Risk Management and Healthcare Policy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Sarcopenia, Depressive Symptoms, and Fall Risk: Insights from a National Cohort Study in the Chinese Population

Xiaoming Zhang[1,*], Dongmei Ye[2,*], Qingli Dou[1,*], Fayi Xie[2], Rui Zeng[2], Ke Zhu[2], Wan Zhu[2], Aizhang Zhu[3,4], Lihuan Chen[5], Yishan Wu[2], Tenghui Fan[2], Pai Peng[2], Yuxu Huang[3,4], Shunrui Xiao[2], Jiahui Bian[2], Mengxia Shi[2], Jiang Wang[3,4], Wenwu Zhang[1]

[1]Department of Emergency, The People's Hospital of Baoan Shenzhen, Shenzhen, Guangdong province, People's Republic of China; [2]School of Clinical Medicine, Jinggangshan University, Ji'an, Jiangxi Province, People's Republic of China; [3]School of Basic Medicine, Jinggangshan University, Ji'an, Jiangxi Province, People's Republic of China; [4]Online Collaborative Research Center for Evidence-Based Medicine Ministry of Education, Jinggangshan University Branch, Ji'an, Jiangxi Province, People's Republic of China; [5]School of Chinese Medicine, Jinggangshan University, Ji'an, Jiangxi Province, People's Republic of China

*These authors contributed equally to this work

Correspondence: Xiaoming Zhang, Department of emergency, The People's hospital of Baoan Shenzhen, Shenzhen, Guangdong province, People's Republic of China, Email zhangmuxi0310@163.com; Jiang Wang, School of Basic Medicine, Jinggangshan University, Ji'an, Jiangxi Province, People's Republic of China, Email 9920070082@jgsu.edu.cn

Background: Previous investigations have indicated that both sarcopenia and depressive symptoms are linked to a heightened risk of falls. However, the potential synergistic effect of these conditions on fall risk remains unclear. This study aims to assess the combined influence of sarcopenia and depressive symptoms on the occurrence of falls in the Chinese population.

Methods: The analysis included 8,405 participants from the China Health and Retirement Longitudinal Study (CHARLS), conducted from 2011 to 2015. Sarcopenia was confirmed using the 2019 Asian Working Group for Sarcopenia (AWGS) algorithm consisting of muscle strength, appendicular skeletal muscle mass (ASM), and physical performance. ASM was calculated using the formula: 0.193 × weight (kg) + 0.107 × height (cm) - 4.157 × sex - 0.037 × age (years) - 2.631. The Center for Epidemiological Research Depression Scale was utilized to assess depressive symptoms, with a cut-off score of 12 points. Depressive sarcopenia is defined as the coexistence of sarcopenia and depression. Multiple logistic regression analyses were conducted to explore the associations among sarcopenia, depressive symptoms, and fall occurrences.

Results: During the four-year follow-up, 1,275 participants reported experiencing falls. A significant synergistic effect was identified between sarcopenia and depressive symptoms regarding fall risk. Compare to robust individuals, those with sarcopenia alone or depression alone had increased falls risks, but those with both conditions exhibited the highest fall risk, with adjusted odds ratios (OR) of 1.21 (95% CI 1.03, 1.42; $P = 0.0174$), 1.53 (95% CI 1.24, 1.88; $P < 0.001$), and 1.78 (95% CI 1.48, 2.15; $P < 0.001$), respectively.

Conclusion: The findings highlight a synergistic effect between sarcopenia and depressive symptoms on fall risk. This study highlights the importance of early detection and intervention for both conditions, especially in older and middle-aged individuals, to mitigate fall risk.

Keywords: sarcopenia, depression, falls, Chinese people

Introduction

According to the World Health Organization (WHO), nearly 30% of individuals aged 65 and older, and about 50% of those aged 80 and above, report experiencing at least one fall each year.[1] Annually, approximately 684,000 fatal falls occur, making them the second leading cause of accidental injury-related deaths, following road traffic accidents.[2] The Global Burden of Disease 2019 study indicates that the fall rate for individuals aged 60 to 79 years is 3,648.3 per 100,000, which increases dramatically to 11,524.4 per 100,000 for those aged 80 and older.[3] Beyond the mortality

Received: 20 September 2024
Accepted: 13 February 2025
Published: 21 February 2025

associated with falls, they are linked to various physical and mental health issues, including fractures,[4] disability,[5] hospitalization,[6] loneliness,[7] and geriatric depression.[8] Additionally, falls significantly contribute to healthcare costs and financial burdens.[9] As the global population ages, preventing and managing falls and related injuries has emerged as a critical challenge.[10]

Depression is a common mental disorder affecting over 264 million people worldwide and significantly contributes to the overall burden of disease.[11] Growing evidence indicates that depression is linked to adverse health outcomes, such as decreased quality of life, the onset of multiple chronic diseases, and higher all-cause mortality. With aging, individuals experience various physiological changes, such as a decline in muscle mass and functional capacity, which can lead to sarcopenia.[12] The prevalence of sarcopenia among older adults in Asia has been reported to range from 5.5% to 25.7%.[12,13] Both depression and sarcopenia are common among the elderly, sharing similarities in their etiology, clinical features, and prognostic outcomes.[14] Furthermore, both conditions have been shown to elevate the risk of falls in older adults.[15,16]

Recent studies have suggested a potential link between sarcopenia and depression. A meta-analysis found an independent association between these two conditions,[17] revealing a relatively high prevalence of depression among individuals with sarcopenia.[14] Moreover, more extensive research has indicated that depression may causally contribute to decreased muscle mass, while reduced muscle strength can heighten the risk of depression.[18] These findings consistently highlight a significant association between sarcopenia and depression. Consequently, these conditions often co-occur in older populations, attracting increasing attention within the field of geriatrics. Recent studies have examined the relationship between depressive sarcopenia and the risks of all-cause mortality or cardiovascular disease, indicating the combined effects of these conditions on adverse health outcomes.[19,20] As falls emerge as a critical issue for older individuals, it is essential to investigate the relationship between depressive sarcopenia and falls.

Previous studies had reported that both sarcopenia alone or depression alone was a risk factor for fall risk among people.[21–23] However, no study assessed the combined effects of sarcopenia and depression on fall risk, leading to insufficient attention on how both conditions interact to influence fall susceptibility. Thus, this study aims to assess the combined impact of sarcopenia and depression on falls among middle-aged and elderly individuals in China, using data from the CHARLS Public database.

