frontiers | Research Topics

Sarcopenia and frailty: The role of physical activity for better aging

Edited by
Ricardo Aurélio Carvalho Sampaio, Marco Carlos Uchida, Hidenori Arai, Priscila Yukari Sewo Sampaio and Luciane Portas Capelo

Published in
Frontiers in Public Health

ISSN 1664-8714
ISBN 978-2-8325-3999-6
DOI 10.3389/978-2-8325-3999-6

About Frontiers

Frontiers is more than just an open access publisher of scholarly articles: it is a pioneering approach to the world of academia, radically improving the way scholarly research is managed. The grand vision of Frontiers is a world where all people have an equal opportunity to seek, share and generate knowledge. Frontiers provides immediate and permanent online open access to all its publications, but this alone is not enough to realize our grand goals.

Frontiers journal series

The Frontiers journal series is a multi-tier and interdisciplinary set of open-access, online journals, promising a paradigm shift from the current review, selection and dissemination processes in academic publishing. All Frontiers journals are driven by researchers for researchers; therefore, they constitute a service to the scholarly community. At the same time, the *Frontiers journal series* operates on a revolutionary invention, the tiered publishing system, initially addressing specific communities of scholars, and gradually climbing up to broader public understanding, thus serving the interests of the lay society, too.

Dedication to quality

Each Frontiers article is a landmark of the highest quality, thanks to genuinely collaborative interactions between authors and review editors, who include some of the world's best academicians. Research must be certified by peers before entering a stream of knowledge that may eventually reach the public - and shape society; therefore, Frontiers only applies the most rigorous and unbiased reviews. Frontiers revolutionizes research publishing by freely delivering the most outstanding research, evaluated with no bias from both the academic and social point of view. By applying the most advanced information technologies, Frontiers is catapulting scholarly publishing into a new generation.

What are Frontiers Research Topics?

Frontiers Research Topics are very popular trademarks of the *Frontiers journals series*: they are collections of at least ten articles, all centered on a particular subject. With their unique mix of varied contributions from Original Research to Review Articles, Frontiers Research Topics unify the most influential researchers, the latest key findings and historical advances in a hot research area.

Find out more on how to host your own Frontiers Research Topic or contribute to one as an author by contacting the Frontiers editorial office: frontiersin.org/about/contact

Sarcopenia and frailty: The role of physical activity for better aging

Topic editors
Ricardo Aurélio Carvalho Sampaio — Federal University of Sergipe, Brazil
Marco Carlos Uchida — State University of Campinas, Brazil
Hidenori Arai — National Center for Geriatrics and Gerontology (NCGG), Japan
Priscila Yukari Sewo Sampaio — Federal University of Sergipe, Brazil
Luciane Portas Capelo — Federal University of São Paulo, Brazil

Citation
Sampaio, R. A. C., Uchida, M. C., Arai, H., Sampaio, P. Y. S., Capelo, L. P., eds. (2024). *Sarcopenia and frailty: The role of physical activity for better aging*. Lausanne: Frontiers Media SA. doi: 10.3389/978-2-8325-3999-6

Table of contents

frontiers | Frontiers in Public Health

TYPE Editorial
PUBLISHED 10 November 2023
DOI 10.3389/fpubh.2023.1303223

Check for updates

OPEN ACCESS

EDITED AND REVIEWED BY
Marcia G. Ory,
Texas A&M University, United States

*CORRESPONDENCE
Ricardo Aurélio Carvalho Sampaio
sampaiorac@academico.ufs.br

RECEIVED 27 September 2023
ACCEPTED 23 October 2023
PUBLISHED 10 November 2023

CITATION
Sampaio RAC, Sewo Sampaio PY, Capelo LP, Uchida MC and Arai H (2023) Editorial: Sarcopenia and frailty: the role of physical activity for better aging.
Front. Public Health 11:1303223.
doi: 10.3389/fpubh.2023.1303223

Editorial: Sarcopenia and frailty: the role of physical activity for better aging

Ricardo Aurélio Carvalho Sampaio[1]*, Priscila Yukari Sewo Sampaio[2], Luciane Portas Capelo[3], Marco Carlos Uchida[4] and Hidenori Arai[5]

