected by clicking. The right side of the interface is divided into two parts: the upper section displays the predicted sarcopenia status after 4 years, while the lower section provides a personalized analysis report to guide precise intervention strategies.

An example application of the prediction system is shown in Figure 4B. After entering relevant information on the left, the system predicts a 28.83% probability of developing sarcopenia within 4 years. Below, the SHAP plot visualizes how each feature influences the prediction. The length of the bars reflects the strength of the effect: red bars indicate positive influences, and blue bars indicate negative influences. Features positively associated with the prediction include F3 and H24, while H47, F2, F17, H5, and H33 had negative impacts. Based on this analysis, preventive measures such as installing running water facilities and improving maximum breathing values could reduce the user's future sarcopenia risk.

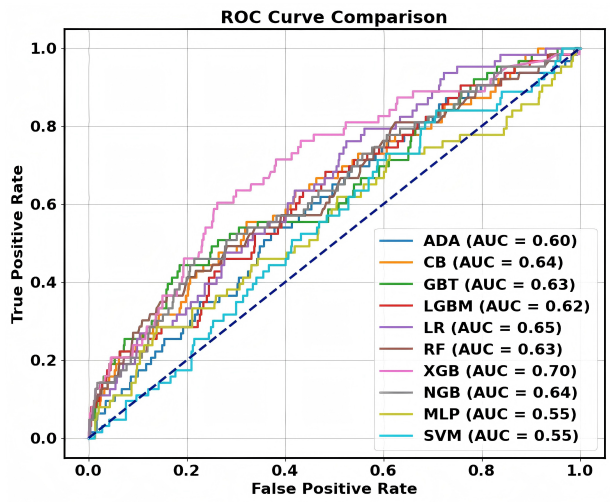

FIGURE 2
ROC curves for different machine learning models.

3 Discussion

This study successfully developed a sarcopenia risk prediction system for the older adult based on the CHARLS database using multiple machine learning algorithms. The system not only identifies high-risk individuals but also enhances usability and user experience through a visualized web interface, providing intuitive decision support for medical professionals.

Unlike previous studies that primarily relied on cross-sectional data (11–13), this study employed longitudinal data to conduct a cohort analysis of sarcopenia risk in the older adult. Cross-sectional studies often capture sarcopenia-related features at a single time point, limiting their ability to reflect dynamic changes and time-dependent risk factors during the disease progression. This limitation can lead to an incomplete understanding of the critical stages in sarcopenia development, reducing the accuracy and clinical applicability of predictive models. In contrast, longitudinal data enable the observation of individual characteristic trends over time, capturing dynamic processes and time-dependent risk factors, thus improving the predictive accuracy and clinical relevance of the model.

After comparing the performance of the models, the XGB model performed the best. In building the risk prediction model using the XGB algorithm, we employed the KNN algorithm for missing value imputation and used the SMOTE algorithm to address class imbalance. Although these methods may introduce some bias, the KNN algorithm, through its imputation strategy based on data similarity, better preserves the original structure and distribution of the data. Moreover, the SMOTE algorithm effectively alleviates class imbalance by generating synthetic samples, thereby improving the model's ability to recognize the minority class (18). To validate the effectiveness of these methods, we compared the performance of models under different preprocessing strategies. The experimental results showed that the model built using KNN imputation and SMOTE for data balancing had a significantly higher ROC-AUC than models using mean imputation, mode imputation, or no data balancing (Supplementary Figure S3). This result supports the rationale for choosing KNN and SMOTE during the preprocessing stage.

We selected the optimal F1-score threshold for prediction probability (Supplementary Code S3). This threshold selection method maximizes the F1-score, balancing the model's precision and recall. Clinically, the optimal F1-score threshold helps improve the diagnostic accuracy of sarcopenia while minimizing false positives and false negatives. According to the confusion matrix analysis of the XGB model (Supplementary Figure S2), among the 753 participants who did not develop sarcopenia after 4 years, the model correctly classified 73.84% of individuals, with a low false-positive rate, indicating that the model effectively avoids misclassifying healthy individuals as diseased, thus reducing unnecessary medical tests and treatment costs. However, among the 63 participants who developed sarcopenia after 4 years, the model correctly classified only 60.32%, with a relatively high false-negative rate. This may result in some patients who require treatment not being identified in time, missing the best opportunity for early intervention, potentially leading to worsening conditions and increasing the complexity and cost of subsequent treatments.

To enhance model interpretability, SHAP technology was used for visual explanations. Traditional machine learning models are often considered "black boxes" (19–21), with their decision-making processes and feature contributions remaining opaque. SHAP assigns contribution values to features, clarifying their roles in predictions. Analysis of SHAP values in this study revealed that features such as living conditions, health status, and behavioral habits significantly influenced the model's predictions. Among these, "Does your residence have running water?" (F3) had the most substantial impact, showing a negative correlation with sarcopenia risk. While no direct association between access to running water and sarcopenia risk has been established in existing studies, it is hypothesized that water, as an essential nutrient, plays a crucial role in overall health (22–24). This finding underscores the importance of improving infrastructure for promoting healthy aging and offers insights for public health policy. Additionally, "Have you lost all of your teeth?" (H47) was the second most influential feature in the model, suggesting that tooth loss is a significant indicator of sarcopenia risk. This aligns with studies such as Kusama et al. (25), which linked tooth loss to reduced protein intake, and Azzolino et al. (26), which found that poor oral health can influence food choices and nutritional intake, leading to frailty and sarcopenia. Other important predictive factors include lower breathing test values (H24) and smoking (F2). Research by Rahimi et al. (27) demonstrated that improved respiratory function significantly enhances muscle strength in older adult women, while Rom et al. (28) reported that smoking accelerates skeletal muscle loss through inflammation and oxidative stress. Consistent with the SHAP analysis results from the overall data, in different gender subgroups (Supplementary Figures S4 and S5), tap water (F3) and breathing test values (H24) have significant effects on the likelihood of sarcopenia in both men and women. However, the impact of alcohol consumption (F1) is greater for men, and marital status (D2) has a stronger influence on women regarding the risk of sarcopenia. These findings not only validate the model's predictions

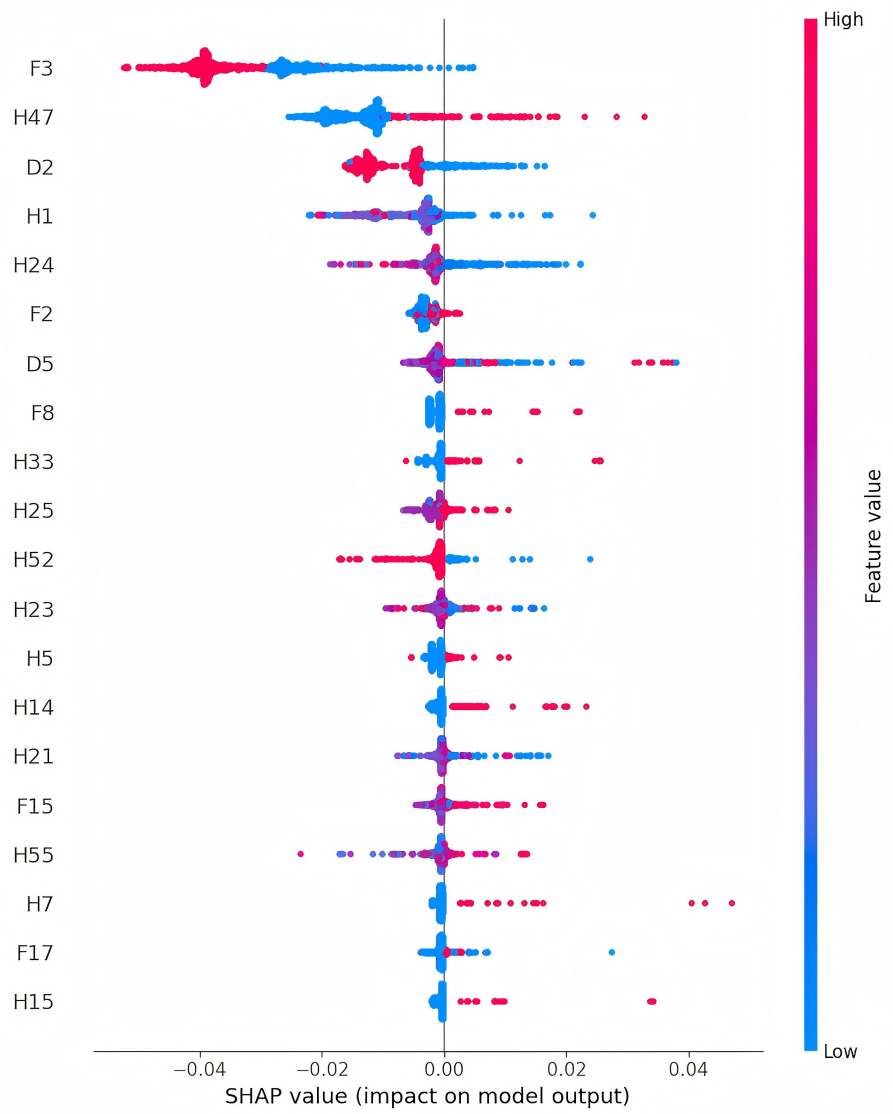

FIGURE 3
Feature importance charts for sarcopenia in older adults (The detailed description of the features can be found in Supplementary Table S1).

but also reveal potential mechanisms influencing sarcopenia. The developed system integrates the prediction model into a web platform, enabling users to input individual characteristics and generate personalized risk assessment reports based on SHAP analysis. This enhances accessibility and provides an intuitive understanding of the results.

However, the study has several limitations. First, the data were derived exclusively from Chinese older adult populations, potentially limiting its generalizability across different cultural or ethnic groups. Second, the model did not include certain potentially critical variables, such as genetic information, long-term exercise habits, and detailed dietary patterns, which may affect prediction accuracy. Additionally, although this study is based on longitudinal data from CHARLS, the temporal changes of predictive factors (such as the dynamic changes in health behaviors) were not adequately considered during model development, which may affect the long-term predictive ability of the model. Lastly, while SHAP technology elucidates the contributions of various features, the specific mechanisms linking certain features to sarcopenia remain underexplored. Future research should expand data sources, incorporate key variables such as genetic information, and optimize model performance. Experimental studies are also needed to further investigate the mechanisms between features and sarcopenia, providing scientific evidence for clinical interventions.

4 Conclusions

This study successfully developed a sarcopenia risk prediction model for the older adult based on the CHARLS database, enhancing its interpretability through SHAP technology and building a visualized web platform to make prediction results more accessible and applicable. The findings highlight the significant role of factors such as living conditions, dental health, and

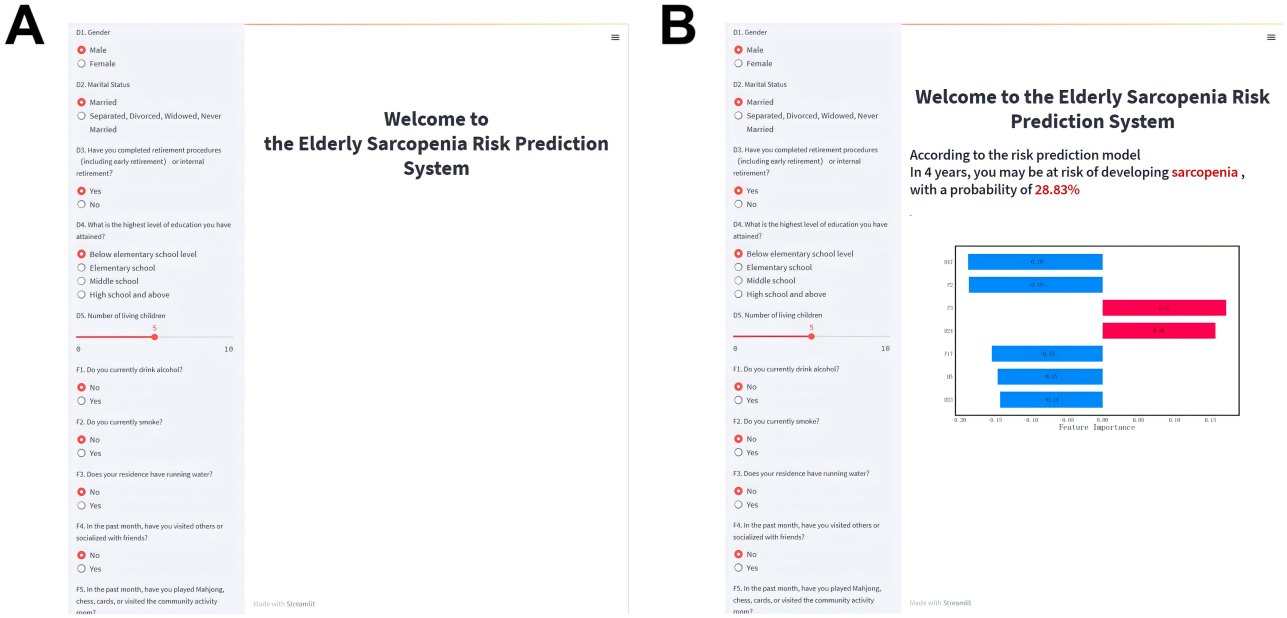

FIGURE 4
Visualized risk prediction system for older adults. **(A)** System homepage; **(B)** Information output page.

respiratory function in predicting sarcopenia risk, providing a foundation for policy development and clinical decision-making. However, the study has limitations, including the restricted data scope. Future efforts should aim to expand the sample range and integrate key variables to further optimize the model, offering more comprehensive support for precise sarcopenia prediction and promoting healthy aging.

5 Methods

5.1 Study population

This study utilized data from the China Health and Retirement Longitudinal Study (CHARLS), a multidisciplinary nationwide survey led by the National School of Development at Peking University. CHARLS covers 28 provinces, 150 counties, and 450 communities (villages) in China, involving ~10,000 households (29, 30). High-quality longitudinal data were collected through in-home visits from individuals aged 45 years and older. The study was approved by the Peking University Institutional Review Board (IRB00001052-11015), and all participants provided informed consent prior to participation. Ethical standards were strictly adhered to, ensuring transparency and integrity throughout the research process. As shown in Figure 1, the study sample was derived from the first (2011) and third (2015) waves of CHARLS. A total of 2,717 eligible participants were included in the final analysis after applying the following exclusion criteria: (1) Participants in 2011 who did not complete sarcopenia testing or had low muscle mass, low muscle strength, or poor physical function; (2) Participants in 2015 who did not complete sarcopenia testing; (3) Participants under 60 years old or with missing age data.

5.2 Research variables

Sarcopenia was assessed based on the Asian Working Group for Sarcopenia (AWGS 2019) criteria, encompassing three components: muscle strength, appendicular skeletal muscle mass (ASM), and physical function (31). Muscle strength was evaluated by measuring handgrip strength using a Yuejian™ WL-1000 hand dynamometer (Nantong Yuejian Measuring Instruments Co., Ltd., Nantong, China). Participants were instructed to squeeze the dynamometer with maximum effort, and two measurements were taken for both the dominant and non-dominant hands. The maximum grip strength was recorded, and the average was used. According to AWGS 2019, the thresholds for low grip strength are <28 kg for men and <18 kg for women. ASM was estimated using a validated body composition formula (Supplementary Equation S1), which has been shown to correlate strongly with dual-energy X-ray absorptiometry (DXA) results (32, 33). ASM adjusted for height squared (ASM/Ht^2) was calculated by dividing ASM by the square of height in meters. Low muscle mass was defined as the lowest 20th percentile of height-adjusted muscle mass in the study population: ASM/Ht^2 <4.90 kg/m^2 for women and <6.79 kg/m^2 for men. Physical function was assessed by gait speed, measured as the time taken to walk 2.5 m back and forth at a normal pace. Low physical function was defined as gait speed <1.0 m/s based on AWGS 2019 recommendations. Participants were classified into two groups: non-sarcopenia and sarcopenia, with the latter defined as low muscle mass combined with either low

muscle strength or low physical function. This study included 78 feature variables (Supplementary Table S1), with missing data rates below 10% for all variables. Given the strong correlation between age and muscle mass, the remaining 77 features were used as predictors, encompassing three categories: demographics, family lifestyle, and health status. Demographic variables included five features (excluding age), such as sex and marital status; family lifestyle included 17 variables, such as current smoking and alcohol consumption; and health status included 55 variables, such as self-rated health and bodily pain.

5.3 Prediction system development

A visualized risk assessment system for sarcopenia in older adults was developed using Python 3.11. The dataset was randomly split into training and testing sets at a 7:3 ratio. Missing data were imputed using the K-Nearest Neighbors (KNN) algorithm, and the Synthetic Minority Oversampling Technique (SMOTE) was employed on the training set to address class imbalance (18). We selected the optimal hyperparameters through 10-fold cross-validation with grid search and constructed XGB, LGBM, ADA, RF, GBT, CB, NGB, LR, MLP, and SVM models. Optimal hyperparameters were determined through grid search with 10-fold cross-validation. Eight models—XGB, LGBM, ADA, RF, GBT, CB, NGB, and LR—were constructed, with performance metrics including accuracy, precision, F1-score, and area under the ROC curve. The model with the best performance was selected as the sarcopenia risk assessment model. Feature importance indices were calculated using SHapley Additive exPlanations (SHAP), and an online risk assessment system was developed. Additionally, to validate the effect of data processing, we also applied mean imputation, mode imputation, and no data balancing strategies, using the best model construction algorithms.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: https://charls.charlsdata.com/pages/data/111/zh-cn.html.

Ethics statement

The studies involving humans were approved by Peking University Institutional Review Board (IRB00001052-11015). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

Author contributions

JD: Conceptualization, Methodology, Resources, Writing – review & editing, Writing – original draft. XT: Data curation, Writing – original draft, Writing – review & editing. LZ: Data curation, Writing – review & editing. HW: Methodology, Writing – review & editing. WQ: Methodology, Writing – review & editing. XM: Data curation, Writing – review & editing. SW: Validation, Writing – review & editing. XZ: Validation, Writing – review & editing. QL: Resources, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2025.1544894/full#supplementary-material

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Low-volume resistance training: a feasible, cost-effective strategy for musculoskeletal frailty in older adults attending daycare centers

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Introduction: Frailty is a prevalent geriatric syndrome, posing significant health risks for older adults attending daycare centers or residing in institutional settings. Addressing frailty with interventions that are feasible and cost effective and also promote high adherence within these environments is crucial.
Objective: This study aimed to evaluate the impact of a low-volume, remotely supervised resistance training protocol on physical frailty among frail older adults attending daycare centers. Secondary outcomes included changes in sarcopenia prevalence and fall risk.
Methods: Thirty-one frail older adults participated in a 12-week usual care period, followed by a 12-weeks intervention featuring low-volume (10-minute sessions) resistance training three times weekly. The program was delivered locally by non-specialized staff under remote supervision. Musculoskeletal, functional, and clinical assessments were conducted at three-time points: baseline, pre-intervention, and post-intervention.
Results: During the usual care period, a decline was observed in handgrip strength (19.2–18.5 kg) and sit-to-stand time (14.5–17.4s) ($p < 0.05$). However, these measures were preserved during the intervention. Relative muscle power decreased during the usual care but improved with training (4.3–5.2 W/Kg, $p < 0.001$). While body composition, physical function, gait speed, and Short Performance Physical Battery scores remained stable, reductions were observed in exhaustion and physical inactivity prevalence ($p < 0.05$). Frailty prevalence showed a decreasing trend (48%–26%, $p = 0.099$), with significant reductions in sarcopenia prevalence (29%–10%, $p = 0.045$), and fall frequency ($p = 0.022$).
Conclusion: The low-volume strength training protocol was a feasible, cost-effective strategy for mitigating musculoskeletal frailty criteria, sarcopenia and fall risk among older adults in daycare centers, potentially delaying the progression of these conditions.