Methods

Study Population

The CHARLS project aims to collect high-quality micro-data representing individuals aged 45 and older in China. This research provides valuable insights into various socio-economic and health-related factors, serving as a foundation for analyzing population aging in China and facilitating interdisciplinary studies on the subject. The national baseline survey for CHARLS was carried out between 2011 and 2012, followed by four rounds of regular questionnaire follow-ups in 2013, 2015, 2018, and 2020. Additionally, a comprehensive life course survey of middle-aged and elderly individuals was completed in 2014. To ensure the sample's representativeness, the CHARLS baseline survey included 150 counties/regions and 450 villages/urban communities nationwide, involving 17,708 individuals from 10,257 households. This design reflects the overall status of the middle-aged and elderly population in China. Detailed information about CHARLS has been published in previous literature.[24] The CHARLS dataset is available for download from the official CHARLS website (http://charls.pku.edu.cn/en).

This study included individuals aged 45 years or older from the China Health and Retirement Longitudinal Study (CHARLS). The inclusion and exclusion criteria are outlined as follows: Inclusion criteria: (1) Participants who took part in the 2011 baseline survey of CHARLS; (2) Participants who completed assessments for both sarcopenia and depressive symptoms. Exclusion criteria: (1) Individuals younger than 45 years; (2) Participants who reported falls in 2011; (3) Participants with missing follow-up data; (4) Participants with more than 30% missing data on covariates. This analysis utilized data from two waves of CHARLS: the 2011 baseline survey (wave 1) and the 2015 follow-up survey (wave 3). The initial national baseline survey included 17,708 participants, but after applying the specified inclusion and exclusion criteria, 8,405 participants remained for the final analysis. The detailed selection process is illustrated in Figure 1.

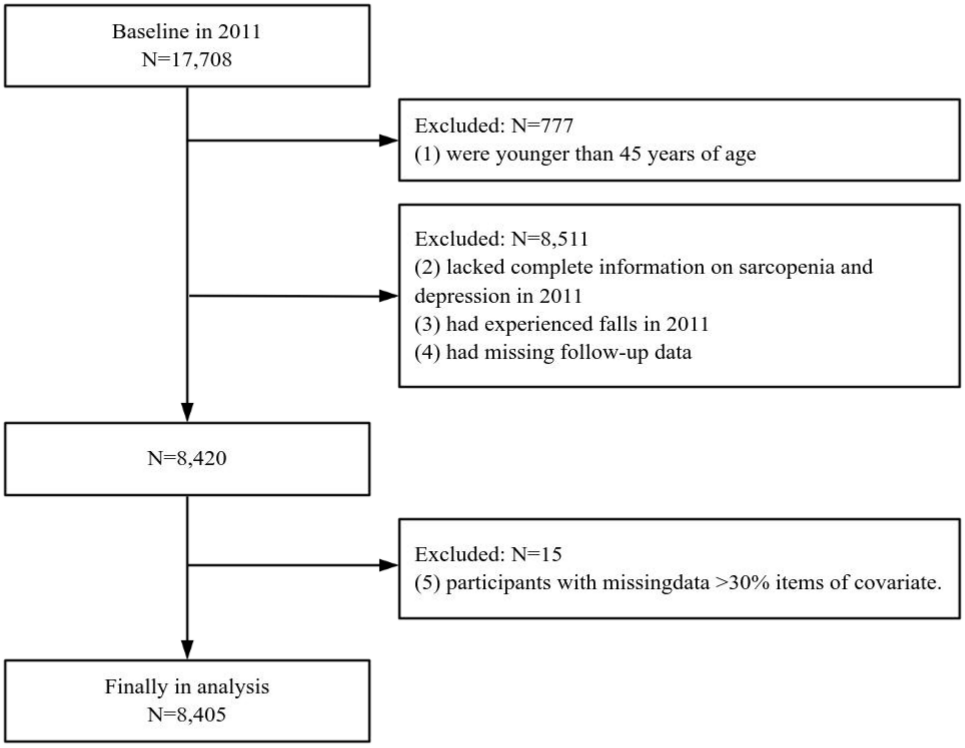

Figure 1 Flow chart of sample selection and the exclusion criteria.

Assessment of Sarcopenia and Depression Status

The Center for Epidemiological Research Depression Scale (CES-D-10) was used to assess the depressive symptom, which has been validated as a reliable tool for detecting depression among Chinese adults.[25] The scale comprises 10 items reflecting participants' experiences over the past week, such as feeling troubled, distracted, depressed, and hopeful about the future.[26] Total scores range from 0 to 30, with higher scores indicating more severe depressive symptoms.[27] A critical cutoff score of ≥12 points was used to classify participants with depression. The CES-D-10 exhibited good internal consistency in this study.

Sarcopenia was defined according to (AWGS) 2019 algorithm, which incorporates measures of muscle strength, appendicular skeletal muscle mass (ASM), and physical performance.[28] Grip strength was obtained by squeezing a YuejianTM WL-1000 dynamometer (Nantong Yuejian Physical Measurement Instrument Co., Ltd., Nantong, China) as forcefully as possible with thresholds set at < 28 kg for males and < 18 kg for females.[28] ASM was calculated using a validated anthropometric equation for Chinese residents: ASM = 0.193 × weight (kg) + 0.107 × height (cm) – 4.157 × sex – 0.037 × age (years) – 2.631, with sex coded as 1 for males and 2 for females.[29] Low muscle mass was categorized using height-adjusted muscle mass, with ASM/HT² values of <5.63 kg/m² for women and <7.05 kg/m² for men indicating low muscle mass.[19] Low physical performance was defined as completing a five-time chair stand test in ≥12 seconds, a gait speed on a 6-m walk of <1.0 m/s, or a Short Physical Performance Battery (SPPB) score ≤9, as per the AWGS 2019 consensus.[30,31] Possible sarcopenia is defined as low muscle strength or low physical performance, whereas sarcopenia is characterized by low muscle mass in conjunction with either low muscle strength or low physical performance.[30] For this study, participants with possible sarcopenia were included in the sarcopenia group.