[1]Graduate Program in Physical Education, Federal University of Sergipe, São Cristóvão, Sergipe, Brazil, [2]Department of Occupational Therapy, Federal University of Sergipe, Lagarto, Sergipe, Brazil, [3]Institute of Science and Technology, Federal University of São Paulo, São José dos Campos, São Paulo, Sergipe, Brazil, [4]Department of Adapted Physical Activity, School of Physical Education, University of Campinas, São Paulo, Sergipe, Brazil, [5]National Center for Geriatrics and Gerontology, Obu, Aichi Prefecture, Japan

KEYWORDS

aging, body composition, disability, muscle strength, physical function, public health

Editorial on the Research Topic
Sarcopenia and frailty: the role of physical activity for better aging

As the global population continues to age, the prevalence of age-related health conditions such as sarcopenia and frailty has become a significant concern for public health worldwide. These conditions affect the quality of life of older adults and place a substantial burden on healthcare systems. Especially because they increase the likelihood of falls, hospitalizations, multimorbidity, and functional disability (1, 2). In addition, sarcopenia and frailty are mortality indicators in both community-dwelling and institutionalized older adults (3).

In this Research Topic, we have assembled a collection of 10 research articles that delve into the complex relationship between sarcopenia, frailty, physical activity, and aging. These articles shed light on crucial aspects of these conditions and provide valuable insights for aging and public health, including those related to lifestyle factors for healthful and successful aging, chronic disease management across the life-course to promote healthy aging, and evidence-based programs and practices.

The article by Gomez-Campos et al. explored the relationship between age and handgrip strength (HGS), a key component of frailty and a predictor of future morbidity and mortality. Their research analyzed data from 5,376 Chilean participants (from 6 to 80 years old). They found that there is a non-linear relationship between chronological age and HGS from childhood to senescence. The proposed percentiles offer valuable insights into monitoring HGS, providing clinicians and researchers with percentiles by age and sex for assessing muscle strength levels.

Considering that low hemoglobin levels/anemia, osteoporosis, and sarcopenia are common in older people, two studies were conducted to verify such associations. Firstly, Liu Q. et al. investigated the correlation between hemoglobin levels and osteoporosis among older Chinese individuals. Their cross-sectional study had a sample of 1,068 individuals aged 55–85 years, and revealed a significant link between lower hemoglobin levels and bone mineral density, even after controlling for several confounders. This emphasizes the importance of considering both hematological and musculoskeletal factors in the assessment of frailty and bone health.

In another exploration of hemoglobin's role, Liu Y. et al. used data from the China Health and Retirement Longitudinal Study (CHARLS) to delve into the relationship between hemoglobin levels and sarcopenia in the Chinese population aged 60 and above ($n = 3{,}055$). Cross-sectionally, their findings highlighted a negative association between hemoglobin levels and sarcopenia, and low appendicular skeletal muscle mass adjusted by height. The cohort study data ($n = 1{,}022$) showed a negative association of hemoglobin level and low physical performance; with sarcopenia; and skeletal muscle mass.

Chen X. et al. addressed the critical issue of mortality in hemodialysis patients. They aimed to identify physical performance (i.e., gait speed, the Timed Up and Go, and the Short Physical Performance Battery) and muscle strength (i.e., HGS) as key predictors. The authors showed that muscle strength and physical performance, rather than muscle mass, predict all-cause mortality ($n = 923$ hemodialysis patients from China; 8.6% have died after a median of 14 months). These findings present the role of strength and physical performance rather than muscle mass in sarcopenia, as well as in hemodialysis patients, with implications for the care and management of this condition.

Supporting that physical exercise is an important intervention to promote health and fitness in sarcopenia, Xiang et al. conducted a bibliometric analysis of research on exercise interventions for this disease published between 2003 and 2022. Specifically, the United States of America is currently the country with the largest number of publications, and Alfonso Cruz-Jentoft, from Spain, first author of both European Consensus on the definition and diagnosis of sarcopenia (4, 5), the most cited author. Their study provided an overview of the current state of research and identified hotspots and trends in the field.

Takahashi et al. investigated the relationship between activity diversity (i.e., type, frequency, evenness) and frailty in a 2-year longitudinal study of Japanese community-dwelling older adults. A total of 207 non-frail participants at baseline were enrolled and 30.9% of them had incident frailty during the follow-up period. Their findings indicated that activity type and evenness were predictors of frailty after adjustments for sociodemographic and psychosomatic factors, underscoring the importance of considering not only the quantity but also the variety of activities in promoting healthy aging.