KEYWORDS

resistance training, older adults, falls, frailty, sarcopenia

Introduction

Frailty is a multifaceted geriatric syndrome characterized by reduced physiological reserves and heightened vulnerability to stressors (1). This condition results in diminished strength, aerobic capacity and physical function (2). With a high prevalence among institutionalized older adults and those attending daycare centers (3–5), adverse outcomes such as loss of quality of life and independence (6), increased healthcare costs (7), and premature mortality (8) are real concerns for caregivers. Although standardizing criteria and algorithms for diagnosing frailty remains challenging (3, 9), Fried's physical frailty phenotype (1) has become a widely accepted approach. This phenotype identifies frailty based on at least three of five criteria: muscle weakness, gait slowness, low physical activity, unintentional weight loss and exhaustion.

Given the substantial neuromuscular involvement in frailty (10, 11), resistance training has emerged as a cornerstone for prevention and management (12–15). Evidence indicates that resistance training (16, 17) can improve gait speed (18), muscle strength (19) and muscle mass (20, 21). Consequently, resistance training is recommended as first-line therapy for frailty management as part of multicomponent physical activity programs, as the International Clinical Practice Guidelines for Sarcopenia (ICFSR) (22) emphasize. Additionally, frailty often overlaps and co-occurs with sarcopenia (23–25)—an age-related disease characterized by the progressive loss of muscle mass and function (26)—and the risk of falls (27), a major cause of death and disability in older adults. These geriatric syndromes share disability pathways as well as clinical and functional outcomes. Therefore, given the typical neuromuscular decline, a program focusing on frailty management could also target these conditions (28, 29).

Despite its well-documented benefits, structured resistance training programs tailored to frail older adults remain rare in institutional and daycare settings (28). Barriers include institutional limitations, such as insufficient resources and trained staff, and individual challenges, including low adherence due to fatigue or functional limitations (30). Addressing these barriers requires innovative approaches, such as low-cost, low-time-demand programs that can be implemented without significantly disrupting participants' daily routines. Furthermore, research highlights the importance of tailoring exercise interventions to participants' needs, including minimal-dose protocols that still achieve meaningful clinical benefits (31, 32). Several proposed resistance exercise programs have been based on the dose-response relationship for healthy older adults (33), which might disregard specific characteristics of frail individuals (34) (e.g., low adherence, reduced energy and exercise tolerance). Therefore, planning programs adapted to participants' abilities is essential, focusing on low-volume yet highly effective approaches (35, 36). The conception of how much resistance training is enough has not yet been clarified (35, 37), but investigating minimal dose methodologies is a vital step towards defining ideal protocols for managing and treating geriatric syndromes.

The present study evaluated the feasibility and effectiveness of a low-volume, remotely supervised resistance training program for frail older adults attending daycare centers. The program was tailored to institutional constraints and participant capabilities, addressing frailty while assessing secondary outcomes such as sarcopenia and fall prevalence. By exploring a minimal-dose approach, this study seeks to inform the development of scalable exercise protocols for managing frailty and related geriatric syndromes.

Materials and methods

Study design and participants

This study recruited 62 participants from four Portuguese daycare centers. Before the intervention began, one center withdrew, and several participants were unable to continue, living a final cohort of 44 individuals. Participants were required to be 65 years or older, classified as frail or pre-frail, and physically and cognitively able to follow basic exercise instructions. A physician provided medical clearance for all participants.

The study employs a repeated measures design, with each participant undergoing a 12-week usual care phase (control) followed by a 12-week exercise intervention. Assessments were conducted at three-time points: baseline (T_I), pre-intervention (T_{II}), and post-intervention (T_{III}).

Musculoskeletal evaluation

Musculoskeletal fitness was assessed through handgrip strength (Leonardo Mechanography, Novotec Medical, Pforzheim, Germany) and appendicular skeletal muscle mass (ASMM) measured via bioimpedance (Bio 101, Akern, Wurzburg, Germany). After a brief explanation and familiarization with the device, maximal handgrip strength was measured twice, with participants seated on a 45 cm high armless chair and the dominant arm's elbow flexed at 90°. The highest value was recorded. ASMM assessment was conducted five minutes after participants were immobilized in a lying position, with the skin prepared and bioimpedance electrodes placed. Resistance and reactance were recorded, converted to ASMM (38), and adjusted for body mass.

Functional evaluation

Physical function was assessed using the Short Physical Performance Battery (39) (SPPB), which includes gait speed, standing balance, and a five times sit-to-stand test (5STS). Gait speed was measured during two attempts of a 2.44 m walk at the participant's usual pace. Due to potential alterations in gait fluency, which are common among older adults, the fastest attempt was recorded for analysis. Balance was assessed using three progressively challenging foot placements: parallel,

semi-tandem, and full tandem. Participants were required to maintain each position for up to 10 s. The test was concluded for any participant unable to sustain balance for the full duration in any position. Lower-limb strength was assessed with the 5STS test, which measured the time required for participants to rise from a seated position (45 cm high) five times without using their hands. The test was performed on a force reaction platform (Leonardo Mechanography, Novotec Medical, Pforzheim, Germany) that recorded both the completion time and muscle power generated during movements.

The three physical function tests (gait speed, balance and lower-limb strength) were scored from 0–4, resulting in a maximum total of 12 points on the SPPB Scale, with higher scores representing better physical function. Participants who were unable to stand or walk independently received a score of 0 on the respective SPPB test and were excluded from the statistical analysis of gait speed.

In addition, the perceived capacity to perform activities of daily living (ADL) was assessed using the 12-item Composite Physical Function (40) (CPF) scale. This self-reported questionnaire evaluates physical function across three domains: basic, instrumental, and advanced ADLs. Each of the 12 items was scored from 0–2, with a maximum possible score of 24 indicating high physical function. The caregiving staff also reported the number of falls experienced by each participant over the previous 12 weeks.

Clinical evaluation

Frailty was diagnosed using Fried's phenotype (1), which includes five criteria: muscle weakness, unintentional weight loss, gait slowness, low physical activity, and self-reported exhaustion. Muscle weakness was determined by handgrip strength thresholds based on sex and body mass index. Unintentional weight loss was defined as a loss exceeding 5 kg or 5% of body mass within the past 12 months. Gait slowness was identified if walking velocity fell below 0.6 or 0.7 m/s, depending on sex and height. Self-reported exhaustion was assessed using the two questions from the Center of Epidemiology Scale for Depression (CES-D) questionnaire while low physical activity was evaluated based on daily mobility with International Physical Activity Questionnaire—Short Form (41, 42). Participants meeting one or two of these criteria were classified as prefrail while those meeting three or more were categorized as frail.

Sarcopenia was assessed according to the EWGSWOP 2019 algorithm (26). Dynapenia was identified if handgrip strength was $\leq$27 kg in men and 16 kg in women. Sarcopenia was confirmed if appendicular skeletal muscle mass index (ASMMI), calculated as ASMM divided by height squared, was $\leq$7 kg/m^2 in men and $\leq$5, 5 kg/m^2 in women.

Physical exercise training protocol

All participants followed a low-volume resistance exercise program conducted without specialized supervision. To enable autonomous delivery of the program, two formal training sessions were provided to caregiving staff at the daycare centers, including occupational therapists and sociocultural animation professionals. This approach addressed the limitation of needing an exercise physiologist for training sessions at each institution. Although the caregiving staff were not exercise specialists, they were experienced in leading various activities and were familiar with the specific care needs of frail older adults.

Each exercise session included two sets of three different resistance band (35) exercises, with 6–10 repetitions per set and 90 s rest intervals between sets and exercises. Sessions were designed to last no more than 15 min and were conducted thrice weekly, with a minimum 48 h rest period between sessions. Participants were encouraged to perform each set to volitional fatigue, which was defined as the point at which they either reported an inability to continue or were unable to maintain proper technique, emphasizing an explosive concentric phase followed by a slower eccentric phase. Supervisors were instructed to adjust the elastic band resistance if volitional fatigue was not reached during a given exercise. This was achieved by replacing the band with one of higher tension (three tension levels were available). If the participants already used the highest-tension band, their grip position was adjusted by shortening the distance to the elastic band's fixed point by approximately 20 centimeters.

Once training routines were established, staff reported that participants usually did not reach high fatigue levels and tended to rest for smaller periods, which meant that session time did not surpass 10 min. The program comprised nine different exercises distributed unevenly across the 12-week intervention. The primary exercises—chest press, squat, and seated rows—were prioritized, averaging 3.3 ± 1.6 sets per week, as they were considered critical for achieving the study's primary outcomes (36). Secondary exercises (leg extension, seated hip abduction, seated hip flexion, side raises, elbow flexion, and seated reverse flies), were performed less frequently, with an average of 1.2 ± 0.6 sets per week.

A pre-recorded video displayed on a large screen demonstrating the correct form for each exercise, ensured participants could easily follow and perform the routines as intended. Exercise sessions were conducted in groups of up to eight participants per supervising caregiving staff member. To qualify for inclusion in the study, participants were required to attend at least 31 sessions, representing an adherence rate of over 85%.

Initially designed as a low-volume resistance training protocol (36), the program can also be classified as minimum-dose power training (17), due to its focus on rapid concentric movements and the avoidance of high muscle fatigue levels during exercise.

Statistical analysis

All statistical analyses were performed using the SPSS statistics software package (version 28.0 for Mac; IBM, Chicago, IL, USA). The analysis comprised descriptive statistics (mean and standard deviation) to characterize the sample's anthropometric (height,

weight and body mass index), neuromuscular (ASMM, handgrip strength, 5STS time and muscle power), and functional (gait speed, SPPB, CPF and number of falls) variables. The prevalence of frailty, sarcopenia, falls, and related criteria (weight loss, muscle weakness, gait slowness, low physical activity and exhaustion) was also determined at each time point.

A repeated-measures ANOVA was used to evaluate the effects of the control and intervention periods on continuous variables (anthropometric, neuromuscular and functional). Mauchly's test was performed to assess whether the sphericity assumption had been met. When the assumption was violated, Greenhouse-Geisser or Huynh-Feldt corrections were applied to adjust the degrees of freedom. *Post-hoc* pairwise comparisons using the Bonferroni correction were performed if significant results were found in the repeated-measures ANOVA.

For categorical variables, including the prevalence of syndromes and positive frailty or sarcopenia criteria, a Cochran's *Q* Test was employed to detect significant differences between time points during the control and intervention periods. If significant differences were observed, *post-hoc* pairwise comparisons with Bonferroni corrections were conducted to identify specific time-point differences. A *p*-value of less than 0.05 was considered statistically significant for all analyses.

Results

Of the 44 participants who began the 12-week exercise intervention, 31 (61% females) completed it. Dropouts were primarily due to participants changing daycare centers ($n = 11$), falls requiring surgery ($n = 1$), and severe pre-existing illness ($n = 1$). Despite the lower completion rate, those who remained in the program demonstrated high adherence to the exercise sessions, with attendance exceeding 90% across all participants. No participants voluntarily withdrew from the study, and only minimal adverse effects, such as mild muscle soreness during initial sessions, were observed, highlighting the program's safety for this population. All daycare centers that initiated the exercise program continued until the end of the 12 weeks, demonstrating its feasibility and adaptability within institutional settings.

At the baseline (T_I), participants had an average age of 82.29 years, with 38.7% classified as frail, 22.6% diagnosed with sarcopenia, and 35.5% reporting a recent fall. Gait slowness and muscle weakness emerged as the most prevalent frailty criteria throughout the 24-weeks study period.

Neuromuscular function declined significantly from T_I to T_{II}, particularly handgrip strength (Figure 1b), 5STS time (Figure 1c), and absolute and relative muscle power (Table 1). However, this

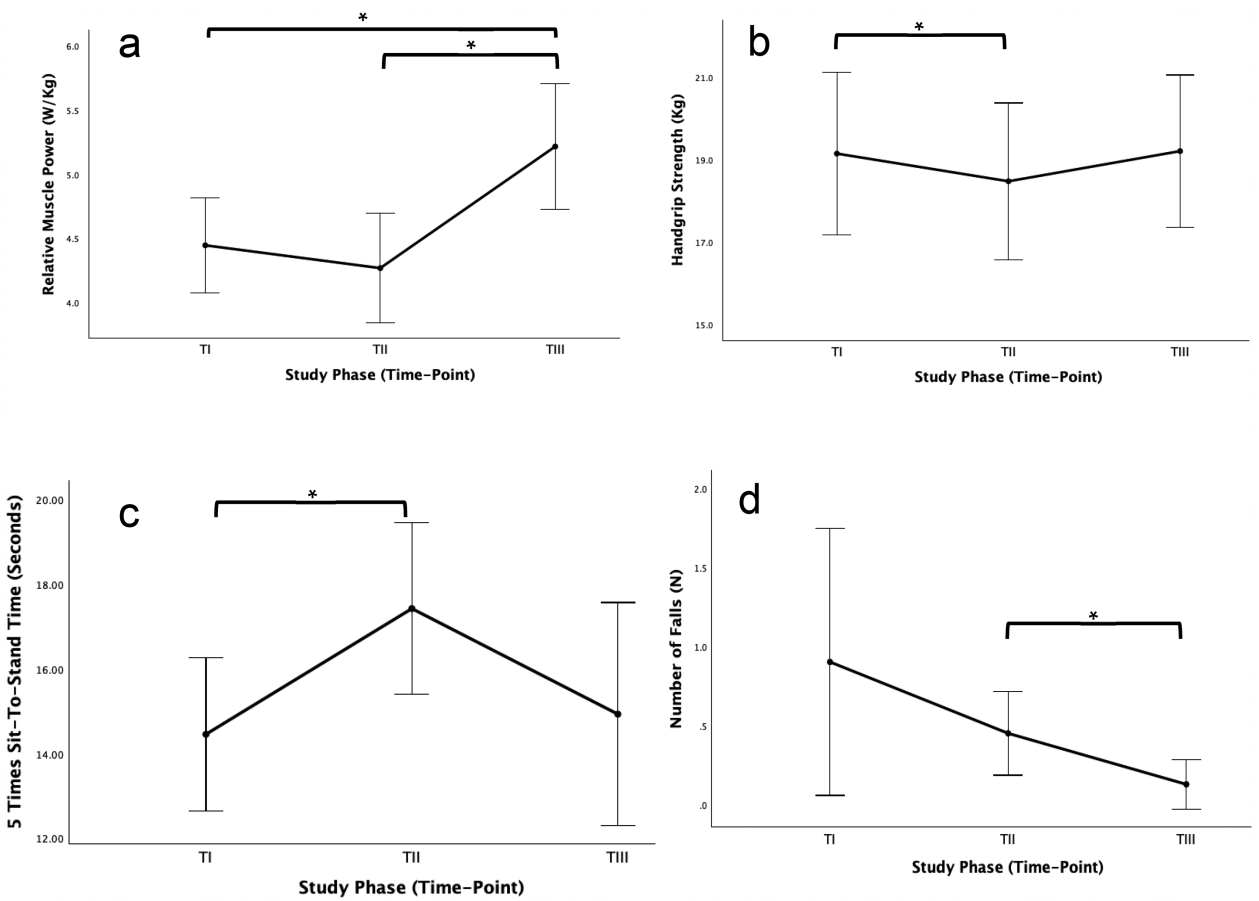

FIGURE 1
Effect of physical exercise intervention in relative muscle power (**a**), handgrip strength (**b**), 5 times sit-to-stand time (**c**) and number of falls (**d**).

TABLE 1 Effects of exercise intervention in neuromuscular and functional parameters (Mean ± SD).

Variables	T_I	T_{II}	T_{III}	>	*p*-value
BMI, kg/m^2	28.53 ± 5.40	28.32 ± 5.45	28.73 ± 5.20	-	0.204
ASMM, kg	17.48 ± 3.27	17.21 ± 3.19	17.03 ± 3.22	-	0.322
ASMMI, kg/m^2	7.15 ± 1.11	7.04 ± 1.10	6.96 ± 1.15	-	0.339
Gait Speed, m/s	0.65 ± 0.28	0.59 ± 0.21	0.62 ± 0.25	-	0.256
SPPB, pts	7.61 ± 2.26	7.42 ± 2.53	7.77 ± 2.82	-	0.609
CPF, pts	13.00 ± 6.75	13.30 ± 6.36	13.73 ± 5.63	-	0.545
Muscle Power, kw	0.31 ± 0.08	0.29 ± 0.08	0.36 ± 0.09	$T_{III} > T_I, T_{II}$	<0.001*
Relative Muscle Power, W/kg	4.45 ± 1.01	4.27 ± 1.16	5.21 ± 1.34	$T_{III} > T_I, T_{II}$	<0.001*
Grip Strength, kg	19.15 ± 5.37	18.48 ± 5.18	19.21 ± 5.03	$T_I > T_{II}$	0.107*
5x Sit-to-Stand, s	14.45 ± 4.92	17.42 ± 5.51	14.93 ± 7.18	$T_{II} > T_I$	0.053*
Number of Falls, n	0.90 ± 2.30	0.45 ± 0.72	0.13 ± 0.43	$T_{II} > T_{III}$	0.138*

T_I, baseline; T_{II}, pre-intervention; T_{III}, post-intervention; >, study phase comparison when significant differences were found; *p*-value, significance for the repeated-measures ANOVA; BMI, body mass index; ASSM, appendicular skeletal muscle mass; ASSMI, appendicular skeletal muscle mass index; SPPB, short performance physical battery; CPF, composite physical function; *, indicates significant differences between study phases.

TABLE 2 Effects of exercise intervention in syndrome prevalence.

Syndromes	T_I	T_{II}	T_{III}	>	*p*-value
Frailty Criteria					
Gait Slowness, %	61.3	71.0	58.1	-	0.273
Weakness, %	87.1	90.3	93.5	-	0.368
Low PA, %	32.3	25.8	0.0	$T_I, T_{II} > T_{III}$	<0.001*
Exhaustion, %	22.6	41.9	25.8	$T_I, T_{II} > T_{III}$	0.012*
Weightloss, %	16.1	16.1	9.7	-	0.670
Frailty, %	38.7	48.4	25.8	-	0.099
Sarcopenia Algorithm					
Upper-Limb Low Muscle Strength, %	64.5	74.2	48.4	$T_I, T_{II} > T_{III}$	0.004*
Lower-Limb Low Muscle Strength, %	51.6	67.7	29.0	$T_I, T_{II} > T_{III}$	0.001*
Low ASMMI, %	25.8	32.3	25.8	-	0.607
Low ASMM, %	41.9	48.4	58.1	$T_{III} > T_I$	0.042*
Low Physical Performance, %	64.5	64.5	54.8	-	0.500
Sarcopenia, %	22.6	29.0	9.7		0.045
Fallers, %	35.5	32.3	9.7	$T_I, T_{II} > T_{III}$	0.022*

T_I, baseline; T_{II}, pre-intervention; T_{III}, post-intervention; >, study phase comparison when significant differences were found; *p*-value, significance for the Cochran's *Q* Test; PA, physical activity; ASSM, appendicular skeletal muscle mass; ASSMI, appendicular skeletal muscle mass index; *, indicates significant differences between study phases.

trend was markedly reversed during the intervention period (T_{II} to T_{III}), with significant improvements observed in muscle power (Figure 1a). Nevertheless, no statistically significant effects of the intervention or the usual care period were found on anthropometric measures (BMI and ASMM) or physical function variables (SPPB, CPF and gait speed).

Apart from muscle weakness, the prevalence of all frailty criteria tended to decrease from T_{II} to T_{III}, with the most significant reductions observed in low physical activity and exhaustion (Table 2). While the percentage of participants below the threshold for gait slowness increased from T_I to T_{II} (61.3%–71.0%) and subsequently decreased from T_{II} to T_{III} (71.0%–58.3%), these changes were not statistically significant. However, changes in neuromuscular and behavioral variables contributed to a clear trend of reduced frailty prevalence, which dropped from 48.4% at T_{II} to 25.8% at T_{III}.