Assessment of Falls

Falls were identified based on respondents' self-reported health status. New respondents who answered "Yes" to the question "Have you fallen down?" were categorized as having experienced a fall.

https://doi.org/10.2147/RMHP.S497087

Covariate Assessments

At baseline, trained interviewers gathered data on sociodemographic and health-related factors using a structured questionnaire. Sociodemographic variables included age, gender, educational level, marital status, and hukou (household registration).Educational levels were categorized as middle school or below and high school or above. Marital status was classified as married or other (including separated, divorced, widowed, and never married). Hukou status was divided into agricultural and non-agricultural.

Health-related variables included drinking status, smoking status, sleep duration, and physician-diagnosed chronic diseases such as hypertension, heart disease, stroke, arthritis, asthma, cancer, dyslipidemia, lung disease, liver disease, kidney disease, digestive disorders, psychological problems, and memory issues. Smoking status, drinking status, and sleep duration were self-reported by participants.

Statistical Analysis

To address missing data in the CHARLS database, the Template method (R Package "VIM")[32] and multiple imputation method (R Package "mice")[33] were utilized to enhance the accuracy of the research findings. Predictive mean matching was employed, with five cycles of imputation performed (m=5). A density plot based on imputed data was generated to illustrate differences between imputation methods. The final imputed datasets were used for subsequent analyses.

Participants were categorized into four groups according to their sarcopenia and depressive symptoms: (1) robust (absence of both sarcopenia and depression), (2) sarcopenia only, (3) depression only, and (4) depressive sarcopenia. The baseline characteristics were presented as percentages for categorical variables and as means with standard deviations for continuous variables. The Kruskal–Wallis rank sum test was used to compare continuous variables across groups, while the Chi-square test or Fisher's exact test was employed for categorical variables.

Univariate analysis identified potential confounders influencing fall occurrences. Multiple logistic regression analysis was conducted to examine the relationship between different groups (sarcopenia only, depression only, and depressive sarcopenia) and fall risk, using the robust group as a reference. Three models were constructed: Model I was not adjusted for any variables; Model II adjusted for the minimal sufficient adjustment set (MSAS) identified using a causal directed acyclic graph (DAG), including age, gender, educational level, marital status, hukou, drinking, and smoking (Supplementary Figure 1); Model III further adjusted for covariates identified in the univariate analysis, including hypertension, heart, memory, psychology, lung, stroke, arthritis, liver disease, kidney disease, digestive system disease, asthma and sleep duration. The logistic regression analysis results were reported as odds ratios (ORs) accompanied by 95% confidence intervals (CIs), with statistical significance assessed using p-values. Additionally, subgroup analyses were conducted to evaluate the combined effect of sarcopenia and depressive symptoms on fall risk across different strata, including age, gender, hukou status, educational level, marital status, smoking status, and drinking status. All statistical analyses were performed using R version 4.2.2 and EmpowerStats version 4.1 (www.empowerstats.com; X&Y Solutions Inc).

Results

Baseline Characteristics According to Sarcopenia and Depression Status

This study comprised 8,405 middle-aged and elderly participants, with a mean age of 58.68 years (SD = 9.15). Participants were categorized into four groups based on their depressive status and sarcopenia: 3,805 individuals were classified as robust (neither condition), 2,552 had sarcopenia only, 826 had depression only, and 1,222 exhibited both depression and sarcopenia. Notably, individuals with both conditions were typically older, predominantly female, primarily residing in rural areas, and exhibited a higher proportion with educational attainment of junior middle school or lower. This group also demonstrated a greater likelihood of being married or cohabiting, reported shorter sleep duration, and had a higher prevalence of chronic diseases. Moreover, they exhibited a lower body mass index (BMI) and a higher prevalence of various health conditions, such as hypertension, chronic lung disease, heart disease, stroke, psychiatric disorders, arthritis, dyslipidemia, kidney disease, liver disease, digestive disorders, asthma, and memory impairments. Interestingly, the prevalence of alcohol consumption and smoking was lower in the depressive sarcopenia group. No significant differences in the prevalence of diabetes or cancer were observed among the groups (Table 1).

Table 1 Baseline Characteristics of the Study Participants According to Sarcopenia and Depression Status in Baseline