Ohta et al. highlighted the intricate interplay between physical and cognitive aspects of aging and emphasized the need for tailored interventions based on sex and age. They identified a stronger linear association of sarcopenia severity with poor cognitive function in women compared with men in their study. The study had a cross-sectional approach of regional cohorts of the Integrated Research Initiative for Living Well with Dementia (IRIDE) Cohort Study with 6,426 Japanese older people.

De lima et al. investigated, in a randomized 14-week interventional study, the effects of agility ladder training with a cognitive task in healthy older adults. This approach demonstrated the potential for improving both physical function and cognitive performance, through innovative interventions in aging populations considering sarcopenia and frailty.

Chen A. et al. conducted a comprehensive analysis of the relationship between body habitus and frailty in a community-based sample of 840 Chinese adults. Their research identified high body mass index (BMI) and waist-hip ratio (WHR) as significant risk factors for frailty, underpinning the importance of considering multiple body composition measures in assessing frailty risk.

Finally, Veen et al. highlighted the benefits of exceeding minimum activity guidelines to optimize performance in activities of daily living and overall functioning. They investigated the impact of accumulating twice the recommended minimum amount of moderate-to-vigorous physical activity (MVPA) on physical function (i.e., HGS, 5 times sit-to-stand, squat jump, and 6-min walk test) in older adults ($n = 193$). Their study revealed that individuals who engaged in more than 300 min of MVPA per week exhibited better physical function, particularly in walking performance.

Collectively, the articles on this Research Topic make an important step forward approach to sarcopenia, frailty, and the role of physical activity in aging populations, as well as underlying factors. As we continue to grapple with the implications of global aging, the insights gained from these studies may inform public health policies and interventions, inspire further research, and lead to strategies with the aim of mitigating sarcopenia and frailty in older adults, promoting healthy and wellbeing aging.

Author contributions

RS: Writing—original draft, Writing—review and editing. PS: Writing—original draft, Writing—review and editing. LC: Writing—original draft, Writing—review and editing. MU: Writing—original draft, Writing—review and editing. HA: Writing—original draft, Writing—review and editing.

Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

Acknowledgments

We would like to thank all the authors who contributed to this Research Topic.

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.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

Publisher's note

References

1. Lu L, Mao L, Feng Y, Ainsworth BE, Liu Y, Chen N. Effects of different exercise training modes on muscle strength and physical performance in older people with sarcopenia: a systematic review and meta-analysis. *BMC Geriatr.* (2021) 21:708. doi: 10.1186/s12877-021-02642-8

2. Bauer J, Morley JE, Schols AMWJ, Ferrucci L, Cruz-Jentoft AJ, Dent E, et al. Sarcopenia: a time for action. An SCWD position paper. *J Cachexia Sarcopenia Muscle.* (2019) 10:956–61. doi: 10.1002/jcsm.12483

3. Xu J, Wan CS, Ktoris K, Reijnierse EM, Maier AB. Sarcopenia is associated with mortality in adults: a systematic review and meta-analysis. *Gerontology.* (2022) 68:361–76. doi: 10.1159/000517099

4. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on Sarcopenia in Older People. *Age Ageing.* (2010) 39:412–23. doi: 10.1093/ageing/afq034

5. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing.* (2019) 48:16–31. doi: 10.1093/ageing/afy169

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 26 January 2023
DOI 10.3389/fpubh.2022.1072684

Check for updates

OPEN ACCESS

EDITED BY
Ricardo Aurélio Carvalho Sampaio,
Federal University of Sergipe, Brazil

REVIEWED BY
Shirko Ahmadi,
Montreal University, Canada
David Hollar,
Mercer University School of Medicine,
United States

*CORRESPONDENCE
Marco Cossio-Bolaños
✉ mcossio1972@hotmail.com

SPECIALTY SECTION
This article was submitted to Aging and Public Health, a section of the journal Frontiers in Public Health

RECEIVED 18 October 2022
ACCEPTED 29 December 2022
PUBLISHED 26 January 2023

CITATION
Gómez-Campos R, Vidal Espinoza R, de Arruda M, Ronque ERV, Urra-Albornoz C, Minango JC, Alvear-Vasquez F, la Torre Choque Cd, Castelli Correia de Campos LF, Sulla Torres J and Cossio-Bolaños M (2023) Relationship between age and handgrip strength: Proposal of reference values from infancy to senescence. *Front. Public Health* 10:1072684. doi: 10.3389/fpubh.2022.1072684

Relationship between age and handgrip strength: Proposal of reference values from infancy to senescence