The proportion of participants falling below the muscle strength threshold for sarcopenia decreased significantly from T_{II} to T_{III} (Figures 2a,b), irrespective of the assessment site (upper or lower limb). According to the applied algorithm, this resulted in a reduction in sarcopenia prevalence ($p = 0.014$), even in the absence of measurable increases in muscle mass (Figure 2c). Additionally, the total number of falls (Figure 1d), particularly the percentage of fallers (Figure 2d), decreased during the intervention, dropping from over 30% at T_I and T_{II} to just 9.7% at T_{III}.

Discussion

The present study investigated the impact of a low-volume, remotely supervised resistance training program on frailty criteria among frail older adults attending daycare centers. The findings demonstrate that this approach can effectively prevent decline or promote improvements in key physical frailty indicators, potentially reversing or delaying its progression.

During the usual care period, significant declines were observed in handgrip strength and 5STS time, both crucial parameters of neuromuscular function in older adults. Although the loss of muscle strength and function was anticipated (43, 44), the rate of deterioration was notable given the relatively short duration of the usual care phase. In line with current knowledge (20, 45), the implementation of the resistance training program successfully halted this decline, effectively preserving muscle capacity. Furthermore, muscle power improved by 22% during the intervention period. While previous research has linked improvements in muscle power to enhanced gait speed, evidence suggests that a minimum 30% increase in muscle power may be required to impact gait speed significantly (46). Although resistance training is known to strongly affect gait speed (18), our results did not show significant changes in this variable, possibly due to a type II statistical error. This is supported by the observed trend: a decline in gait speed during the usual care phase, followed by a slight improvement during the intervention.

The absence of significant changes in objective physical function (SPPB) or perception of capacity (CPF) may reflect the intervention's duration and low volume, which may have been

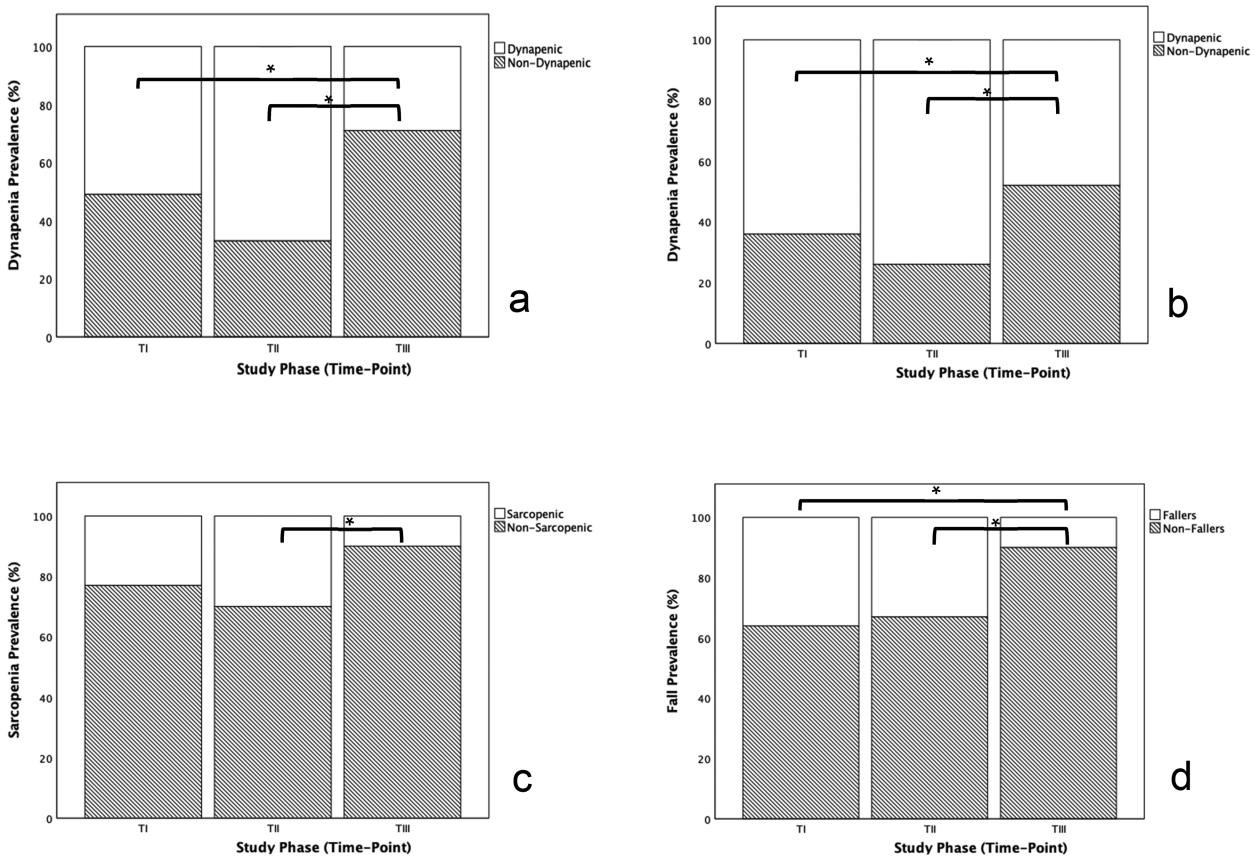

FIGURE 2
Effect of physical exercise intervention in the prevalence of dynapenia assessed in the upper limb (a), dynapenia assessed in the lower limb (b), sarcopenia (c) and falls (d).

insufficient to elicit detectable adaptations. Previous studies have shown that a minimum of 8.2% improvement in one-repetition maximum (1RM) strength is required for significant increases in physical function, a measure that is challenging to achieve with resistance band exercises (46).

Variations in physical function and neuromuscular capacity following the intervention translated into mixed effects on specific frailty criteria. Although the prevalence of gait slowness showed a slight but statistically insignificant reduction, there were no substantial changes in the prevalence of muscle weakness or unintentional weight loss. Importantly, however, significant reductions were observed in the prevalence of exhaustion and low physical activity, both of which are perceptive, self-reported measures. These changes likely reflect participants' subjective sense of increased energy and greater engagement in daily activities rather than objectively measured physical improvements. Previous research has consistently shown that resistance training alone does not improve habitual physical activity (47, 48). Nevertheless, the increase in physical activity observed in this study was sufficient to bring all participants above the low physical activity criterion threshold.

Overall, these changes contributed to a tendency towards a decrease in frailty prevalence, aligning with previous findings (13, 19, 49, 50) that support resistance training as a therapeutic tool for frailty management.

Supervision has consistently been shown to enhance outcomes in exercise programs for older adults (51, 52) and to improve adherence (53). This study represents the first attempt to implement a remotely supervised exercise program at an institutional level for this population. The findings suggest that unspecialized local supervision is sufficient to drive meaningful changes in physical function and frailty-related measures. Nevertheless, direct specialized supervision may have yielded even greater improvements emphasizing the potential for hybrid supervision models that combine remote and on-site expertise. On the other hand, the program's design achieves full adherence by participants and institutions, addressing common barriers to implementation (30, 32), enabling consistent participation.

The intervention had no measurable effect on ASMM, despite resistance training being recognized as a primary intervention for increasing muscle mass (45). High-intensity effort is typically necessary to stimulate muscle growth (20) and this program's intensity may not have met that threshold (35). Additionally, nutritional support is often needed to optimize muscle hypertrophy outcomes (54, 55). The limitations of bioimpedance analysis, a tool with known constraints, may have further

hindered the accurate detection of changes in muscle mass (56). Despite the lack of significant muscle mass or strength gains, the observed improvement trend in handgrip strength and the 5STS time which progressed, was sufficient to reduce the prevalence of dynapenia following resistance training. According to the EWGSWOP2 (26) algorithm, this represented a substantial decline in sarcopenia prevalence. Notably, different thresholds for low muscle strength in diagnosing sarcopenia (26) and frailty (1) led to significantly divergent results.

Finally, the observed reduction in fall frequency and the percentage of fallers is a critical finding, given the severe consequences of falls in older adults. This finding is consistent with previous studies demonstrating the efficacy of resistance training in improving balance and reducing fall incidence (57). However, the magnitude of this reduction is especially noteworthy.

Our results indicate that even a low-volume resistance training program can yield meaningful benefits for managing frailty, sarcopenia and fall prevalence. However, the study has limitations. The repeated measures design suggests that participants may have experienced physical decline before the intervention began, potentially complicating comparisons between the control and intervention periods. The use of resistance bands, while enhancing adherence and addressing institutional constraints, limited the ability to precisely control exercise intensity, progression, and task-specific muscle strength assessment. Furthermore, the absence of nutritional support and more robust tools for measuring muscle hypertrophy likely affected the evaluation of muscle mass changes.

Future research should focus on developing feasible exercise programs tailored to individual and institutional needs. Studies exploring optimal volumes and frequencies in larger samples and over longer durations are essential to understand better how older adults adapt to low-volume resistance training protocols.

Conclusion

This study highlights the benefits of a low-volume, remotely supervised resistance training program for frail older adults attending daycare centers. The findings demonstrate that such a program can overcome common institutional and individual barriers to implementing exercise interventions in senior care settings. Despite its limitations, this study underscores the potential of this approach to improve outcomes related frailty, sarcopenia, and falls. Further research is needed to refine the program design balancing individual and institutional adherence with meaningful clinical improvements.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Conselho de Ética para a Investigação da Faculdade de Motricidade Humana. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

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Sarcopenia prediction model based on machine learning and SHAP values for community-based older adults with cardiovascular disease in China

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Background: Sarcopenia (SP), is recognized as a complication of cardiovascular disease (CVD), but few relevant diagnostic models have been developed. This study aims to establish an interpretable diagnostic model for the occurrence of SP in older adult CVD patients living in Chinese community-dwelling (CD).

Methods: We randomly selected participants with CVD recruited from CHARLS from 2011 to 2015 and divided them into a training set and a test set. In the training set, we processed and screened the predictor variables and addressed the data imbalance by the synthetic minority oversampling technique (SMOTE). Subsequently, we built four machine learning (ML) models to predict SP. After 100 iterations, we selected the best performing model for risk stratification by comparing model discrimination and calibration. Then, we analyzed the relationship between ML risk and SP using scatterplots and logistic regression (LR). Finally, the Shapley's Additive Explanatory Plot (SHAP) illustrates how each feature level affects the predicted probability of SP.

Results: We ultimately included 1,088 CD older adults, 18.61% of whom reported SP. The optimal model, XGBoost, was selected for prediction and risk stratification. After both univariate (odds ratio [OR]: 12.45, $p = 4.74 \times 10^{-10}$) and multivariate analyses (OR: 6.98, $p = 3.96 \times 10^{-10}$), participants with higher ML scores had a higher risk of SP. In sex-specific subanalyses, BMI, height, age, DBP, HDL, etc. were all significant predictors.

Conclusion: This study develops a novel clinically-integrated tool that can be used to easily predict SP in the older adults population with CVD, providing a basis for the development of personalized therapeutic measures.

KEYWORDS

sarcopenia, CHARLS, cardiovascular disease, SHAP, diagnostic performance

1 Introduction

Cardiovascular disease (CVD) is a group of diseases involving the heart and peripheral vasculature, which is characterized by the interplay of atherosclerosis and myocardial ischemia leading to impaired cardiac function. Statistically, it accounts for 31% of deaths in the global population (1) and up to 40% in China, making it the leading cause of death (2). Previous studies have shown that CVD is associated with irreversible damage and decreased function of multiple organs such as the liver (3) and lungs (4), usually affecting the body's metabolic, detoxification, and neurological functions. Recent studies have found that chronic inflammatory states and reduced exercise tolerance are associated with CVD; and that the accelerated muscle loss resulting from both is a precursor to the development of sarcopenia (SP), which has become a recognized complication of CVD (5, 6).

Irving Rosenberg first defined SP as muscle atrophy in the older adults (7), and the Asian sarcopenia working group expanded it to include age-related loss of skeletal muscle mass, plus low muscle strength, and/or low physical performance (8). In general, a decrease in skeletal muscle mass usually begins to appear after the age of 40, and the incidence of SP is about 1–33% among people over 50 years old. Among subjects aged 60–70, 5–13% are affected by it, while among older adults aged 80 and above, this proportion can even reach as high as 50%. Studies have shown that SP is widely recognized as a risk factor for CVD and that the overall prevalence of SP in patients with high blood pressure (HBP) and coronary heart disease (CHD) is quite high (9). A systematic evaluation and meta-analysis reported that the prevalence of stroke-related SP was 42% (95% CI 33–52%) and that the prevalence of SP was even higher in the early post-stroke period (10). Research has shown that various characteristics of CVD (such as neuroendocrine disorders, endothelial dysfunction, etc.) affect the balance between protein synthesis and degradation in skeletal muscle, leading to SP (11). These risks can exacerbate the occurrence of related adverse outcomes such as falls, cachexia, and even death in SP patients, and vice versa (12). Therefore, we urgently need to determine methods for early screening of SP in patients with CVD.

Currently, SP diagnosis requires measurement of bone mass. Still, there are some methodological limitations, such as bioimpedance analysis (BIA) which is limited to specific groups of people, and X-ray computed tomography (CT) which exposes the body to radiation and is expensive (13, 14). Currently, there is a paucity of review literature that systematically summarizes and analyzes studies on SP prediction using machine learning (ML) techniques (15). It is worth noting that now with the rapid development of AI-assisted diagnostic technologies, relevant predictive models for this disease have been developed and have high accuracy and sensitivity (13, 16–18). For example, one study used clinical and laboratory metrics data from the West China Health and Aging Trends (WCHAT) study to predict SP using Support Vector Machine (SVM), Random Forest (RF), Extreme Gradient Boosting (XGBoost), and Wide and Deep (W&D) models, and showed that the W&D model had the highest area under the receiver operating curve (AUC) and accuracy (13). Another study using the National Health and Nutrition Examination Survey (NHANES) database in type 2 diabetes developed a novel and practical column chart based on three independent factors: gender, height, and waist circumference, which may be useful to clinicians in predicting the risk of pre-sarcopenia in young people with diabetes mellitus (16). Nevertheless, there is a lack of research on ML's diagnostic prediction of SP in CVD patients. In addition, although ML has performed well in previous studies, there is limited evidence of its application in Asian populations and interpretable risk prediction models to assist in disease diagnosis. Logistic regression (LR), random forest (RF) (19), support vector machine (SVM) (20), and XGBoost (21) were selected for this study in view of their excellent performance in dealing with high-dimensional and complex data; RF effectively reduces the risk of overfitting, SVM can find the optimal classification hyperplane in high-dimensional space, and XGBoost, with its powerful learning ability and fast training speed, has shown excellent performance in many medical prediction research, and XGBoost has shown excellent performance in many medical prediction studies with its strong learning ability and fast training speed.

In order to address the above limitations, this study develops a diagnostic model for SP in Chinese older adults with the help of an ML approach combined with SHAP in a CVD population. The objectives were to (1) screen the main influencing factors affecting the occurrence of SP in the older adults to provide a basis for early intervention; (2) build a highly interpretable SP diagnostic model to provide a non-invasive, economical, and harmless alternative imaging method for early detection of these patients.

2 Methods

2.1 Study population

The China Health and Retirement Longitudinal Study (CHARLS), a nationwide longitudinal survey of people >45 years old and their spouses in China, recruited 17,708 participants from June 2011 to March 2012, with multiple follow-ups after that (22). The database used face-to-face computer-assisted personal interviews (CAPI) to examine nearly 10,000 households in 150 counties and 450 villages across 28 provinces in China over an average of 2–3 years, providing information on relevant social, economic, and health status of community residents (22). Ethical approval for all the CHARLS waves was granted from the Institutional Review Board at Peking University. The IRB approval number for the main household survey, including anthropometrics, was IRB00001052-11,015; the IRB approval number for biomarker collection, was IRB00001052-11,014.

Blood tests and physical measurements were performed in the 2011 and 2015 waves, respectively (not available in 2018), so we used the 2011 and 2015 waves to develop a diagnostic model for SP. We excluded participants diagnosed with SP at baseline and included participants aged ≥60 years with a history of CVD (n = 1,080) who had blood tests and other health-related data available at baseline (Figure 1).

2.2 Ascertainment of outcomes

The diagnostic criteria for SP we defined regarding the latest edition of the Asian Working Group on Muscle Attenuation Syndrome 2019 (AWGS2019) (8), which included three components: low muscle mass (<5.61 kg/m^2 for females and <7.35 kg/m^2 for

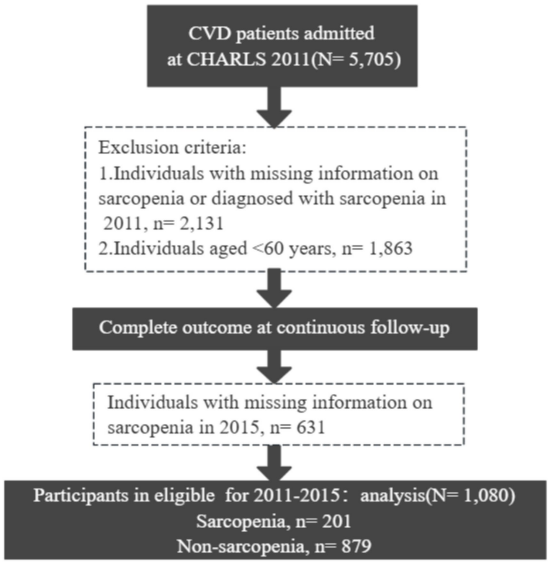

FIGURE 1
The flowchart for data processing and statistical analysis using the CHARLS in the present work.

males), muscle strength (<28.0 kg for males and <18.0 kg for females), or low physical performance (gait speed<1 m/s, chair stand test≥12 s) (23, 24).

First, muscle mass was assessed by appendicular skeletal muscle mass (ASM) and height. The equation model of ASM, which was validated on Chinese residents, was in strong agreement with DXA (25, 26):

$$\text{ASM} = 0.193 \times \text{body weight} + 0.107 \times \text{height} - 4.157 \times \text{sex} - 0.037 \times \text{age} - 2.631$$

Height, weight, and age are given in centimeters, kilograms, and years, respectively. For sex, value 1 represents males and value 2 represents females. Subsequently, we determined the threshold value for low muscle mass based on the lowest 20% of sex for height-adjusted muscle mass (ASM/height^2) in the study population (26, 27). Xu Wen et al. applied multiple linear regression to develop a height-weight model using DXA-measured ASM as the dependent variable and anthropometric variables as independent variables. The developed regression model was then cross-validated using data from the CV group. The adjusted R^2 of the equation model was 0.90 and the estimated standard error was 1.63 kg.

Additionally, participants' muscle strength in their dominant and non-dominant hands was assessed by a Yuejian TM WL-1000 dynamometer (22).

Finally, regarding physical performance, we chose to assess gait speed and chair stand tests. To measure gait speed, participants were asked to walk a 2.5-meter route twice at normal speed and take the average. To measure the chair stand test, participants were asked to stand five times in a row from a 47 cm high chair, keeping their arms crossed in front of their chest, and the time taken (in seconds) was recorded.

2.3 Ascertainment of CVD

This study focused on a population of people with CVD and HBP. In previous definitions (28, 29), CVD was identified by assessing two questions, "Have you ever been told by your doctor that you have had a heart attack, angina, CHD, heart failure, or other heart problem?" or "Have you ever been told by a doctor that you have had a stroke?" Study participants also answered the question about HBP, "Have you ever been told by a doctor that you have HBP?"

2.4 Feature selection and data preprocessing

To efficiently and comprehensively extract relevant features, we performed feature selection in three categories, including socio-demographic information, physical、exercise, nutritional factors, and clinical factors. Details of the candidate variables measured at baseline for all participants are shown in Supplementary Table 1. The selection of each feature was based on the following factors: (1) the feature had a missingness rate of less than 30% [populated with multiple imputation (30)], We use the mice package in R studio for multiple imputation, where each regression model can be expressed using the following equation:

$$Y_{\text{missing}} = \beta_0 + \beta_1 X_1 + \cdots + \beta_p X_p + \in$$

where Y_{missing} missing denotes the missing value of the target variable, $X_1, \cdots + X_p$ denotes the other predictor variables, $\beta_0, \beta_1, \cdots + \beta_p$ are the regression coefficients and υ is the error term. During interpolation, the regression model needs to be appropriately chosen to match the nature of the data (e.g., linear or logistic regression). The error term υ is usually assumed to be normally distributed, allowing the interpolation process to reflect the uncertainty in the predictions. Compared to other interpolation methods, it has the following significant advantages: consideration of uncertainty, efficient use of information, applicability to a wide range of analysis methods, and reduction of bias.