Variable	Total	Robust	Sarcopenia Only	Depression Only	Depressive Sarcopenia	*P*-value
No. of subjects	8405	3805	2552	826	1222	
Age	58.68 ± 9.15	55.26 ± 7.53	62.83 ± 9.40	55.89 ± 7.62	62.58 ± 9.09	<0.001
Gender						<0.001
Male	4184 (49.78%)	2227 (58.53%)	1167 (45.73%)	368 (44.55%)	422 (34.53%)	
Female	4221 (50.22%)	1578 (41.47%)	1385 (54.27%)	458 (55.45%)	800 (65.47%)	
Educational level						<0.001
Middle school or below	5677 (67.54%)	2063 (54.22%)	1991 (78.02%)	584 (70.70%)	1039 (85.02%)	
High school or above	2728 (32.46%)	1742 (45.78%)	561 (21.98%)	242 (29.30%)	183 (14.98%)	
Marital status						<0.001
Married	1015 (12.08%)	230 (6.04%)	407 (15.95%)	113 (13.68%)	265 (21.69%)	
Other	7390 (87.92%)	3575 (93.96%)	2145 (84.05%)	713 (86.32%)	957 (78.31%)	
Hukou						<0.001
Agricultural	6903 (82.13%)	2955 (77.66%)	2127 (83.35%)	705 (85.35%)	1116 (91.33%)	
Non-agricultural	1502 (17.87%)	850 (22.34%)	425 (16.65%)	121 (14.65%)	106 (8.67%)	
Drinking						<0.001
No	5612 (66.77%)	2288 (60.13%)	1820 (71.32%)	568 (68.77%)	936 (76.60%)	
Yes	2793 (33.23%)	1517 (39.87%)	732 (28.68%)	258 (31.23%)	286 (23.40%)	
Smoking						<0.001
No	5699 (67.80%)	2469 (64.89%)	1773 (69.47%)	576 (69.73%)	881 (72.09%)	
Yes	2706 (32.20%)	1336 (35.11%)	779 (30.53%)	250 (30.27%)	341 (27.91%)	
Hypertension						<0.001
No	6276 (74.67%)	2914 (76.58%)	1898 (74.37%)	611 (73.97%)	853 (69.80%)	
Yes	2129 (25.33%)	891 (23.42%)	654 (25.63%)	215 (26.03%)	369 (30.20%)	
Diabetes						0.058
No	7916 (94.18%)	3580 (94.09%)	2424 (94.98%)	764 (92.49%)	1148 (93.94%)	
Yes	489 (5.82%)	225 (5.91%)	128 (5.02%)	62 (7.51%)	74 (6.06%)	
Cancer						0.207
No	8336 (99.18%)	3778 (99.29%)	2534 (99.29%)	815 (98.67%)	1209 (98.94%)	
Yes	69 (0.82%)	27 (0.71%)	18 (0.71%)	11 (1.33%)	13 (1.06%)	
Lung						<0.001
No	7629 (90.77%)	3557 (93.48%)	2291 (89.77%)	735 (88.98%)	1046 (85.60%)	
Yes	776 (9.23%)	248 (6.52%)	261 (10.23%)	91 (11.02%)	176 (14.40%)	
Heart						<0.001
No	7467 (88.84%)	3453 (90.75%)	2275 (89.15%)	714 (86.44%)	1025 (83.88%)	
Yes	938 (11.16%)	352 (9.25%)	277 (10.85%)	112 (13.56%)	197 (16.12%)	
Stroke						<0.001
No	8238 (98.01%)	3765 (98.95%)	2493 (97.69%)	805 (97.46%)	1175 (96.15%)	
Yes	167 (1.99%)	40 (1.05%)	59 (2.31%)	21 (2.54%)	47 (3.85%)	
Psychology						<0.001
No	8323 (99.02%)	3784 (99.45%)	2542 (99.61%)	806 (97.58%)	1191 (97.46%)	
Yes	82 (0.98%)	21 (0.55%)	10 (0.39%)	20 (2.42%)	31 (2.54%)	
Arthritis						<0.001
No	5717 (68.02%)	2844 (74.74%)	1776 (69.59%)	457 (55.33%)	640 (52.37%)	
Yes	2688 (31.98%)	961 (25.26%)	776 (30.41%)	369 (44.67%)	582 (47.63%)	
Dyslipidemia						<0.001
No	7627 (90.74%)	3421 (89.91%)	2376 (93.10%)	740 (89.59%)	1090 (89.20%)	
Yes	778 (9.26%)	384 (10.09%)	176 (6.90%)	86 (10.41%)	132 (10.80%)	
Liver disease						0.002
No	8150 (96.97%)	3709 (97.48%)	2480 (97.18%)	793 (96.00%)	1168 (95.58%)	
Yes	255 (3.03%)	96 (2.52%)	72 (2.82%)	33 (4.00%)	54 (4.42%)	

(*Continued*)

Table 1 (Continued).

Variable	Total	Robust	Sarcopenia Only	Depression Only	Depressive Sarcopenia	*P*-value
Kidney disease						<0.001
No	7975 (94.88%)	3652 (95.98%)	2441 (95.65%)	757 (91.65%)	1125 (92.06%)	
Yes	430 (5.12%)	153 (4.02%)	111 (4.35%)	69 (8.35%)	97 (7.94%)	
Digestive system disease						<0.001
No	6641 (79.01%)	3141 (82.55%)	2067 (81.00%)	590 (71.43%)	843 (68.99%)	
Yes	1764 (20.99%)	664 (17.45%)	485 (19.00%)	236 (28.57%)	379 (31.01%)	
Asthma						<0.001
No	8042 (95.68%)	3700 (97.24%)	2439 (95.57%)	772 (93.46%)	1131 (92.55%)	
Yes	363 (4.32%)	105 (2.76%)	113 (4.43%)	54 (6.54%)	91 (7.45%)	
Memory						<0.001
No	8308 (98.85%)	3787 (99.53%)	2512 (98.43%)	820 (99.27%)	1189 (97.30%)	
Yes	97 (1.15%)	18 (0.47%)	40 (1.57%)	6 (0.73%)	33 (2.70%)	
BMI	24.18 ± 20.68	25.21 ± 14.40	23.27 ± 32.93	24.58 ± 3.41	22.55 ± 3.96	<0.001
CESD_2011	7.86 ± 6.08	4.73 ± 3.26	5.50 ± 3.33	16.05 ± 3.76	16.98 ± 4.25	<0.001
Sleep duration	6.43 ± 1.83	6.75 ± 1.55	6.55 ± 1.83	5.90 ± 1.92	5.59 ± 2.17	<0.001
Cognitive	9.05 ± 3.46	7.90 ± 3.01	9.71 ± 3.52	9.50 ± 3.19	10.95 ± 3.53	<0.001

Notes: Continuous variables are expressed as mean ± standard deviation, or as median (interquartile range). Categorical variables are expressed as frequency (percent). Units for Variables: Sleep duration is presented in "hours"; BMI is expressed in "kg/m²". Cognition: 21–(memory test score + orientation test score + serial 7's test + drawing test).

Univariate Analysis for the Incidence of Falls

A univariate analysis was conducted to evaluate the association between individual independent variables and the frequency of falls. The results indicated that factors such as age, gender, educational level, marital status, hukou, sarcopenia alone, depression alone, depressive sarcopenia, hypertension, heart, memory, psychology, lung, stroke, arthritis, liver disease, kidney disease, digestive system disease, asthma and sleep duration were significantly linked to the risk of falls ($P < 0.05$). Consequently, these variables were incorporated into the multivariate model. Conversely, conditions like diabetes mellitus and hyperlipidemia did not show statistical significance in the univariate analysis (Supplementary Table 1).

Relationship Between Sarcopenia, Depressive Symptoms, and Falls Analyzed via Multiple Logistic Regression

The relationship between depressive sarcopenia and fall incidents was assessed using a multivariate logistic regression model, adjusting for various covariates. In the unadjusted model, individuals with sarcopenia only showed an increased risk of falls (OR = 1.49, 95% CI: 1.28, 1.72, $P < 0.0001$), as did those with depression only (OR = 1.97, 95% CI: 1.61, 2.41, $P < 0.0001$). The risk was significantly elevated among individuals with both conditions (OR = 2.70, 95% CI: 2.29, 3.18, $P < 0.0001$). After adjusting for confounders, the results remained consistent: the sarcopenia-only group exhibited an increased risk (OR = 1.21, 95% CI 1.03, 1.42; $P = 0.0174$), as did the depression-only group (OR = 1.53, 95% CI: 1.24, 1.88; $P < 0.001$). Similarly, individuals with both conditions had a significantly heightened risk of falls (OR = 1.78, 95% CI: 1.48, 2.15; $P < 0.001$) (Table 2). Further analysis revealed a Relative Excess Risk due to interaction (RERI) of 0.05 (−0.36, 0.43), an Attributable Proportion (AP) of 0.03 (−0.22, 0.22), and a Synergy Index (SI) of 1.08 (0.63, 1.85), indicating no interaction between sarcopenia and depressive symptoms on fall risk.