Rossana Gómez-Campos[1,2], Rubén Vidal Espinoza[3], Miguel de Arruda[4], Enio Ricardo Vaz Ronque[5], Camilo Urra-Albornoz[6], Juan Carlos Minango[7], Fernando Alvear-Vasquez[8], Christian de la Torre Choque[9], Luis Felipe Castelli Correia de Campos[10], Jose Sulla Torres[11] and Marco Cossio-Bolaños[2,12]*

[1]Departamento de Diversidad e Inclusividad Educativa, Universidad Católica del Maule, Talca, Chile, [2]Faculty of Education, Psychology and Sport Sciences, University of Huelva, Huelva, Spain, [3]Universidad Católica Silva Henriquez, Santiago, Chile, [4]Universidad Estadual de Campinas, São Paulo, Brazil, [5]Departamento de Educação Física (DEF), Universidade Estadual de Londrina, Londrina, Brazil, [6]Escuela de Ciencias del Deporte, Facultad de Salud, Universidad Santo Tomás, Santiago, Chile, [7]Instituto Tecnológico Universitario Ruminahui, Sangolqui, Ecuador, [8]Facultad de Educación, Universidad Autónoma de Chile, Talca, Chile, [9]Universidad San Ignacio de Loyola, Lima, Perú, [10]Departamento de Ciencias de la Educación, Facultad de Educación y Humanidades, Universidad del Bio-Bio, Chillán, Chile, [11]Universidad Católica de Santa María, Arequipa, Perú, [12]Departamento de Ciencias de la Actividad Física, Universidad Católica del Maule, Talca, Chile

Introduction: Measurement of hand grip strength (HGS) has been proposed as a key component of frailty and has also been suggested as a central biomarker of healthy aging and a powerful predictor of future morbidity and mortality.

Objectives: (a) To determine whether a nonlinear relationship model could improve the prediction of handgrip strength (HGS) compared to the linear model and (b) to propose percentiles to evaluate HGS according to age and sex for a regional population of Chile from infancy to senescence.

Methods: A cross-sectional descriptive study was developed in a representative sample of the Maule region (Chile). The volunteers amounted to 5,376 participants (2,840 men and 2,536 women), with an age range from 6 to 80 years old. Weight, height, HGS (right and left hand) according to age and sex were evaluated. Percentiles were calculated using the LMS method [(L (Lambda; asymmetry), M (Mu; median), and S (Sigma; coefficient of variation)].

Results and discussion: There were no differences in HGS from 6 to 11 years of age in both sexes; however, from 12 years of age onwards, males presented higher HGS values in both hands ($p < 0.05$). The linear regression between age with HGS showed values of $R^2 = 0.07$ in males and $R^2 = 0.02$ in females. While in the non-linear model (cubic), the values were: $R^2 = 0.50$ to 0.51 in men and $R^2 = 0.26$ in women. The percentiles constructed by age and sex were: P5, P15, P50, P85, and P95 by age range and sex. This study demonstrated that there is a nonlinear relationship between chronological age with HGS from infancy to senescence. Furthermore, the proposed percentiles can serve as a guide to assess and monitor upper extremity muscle strength levels at all stages of life.

KEYWORDS

dynamometer, hand grip strength, percentiles, infancy, senescence

Introduction

Hand grip strength (HGS) is the amount of static force that the hand can generate around the dynamometer. It is defined as the ability of the hand to grasp objects between the thumb and fingers (1). It is characterized by completing a maximal isometric grip strength task, in which individuals squeeze a grip dynamometer with maximal effort for a short period of time and then the contracted musculature is relaxed (2).

Overall muscle strength is conveniently assessed by measuring (HGS) with a hand grip dynamometer (3). This equipment objectively measures upper extremity isometric strength (4) and is considered a prime candidate for use in routine medical examinations given its simplicity and low cost for assessing isometric strength in children, youth and adults (5).

Measurement of HGS has been proposed as a key component of frailty phenotypes and has also been suggested as a central biomarker of healthy aging and a powerful predictor of future morbidity and mortality in both young, as well as older adult populations (6, 7).

Indeed, measures of muscle strength and physical performance are increasingly used for research and practice. It is timely to review and identify appropriate tools for their assessment (8), so norm-referenced percentiles are an alternative to help interpret the performance of an individual compared to a reference population (9).