(1) The feature was associated with SP or a potential causative factor that turned out to be significant after analyses using logistic regression (LR), and (2) features with low variance and strong correlation (correlation coefficient>0.90) have been remove. The absence of significant linear relationships for the variables was checked using the findLinearCombos function from the Matrix package.

Since different features may have different ranges of values and some ML algorithms are sensitive to the scale of the features, we standardized or normalized the continuous variables and One-Hot the categorical variables.

2.5 Derivation and evaluation of prediction models

We predict whether SP occurs or not in four ML models, namely, LR, support vector machine (SVM), random forest (RF), and extreme gradient boosting (XGBoost), which is a scalable tree boosting system that has a wide range of application scenarios in ML. Its loss function does a second-order Taylor expansion of the error part; and also adds

a regularization part and parallel selection of each weak classifier, which prevents model overfitting and improves model generalization (31). We randomly divided 1,080 participants into a training set and a test set in a 7:3 ratio. Preprocessing, parameter tuning, and model training were performed on the training set. Considering the imbalance between positive and negative classes, we chose the synthetic minority oversampling technique (SMOTE) (32) for class balancing treatment. The new data are generated by calculating the distance between samples, finding the nearest neighbor samples of a certain minority class of samples, and then by linear interpolation. The specific process is as follows:

Step 1, select a minority class sample: randomly select a sample x_i from the minority class sample set.

Step 2, find the nearest neighbor samples: among the minority class samples, find the k nearest neighbor samples of x_i by Euclidean distance, and the value of k is set to 5 in this study.

Step 3, randomly select a neighbor sample: from these k nearest neighbor samples, randomly select a sample x_{nn}.

Step 4, generate a new sample: randomly interpolate between x_i and x_{nn} to generate a new sample according to the following equation. Where λ is a random number between 0 and 1.

$$x_{new} = x_i + \lambda \times \left(x_{nn} - x_i\right)$$

Step 5, Repeat the above process: repeat steps 1–4, and in our study we set the ratio of the number of diseased to non-diseased samples to 1:1.

After that, this study used a grid search method with a five-fold CV to optimize the hyperparameter combinations, and the specific tuning parameters are detailed in Supplementary Table 2. Finally, we chose the area under the receiver operating characteristic curve (AUC), accuracy, sensitivity, specificity, and F1 scores to assess the model's discrimination and the Brier scores to assess the model's calibration. To ensure the robustness of the results and to limit overfitting, we set up 100 different random seeds to repeat the above process and calculate the average performance of these 100 repetitions (33) (Figure 2). In this paper, the TRIPOD process is strictly followed to construct the prediction model (34).

2.6 Model interpretation and feature importance

The "black box" problem is considered to be one of the main obstacles to the further development of ML, and we need to increase the interpretability of the results by visualizing the model results both globally and locally. SHapley additive exPlanations (SHAP) (35) assign the contribution of the feature values to the different features. SHAP generates graphical and quantitative interpretations to help interpret the model and make more accurate clinical decisions. Its performance has been validated in previous studies (36). The calculation of SHAP value is based on evaluating all possible combinations of features with the following mathematical formula:

$$\phi_i = \sum_{S \subseteq N \setminus \{i\}} \frac{|S|!\left(|N| - |S| - 1\right)!}{|N|!} \left(v\left(S \cup \{i\}\right) - v\left(S\right)\right)$$

ϕ_i is the SHAP value of the features, S is the subset of features (excluding features i); N is the total set of features; $v\left(S\right)$ is the model output of the feature set S, and $v\left(S \cup \{i\}\right)$ is the model output after feature set S plus feature i.

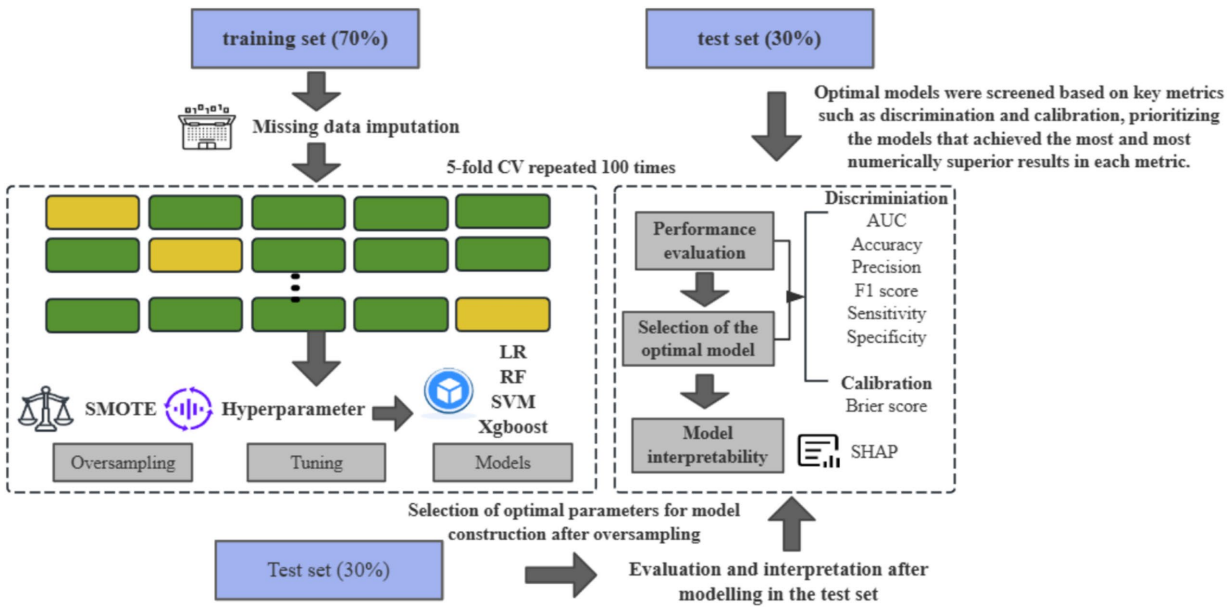

FIGURE 2
Flow chart of model derivation and test.

Afterward, we calculated the importance of the variables in the optimal model to identify the main predictors of the occurrence of SP in the older adults population with CVD.

2.7 Statistical analysis

First, to better understand the data distribution and characteristics, continuous data are presented as means (standard deviations) and were tested using independent samples t-tests or Mann–Whitney U-tests. Categorical variables were presented as frequencies (percentages) and tested using chi-square tests. The highest Youden's index was used to define the optimal threshold and to differentiate between low-risk and high-risk participants. Scatterplots were then drawn to describe the high and low ML risk distribution. Finally, the relationship between ML risk and 4-year SP was assessed using univariate and multivariate LR (controlling for the top 5 significant predictors). Statistical significance was based on a two-tailed p value$\leq$0.05.

All analyses and calculations were performed using R version 4.2.1 (caret, XGBoost, kernlab, randomForest, DMwR, and shapviz packages).

3 Results

3.1 Patient characteristics of the internal training and testing sets

The baseline characteristics of all participants in this study are shown in Supplementary Table 3. The baseline characteristics of participants after feature screening are shown in Table 1. The data were divided into a training set (70%) and a test set (30%). The prevalence of SP in the older adults population with CVD was 18.61% of the total number of subjects, 18.63% in the training set (141 subjects), and 18.58% in the validation set (60 subjects). The differences between the training and test sets were not statistically significant on the remaining variables such as gender, any weekly contact with children, taking any medications for HBP, CESD scale, visual or hearing problem, complication, BUN, glucose, age, average

TABLE 1 Training and testing set demographics.

Characteristics	Level	Participants, No. (%)			p value
		Total (N = 1,080)	Train (N = 757)	Test (N = 323)	
Sarcopenia (%)	No	879 (81.39)	616 (81.37)	263 (81.42)	0.089
	Yes	201 (18.61)	141 (18.63)	60 (18.58)	
Gender (%)	Male	513 (47.50)	346 (45.71)	167 (51.70)	0.082
	Female	567 (52.50)	411 (54.29)	156 (48.30)	
Any weekly contact with children (%)	No	93 (8.61)	63 (8.32)	30 (9.29)	0.690
	Yes	987 (91.39)	694 (91.68)	293 (90.71)	
Takes any medications for HBP (%)	No	407 (37.69)	295 (38.97)	112 (34.67)	0.206
	Yes	673 (62.31)	462 (61.03)	211 (65.33)	
CESD scale (%)	No	630 (58.33)	442 (58.39)	188 (58.20)	0.873
	Yes	450 (41.67)	315 (41.61)	135 (41.80)	
Visual or hearing problem (%)	No	867 (80.28)	603 (79.66)	264 (81.73)	0.483
	Yes	213 (19.72)	154 (20.34)	59 (18.27)	
Complication (%)	No	708 (65.56)	510 (67.37)	198 (61.30)	0.064
	Yes	372 (34.44)	247 (32.63)	125 (38.70)	
BUN (mg/dL) (Mean ± SD)		16.29 (4.42)	16.27 (4.50)	16.32 (4.23)	0.878
HDL (mg/dL) (Mean ± SD)		47.57 (14.03)	48.53 (14.24)	45.32 (13.25)	0.001
Glucose (mg/dL) (Mean ± SD)		117.07 (40.51)	116.47 (39.94)	118.49 (41.86)	0.453
UA (mg/dL) (Mean ± SD)		4.71 (1.28)	4.65 (1.24)	4.86 (1.37)	0.018
Age (y) (Mean ± SD)		66.32 (5.23)	66.26 (5.12)	66.46 (5.47)	0.567
Nst (h, Mean ± SD)		6.19 (1.93)	6.20 (1.95)	6.18 (1.90)	0.848
DBP (mmHg) (Mean ± SD)		78.28 (11.72)	78.37 (11.59)	78.05 (12.06)	0.682
Height (m) (Mean ± SD)		1.57 (0.10)	1.57 (0.08)	1.57 (0.12)	0.555
BMI (kg/m^2) (Mean ± SD)		26.67 (21.55)	25.82 (4.23)	28.68 (38.85)	0.046
Waist (cm) (Mean ± SD)		91.33 (11.46)	91.45 (11.17)	91.05 (12.13)	0.600

CESD, Center for Epidemiologic Studies Depression Scale; BUN, blood Urea Nitrogen; DBP, diastolic blood pressure; BMI, body mass index; Nst, average hours for one night sleeping time during the past month; UA, uric acid.

hours for one night sleeping time during the past month, DBP, height and waist, except for significant differences on HDL (48.53 vs. 45.32, $p = 0.001$) and uric acid (UA) (4.65 vs. 4.86, $p = 0.018$).

3.2 ML to predict outcomes

Table 2 shows the prediction performance of the four ML models in the test set. Overall, the new ML models all performed better than the traditional LR model. More specifically, comparing the AUC first, it can be seen from Supplementary Figure S1 that the RF has the highest AUC (all the following values are averages: 0.8769, 95% CI: 0.8367 ~ 0.9171) and the lowest LR (AUC = 0.8459, 95% CI: 0.7922 ~ 0.8996). Next, SVM has the highest precision (0.9681, 95% CI: 0.9429 ~ 0.9932) and specificity (0.9000, 95% CI: 0.8241 ~ 0.9759). However, taken together, the XGBoost had the highest accuracy (0.8050, 95%CI: 0.7575 ~ 0.8467), F1 score (0.8706, 95% CI: 0.8408, 0.9004), sensitivity (0.8061, 95% CI: 0.7583 ~ 0.8539) and Brier score (0.1950, 95% CI: 0.1486 ~ 0.2414) performed best. In addition, its AUC (0.8670, 95% CI: 0.8184 ~ 0.9156) is second only to the RF (Table 2). Therefore, XGBoost was selected for further prediction in this study.

3.3 Categorization of prediction score and risk stratification

We categorized patients into high-risk and low-risk groups after establishing the XGBoost in the test set using the maximum Youden's index as the optimal threshold (0.457, sensitivity = 0.8500, specificity = 0.7985) (Figure 3a). The results of the risk probability scatterplot determined by the optimal model showed a clear aggregation of SP in the older adults population with CVD, further demonstrating the accuracy of the model in stratifying high-risk and low-risk (Figure 3b).

3.4 Logistic regression analysis

After categorizing participants into low-risk and high-risk based on thresholds in a one-way LR analysis, high ML risk was significantly associated with SP diagnosis (unadjusted odds ratio [OR]: 12.45; 95%CI: 1.87 ~ 23.02; $p = 4.74 \times 10^{-10}$). After controlling for the five most important predictors (BMI, height, age, waist, and DBP), the correlation remained (adjusted OR: 6.98; 95%CI: 1.33 ~ 12.63; $p = 3.96 \times 10^{-10}$). The results of the multivariate LR analysis are shown in Figure 4.

3.5 Visualization of feature importance and interpretation of personalized predictions

SHAP can globally interpret and visualize the contribution of each feature in the XGBoost model to the prediction. In each feature importance row, all patient attributions to the results are represented by dots of different colors, with purple dots representing a negative correlation between the feature and the result, and yellow dots representing a positive correlation (Figure 5a). Figure 5b shows the importance of all screened variables using the optimal model. *X* and *y*-axis represent a unified index that responds to the influence of a certain feature in the model and variable importance, respectively. Age, UA, glucose, HDL, CESD scale, BUN, complication, taking any medications for HBP, and visual or hearing problems are positively correlated with SP. In contrast, BMI, height, waist, DBP, average hours for one night sleeping time during the past month, gender, and any weekly contact with children were negatively associated with SP (Figure 5a). We also provide an example to illustrate the function of SHAP in locally explaining individual features (Figure 6). Although the specific contribution of each individual may differ, the overall trend remains consistent with what we perceive.

3.6 Gender-based analysis

In the sex-specific subanalysis, we compared the top 10 predictors, average hours for one night sleeping time during the past month and HDL, as significant predictors only in males; they were not among the top 10 predictors in females. Similarly, some factors, such as CESD score and complication, were significant predictors in females only; in males, they were not among the top 10 predictors (Figures 7a,b).

The results of the risk probability scatterplot stratified according to different genders also showed an aggregation of SP in the older adults population with CVD, suggesting that the accuracy of the XGBoost for high-risk and low-risk stratification of different gender groups is also high (Figures 7c,d).

TABLE 2 Scores of each model on the test set.

Indicators	LR	RF	SVM	XGBoost
AUC	0.8459 (0.7922 ~ 0.8996)	**0.8760 (0.8367 ~ 0.9171)**	0.8645 (0.8204 ~ 0.9086)	0.8670 (0.8184 ~ 0.9156)
Accuracy	0.7709 (0.7211 ~ 0.8156)	0.8019 (0.7541 ~ 0.8439)	0.7307 (0.6787 ~ 0.7783)	**0.8050 (0.7575 ~ 0.8467)**
Precision	0.9565 (0.9287 ~ 0.9843)	0.9462 (0.9165 ~ 0.9758)	**0.9681 (0.9429 ~ 0.9932)**	0.9464 (0.9169 ~ 0.9759)
F1 score	0.8426 (0.8096 ~ 0.8755)	0.8683 (0.8382 ~ 0.8984)	0.8071 (0.7707 ~ 0.8435)	**0.8706 (0.8408 ~ 0.9004)**
Sensitivity	0.7529 (0.7007 ~ 0.8050)	0.8023 (0.7541 ~ 0.8504)	0.6920 (0.6362 ~ 0.7478)	**0.8061 (0.7583 ~ 0.8539)**
Specificity	0.8500 (0.7596 ~ 0.9404)	0.8000 (0.6988 ~ 0.9012)	**0.9000 (0.8241 ~ 0.9759)**	0.8000 (0.6988 ~ 0.9012)
Brier score	0.2291 (0.1826 ~ 0.2755)	0.1981 (0.1578 ~ 0.2383)	0.2693 (0.2136 ~ 0.3250)	**0.1950 (0.1486 ~ 0.2414)**

LR, logistic regression; RF, random forest; SVM, Support Vector Machine. Bolded representations perform better in the 4 models.

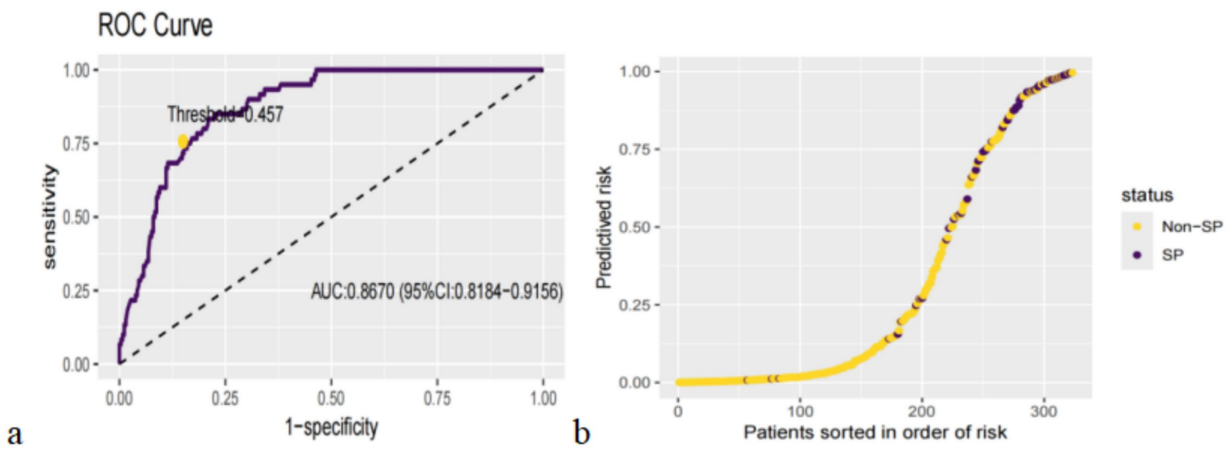

FIGURE 3
Categorization threshold of prediction score **(a)** and prediction distributions in participants with SP **(b)**.

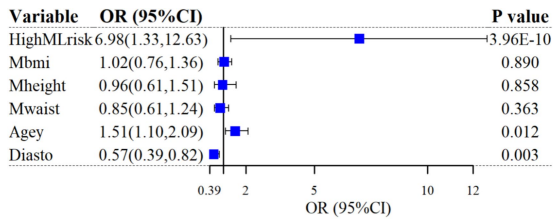

FIGURE 4
Multivariable logistic regression for SP prediction.

4 Discussion

4.1 Summary and comparison with existing studies

The occurrence of SP in the real world is still not properly and fully recognized clinically, especially in patients with CVD. Our literature review shows that the number of SP patients in CVD is higher than that in diabetes and respiratory diseases (6). In addition, early stroke is particularly likely to be associated with SP (10), suggesting that early diagnosis and intervention are of great importance in the prevention and treatment of SP in the older adults population with CVD.

In the current study, we developed an interpretable diagnostic prediction model for SP in the older adults population with CVD based on factors such as clinical assessment and socio-demographic information, which may be useful for clinicians to predict the risk of SP in CVD patients. Afterward, performance comparisons were made in terms of both calibration and discrimination of the models, and XGBoost had the best overall performance among the four ML models. The ML risk score generated from this model also indicates high accuracy. In addition, SHAP was used to interpret the features in the model both holistically and locally.

Firstly, regarding the clinical aspects, our study found that lower BMI was a relevant factor for the diagnosis of SP in the older adults population with CVD. Previous studies have shown that lower weight older adults are more likely to have a negative impact on nutritional status due to insufficient protein intake, whereas those with a higher BMI consume sufficient protein which may be protective against SP (37). Also, lower heights also have a higher risk of CVD (38) and the perspective that greater height loss is more likely to be diagnosed with SP has been observed in previous cohort studies (39), which is consistent with our findings. Interestingly, waist is also a correlate of SP because high levels of sex hormones stored within waist fat positively affect skeletal muscle (40), which is consistent with our findings.