Stratified Analyses of the Relationship Between Depressive Sarcopenia and Falls

Stratified analyses were conducted to explore the association between depressive sarcopenia and fall risk across various subgroups, including age, gender, hukou, educational level, marital status, smoking, and drinking. The results indicated that the association between depressive sarcopenia and falls was statistically significant across all subgroup variables. Notably, significant interactions between depressive sarcopenia and fall risk were observed only for gender (*P* for

Table 2 Association of Sarcopenia and Depression with New-Onset Fall Events

Variable	Robust	Sarcopenia Only	Depression Only	Depressive Sarcopenia
Fall events				
Case, n (%)	3805 (45.27%)	2552 (30.36%)	826 (9.83%)	1222 (14.54%)
Model 1	1.00 (Ref)	1.49 (1.28, 1.72) <0.0001	1.97 (1.61, 2.41) <0.0001	2.70 (2.29, 3.18) <0.0001
Model 2	1.00 (Ref)	1.26 (1.07, 1.47) 0.0049	1.80 (1.47, 2.21) <0.0001	2.18 (1.82, 2.60) <0.0001
Model 3	1.00 (Ref)	1.21 (1.03, 1.42) 0.0174	1.53 (1.24, 1.88) <0.0001	1.78 (1.48, 2.15) <0.0001

Notes: Model 1 was non-adjusted model. Model 2 was adjusted for the minimal sufficient adjustment set (MSAS) identified using a causal directed acyclic graph (DAG) including adjusted for age categorical (age≥65; age<65); gender; educational level; marital status; hukou; drinking; smoking. Model 3 was further adjusted for hypertension; heart; memory; psychology; lung; stroke; arthritis; liver disease; kidney disease; digestive system disease; asthma and sleep duration based on Model 2.

interaction = 0.0371), with males exhibiting a stronger synergistic effect compared to females. No significant interactions were identified with age, educational level, marital status, hukou status, smoking, or drinking (*P* for interaction > 0.05) (Figure 2; Supplementary Table 2).

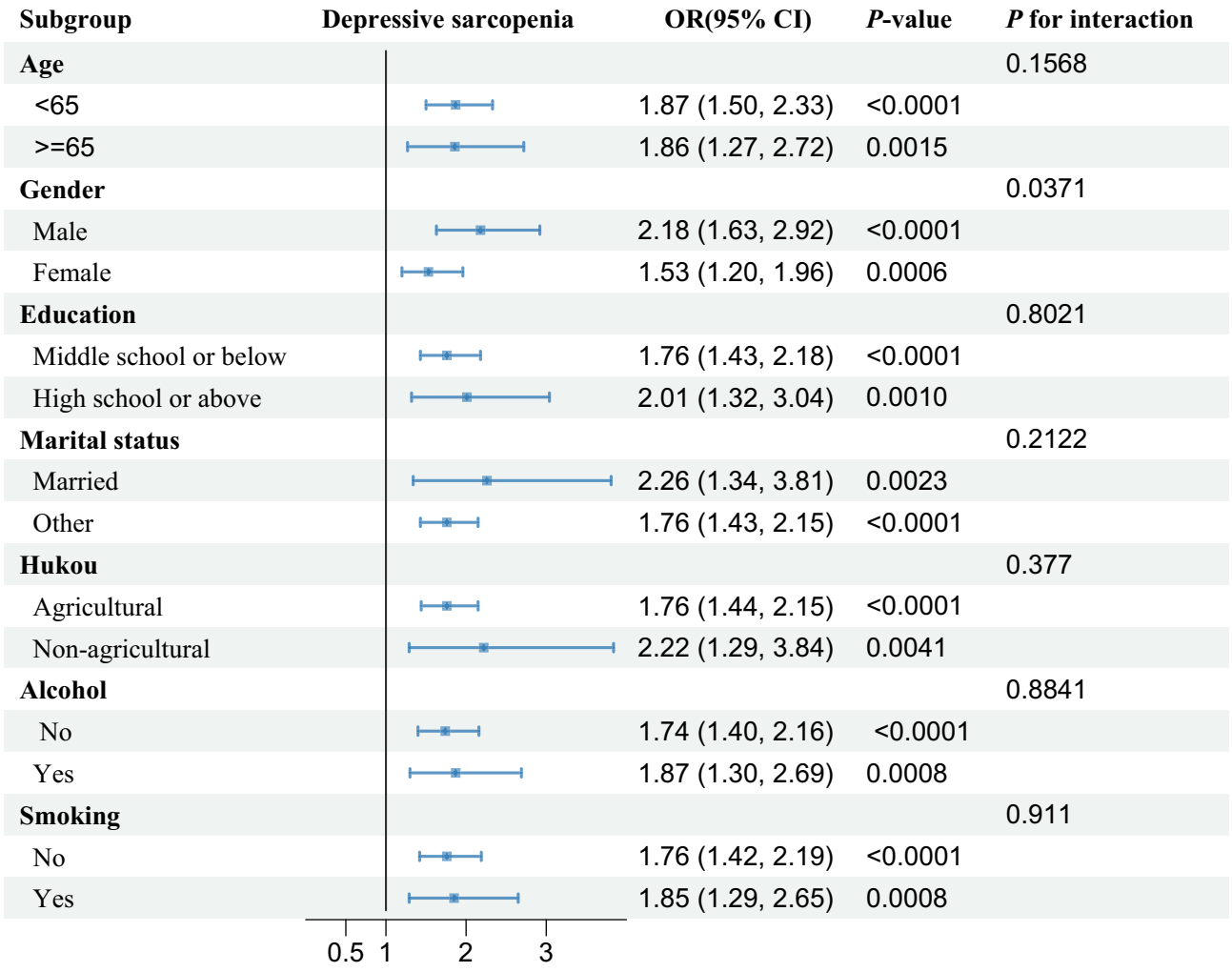

Figure 2 Subgroup Analysis of Associations between Sarcopenia, Depression, Depressive Sarcopenia, and Fall Risk by Sociodemographic Factors.

https://doi.org/10.2147/RMHP.S497087

Discussion

This cohort analysis utilized data from the China Health and Retirement Longitudinal Study (CHARLS) to examine the relationships between sarcopenia, depressive symptoms, and their co-occurrence—termed depressive sarcopenia—in relation to fall incidents. The findings underscore the significant roles that both depressive symptoms and sarcopenia play as correlates of fall risk among older Chinese adults. Notably, our study reveals a significant synergistic effect between these two conditions, indicating that their coexistence markedly increases the likelihood of falls. This interaction poses a substantial threat to individual health and safety, underscoring the urgent need for preventive measures.