In that sense, reference ranges for HGS from infancy to senescence have been reported in several studies in high-income countries such as England (10) Canada (11) and the United States (12, 13). These scales are comparable and measurable to aid in interpetation of test results and decision making (13), such as the reference values proposed by the Center for Disease Control and Prevention [CDC] (14), developed from the United States National Health and Nutrition Examination Survey (NHANES).

These references are very scarce in South America, such as the study developed in Colombia (15). However, in Chile, as far as is known, no studies have been identified that cover a wide age range that would allow the assessment of HGS from 6 to 80 years of age, as has been observed in previous studies.

In general, reference values should be interpreted using specific ranges according to geographic region, ethnicity (16), age, sex, height (7). This is due to the fact that, not all country populations present similar characteristics (social, economic, cultural, demographic, nutritional and anthropometric). Therefore, their trajectories usually present varied levels of muscular strength performances, being higher in men in relation to women. These differences appear during the stage of growth and maturation, passing through youth, middle adulthood and old age) (10, 11).

Consequently, studying HGS from infancy to senescence is relevant, due to its ability to predict skeletal muscle strength throughout life, as studies generally use linear regression models to predict HGS (1, 17, 18). However, it is possible that there is a nonlinear relationship between age and HGS, as the cubic model could improve the predictive power of isometric strength when it is intended to be analyzed from infancy to senescence.

Therefore, the objectives of the study were (a) to determine whether a nonlinear relationship model could improve the prediction of HGS compared to the linear model and (b) to propose percentiles to assess HGS according to age and sex for a regional population of Chile from infancy to senescence.

Methodologic

Type of study and sample

A descriptive cross-sectional study was developed in a representative sample of the Maule region (Chile). The details of the sampling process were described in a previous study (19). Sampling was probabilistic (random). The volunteers amounted to 5,376 participants (2,840 males and 2,536 females), with an age range of 6 to 80 years old. They were recruited from public schools (schoolchildren aged 6 to 17 years), public and private universities (aged 18 to 30 years) and middle-aged and older adults from social programs offered by the Municipality of Talca (Maule Region). Maule is located in the seventh region of Chile 230 km south of the capital Santiago and the Development Index (HDI) for 2018 was 0.872, while for the country it was 0.847 (20).

Regarding the socio-demographic indicators of the Maule region (Chile), according to the Ministerio de Desarrollo Social Chile (21), there are small differences in relation to the capital of chile (Santiago). For example, the average years of schooling in the Maule region are around ∼9.8 years, the employment rate is 55.7%, unemployment rate 6.9%, state social welfare 55.7%, private social welfare 5.9%. While, in the capital Santiago, the average years of schooling are ∼11.6 years, the employment rate is 58.9%, unemployment rate 6.9%, state social security 71.0%, and private social security 21.3%.

All study participants signed the informed consent form, in which they authorized the anthropometric measurements and the assessment of HGS. For those under 18 years of age, it was the parents and/or guardians who signed the informed consent. Participants who were of a nationality other than Chilean were excluded, as well as those who presented some type of physical disability (that prevented them from being able to look after themselves). People who previously reported stroke, spinal cord or brain injury, or upper extremity disabilities were also excluded from the study.

The research was conducted from 2015 to 2018 and was developed according to the Declaration of Helsinki for human beings and had the approval of the University Ethics Committee (UA-238-2014).

Techniques and procedures

A team of 6 evaluators was formed to collect data from the study sample. The anthropometric variables and the HGS were collected in schools, universities, and in the facilities of the social programs of the Municipality of Talca. This procedure was carried out from Monday to Friday from 8:30 am to 12:30 pm. Data such as age and date of birth were collected from the registration forms of each institution.

Anthropometric measurements of weight and height were evaluated according to the recommendations of Ross and Marfell-Jones (22). All participants wore as little clothing as possible (shorts, T-shirt, and bare feet). Body weight (kg) was measured using an electric scale (Tanita, Glasgow, UK, Ltd), accurate to 100g and with a scale from 0 to 150 kg. Height was measured in the standing position and according to the Frankfort plane (23). A portable stadiometer (Seca Gmbh and Co. KG. Hamburg, Germany), with an accuracy of 0.1 mm, and a scale of 0 to 205 cm, was used. Both anthropometric

TABLE 1 Characteristics of the sample studied.