The absence of adequate blood supply during diastole due to low DBP may affect the nutritional status of the muscle the lower the DBP the more likely it is to develop into SP (41). A meta-analysis (42) mentioned a significant correlation between HBP and SP in older adults, which is similar to the results of our study, which defined taking HBP-related medications as HBP. Our results also showed a significant association between depressive symptoms (43), visual or hearing impairment (44), and having other comorbidities (renal disease, dyslipidemia, diabetes mellitus, and cancer) (45–48) were predictors of SP, which is a recognized finding in previous studies.

Regarding blood tests, we found that BUN associated with kidney function and glucose associated with diabetes may increase the risk of developing SP. Although the current study has not confirmed that BUN and glucose are associated with skeletal muscle, it is hypothesized that they may further increase the prevalence of SP by affecting renal function and the development of diabetes. Miao Lu et al. (49) demonstrated that UA is a potential risk factor for SP in patients with heart failure with preserved ejection fraction (HFpEF), which is consistent with our findings. Meng Wang et al. (50) noted that for every 1-unit increase in HDL levels, there was a 42% increase in the odds of developing SP, and HDL also showed a positive correlation with SP in the current study.

Regarding socio-demographic information, in addition to gender and age mentioned in previous studies (16, 51), we found that any weekly contact with children in person/phone/emails may be a protective factor. Living alone and social isolation were identified as risk factors for SP by Jiaqing Yang (52). In the Chinese CD, many older adults live alone, and they alleviate their loneliness by talking to their children on the phone, which helps to reduce their risk of SP. After that, regarding physical、exercise, and nutritional aspects, the shorter the average hours for one night sleeping time during the past, the more likely it is to develop

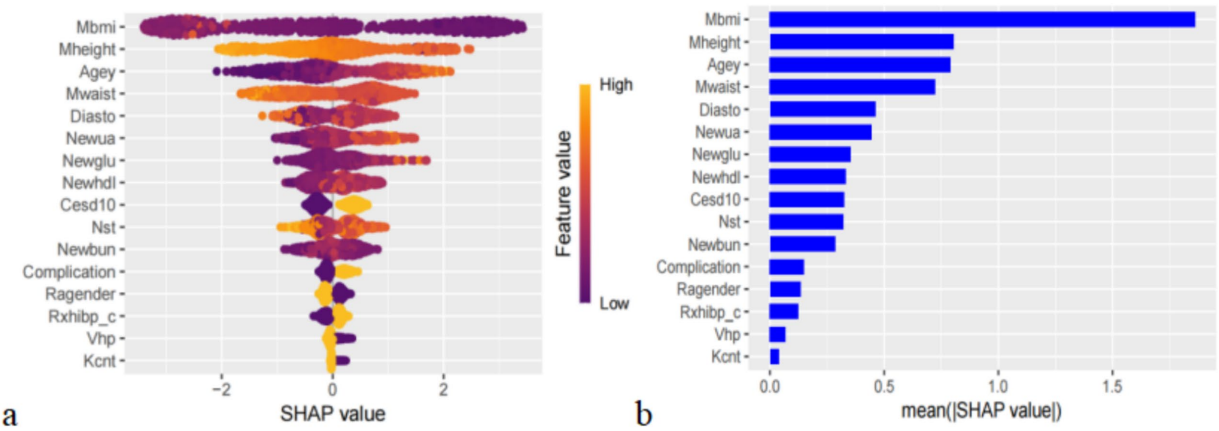

FIGURE 5
(a) Importance of all screened variables according to the mean (|SHA*p* value|), **(b)** the importance of all screened variables using the optimal model.

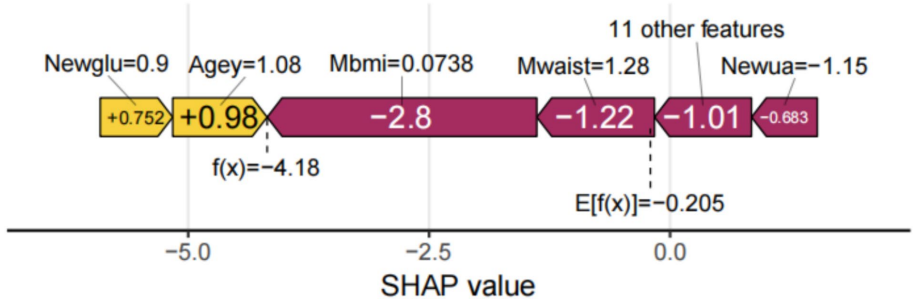

FIGURE 6
Interpretation of single sample model predictions.

SP. Ronaldo D. Piovezan (53) pointed out that with age, the decrease in sleep duration and quality favors protein hydrolysis and increases the risk of insulin resistance, which in turn reduces muscle fibers and strength.

The model constructed in this study brings new ideas for personalized treatment of older adults CVD patients. Through accurate risk stratification, appropriate treatment plans can be formulated according to the different levels of low, medium and high, from low-risk life interventions to high-risk intensive treatment, so as to improve the accuracy of treatment and the efficiency of resource utilization.

4.2 Strengths and limitations

Compared with previous studies (54), our work has several advantages. First, considering the possibility of increased sampling error in small, unrepresentative samples, this study used a large Asian-based cohort to increase the accuracy and breadth of the results. Second, the ML model combined with SHAP to analyze the importance and direction of action of each variable in the model helps to identify factors with high impact and improve clinical outcomes through early intervention.

Our study also has limitations. First, in terms of model selection, we did not select deep learning models. In the future, we will try to build deep learning models to predict SP and combine a wider range of data and information for different levels of research. After that, our study lacked external validation from an independent cohort, which may affect the superiority and generalization ability of the model. Finally, in terms of feature selection, we extracted some structured self-reported data and lacked imaging and genetic data. The absence of imaging data, which can visualize muscle morphology and structure (55), and genetic data, which can reflect an individual's genetic susceptibility (56), may prevent the model from comprehensively capturing the factors affecting the development of SP, thus affecting the accuracy of the prediction. Future studies may consider collecting related data to further improve the prediction model.

5 Conclusion

In an older adult CVD population in a Chinese CD, this study demonstrated the feasibility of using advanced ML methods and easily accessible features for effective prediction of SP risk. The ML-based SP risk prediction model can help physicians identify high-risk older adults CVD patients at an early stage, and combined with SHAP values can guide personalized treatment. At the policy level, this model can be used for mass screening to improve the efficiency of resource allocation, and can also promote relevant policies to facilitate the integration of the technology into the clinic.

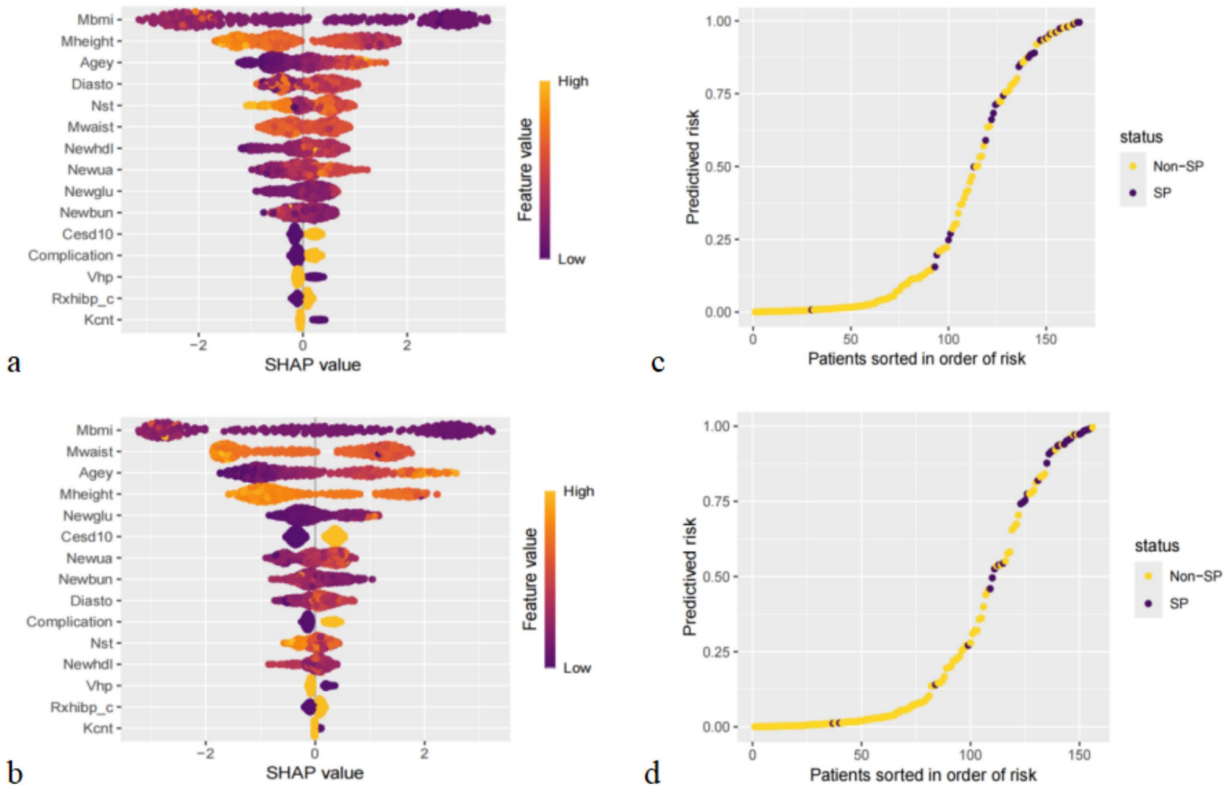

FIGURE 7
Importance of all screened variables according to the mean (|SHAP value|) for male **(a)** and female **(b)**, and prediction distributions in participants with SP for male **(c)** and female **(d)**.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Ethical approval for all the CHARLS waves was granted from the Institutional Review Board at Peking University. The IRB approval number for the main household survey, including anthropometrics, was IRB00001052-11,015; the IRB approval number for biomarker collection, was IRB00001052-11,014. Written informed consent was not required to participate in this study in accordance with the local legislation and institutional requirements.

Author contributions

PY: Conceptualization, Data curation, Formal analysis, Investigation, Validation, Visualization, Writing – original draft, Writing – review & editing. XZ: Investigation, Methodology, Supervision, Writing – original draft. GS: Conceptualization, Investigation, Writing – original draft. PZ: Funding acquisition, Resources, Validation, Visualization, Writing – review & editing. CZ: Investigation, Supervision, Validation, Writing – review & editing. KW: Funding acquisition, Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2025.1527304/full#supplementary-material

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Glossary

CVD - Cardiovascular disease

SP - Sarcopenia

HBP - High blood pressure

CHD - Coronary heart disease

BIA - Bioimpedance analysis

CT - Computed tomography

ML - Machine learning

CHARLS - China Health and Retirement Longitudinal Study

CAPI - Computer-assisted personal interviews

ASM - Appendicular skeletal muscle mass

LR - Logistic regression

SVM - Support vector machine

RF - Random forest

XGBoost - Extreme gradient boosting

SMOTE - Synthetic minority oversampling technique

AUC - Area under the receiver operating characteristic curve

SHAP - SHapley additive exPlanations

CESD - Center for Epidemiologic Studies Depression Scale

BUN - Blood Urea Nitrogen

DBP - Diastolic blood pressure

BMI - Body mass index

UA - Uric acid

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Differential effects of concentric and eccentric contractions on the primary motor cortex in healthy young and elderly participants

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Introduction: Aging is associated with a decline in musculoskeletal function, particularly muscle weakness, which affects a significant proportion of older adults and is associated with reduced quality of life and increased mortality. Two major contributors to age-related muscle weakness are muscle atrophy and cortical alterations. Eccentric exercise has been identified as a promising intervention to counteract these declines, as it has the potential to increase both muscle mass and cortical activity in young people. However, while the benefits of eccentric contractions on muscle mass in older adults are well documented, their effects on cortical activity, particularly in the lower limbs, remain unclear. The aim of this study was to compare cortical activity during concentric and eccentric quadriceps contractions of young and older adults.

Methods: This prospective study included 32 healthy participants: 17 young (23 ± 4 years, 6 women, 11 mens) and 15 older (62 ± 7 years, 7 women, 8 mens). Muscle strength was assessed using an isokinetic ergometer, muscular activity with electromyography electrodes positioned on quadriceps, and cortical activity using electroencephalography (EEG). Participants performed 40 concentric and 40 eccentric voluntary contractions against 20% of their maximal voluntary isometric contraction. EEG data were processed to analyze motor-related cortical potentials, specifically the negative potential (NP). The NP was divided into two main components: latency and amplitude as indicators of cortical activity during movement preparation and execution.

Results: There were no significant differences in participants characteristics between groups, except for age. Muscular activity was lower during eccentric than concentric contractions ($p < 0.05$). Cortical activity was significantly lower in older compared to young adults, which was reflected in reduced NP latency across several electrodes (Cz, $p = 0.03$; C4, $p = 0.02$; FC2, $p = 0.02$). However, regarding NP amplitude, it was significantly higher during eccentric contractions in Cz, C4, FC5, and C2 electrodes ($p < 0.05$) across both age groups.

Conclusion: This study is the first to investigate cortical activity during eccentric lower limb contractions in older adults. The results suggest that eccentric contractions induce greater cortical activation compared to concentric, even in older adults who generally exhibit reduced cortical activity. These findings

support the potential of eccentric as an effective intervention to improve motor function and muscle strength in older adults.

KEYWORDS

EEG, movement related cortical potential, muscle weakness, aging, eccentric

1 Background

Aging is a complex and inevitable biological process, associated with the decline of multiple systems such as the cardiovascular, respiratory, musculoskeletal or immune systems, increasing vulnerability to chronic disease and infections (López-Otín et al., 2013). Risk of lower limb muscle weakness is increasing during aging. Defined as the loss of muscle strength, this comorbidity affects between 9 and 13% of individuals over 60 years and more than 50% of those over 80 years (Cruz-Jentoft et al., 2010). It is associated with a reduced quality of life, postural instability and increased risk of falls and injuries, and with an increased hospitalization rate (Orr, 2010). Additionally, a low quadriceps strength is associated with an increased mortality rate (Newman et al., 2006).

In order to determine the most appropriate intervention to increase quadriceps strength when muscle weakness occurs, it is essential to understand its underlying main factors. In literature, two stand out as primary contributors: muscle atrophy and cortical alterations (Clark et al., 2015; Clark and Fielding, 2012; Clark and Taylor, 2011). Muscle atrophy is characterized by alterations in muscle fiber, loss of motor units and impaired protein synthesis (Degens, 2007; Narici et al., 2004; Ryall et al., 2008; Seene and Kaasik, 2012). While several studies, particularly in clinical populations such as individuals with chronic obstructive pulmonary disease (COPD), have estimated that muscle atrophy may account for up to 50–60% of age-related muscle weakness (Bernard et al., 1998; Menon et al., 2012; Seymour et al., 2010), evidence from large longitudinal studies in healthy older adults suggests a much smaller contribution. Delmonico et al. (2009) reported that changes in muscle mass explained only about 6–8% of the variance in strength decline, indicating that other factor play an important role (Delmonico et al., 2009). The cortical alterations are also a significant contributor of muscle weakness since they explain between 20 and 30% of the variance of muscle force (Clark et al., 2015; Clark and Taylor, 2011). Among abnormalities, a decrease in gray and white matter, a reduction in dendrite arborization and spine number, and neural dysfunction are classically reported (Clark and Fielding, 2012). Consequently, to fight efficiently against muscle weakness, and maximize strength improvement, it is thus necessary to promote interventions that target both muscle atrophy (i.e., increasing muscle mass) and cortical alterations (i.e., increasing cortical activity).

Among interventions well documented (among them nutrition, electrostimulation or stretching. . .), eccentric exercise appears to be a potential promising and relevant candidate. First of all, it is a safe intervention mode already used in elderly. Among its main advantages, this mode of contraction allows work at higher intensities with a lower perception of effort, oxygen consumption, and energy cost than concentric ones (Kim et al., 2022). This implies that a greater amount of work can be easily performed even in conditions with reduced functional capacities as in older individuals. Further, its efficacy on the determinants of muscle strength gain is documented by numerous studies. Eccentric contractions significantly increase quadriceps muscle mass and strength in both young and old people. Studies indicate up to 24% quadriceps hypertrophy and significant strength gains in young individuals following eccentric training (Brasileiro et al., 2011; Higbie et al., 1996; Hortobágyi et al., 1996; Leong et al., 2014). Similar results were observed, with up to 22% increases in quadriceps muscle thickness (Čretnik et al., 2022; Gluchowski et al., 2015; Katsura et al., 2019; LaStayo et al., 2009; Molinari et al., 2019). These studies suggests that eccentric contractions could be efficient to fight against muscle atrophy, the first key factor of age-related muscle weakness. The literature dedicated to eccentric training effects on cortical activity, is unfortunately less conclusive, due to a limited number of studies carried out on this topic. Nonetheless, understanding the cortical mechanisms underlying eccentric training is equally essential. In clinical contexts such as pulmonary rehabilitation, approximately half of COPD patients fail to achieve significant strength gains despite mechanical loading, which may be due to insufficient neural adaptations (Desachy et al., 2023). Identifying whether eccentric contractions promote cortical activation could therefore help optimize rehabilitation strategies by targeting both muscular and neural pathways of adaptation. However, some data are available concerning acute cortical responses during eccentric contractions. In young subjects, the literature highlights a greater cortical activity measured by EEG during the preparation and execution phases of the movement (Koohestani et al., 2020). In older people, fMRI indicate that a greater number of cortical regions are activated during eccentric movement (Yao et al., 2014). Taken together, these studies are consistent with the interest of eccentric contraction increase of cortical circuit functioning.

Unfortunately, findings on older people were systematically obtained on the upper limb. Therefore, these results cannot be directly extrapolated to the lower limbs due to their association with functional independence (e.g., gait, walking speed, fall prevention and more generally autonomy). This issue is all the more serious as some elements can act to induce different results in lower limbs. Indeed, researches have demonstrated that movements of the upper and lower limbs are associated with different patterns of cortical activation. Specifically, upper limb movements are characterized by greater cortical lateralization measured by fMRI, with substantial excitatory input to the contralateral motor cortex and significant interhemispheric inhibition, reflecting their role in fine and controlled movements (Volz et al., 2015). In contrast, lower limb movements involve more central, symmetrical interactions

between hemispheres with reduced inhibition (Harirchian et al., 2008, fMRI study). This distinction is related to the nature of the tasks: lower limb movements are generally less analytic and more coordinated (Martínez-Expósito et al., 2017). Consequently, these movements generate less intense cortical activity compared to upper limb movements, which require higher activity due to the complexity and fine motor control involved (Wheaton et al., 2008). Furthermore, the literature reports systematically lower cortical activity measured by EEG during movements of the lower limbs (potentially up to 50% lower compared to similar movements of the upper limbs) (Kline et al., 2016; Luft et al., 2002). Consequently, it remains uncertain whether eccentric movements of the lower limbs generate sufficient cortical activity to effectively combat age-related declines in both age-related brain alterations and muscle weakness.

In summary, eccentric exercise appears promising because it induces positive adaptations on major key factors of muscle weakness (atrophy and cortical alterations) in young subjects. However, no strong knowledge is available for older adults during lower limb eccentric contractions. Before proposing its use in a pathological context, we need to determine its effects on healthy older adults and on the lower limbs. Thus, the objective of this study was to compare cortical activity during quadriceps concentric and eccentric contractions in young vs. older healthy participants. The inclusion of a young adult group was intended to validate the experimental protocol in a population with preserved neuromuscular function. This ensured that the protocol was able to detect expected cortical activation patterns during lower limb contractions, before evaluating potential alterations related to aging.