Extensive prior research has consistently demonstrated that sarcopenia is associated with an increased likelihood of falls.[21,22] Research has identified sarcopenia as a factor contributing to various adverse health outcomes, such as falls, fractures, functional decline, cognitive decline, depression, and increased mortality.[34,35] Furthermore, evidence suggests that both suspected and confirmed sarcopenia, as defined by the AWGS 2019 criteria, show a significant positive correlation with fall occurrences.[36] Our study aligns with these findings, indicating that individuals with sarcopenia (including possible, confirmed, and severe sarcopenia assessed via the AWGS 2019 algorithm) have an 18% higher risk of falls, based on CHARLS data from 2011 to 2015.

Additionally, depressive symptoms have been established as a key risk factor for falls.[23,37] A study involving 89,076 subjects from the UK Biobank utilized a genome-wide association study (GWAS) to explore genetic factors associated with fall risk, revealing correlations with insomnia, neuroticism, and depressive symptoms.[37] Our study corroborates these findings, demonstrating that participants with depressive symptoms, as measured by the CES-D 10, had a 77% higher risk of falls compared to healthy individuals.

The significant synergistic effect observed between sarcopenia and depressive symptoms in our study suggests that these conditions may collectively exacerbate fall risk. Individuals with both conditions (depressive sarcopenia) exhibited the highest fall risk (OR = 1.78, 95% CI: 1.48, 2.15) compared to those with sarcopenia only (OR = 1.21, 95% CI: 1.03, 1.42) or depression only (OR = 1.53, 95% CI: 1.24, 1.88). This supports previous research that identified synergistic effects of sarcopenia and depression on adverse outcomes, including overall mortality and cardiovascular risk.[19,20] Given the prevalence of sarcopenia and depression among older populations, it is crucial for healthcare providers to screen for both conditions, especially in middle-aged and older adults. Timely assessment enables the implementation of necessary interventions, and recent advancements in exercise programs, such as the novel multicomponent program for sarcopenic older adults designed by Kumar et al, hold promise for significantly improving the functional status of sarcopenic individuals. This innovative approach, known as ReStart-S, targets older adults residing in long-term care settings and emphasizes the importance of tailored, exercise-based strategies for combating sarcopenia.[38]

While the specific mechanisms linking sarcopenia and depression to increased fall risk remain unclear, several potential explanations can be posited. These are likely associated with multifactorial, molecule-driven pathways, encompassing neurotrophins, chronic inflammation, and oxidative stress,[39,40] alongside common lifestyle factors such as malnutrition and physical inactivity.[12,13] Falls, sarcopenia, and depression share clinical manifestations and underlying causes, such as physical inactivity, disrupted sleep, and depressive symptoms.[41] Chronic inflammation may play a pivotal role,[42] as elderly individuals often contend with poly-chronic illnesses where inflammatory cytokines activate the ubiquitin-proteasome pathway, leading to muscle fiber degradation.[43] This results in decreased muscle strength, function, and mass, thereby accelerating the development of sarcopenia.[44]

The muscle-brain endocrine axis, mediated by myokines, may also connect sarcopenia with various health issues, including depression and cognitive decline,[45–47] further elevating fall risk. Conversely, evidence suggests that physical activity can enhance antioxidative capacity, reduce oxidative stress, and exert anti-inflammatory effects.[45,48,49] Exercise has been shown to mitigate the progression of both sarcopenia and depression.[12,13,29] Further extensive research is essential to investigate the relationships between these conditions and fall risk, as well as to elucidate the specific mechanisms underlying these connections.

This research has several significant merits. Notably, it is one of the first studies to explore the relationships among depression alone, sarcopenia alone, and the combined condition of depressive sarcopenia concerning fall risk, utilizing data from the nationally representative CHARLS survey. The representativeness of the CHARLS dataset enhances the

credibility of our findings for middle-aged and elderly individuals in China. Furthermore, adherence to the AWGS sarcopenia measurement guidelines ensures the accuracy of our results regarding muscle health. Lastly, the cohort design provides evidence of a relevant causal relationship.

However, several limitations warrant consideration. First, the assessment of fall incidents relied on participant self-reporting, which may introduce recall bias and potential underreporting. Second, the use of the CES-D 10 scale limited the evaluation of participants' psychological well-being to a one-week period, which may not accurately capture long-term psychological states; future studies should incorporate longer-term evaluations. Third, the use of the ASM formula to evaluate muscle mass, instead of the more widely recognized dual-energy X-ray absorptiometry (DXA), may introduce potential biases. Fourth, despite accounting for numerous confounding variables, this observational study remains susceptible to biases and unmeasured confounders. Lastly, while utilizing data from two waves (2011 to 2015) offers valuable insights, limitations in accessing updated data may prevent our findings from fully reflecting current epidemiological trends. Temporal, cultural, socio-economic, and environmental factors could influence the relationship between depressive sarcopenia and falls, necessitating further studies to validate our conclusions across diverse regions.

Conclusion

In conclusion, our study confirms that both sarcopenia and depressive symptoms independently increase the risk of falls. Furthermore, we identify a potential synergistic effect between the two conditions, with individuals affected by both sarcopenia and depressive symptoms experiencing an especially high risk of falling. These findings highlight the critical need for comprehensive screening and early recognition of sarcopenia and depressive symptoms in clinical and public health settings. Timely implementing effective preventive measures are essential to reduce the occurrence of falls. Additionally, our study directs future research toward exploring the potential interactions between these two conditions and their biological mechanisms, providing a scientific foundation for developing targeted intervention strategies.

Abbreviations

AWGS, Asian Working Group for Sarcopenia; ASM, appendicular skeletal muscle mass; WHO, World Health Organization; CHARLS, China Health and Retirement Longitudinal Study; CES-D-10, Center for Epidemiological Research Depression Scale; SPPB, Short Physical Performance Battery; MSAS, minimal sufficient adjustment set; DAG, causal directed acyclic graph; GWAS, genome-wide association analysis; USPSTF, United States Preventive Services Task Force; BIA, bioelectrical impedance analysis; DXA, dual-energy X-ray absorptiometry; SD, standard deviation.

Ethics Approval and Consent to Participate

As per the "Measures for Ethical Review of Life Science and Medical Research Involving Human Subjects" (February 18, 2023), the research qualifies for exemption under item [1 or 2] of Article 32. Specifically, analysis with no direct interaction with participants using anonymized data.Therefore, no additional ethical review or approval was required from our institution.

Acknowledgments

The authors thank all the members of the CHALRS for their contributions and the participants who contributed their data.

Author Contributions

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

Disclosure

The authors report no conflicts of interest in this work.

References

1. Li Y, Liu M, Sun X, Hou T, Tang S, Szanton SL. Independent and synergistic effects of pain, insomnia, and depression on falls among older adults: a longitudinal study. *BMC Geriatr*. 2020;20(1):491. doi:10.1186/s12877-020-01887-z
2. Health Organization W. Available from: https://www.who.int/news-room/fact-sheets/detail/falls. Accessed April 26, 2021.
3. Diseases GBD. Injuries C: global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396(10258):1204–1222.
4. Karinkanta S, Piirtola M, Sievänen H, Uusi-Rasi K, Kannus P. Physical therapy approaches to reduce fall and fracture risk among older adults. *Nat Rev Endocrinol*. 2010;6(7):396–407. doi:10.1038/nrendo.2010.70
5. Gill TM, Murphy TE, Gahbauer EA, Allore HG. The course of disability before and after a serious fall injury. *JAMA Intern Med*. 2013;173 (19):1780–1786. doi:10.1001/jamainternmed.2013.9063
6. Hoffman GJ, Tinetti ME, Ha J, Alexander NB, Min LC. Prehospital and posthospital fall injuries in older US adults. *JAMA Network Open*. 2020;3 (8):e2013243. doi:10.1001/jamanetworkopen.2020.13243
7. Yu K, Wu S, Jang Y, Chou C-P, Wilber KH, Aranda MP. Longitudinal assessment of the relationships between Geriatric conditi ons and loneliness. *J Am Med Dir Assoc*. 2021;22(5):1107–1113.e1101. doi:10.1016/j.jamda.2020.09.002
8. Gambaro E, Gramaglia C, Azzolina D, Campani D, Molin AD, Zeppegno P. The complex associations between late life depression, fear of falling and risk of falls. A systematic review and meta-analysis. *Ageing Res Rev*. 2022;73:101532. doi:10.1016/j.arr.2021.101532
9. Davis JC, Robertson MC, Ashe MC, Liu-Ambrose T, Khan KM, Marra CA. International comparison of cost of falls in older adults living in the community: a systematic review. *Osteoporos Int*. 2010;21(8):1295–1306. doi:10.1007/s00198-009-1162-0
10. Montero-Odasso M, van der Velde N, Martin FC, et al. World guidelines for falls prevention and management for older adults: a global initiative. *Age Ageing*. 2022;51(9):afac205.
11. Rudnicka E, Napierała P, Podfigurna A, Męczekalski B, Smolarczyk R, Grymowicz M. The World Health Organization (WHO) approach to healthy ageing. *Maturitas*. 2020;139:6–11. doi:10.1016/j.maturitas.2020.05.018
12. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *Lancet*. 2019;393(10191):2636–2646. doi:10.1016/S0140-6736(19)31138-9
13. Bauer J, Morley JE, Schols AMWJ, et al. Sarcopenia: a time for action. An SCWD position paper. *J Cachexia Sarcopenia Muscle*. 2019;10 (5):956–961. doi:10.1002/jcsm.12483
14. Li Z, Tong X, Ma Y, Bao T, Yue J. Prevalence of depression in patients with sarcopenia and correlation between the two diseases: systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle*. 2022;13(1):128–144. doi:10.1002/jcsm.12908
15. Kao S, Wang Y-C, Tzeng Y-M, Liang C-K, Lin F-G. Interactive effect between depression and chronic medical conditions on fall risk in community-dwelling elders. *Int Psychogeriatr*. 2012;24(9):1409–1418. doi:10.1017/S1041610212000646
16. Woo N, Kim SH. Sarcopenia influences fall-related injuries in community-dwelling older adults. *Geriatr Nurs*. 2014;35(4):279–282. doi:10.1016/j.gerinurse.2014.03.001
17. Chang K-V, Hsu T-H, Wu W-T, Huang K-C, Han D-S. Is sarcopenia associated with depression? A systematic review and meta -analysis of observational studies. *Age Ageing*. 2017;46(5):738–746. doi:10.1093/ageing/afx094
18. Wang D-K, Li Y-H, Guo X-M. Depression and sarcopenia-related traits: a Mendelian randomization study. *World J Psychiatry*. 2023;13 (11):929–936. doi:10.5498/wjp.v13.i11.929
19. Xue T, Gu Y, Xu H, Chen Y. Relationships between sarcopenia, depressive symptoms, and the risk of cardiovascular disease in Chinese population. *J Nutr Health Aging*. 2024;28(7):100259. doi:10.1016/j.jnha.2024.100259
20. Zhang X, Wang W, Zeng R, et al. Relationships between sarcopenia, depressive symptoms, and the risk of all-cause mortality in the Chinese population. *J Nutr Health Aging*. 2024;28(9):100316. doi:10.1016/j.jnha.2024.100316
21. Anderson DE, Quinn E, Parker E, et al. Associations of computed tomography-based trunk muscle size and density with balance and falls in older adults. *J Gerontol a Biol Sci Med Sci*. 2016;71(6):811–816. doi:10.1093/gerona/glv185
22. Kirk B, Zanker J, Duque G. Osteosarcopenia: epidemiology, diagnosis, and treatment-facts and numbers. *J Cachexia Sarcopenia Muscle*. 2020;11 (3):609–618. doi:10.1002/jcsm.12567
23. Lv Z, Deng C. NSAID medication mediates the causal effect of genetically predicted major depressive disorder on falls: evidence from a Mendelian randomization study. *J Affect Disord*. 2024;361:217–223. doi:10.1016/j.jad.2024.06.028
24. Zhao Y, Hu Y, Smith JP, Strauss J, Yang G. Cohort profile: the China Health and Retirement Longitudinal Study (CHARLS). *Int J Epidemiol*. 2014;43(1):61–68. doi:10.1093/ije/dys203
25. Kohout FJ, Berkman LF, Evans DA, Cornoni-Huntley J. Two shorter forms of the CES-D (Center for Epidemiological Studies Depression) depression symptoms index. *J Aging Health*. 1993;5(2):179–193. doi:10.1177/089826439300500202
26. Chen H, Mui AC. Factorial validity of the Center for Epidemiologic Studies Depression Scale short form in older population in China. *Int Psychogeriatr*. 2014;26(1):49–57. doi:10.1017/S1041610213001701
27. Boey KW. Cross-validation of a short form of the CES-D in Chinese elderly. *Int J Geriatr Psychiatry*. 1999;14(8):608–617. doi:10.1002/(SICI)1099-1166(199908)14:8<608::AID-GPS991>3.0.CO;2-Z
28. Chen L-K, Woo J, Assantachai P, et al. Asian Working Group for Sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc*. 2020;21(3):300–307.e302. doi:10.1016/j.jamda.2019.12.012
29. Wu X, Li X, Xu M, Zhang Z, He L, Li Y. Sarcopenia prevalence and associated factors among older Chinese popul ation: findings from the China Health and Retirement Longitudinal Study. *PLoS One*. 2021;16(3):e0247617. doi:10.1371/journal.pone.0247617
30. Hu Y, Peng W, Ren R, Wang Y, Wang G. Sarcopenia and mild cognitive impairment among elderly adults: the fir st longitudinal evidence from CHARLS. *J Cachexia Sarcopenia Muscle*. 2022;13(6):2944–2952. doi:10.1002/jcsm.13081
31. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol a Biol Sci Med Sci*. 2000;55(4):M221–231. doi:10.1093/gerona/55.4.M221
32. Templ M, Alfons A, Filzmoser P. Exploring incomplete data using visualization techniques. *Adv Data Anal Classif*. 2012;6(1):29–47. doi:10.1007/s11634-011-0102-y