2 Materials and methods

2.1 Participants

The prospective study included a total of 38 healthy participants. To be included, participants had to be right leg dominant and aged between 20 and 35 years for the young group, or between 50 and 70 years for the older group. The older group was composed of functionally healthy individuals without clinically significant muscle weakness. This choice allowed us to isolate age-related cortical effects independently of pathological conditions such as sarcopenia, and to establish a clear baseline for future comparisons.

The exclusion criteria were the existence of a lower limb trauma during the last 6 months, the inability to perform full knee extensions, a chronic illness, a neuromuscular pathology, a possession of any medical device (pacemaker, etc.) and the use of treatment known to modify neuronal activity [antidepressants, excessive consumption of caffeine/theine, i.e., more than 5 doses per day (Nehlig et al., 1992)]. Finally, 32 subjects were analyzed (6 subjects were excluded for the poor signal quality) and assigned to young (17 participants, mean age 23.5 ± 4.2 years, 6 women, 11 mens) or older group (15 participants, mean age 61.9 ± 5.7 years, 7 women, 8 mens). All included individuals signed informed written consent before participating to the study. In accordance to the Declaration of Helsinki, the study was approved by the local Ethics Committee (Institutional Review Board, permit number 2101B).

2.2 Procedures

The following procedures were based on the protocol described by Fang et al. (2001, 2004).

2.2.1 Dominant leg identification

The subject's dominant leg was determined based on three distinct tests: (1) ascending a step, (2) striking a ball with foot, and (3) experiencing forward imbalance. The leg naturally used for at least 2 out of the 3 tests was considered as the dominant leg (de Ruiter et al., 2010). Only participants with a right dominant leg were included in the study, for standardization purposes and due to equipment setup constraints.

2.2.2 Strength assessment

An isokinetic ergometer, the BIODEX 3 (Biodex, Shirley, New York), was used to assess the muscle strength of the dominant quadriceps of the subjects.

Participants were comfortably seated on the BIODEX 3 isokinetic ergometer. Adjustments were made to ensure hip and knee angles of 90°. The lever arm was properly adjusted to ensure attachment of the arm in line with the subject's kneecap and 2 cm above the ankle. The subject's right (dominant) leg was attached to the ergometer. The subject's shoulders, torso and arms were secured with belts so that only movements at the knee joint were possible.

Angle and force torque signals were recorded using the DELSYS system (Trigno^{TM} Wireless Systems, Delsys Inc., United States), at an acquisition frequency of 518 Hz.

After a standardized warm-up consisting of concentric and eccentric contractions performed at 120°/s, 70°/s, and 30°/s, the maximal voluntary isometric contraction (MVIC) of the quadriceps was assessed. For this, the leg was positioned at 90° and the ergometer was locked in an isometric position. The subjects were instructed to develop maximal force for 5 s, as if they were attempting to extend the leg (Babault et al., 2001). The contraction was considered valid if a plateau was maintained for at least 2 s. Three maximal contractions were performed, each separated by 1 min of passive rest. If the variation among the three contractions exceeded 10%, a fourth contraction was conducted to ensure three reproducible contractions. Based on the average MVIC value obtained, an external load (kg) corresponding to 20% of the MVIC was calculated and physically attached to the participant's ankle (Fang et al., 2001).

Voluntary concentric and eccentric contractions of the quadriceps were performed against this fixed load (20% of MVIC). Concentric contractions involved raising the leg from 100° to 165° (i.e., from vertical to horizontal position), while eccentric contractions involved lowering the leg from 165° to 90°. Each movement was executed over 3 s, corresponding to a controlled angular velocity of 22°/s (Babault et al., 2001). Although the setup involved an isokinetic dynamometer, the fixed nature of the resistance made the task functionally isotonic.

2.2.3 Electroencephalography recording

The Starstim 20 system (Neuroelectrics, Barcelona, Spain) was used to record EEG signals from the scalp.

The EEG cap containing the electrodes (NG Geltrode, Neuroelectrics) was positioned on the participant's head with Cz at

the center of the head. The electrode positioning was based on the International 10–20 System (Klem et al., 1999). In this experimental design, 9 electrodes (Cz, C1, C2, C3, C4, FC1, FC2, FC5, FC6) were used and positioned overlying the sensorimotor areas of ipsi- and contra-lateral hemispheres (Figure 1). Cz and C3 were considered as the main electrodes due to their proximity to the leg motor cortex area.

Conductive gel (Signa Gel®) was injected into each electrode using a syringe. A color-coded map indicating electrode impedance was displayed to improve the connection between the electrodes and the scalp. Elevated impedance was typically reduced by applying more gel or gently pressing the electrode, in order to keep impedance of each electrode below 10 kΩ. References electrodes (CMS, DRL) were placed over the right earlobe using an ear clip. The EEG was sampled at 500 Hz. The EEG device was connected using WIFI and controlled by the computer through a software interface (Neuroelectrics Instrument Controller, NIC v 2.0).

2.2.4 Electromyography recording

The DELSYS wireless dynamic EMG system (TrignoTM Wireless Systems, Delsys Inc., United States) was used to record the electrical activity of the vastus lateralis, vastus medialis, and rectus femoris of the dominant leg. Before each electrode placement, the skin was shaved, abraded, and cleaned with alcohol. EMG signal quality was automatically assessed by the Delsys Trigno system before each recording using the built-in diagnostic function. This tool provides a visual indicator (green/orange/red) for each sensor, reflecting the quality of electrode-skin contact. We verified that all sensors displayed green status prior to data collection, which corresponds to low contact resistance and optimal signal acquisition (typically equivalent to impedance values below ∼5 kΩ). This ensured consistent EMG signal quality across participants. The sampling frequency was 2148 Hz.

The wireless EMG signals were transmitted to the EMG acquisition software via the electrodes pasted on muscle surfaces, and then processed and analyzed using the EMG software (EMGworks Analysis and MATLAB 2021b).

2.3 Protocol

After the participants' arrival, the dominant leg was identified. The EMG electrodes were attached on the dominant leg, the EEG cap and electrodes were placed and the impedance checked. Once equipped, the participant takes a seat on the ergometer and adjustments were made.

Subjects performed a warm-up composed of 3 sets of 10 concentric-eccentric contractions (leg extension-flexion) at 120°/s, 70°/s, and then 30°/s. After that, the MVIC was assessed. To familiarize with contractions, subjects performed 10 concentric and 10 eccentric contractions to well understand to movement and respect the timing of the task. After that, subjects began with either concentric or eccentric contractions (randomly). They performed 40 concentric contractions (2 sets of 20) and 40 eccentric contractions (2 sets of 20) against a load equal to 20% of their MVIC. Each contraction was preceded by a 3-s isometric contraction (Fang et al., 2001). The movement was calibrated using vocal instructions ("start", "go", "stop"). There was a 20-s rest between each contraction, 5 min of rest between the two sets, and 10 min of rest between the two modes of contractions.

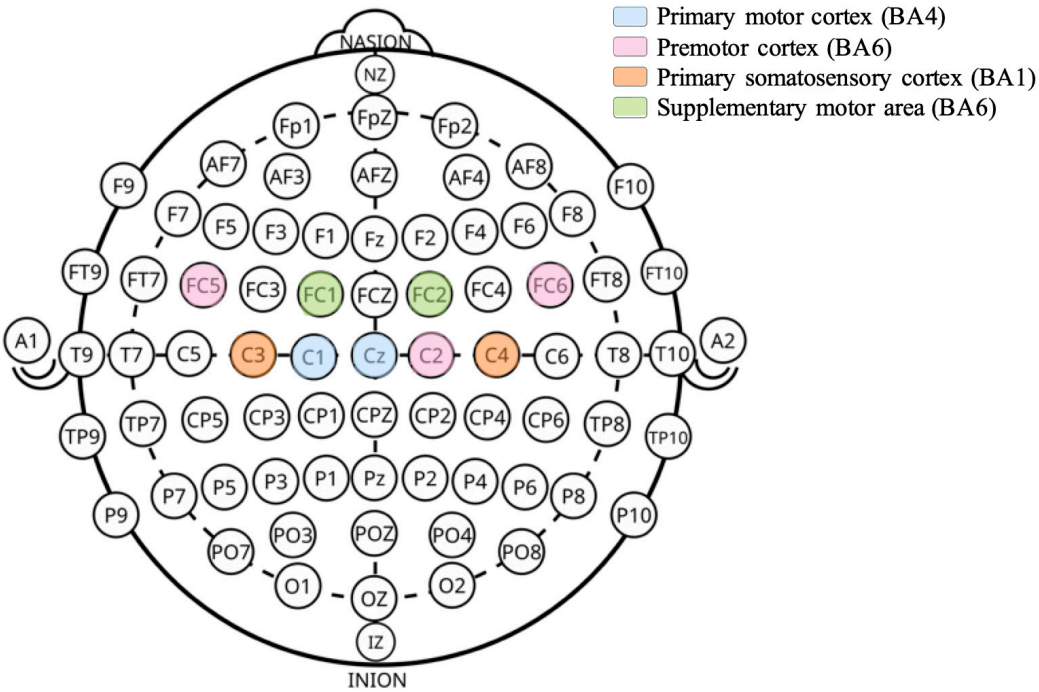

FIGURE 1
Scalp positions of EEG electrodes used. Electrode labels follow the international 10–20 system. The underlying cortical areas and their associated functions are indicated based on anatomical mapping studies (Scrivener and Reader, 2022).

During the contractions, subjects were instructed to remain as relaxed as possible, without moving, speaking, and to focus on a visual cue in front of them (a black cross (approximately 10 × 10 cm), drawn with a marker on a whiteboard, was placed at eye level about 1.5 meters in front of the participant).

2.4 Data analysis

2.4.1 EMG pre-processing

To preprocess the EMG signal, a Butterworth high-pass filter with a cutoff frequency of 10 Hz was applied to remove movement artifacts, followed by a low-pass filter with a cutoff frequency of 400 Hz to eliminate high-frequency noise. The amount of muscle electrical activity was expressed as the root mean square (RMS) of the EMG recording.

2.4.2 EEG pre-processing

Off-line signal processing and analyses were performed using EEGLAB open-source toolbox version 2022.0 (Delorme and Makeig, 2004). Raw continuous EEG data were preprocessed using the pipeline describe in Figure 2. First bandpass filtered between 1 and 40 Hz. To reduce high-amplitude, non-stationary artifacts prior to ICA decomposition, we applied Artifact Subspace Reconstruction (ASR) with a burst criterion of 20 and a window criterion of 0.25. This method allowed automatic detection and correction of transient artifacts by comparing signal characteristics to a baseline estimated from clean EEG segments. ICA was then performed using the Infomax algorithm (runica function in EEGLAB). Artifactual components (e.g., ocular, muscle) were identified using ICLabel and removed. A visual inspection of the cleaned signal was conducted afterward to ensure artifact-free epochs.

Data were segmented into 10-s windows time-locked to each trigger (from −5 to +5 s). Only participants with at least 10 artifact-free trials per condition (eccentric and concentric) were included in the final analysis to ensure quality (Borràs et al., 2022; Boudewyn et al., 2018).

2.4.3 Motor related cortical potential

MRCPs were selected as the primary cortical marker to replicate and extend the work of Fang et al. (2001), who used this approach to compare cortical activation during concentric and eccentric contractions (Fang et al., 2001). MRCPs are well-established, temporally precise indicators of voluntary movement preparation and execution, and allow for trial averaging and robust inter-group comparisons.

For each EEG channel, MRCPs were computed by averaging across artifact-free trials for each condition. EEG epochs were baseline-corrected using a pre-movement resting segment (-10 s), and the mean baseline value was set as the y-axis reference. A linear regression was applied to the descending slope of the waveform

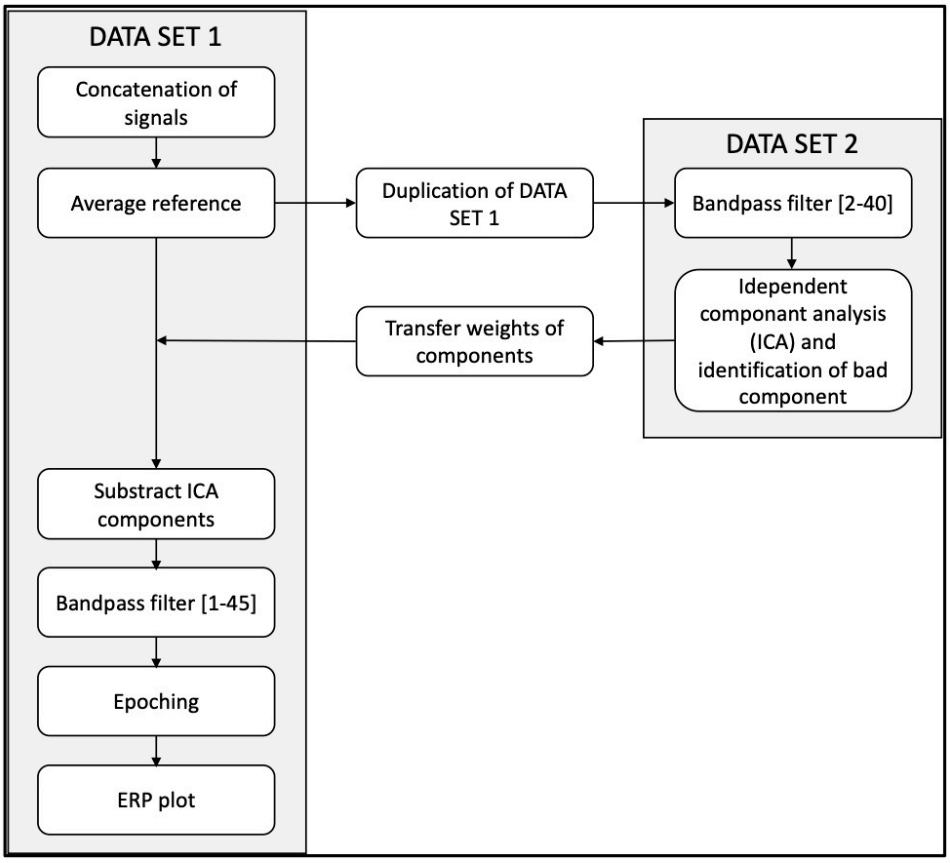

FIGURE 2
Pre-processing EEG pipeline.

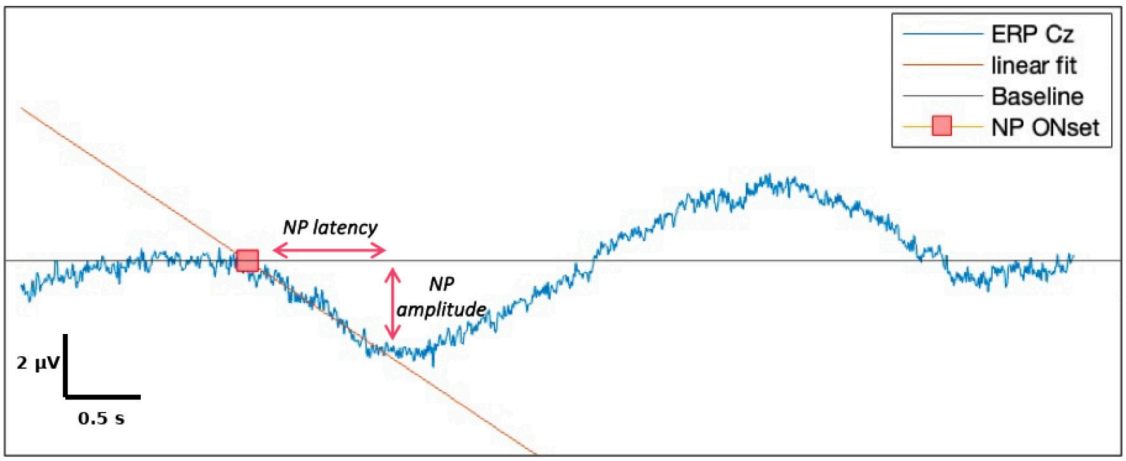

FIGURE 3
Components of negative potential (NP) and illustrations of their measurements.

leading to the negative peak (NP). The onset of cortical motor preparation was defined as the intersection between this regression line and the baseline.

NP latency was defined as the time interval between this onset point and the most negative value (NP). NP amplitude was calculated as the difference between the baseline level and the NP (Figure 3). All waveforms were visually inspected, and manual corrections were made when needed to ensure reliability (Shibasaki and Hallett, 2006).

2.5 Statistical analysis

All statistical analyses were performed using JASP software [JASP Team (2022). JASP (Version 0.16.3)].

Before comparing the participant's characteristics, we assessed the normality of the data distribution using the Shapiro-Wilk test. Since all variables met the assumption of normality ($p > 0.05$ for age, body weight, height, BMI and quadriceps strength), parametric tests were used. An unpaired *t*-test was used to compare differences between young and older participants. A chi-square (χ^2) test was used to compare the distribution of sex (male vs. female) between the two age groups.

For all analyses, data were first averaged across valid trials for each participant and condition. Statistical tests were then conducted on these participant-level averages for EMG RMS values at each muscle, and MRCP features at each EEG electrode.

To compare MRCPs between concentric and eccentric contractions in each group, a two-way repeated-measures ANOVA was performed, with Age Group (young vs. older) as the between-subject factor and Contraction Mode (concentric vs. eccentric) as the within-subject factor. Assumptions of normality (Shapiro–Wilk test) and homogeneity of variances (Levene's test) were confirmed for all dependent variables ($p > 0.05$). The assumption of sphericity for the within-subject factor was assessed using Mauchly's test.

The effect size was estimated with Partial Eta Squared (η_p^2). A Partial Eta Squared of 0.01, 0.06 or 0.14 indicated, respectively, small, medium or large effect.

All results are reported as mean ± standard deviation (SD). An alpha threshold of 0.05 was considered significant for all statistical tests.

3 Results

3.1 Participants characteristics

Participant's characteristics are given in Table 1. Except for age, the participant's characteristics were non-significantly different between groups.

3.2 Muscular activity

The ANOVA conducted on the RMS values of the EMG signals from the rectus femoris, vastus lateralis, and vastus medialis, revealed no significant interactions between age group (young vs. older) and contraction mode (concentric vs. eccentric) across the

TABLE 1 Participant's characteristics.

Variable	Young group (*n* = 17)	Older group (*n* = 15)	*P*-value
Age (years)	23.5 ±4.2	61.9 ± 5.7	<0.001
Male/female	12/5	8/7	ns (0.31)*
Body weight (kg)	63.5 ± 8.6	67.6 ±13.6	ns (0.33)
Height (cm)	168.1 ±10.5	169.2 ±7.1	ns (0.71)
BMI	22.2 ±2.9	24.1 ±3.1	ns (0.09)
Q_{MVIC} (N.m)	196.9 ±60.7	162.6 ±41.4	ns (0.08)
Q_{MVIC} (kg)	50.2 ±13.4	42.5 ±11.2	ns (0.08)

BMI, body mass index; Q_{MVIC}, quadriceps maximal voluntary isometric contraction. ns, non-significant statistical difference. (Independent sample *t*-test were used for all variables except for the comparison of male and female, a Chi-squared was used). *Means that a Chi-squared test was used.

TABLE 2 ANOVA results on NP amplitudes (in μV) on age and contraction mode factors.