33. Zhang Z. Multiple imputation with multivariate imputation by chained equation (MICE) package. *Ann Transl Med*. 2016;4(2):30. doi:10.3978/j.issn.2305-5839.2015.12.63
34. Wang DXM, Yao J, Zirek Y, Reijnierse EM, Maier AB. Muscle mass, strength, and physical performance predicting activities of daily living: a meta-analysis. *J Cachexia Sarcopenia Muscle*. 2020;11(1):3–25. doi:10.1002/jcsm.12502
35. Chen X, Han P, Yu X, et al. Relationships between sarcopenia, depressive symptoms, and mild cognitive impairment in Chinese community-dwelling older adults. *J Affect Disord*. 2021;286:71–77. doi:10.1016/j.jad.2021.02.067
36. Lim SK, Kong S. Prevalence, physical characteristics, and fall risk in older adults with and without possible sarcopenia. *Aging Clin Exp Res*. 2022;34(6):1365–1371. doi:10.1007/s40520-022-02078-z
37. Trajanoska K, Seppala LJ, Medina-Gomez C, et al. Genetic basis of falling risk susceptibility in the UK Biobank Study. *Commun Biol*. 2020;3(1):543. doi:10.1038/s42003-020-01256-x
38. Kumar P, Umakanth S, Marzetti E, Kalra S, G N. Four-step co-designing of the reablement strategies targeting sarcopenia (ReStart-S): an exercise-based multicomponent program for older adults residing in long-term care settings. *J Multidiscip Healthc*. 2024;17:1415–1433. doi:10.2147/JMDH.S452269
39. Schaap LA, Pluijm SMF, Deeg DJH, et al. Higher inflammatory marker levels in older persons: associations with 5-year change in muscle mass and muscle strength. *J Gerontol a Biol Sci Med Sci*. 2009;64(11):1183–1189. doi:10.1093/gerona/glp097
40. Berk M, Williams LJ, Jacka FN, et al. So depression is an inflammatory disease, but where does the inflammat ion come from? *BMC Med*. 2013;11:200. doi:10.1186/1741-7015-11-200
41. Gao K, Ma W-Z, Huck S, et al. Association between sarcopenia and depressive symptoms in Chinese older adults: evidence from the china health and retirement longitudinal Study. *Front Med*. 2021;8:755705. doi:10.3389/fmed.2021.755705
42. Liang C, Shi L, Li B, He Z. The mediating role of sarcopenia in the association between physical activity and falls among Chinese older adults: a cross-sectional study. *Healthcare*. 2023;11(24):3146. doi:10.3390/healthcare11243146
43. Jo E, Lee S-R, Park B-S, Kim J-S. Potential mechanisms underlying the role of chronic inflammation in ag e-related muscle wasting. *Aging Clin Exp Res*. 2012;24(5):412–422. doi:10.1007/BF03654825
44. Collins-Hooper H, Woolley TE, Dyson L, et al. Age-related changes in speed and mechanism of adult skeletal muscle stem cell migration. *Stem Cells*. 2012;30(6):1182–1195. doi:10.1002/stem.1088
45. Chen W, Wang L, You W, Shan T. Myokines mediate the cross talk between skeletal muscle and other organs. *J Cell Physiol*. 2021;236(4):2393–2412. doi:10.1002/jcp.30033
46. Pedersen BK. Physical activity and muscle-brain crosstalk. *Nat Rev Endocrinol*. 2019;15(7):383–392. doi:10.1038/s41574-019-0174-x
47. Scisciola L, Fontanella RA, Surina, Cataldo V. Sarcopenia and cognitive function: role of myokines in muscle brain cross-talk. *Life*. 2021;11(2):173. doi:10.3390/life11020173
48. Mokhtarzade M, Motl R, Negaresh R, et al. Exercise-induced changes in neurotrophic factors and markers of blood- brain barrier permeability are moderated by weight status in multiple sclerosis. *Neuropeptides*. 2018;70:93–100. doi:10.1016/j.npep.2018.05.010
49. Małkiewicz MA, Szarmach A, Sabisz A, Cubała WJ, Szurowska E, Winklewski PJ. Blood-brain barrier permeability and physical exercise. *J Neuroinflammation*. 2019;16(1):15.