		Means SD		ANOVA results			
Area	Modes	Older	Young		Contraction * age	Contraction mode (concentric vs. eccentric)	Group age (young vs. older)
C1	Concentric	2.39 ± 1.63	2.96 ± 1.58	**F**	2.60	0.06	0.04
	Eccentric	2.80 ± 1.80	2.41 ± 1.03	**p**	0.12	0.81	0.84
				η_p^2	0.08	<0.01	<0.01
C2	Concentric	1.86 ± 1.24	2.21 ± 0.95	**F**	0.75	15.79	0.05
	Eccentric	3.19 ± 2.16	3.06 ± 1.21	**p**	0.40	***<0.001***	0.82
				η_p^2	0.03	0.39	<0.01
C3	Concentric	2.55 ± 1.34	3.36 ± 1.81	**F**	1.83	0.02	0.86
	Eccentric	2.91 ± 1.52	2.92 ± 1.25	**p**	0.19	0.89	0.36
				η_p^2	0.06	<0.01	0.03
C4	Concentric	2.21 ± 1.24	2.78 ± 1.03	**F**	1.15	9.66	0.31
	Eccentric	3.44 ± 2.06	3.38 ± 1.24	**p**	0.29	***0.005***	0.58
				η_p^2	0.04	0.27	0.01
Cz	Concentric	3.86 ± 2.21	6.75 ± 4.50	**F**	0.07	6.15	4.66
	Eccentric	5.92 ± 3.91	8.39 ± 4.96	**p**	0.79	***0.02***	***0.04***
				η_p^2	<0.01	0.17	0.14
FC1	Concentric	2.56 ± 1.11	3.22 ± 1.85	**F**	2.41	4.79	0.19
	Eccentric	3.00 ± 1.68	2.70 ± 1.05	**p**	0.13	**0.04**	0.67
				η_p^2	0.07	0.19	<0.01
FC2	Concentric	2.99 ± 1.62	3.00 ± 1.40	**F**	0.01	1.05	0.01
	Eccentric	3.32 ± 1.94	3.40 ± 1.53	**p**	0.94	0.32	0.92
				η_p^2	<0.01	0.04	<0.01
FC5	Concentric	4.16 ± 1.83	4.28 ± 1.60	**F**	0.02	6.80	0.012
	Eccentric	5.60 ± 2.44	5.90 ± 2.67	**p**	0.88	***0.01***	0.73
				η_p^2	<0.01	0.21	<0.01
FC6	Concentric	5.14 ± 2.08	5.52 ± 1.79	**F**	0.07	0.08	0.17
	Eccentric	5.35 ± 1.54	5.52 ± 2.36	**p**	0.79	0.79	0.69
				η_p^2	<0.01	<0.01	<0.01

Bold and italic values indicate statistically significant results.

three muscles (p-values related to $F_{contraction*age}$ ranging from 0.22 to 0.49).

Additionally, there was no significant effect of age, indicating that EMG activity did not differ significantly between younger and older participants (p-values related to F_{age} ranging from 0.14 to 0.74).

However, a significant effect of contraction mode was found for both the rectus femoris and vastus lateralis, with a significantly lower RMS values observed during eccentric contractions compared to concentric ones (respectively, $F = 8.86$, $p < 0.01$, $\eta_p^2 = 0.22$ and $F = 6.65$, $p = 0.01$, $\eta_p^2 = 0.17$). No significant effect of contraction mode was found for the vastus medialis ($F = 1.66$, $p = 0.21$, $\eta_p^2 = 0.05$).

3.3 Cortical activity

3.3.1 NP Amplitude (μV)

NP amplitude on Cz, C2, C4, FC5 were significantly higher during eccentric contractions compared to concentric ones (respectively, $p = 0.02$, $\eta_p^2 = 0.17$; $p < 0.001$, $\eta_p^2 = 0.39$; $p = 0.005$, $\eta_p^2 = 0.27$; $p = 0.01$; $\eta_p^2 = 0.21$) (Table 2 and Figure 4). FC1 amplitude revealed a significant interaction between the age group and the contraction mode ($p = 0.04$, $\eta_p^2 = 0.19$). Older adults exhibited reduced cortical activity during concentric contractions and greater activity during eccentric contractions, whereas younger participants showed the opposite pattern, with higher cortical activity during concentric compared to eccentric contractions.

Cz NP amplitude was significantly lower in the older group compared to young group whatever the contraction mode ($p = 0.04$, $\eta_p^2 = 0.14$).

3.3.2 NP Latency (ms)

The analyses revealed a non-significant interaction between contraction mode and age group. Regarding group effect, NP latency on FC2 was systematically lower in the older group whatever contraction mode ($p = 0.02$, $\eta_p^2 = 0.16$). There were no significant differences on others electrodes (Table 3). No significant effect of contraction mode was observed.

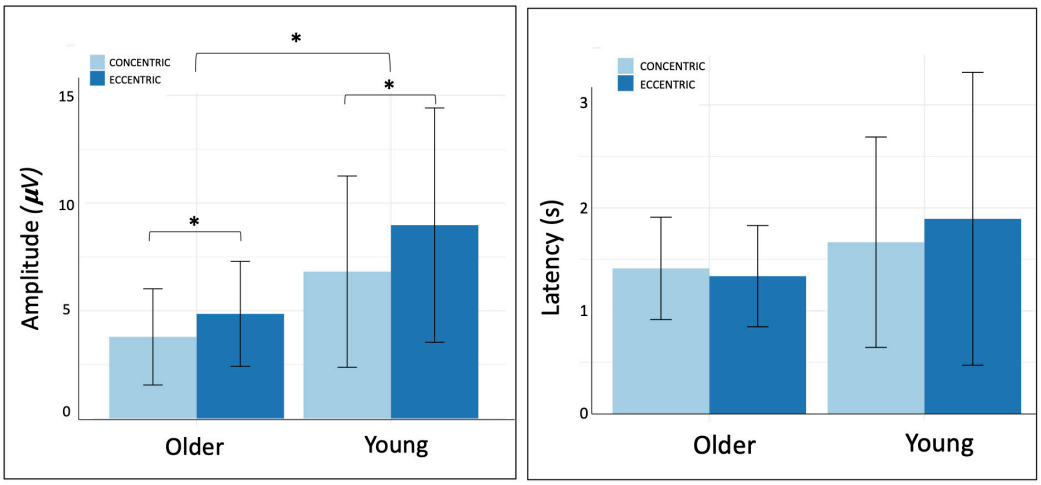

FIGURE 4
Amplitude and latency of negative peak on Cz electrode.

TABLE 3 ANOVA results on NP latency (in ms) on age and contraction mode factors.

		Means SD		ANOVA results			
Area	Modes	Older	Young		Contraction * age	Contraction mode (concentric vs. eccentric)	Group age (young vs. older)
C1	Concentric	1.29 ± 0.75	1.73 ± 1.03	F	0.80	0.31	1.69
	Eccentric	1.36 ± 0.68	1.43 ± 0.66	p	0.38	0.58	0.20
				η_p^2	0.03	0.01	0.05
C2	Concentric	1.18 ± 0.38	1.42 ± 0.71	F	0.11	1.36	1.06
	Eccentric	1.44 ± 0.83	1.56 ± 0.72	p	0.74	0.25	0.31
				η_p^2	<0.01	0.04	0.03
C3	Concentric	1.41 ± 0.88	1.59 ± 0.83	F	0.41	0.20	0.08
	Eccentric	1.45 ± 0.67	1.36 ± 0.57	p	0.53	0.66	0.78
				η_p^2	0.01	<0.01	<0.01
C4	Concentric	1.67 ± 0.82	2.13 ± 1.13	F	1.18	0.02	0.23
	Eccentric	1.92 ± 1.23	1.81 ± 1.51	p	0.29	0.89	0.64
				η_p^2	0.04	<0.01	<0.01
Cz	Concentric	1.44 ± 0.50	1.55 ± 0.64	F	0.94	1.48	<0.01
	Eccentric	1.41 ± 0.33	1.30 ± 0.50	p	0.34	0.24	0.97
				η_p^2	0.03	0.05	<0.01
FC1	Concentric	1.54 ± 0.87	1.69 ± 1.22	F	0.08	2.04	0.19
	Eccentric	1.28 ± 0.58	1.31 ± 0.63	p	0.79	0.16	0.67
				η_p^2	<0.01	0.07	<0.01
FC2	Concentric	1.31 ± 0.52	1.82 ± 0.80	F	<0.01	0.14	5.88
	Eccentric	1.37 ± 0.56	1.89 ± 1.11	p	0.98	0.71	***0.02***
				η_p^2	<0.01	<0.01	0.16
FC5	Concentric	1.45 ± 0.50	1.40 ± 0.69	F	0.02	0.05	0.16
	Eccentric	1.51 ± 0.80	1.41 ± 0.77	p	0.90	0.83	0.69
				η_p^2	<0.01	<0.01	<0.01
FC6	Concentric	1.38 ± 0.52	1.35 ± 0.46	F	0.65	3.00	0.18
	Eccentric	1.50 ± 0.68	1.68 ± 0.71	p	0.43	0.09	0.67
				η_p^2	0.02	0.09	<0.01

4 Discussion

The aim of the study was to compare cortical activity during quadriceps concentric and eccentric contractions in young and older subjects. The major findings were that even though the older group exhibited lower cortical activity compared to the younger group (on Cz and FC2), eccentric contractions were associated higher cortical activity (on Cz, C2, C4, and FC5) in both groups compared to concentric ones. Additionally, a lower muscular activity was found during eccentric contractions compared to concentric ones in young and older group.

From a fundamental perspective, the lower muscular activity observed during eccentric contractions compared to concentric ones aligns with previous research. Eccentric contractions are known to generate high force with reduced neural drive, involving lower motor unit recruitment and firing rates than concentric contractions (Babault et al., 2001; Moritani et al., 1987). This reduced activation is partly due to mechanisms unique to eccentric actions, such as passive force contributions from elastic elements, fewer motor units recruited and the efficient detachment of cross-bridges during lengthening (Kellis and Baltzopoulos, 1998). Additionally, eccentric contractions are metabolically efficient, requiring significantly less ATP and energy expenditure (Enoka, 1996; LaStayo et al., 2003), which makes them advantageous for producing high force levels with minimal muscle activation. This efficiency is reflected in lower EMG amplitudes, indicating that eccentric contractions allow for economical tension development, which is especially useful for strength training and rehabilitation contexts.

Regarding cortical activity, this study revealed two significant differences between age groups. First, elderly individuals showed lower cortical amplitudes at Cz compared to younger participants, regardless of the contraction mode. This reduced amplitude likely reflects decreased cortical motor preparation, as MRCP amplitude, and particularly the negative potential (NP), is known to be a marker of the intensity of cortical recruitment during voluntary movement planning (Shibasaki and Hallett, 2006). This observation aligns with established literature, which attributes such differences to age-related functional and structural cerebral changes. Indeed, numerous studies have highlighted cerebral differences between young and elderly individuals. Structural changes include global cerebral volume reduction, decreased gray matter volume, and lower quality and quantity of white matter (Salat et al., 2009; Seidler et al., 2010). At a functional level, the observed decrease in corticospinal excitability with aging (Fujiyama et al., 2012; Spedden et al., 2018) could be linked to a reduced capacity of elderly individuals to regulate inhibitory processes (Fujiyama et al., 2012). Furthermore, older adults exhibit reduced corticospinal responses during submaximal contractions (Škarabot et al., 2019). In addition, a significantly shorter MRCP onset latency was observed at FC2 in older adults. While this may seem unexpected, FC2 corresponds to the right premotor cortex, which is primarily involved in motor planning. This earlier activation may reflect a compensatory anticipatory mechanism, aimed at maintaining performance despite age-related decline, as suggested by previous findings (Heuninckx et al., 2005; Mattay et al., 2002). More generally, while MRCP amplitude clearly discriminated between groups and conditions, latency appeared less sensitive. This may be due to its tighter temporal constraint within the task and greater interindividual variability, making it less reliable for detecting systematic differences at the group level.

Secondly, this research highlighted greater cortical activity on Cz, C2, C4, and FC5 electrodes during eccentric contractions. These findings are consistent with the literature and confirms several key aspects previously established for upper limb movements or younger individuals. Our results show that the pattern of greater cortical activation during eccentric contractions, compared to concentric contractions, is also observed for the lower limbs (Kline et al., 2016; Luft et al., 2002). Moreover, this pattern persists with aging with a higher cortical activity in eccentric. Functionally, this increased amplitude of the NP suggests that eccentric contractions demand stronger preparatory engagement from the motor system, possibly due to the higher complexity of motor control during lengthening contractions, which require precise modulation of descending commands, and greater reliance on sensorimotor integration (Fang et al., 2001; Enoka, 1996). Additionally, eccentric actions involve controlling an externally imposed movement, rather than generating one from scratch, which has been associated with higher inhibitory demands and the need for fine motor coordination. This may explain the greater activation observed in motor and premotor regions. Another contributing factor may be the relative unfamiliarity of eccentric contractions in daily life. Because these actions are less practiced, they may require more attentional resources and anticipatory planning, further amplifying preparatory cortical activity. This indicates that distinct neuronal control strategies for eccentric movements are maintained whatever the limb engaged and preserved with aging. While these higher cortical activity in eccentric align with the existing literature, our study also revealed an unexpected spatial pattern of cortical activation.

The increased cortical activation during eccentric contractions observed in this study was more localized to central regions (notably Cz, C2, C4, and FC5 electrodes) rather than widespread across the cortex like for upper limb. Although this spatial pattern is consistent with the organization of motor control for lower limb movements, it remains somewhat surprising in light of the literature on eccentric contractions, which has consistently reported broader and more diffuse cortical activation across the cortex during eccentric tasks (Fang et al., 2004). This pattern was consistent across both age groups, contrasting with previous studies reporting more diffuse cortical activation in older adults during eccentric contractions (Fang et al., 2004; Inuggi et al., 2011; Mattay et al., 2002; Perrey, 2018; Sailer et al., 2000; Yao et al., 2014). One relevant explanation lies in the differences between upper and lower limb neural control. Lower limb movements, predominantly engage localized regions in the primary motor cortex, as opposed to the more lateralized and diffuse activation patterns observed for upper limb movements (Volz et al., 2015). These factors likely explain the localized overactivation observed during eccentric contractions in this study, highlighting distinct neural control strategies for lower limb motor tasks.

Finally, these results, and more specifically the higher cortical activity during eccentric contractions, open up very interesting clinical perspectives. Clarifying the cortical effects of eccentric exercise is therefore essential not only to understand the neurophysiological basis of strength gains, but also to improve clinical outcomes by guiding more personalized and targeted

rehabilitation interventions, such as with COPD patients. In young individuals, eccentric exercise not only leads to acute cortical response but also induces significant chronic cortical adaptations as an increased cortical activity, a reduction of intracortical inhibition and silent period, as well as an enhancement of corticospinal excitability (Kidgell et al., 2015). In this context, acute responses refer to immediate neurophysiological changes that occur during or shortly after a single session of exercise. In contrast, chronic responses correspond to longer-term adaptations resulting from repeated exposure to exercise over several weeks, such as structural or functional changes. These chronic adaptations are of prime importance since cortical activity is significantly related to the increase of muscle strength after training (Kidgell and Pearce, 2010). In support of this, we found that MRCP amplitude at Cz and C3 was positively correlated with maximal voluntary force. Specifically, Cz amplitude during concentric contractions explained 39% of the variance in strength ($r = 0.624$, $p < 0.001$), whereas Cz and C3 amplitudes during eccentric contractions explained 18% ($r = 0.421$, $p = 0.017$) and 17% ($r = 0.416$, $p = 0.018$), respectively. One could hypothesize that this difference may, at least in part, reflect the greater familiarity and consistency of concentric contractions, which could reduce interindividual variability and strengthen the association with cortical activation. However, this remains a hypothesis and should be further explored in future studies. These correlations suggests that promoting cortical activation may meaningfully contribute to improving strength. Given that our study shows similar acute cortical responses in older adults and in the lower limb, it is reasonable to infer that similar chronic adaptations could be achieved in the elderly. Although this remain to be confirmed by specific studies, there is indirect evidence to support the idea that chronic brain adaptations may be preserved with age, which could play a crucial role in improving muscle strength through this neural mechanism. Indeed, a recent study examining muscular adaptation after 12 weeks of eccentric training in older adults with COPD reported a significant increase in muscle strength without changes in muscle mass (MacMillan et al., 2017). The authors hypothesized that this improvement may stem from cortical adaptations, supporting the potential of eccentric training to induce central nervous system benefits even in clinical populations. Eccentric exercise could be a promising candidate for enhancing muscle strength in older adults by targeting both muscle atrophy and brain alterations. The increase of muscle strength of elderly is of major concern in order to reduce the risk of falls, improve patients' quality of life, and potentially reduce mortality risk in certain pathologies (Swallow et al., 2007).

5 Methodologials considerations

Several limitations of this study should be acknowledged. First, only quadriceps EMG activity was recorded, without monitoring antagonist muscles such as the hamstrings. This limits our ability to evaluate potential co-contraction strategies, which may influence both movement execution and cortical motor engagement.

Second, although EEG provides high temporal resolution and is well suited for analyzing preparatory cortical dynamics, its spatial resolution remains limited. As a result, deeper or more distributed brain activations, particularly in subcortical or associative regions, may not have been fully captured by our analyses.

Third, due to the structure of the experimental task, participants were required to immediately return their leg to the starting position after each contraction. This continuous movement introduced artifacts in the post-movement period, preventing reliable analysis of termination-related potentials or post-movement cortical dynamics, which may have offered additional insight into inhibitory processes.

Fourth, although a threshold of at least 10 clean trials per condition was applied, the total number of usable trials remained relatively modest for some participants. This could affect the signal-to-noise ratio and reduce the robustness of individual-level averages, particularly in older adults where signal quality is often more variable.

Another limitation is that the older adult group in our study consisted of functionally healthy individuals without clinically significant muscle weakness. While this allowed us to isolate age-related cortical responses under controlled conditions, it limits the generalizability of our findings to frailer or sarcopenic populations. Future studies should examine whether similar cortical responsiveness to eccentric contractions is preserved—or perhaps enhanced—in clinical populations, and whether chronic eccentric training can promote neuroplastic adaptations relevant for rehabilitation.

Finally, all contractions were performed using the right dominant leg. Consequently, the findings may not generalize to the non-dominant limb or to bilateral or functional movements involving interlimb coordination.

6 Conclusion

To conclude, this study is the first one to investigate cortical activity during lower limb eccentric contractions in the elderly. Despite an overall reduction in cortical activity in older adults, eccentric contractions were associated with significantly higher cortical activation compared to concentric ones, as in younger individuals. Interestingly, this greater activation is more localized to brain regions associated with motor control of the lower limbs. These findings enhance our understanding of the neural mechanisms underlying muscle contractions in the elderly, providing valuable insights for developing targeted interventions to improve motor function, prevent falls and increase quadriceps muscle strength in this population.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Institutional Review Board of Euromov. The studies were conducted in accordance with the local legislation and institutional

requirements. The participants provided their written informed consent to participate in this study.

Author contributions

MD: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing, Software, Validation, Visualization. NH: Conceptualization, Funding acquisition, Resources, Supervision, Writing – review & editing, Project administration. JL: Data curation, Methodology, Software, Writing – review & editing. SP: Data curation, Methodology, Resources, Writing – review & editing. AV: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Methodology, Project administration, Resources, Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Indonesian optimal sarcopenia cutoff values of calf circumference, muscle strength, and physical performance: a multicenter descriptive and cross-sectional study

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Introduction: The prevalence of possible sarcopenia among Indonesian older adults using the Asian Working Group for Sarcopenia (AWGS) 2019 consensus cutoffs was abnormally high compared with reported prevalence in other East Asian countries. This suggests that the current AWGS cutoff values may not be applicable to the Indonesian population as it did not contain reference statistical values based on the local population normative studies. This lack of local data may result in inaccurate assessments and diagnoses of sarcopenia

among Indonesian population. We therefore aimed to conduct a nationwide study in the community to obtain optimal cutoff values for calf circumference, muscle strength, and physical performance for the diagnosis of sarcopenia in Indonesia.

Methods: In this multicenter descriptive and cross-sectional study, we collected data from healthy adults aged 20–39 years in different islands in Indonesia. We followed the recommendation by the European Working Group for Sarcopenia in Older People (EWGSOP) of using 2 standard deviations [SD] below the mean of a young healthy cohort for the new cutoff points of sex-specific handgrip strength, calf circumference, and gait speed. The mean +2 SD was used for five times sit-to-stand test (FTSTST).

Results: The mean −2 SD value of male handgrip strength was 21.15 kg, and 14.34 kg for female subjects. The mean −2 SD value of male and female calf circumferences were 29.92 cm, and 26.70 cm, respectively. Two SD below the mean of gait speed results was 0.51 s, whereas 2 SD above mean of FTSTST results was 11.69 s.

Discussion: The suggested cutoff values for low calf circumference, muscle strength, and gait speed in Indonesian population are different from those in previous consensuses. Body morphology, culture, and obesity may be the factors related to this phenomenon. This study contributes to the body of literature of normative data used to determine cutoff values used in the diagnosis of sarcopenia in Indonesian and Asian populations.

KEYWORDS

sarcopenia, walking speed, physical functional performance, muscle strength, Indonesia

1 Introduction

The Asian Working Group for Sarcopenia (AWGS) pioneered the development of diagnostic criteria specific to the Asian population, considering factors such as body composition, muscle strength, and physical performance (1). Systematic review and meta-analysis of the studies following AWGS 2014 guideline concluded that the prevalence of sarcopenia in Asian older adults was as high as 14% (95% confidence interval [CI] 0.12–0.17) (2). Prevalence of sarcopenia in Asian populations is comparable to that of Caucasian populations when using appropriate diagnostic criteria (3). The AWGS 2014 guideline addressed the cutoff points for older Asian people by modifying the European Working Group on Sarcopenia in Older People (EWGSOP) guideline (1), followed by publishing updated guideline in 2019 (4). AWGS 2019 diagnostic algorithm incorporated calf circumference for muscle mass assessment, handgrip strength to assess muscle strength, five times sit-to-stand test (FTSTST), and gait speed to assess physical performance (4). Various studies have highlighted physiological and health-related factors which may affect physical performance, such as muscle strength, age, pain, and cognitive function (5–7). There is also a growing recognition of the influence of ethnicity, cultural background, and even geolocation differences of the same ethnicity on the various components of body composition and muscle health (8).

The most populous nations in Southeast and East Asian regions, namely, Indonesian and People's Republic of China, were not represented among the study populations and were used to determine the cutoffs in both versions of the AWGS consensus guidelines (1, 4). FTSTST was used as a surrogate for gait speed in a single-center Japanese study, with the cutoff for FTSTST estimated based on the linear regression study between FTSTST and gait speed by Nishimura et al. (9). While China had solved the problem by conducting a study to determine the optimal cutoff points for the diagnosis of sarcopenia among mainland Chinese population (10), there was a lack of Indonesian data in AWGS cutoff points. Our previous SARC-F questionnaire-based multicentre study found that 17.6% of Indonesian older adults were at risk of sarcopenia (10). However, a cross-sectional study in Indonesia by Sumandar et al. based on AWGS 2019 cutoff points (4) reported an abnormally high prevalence of possible sarcopenia (45.5%) among Indonesian older adults (11). Sumandar, et al. suggested that the use of current AWGS 2019 cutoff values for the diagnosis of sarcopenia may result in an overestimation of the prevalence of sarcopenia in Indonesia (11).

The cutoffs for the various components of muscle health used in the diagnosis of sarcopenia in the AWGS 2019 are based on a combination of studies using 2-standard deviations, 1-standard deviation, or the lowest quintiles, a cutoff for normality (1, 4). On the other hand, the consensus form the European Working Group on Sarcopenia in Older People in 2010 (EWGSOP) relied on 2 standard deviations (SD) below mean of the numerical data obtained from healthy young adult population as reference statistical value to classify abnormal findings (12, 13).

The abnormally high prevalence of possible sarcopenia reported by Sumandar et al. using cutoff points from AWGS 2019, together with our concerns regarding the lack of Indonesian normative data, and the use of variable standard deviations and lowest quintiles as reference statistical values were the impetus for us to conduct this descriptive and cross-sectional study in an Indonesian healthy young adult

population. We aimed to conduct a multicentre study to obtain Indonesia's optimal sarcopenia cutoff values for calf circumference, muscle strength, FTSTST, and gait speed. We also aimed to use the 2-standard deviations based on the mean of a healthy young adult population as the cutoff for normality as per the European Working Group on Sarcopenia in Older People in 2019 (EWGSOP2) guidelines (12, 13), with slight method adjustment for FTSTST.

2 Materials and methods

2.1 Study design and subjects

We conducted a multicenter descriptive and cross-sectional study in multiple study centers. We utilized consecutive sampling method to collect the data from healthy Indonesian adults aged 20–39 years who met predetermined criteria. The inclusion criterion was the ability to walk without walking aid (e.g., walking stick, frame, wheeled trolley, crutches, walkers, or rollators). The exclusion criteria were history of electronic device or orthopedic metal implantations, heart failure, chronic kidney disease, peripheral oedema, diuretic consumption, hyperthyroidism or hypothyroidism, and later stage of malignancies with cachexia. The history was ascertained through history taking. The hospitals involved in data collection process were Dr. Cipto Mangunkusumo National General Hospital, Jakarta; Prof. Dr. I Goesti Ngoerah Gde Ngoerah Central General Hospital, Denpasar; Dr. Hasan Sadikin Central General Hospital, Bandung; Dr. Zainoel Abidin District General Hospital, Banda Aceh; Dr. M. Djamil Central General Hospital, Padang; Dr. Wahidin Sudirohusodo Central General Hospital, Makassar; Dr. Moewardi District General Hospital, Surakarta; Dr. Saiful Anwar District General Hospital, Malang; Dr. H. Moch. Ansari District General Hospital, Banjarmasin; Prof. Chairuddin P. Lubis Hospital, Medan; and Merauke District General Hospital, Merauke.

We calculated the minimum sample sizes utilizing sensitivity analysis formula. The highest number of calculation result was considered the minimum sample size, which was 676, consisting of 376 of male subjects and 300 of female subjects. We determined the minimum sample size for each of 6 main islands (Java, Bali, Kalimantan [Borneo], Papua, Sumatra, and Sulawesi [Celebes]) based on the ratio of the regional population to the total population in 2022 (n = 252,021,000). Therefore, the minimum sample size calculated for Java was 388 subjects (216 male subjects and 172 female subjects), whereas it was 12 for Bali (7 male subjects and 5 female subjects) and 46 for Kalimantan (25 male subjects and 20 female subjects). The minimum sample size was 15 for Papua (8 male subjects and 7 female subjects), 161 for Sumatra (89 male subjects and 71 female subjects), and 54 for Sulawesi (30 male subjects and 24 female subjects). The minimum sample size for Java was divided into four centers, namely, Jakarta, Bandung, Surakarta, and Malang. Centers in Banda Aceh, Medan, and Padang represented the population of Sumatra, and the minimum sample size for this island was divided into three centers. Makassar represented the population of Sulawesi (Celebes). On the other hand, centers in Denpasar, Banjarmasin, and Merauke represented the population of Bali, Kalimantan (Borneo), and Papua, respectively.

Ethics approval was obtained from the Ethics Committee of the Faculty of Medicine, Universitas Indonesia–Cipto Mangunkusumo Hospital, Jakarta, Indonesia, with registration number KET-712/UN2.F1/ETIK/PPM.00.02/2023. Each subject provided their written informed consent to participate in this study.

2.2 Data collection

Calf circumference was measured in centimeter (cm) at the point where the calf appeared to be the largest. Muscle strength was assessed by handgrip strength assessment. Handgrip strength was documented in kilogram (kg) using hydraulic dynamometer (Jamar Hydraulic Hand Dynamometer, Model J00105, Lafayette Instrument, Lafayette, Indiana, United States). We defined handgrip strength as the highest grip strength of the dominant handgrip of three attempts with maximum effort of isometric contractions. Test was done in sitting position with 90-degree elbow flexion following the recommended standard (2).

We assessed the physical performance through FTSTST and gait speed assessments. The former was done prior to the latter. To assess FTSTST, we asked the study subjects to sit down on a chair with back support initially. The subjects were asked to move from sitting position to standing position five times in a row non-stop as quick as possible. The measurement stopped when the individual stands for the fifth time. For gait speed assessment, we instructed each study subject to walk on their usual walking pace for 6 m without deceleration. The patient was not forced to walk as fast as possible. Walking attempts were made two times, and the average of both results was considered as the subject's gait speed.

2.3 Statistical analyses

Statistical analyses relied on SPSS version 21 (IBM, Armonk, New York, United States). We provided the characteristics of study subjects descriptively. Numerical data with normal distribution were reported as mean (standard deviation [SD]). We reported numerical data with skewed data distribution by providing the median (interquartile range [IQR]). We determined cutoff points for sex-specific handgrip strength and calf circumference, as well as for general gait speed, by finding 2 SD below the mean of each variable (13, 14). Values less than the 2 SD below mean for gait speed were classified as low physical performance. Values less than the 2 SD below mean for sex-specific handgrip strength and calf circumference were considered low or abnormal. We also showed the SD value above mean and 20th percentile for FTSTST. We also provided the 20th percentile value of each variable, as an alternative method used previously by sarcopenia experts in China (14).

3 Results

We collected data from 905 Indonesian adults (Table 1). The mean age of the subjects was 26.98 years. Of all study subjects, 22.7% of study subjects were from Jakarta and 55.9% were female. A larger proportion of study subjects were either overweight or obese (53.3%). Each study center exceeded the minimum sample size required in this study.

The mean −2 SD value of male subject handgrip strength was 21.15 kg, and 14.34 kg for female subjects. The mean −2 SD value of

TABLE 1 Characteristics of study population (n = 905).

Characteristics, unit if indicated	Frequency (n)	Percentage (%)
Age, years, mean (SD)	26.98 (4.91)	
Sex		
Male	399	44.1
Female	506	55.9
Body weight, kg, median (IQR)	65.41 (15.31)	
Body height, cm, mean (SD)	162.67 (8.25)	
Body mass index, kg/m^2, median (IQR)	23.83 (5.46)	
Nutritional status		
Underweight (<18.5 kg/m^2)	51	5.6
Normal body mass index (18.5–23.5 kg/m^2)	372	41.1
Overweight and obesity (>23.5 kg/m^2)	482	53.3
Study center		
Aceh	54	5.9
Bandung	91	10
Banjarmasin	78	8.6
Denpasar	15	1.7
Jakarta	206	22.7
Makassar	53	5.9
Malang	95	10.5
Medan	54	5.9
Merauke	109	12.0
Padang	56	6.2
Surakarta	94	10.4
Last completed formal education		
No formal education	5	0.6
Primary school	0	0
Junior high school	4	0.4
Senior high school	109	12
Higher education	787	86.9

The data were reported in frequency and percentage, unless stated otherwise.
IQR, interquartile range; SARC-CalF, SARC-F combined with calf circumference; SD, standard deviation; SPPB, The Short Physical Performance Battery.

male subject calf circumference was 29.92 cm, and 26.70 cm for female subjects. The mean +2 SD value of FTSTST result of all subjects was 11.69 s. The mean −2 SD value of gait speed of all subjects was 0.51 m/s (Table 2).

4 Discussion

These suggested cutoff points are different from the criteria set by AWGS in 2019. To detect low calf circumference, we suggested using <29.92 cm and <26.70 cm for male and female Indonesians, respectively. The values are much lower than the reference values in AWGS consensus (<34 cm for male subjects and <33 cm for female subjects) (4). Similarly, the suggested cutoff points to detect lower handgrip strength for male and female Indonesians are also lower than the values in AWGS consensus (<21.15 kg vs. < 28 kg for male subjects; and <14.34 kg vs. < 18 kg for female subjects) (4). Handgrip strength has been identified as a reliable proxy for muscle mass in older Asian adults (15), and therefore, appropriate cutoff point is crucial for handgrip strength assessment.

Low physical performance may be detected in Indonesians walking at pace slower than 0.51 m/s. The cutoff pace is much lower than the values in AWGS and EWGSOP2 consensuses (4, 14). Despite the different methods used in determining the optimal FTSTST cutoff value between our study and the study conducted by Nishimura et al. (9), our proposed cutoff point of FTSTST (11.69 s) is similar to that of AWGS consensus (12 s) (4). FTSTST alone was not included in EWGSOP2's sarcopenia diagnostic algorithm, although it was incorporated in the short physical performance battery (SPPB) (12, 13).

There are several possible reasons why muscle-related assessment result in healthy Indonesian adults may not be comparable to that of other Asian populations. First, lower mean result and cutoff points of sarcopenia assessment of the lower limb may be related to being overweight and obesity. More than half of our study subjects were either overweight or obese (53.3%). The proportion of overweight and obese young adults in our study was similar to the most recent Indonesian Health Survey result in 2023. Being overweight and obese were found in 26.2% of Indonesians aged 20–24 years, 41.9% of those aged 25–29 years, 50.9% of those aged 30–34 years, and 55.4% of those aged 35–39 years (16). In contrast, the prevalence of obesity among Singaporeans aged 30–39 years was only 12.4% (17). Reduced lower limb strength relative to body mass in overweight and obese individuals may be affected by a reduced functional capacity (e.g., walking difficulties, stairs negotiation, and rising from a chair or bed) (18, 19), neural adaptations, and changes in muscle morphology (19).

Second, developed Asian nations, from which the AWGS data were obtained, may have different body morphologies compared with the body morphology of Indonesians. Body growth is multifactorial (20), and this might indirectly affect an individual's physical performance (e.g., gait speed). The factors included chronic/non-communicable diseases, nutrition, urbanization, socioeconomic status, physical activity, psychosocial deprivation, and climate (20). Higher income in developed Asian nations may be associated with better education, leading to improved childcare, nutrition, and better access to medical services. The improvement in different fields will increase overall stature (21, 22). One of the body dimensions was body height, which was strongly associated with gait speed, as suggested by previous study in Singapore (23). Mean (SD) of body height of subjects in our study was only 162.67 cm (8.25 cm). A comparative anthropometric study was conducted comparing Indonesian versus Singaporean population as an example of a developed Asian nation. Although both nations are technically Asian, the study showed that both female and male subjects in Singapore tend to have larger physical dimensions than Indonesians (22).

Third, it is hypothesized that local culture may affect individual's physical performance. While various studies have highlighted physiological and health-related factors affecting physical performance, there is a growing recognition of the influence of cultural backgrounds on this aspect of mobility (5–7). Indonesian citizens only walked 3,513 steps per day and were at the 46th place of 46 countries assessed in previous study about daily step count (23). Furthermore, the mean (SD) of Indonesian healthy adult's gait speed

TABLE 2 Mean, standard deviation, 2 standard deviations below mean, median, and 20th percentile of the data from different study variables.

Diagnostic component (unit)	Results
Male handgrip strength (kg)	
Mean	38.95
SD	8.90
Mean −2 SD	21.15
Median	38
20th percentile	31
Female handgrip strength (kg)	
Mean	25.45
SD	5.56
Mean −2 SD	14.34
Median	25
20th percentile	20.30
Male calf circumference (cm)	
Mean	38.13
SD	4.11
Mean −2 SD	29.92
Median	38
20th percentile	35.00
Female calf circumference (cm)	
Mean	34.74
SD	4.02
Mean −2 SD	26.70
Median	34
20th percentile	31.50
Five times sit-to-stand test (s)	
Mean	7.43
SD	2.13
Mean +2 SD	11.69
Median	7.07
20th percentile	5.55
Gait speed (m/s)	
Mean	1.09
SD	0.29
Mean −2 SD	0.51
Median	1.09
20th percentile	0.87

Two standard deviations above mean were used for five times sit-to-stand test.
SD, standard deviation.

in our study was 1.09 m/s (±0.29 m/s), as opposed to the result in previous study among Japanese adults being 1.30 m/s (±0.10 m/s) (24). Indonesian gait characteristics include a shorter stride length of 1.15 m and a slower cadence of 110 steps per minute compared to other populations (25). Reluctance to walk was seen in a study of the population of Kupang, people of which were willing to walk an average distance of 115 m only to access public transit (26). Such habit of slow walking and reluctance to walk may be influenced by environmental factors related to safety and comfort of pedestrians in Indonesia (27). However, we should not normalize slow gait speed, as slow gait speed is a significant risk factor for all-cause and cardiovascular mortality, independent of other major risk factors (28). Slow gait speed has also been associated with a higher risk of adverse health outcomes, including all-cause mortality in adults with knee osteoarthritis (29).

This study has several strengths. First, this is the first multicentre study to estimate the sarcopenia-related measurement data of this multiethnic archipelagic state. We also determined the minimum sample size appropriately by considering regional population of each main island. Second, we followed the recommendations by the European Working Group for Sarcopenia in Older People of using 2 SD below the mean of a young healthy cohort to determine the cutoffs for normality (12, 13). Our results may also add to the body of literature with regard to the normative values for muscle health and diagnosis of sarcopenia in this region. However, we also acknowledged our limitation. This study population did not include the rural population of each island, although more than 50% of Indonesian older adults are now living in the cities (30). Caution should be exercised if extrapolating these cutoff points to other populations, as there may be distinct differences in cutoffs of other Asian groups. Future studies are required to establish optimal cutoff points in Indonesian population regarding muscle mass using other modalities of muscle mass assessment such as dual energy X-ray absorptiometry or bioelectrical impedance analysis. Third, we did not perform stratified analysis of data from this age group.

In conclusion, we propose the use of calf circumference <29.92 cm and <26.70 cm for the detection of low calf circumference among male and female Indonesians, respectively. We also propose that the optimal cutoff points to detect low handgrip strength are <21.15 kg and <14.34 kg for male and female Indonesians, respectively. Low gait speed can be defined as a walking pace <0.51 m/s. Abnormal physical performance is considered in those completing FTSTST >11.69 s. This study provides important contribution to the body of literature with regard to normative data required to determine cutoff values used in the diagnosis of sarcopenia in Indonesian and Asian populations. We suggest that the process of determining cutoff points should consider our multicentre study results. Future clinical screening or community-based programs in this region are subject to further discussion with health policymaker.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the Ethics Committee of the Faculty of Medicine, Universitas Indonesia – Cipto Mangunkusumo Hospital, Jakarta, Indonesia. The subjects provided their written informed consent to participate in this study (registration number KET-712/UN2.F1/ETIK/PPM.00.02/2023). The studies were conducted in accordance with the local legislation and institutional

requirements. The participants provided their written informed consent to participate in this study.

Author contributions

SiS: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. SK: Conceptualization, Funding acquisition, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. SC: Conceptualization, Funding acquisition, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. NK: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. KH: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. PL: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. IA: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. SrS: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. ND: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. IF: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. AA: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. MA: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. RM: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. DA: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. WC: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. LD: Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing, Conceptualization, Data curation. FB: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. AS: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. MH: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. CI: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. MS: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. RI: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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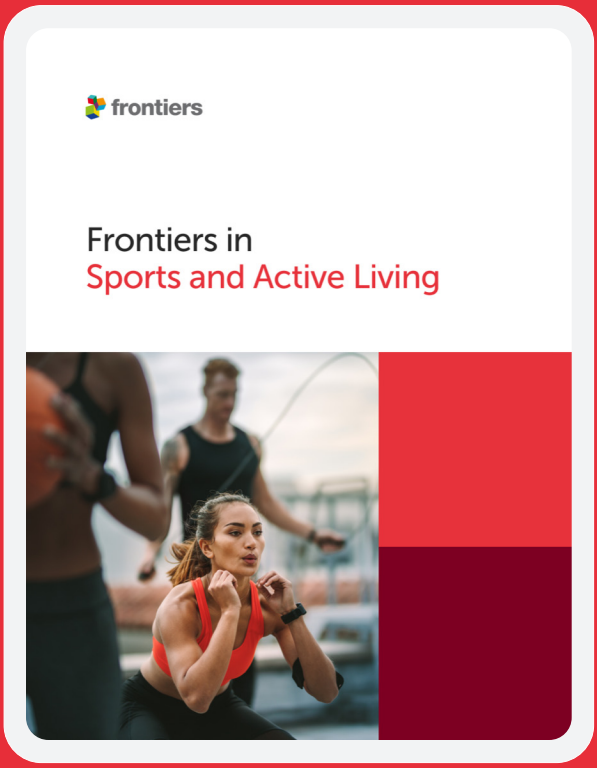

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