Age (years)	n	Weight (kg)		Height (cm)		HGS- RA(kgf)		HGS-LA (kgf)	
		X	SD	X	SD	X	SD	X	SD
Males									
6 a 11	735	35.3	11.2	133.7	11.6	10.9	7.3	10.6	7.2
12 a 19	1534	64.8	13.9*	167.6*	9.8	31.7	13.7*	30.4	13.1*
20 a 29	322	77.3	12.3*	173.1*	6.7	43.8	12.3*	41.9	12.1*
30 a 39	49	82.9	12.8*	175.3*	9.4	33.4	17.4*	31.1	16.1*
40 a 49	43	84.3	15.4*	170.0*	5.5	27.2	12.7*	26.8	13.4*
50 a 59	53	86.9	11.6*	169.6*	6.8	25.8	11.1*	26.2	10.9*
60 a 69	52	81.5	13.0*	167.9*	6.6	29.4	15.3*	27.7	13.5*
70 a 80	52	78.6	11.7	165.6*	6	27.4	12.7*	25.3	13.0*
Total	2840	59.7	20.3	159.4	18.4	27.5	16.3	26.3	15.6
Females									
6 a 11	630	36.1	10.9	135.2	12.1	10.8	5.9	10.1	5.6
12 a 19	787	59.7	12.1	158,0	6.3	22.9	7.6	21.6	7.3
20 a 29	240	64.3	12.5	160.6	6.1	23.5	8.7	22,0	8.3
30 a 39	72	70.5	13.8	160,0	8.1	23.7	10.2	22.8	9.5
40 a 49	110	70.7	14,0	156.8	10.4	23.5	8.8	23,0	8.7
50 a 59	162	70.4	12.4	156.2	5.7	20.2	8.2	19.7	8.5
60 a 69	294	70.2	12.2	153,0	6.7	20.3	6.9	19.4	6.9
70 a 80	241	67.5	12.5	151.3	6.4	18.7	7.1	17.8	7.1
Total	2536	57.7	17.8	151.3	13.1	19.3	8.8	18.4	8.5

X, Average; SD, Standard deviation; HGS, Handgrip strength; RA, Right arm; LA, Left arm.

measurements were evaluated 2 times, where the relative technical error of measurement (TEM%) was 1.2%.

The HGS of both hands (right and left) was assessed by dynamometry. A JAMAR hydraulic dynamometer (brand name) (Hydraulic Hand Dynamometer® Model PC-5030 J1, Fred Sammons, Inc., Burr Ridge, IL: USA) was used. This equipment has an accuracy of 0.1 kg and a scale up to 100 kg/f. We used the protocol proposed by Richards et al. (24), where participants were tested one by one in a seated position (standard position in a straight-backed chair). Each subject performed two attempts with each hand and one of the evaluators adjusted the dynameter to the grip size of the equipment. The hands performing the grips were alternated to minimize fatigue effects (1 to 2 min rest between each attempt). The best measurement was recorded for each of the two attempts. The TEM% between the two evaluations ranged from 1.2 to 1.5%.

Statistics

The normality of the distribution of the data (weight, height and HGS) was verified by means of the Kolmogorov-Smirnov test. Descriptive statistics (mean and standard deviation) were calculated by age and sex strata. Significant differences between both sexes were verified by means of the Student's *t*-test for two samples. Different linear and nonlinear (cubic) regression analysis models were used, being the third degree cubic polynomial model the most adequate for both sexes (between age and HGS): HGS = a + b1(age) + b2(age)2 + b3(age)3, where: a is the intercept, b1, b2 and b3 are regression parameters, estimated from the data. The regression analysis was performed separately for each sex. For significance, $p < 0.05$ was adopted and calculations were performed in Microsoft Excel spreadsheets, SPSS 16.0 software and R. Percentile curves were created for HGS for both hands (P5, P15, P50, P85, and P9) using the LMS method [L (Lambda; skewness), M (Mu; median) and S (Sigma; coefficient of variation)] proposed by Cole et al. (25). The LMS Chart Maker software version 2.3 (26) was also used.

Results

Table 1 shows the anthropometric characteristics, and HGS values of both sexes by age ranges. The boys categorized from 6 to 11 years of age presented similar values of weight, height, and HGS (right and left arm) in relation to their female counterparts ($p > 0.05$). On the contrary, in the age ranges (12 to 19 years, 20 to 29 years, 30 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 and 70 to 80 years), males presented significant higher values in relation to females ($p < 0.05$).

The results of the linear and nonlinear regression between age and HGS can be seen in Figure 1. In the linear relationship, age with HGS showed low explanatory power in both sexes ($R^2 = 0.07$ in men and 0.02 in women). While when analyzed by the cubic (non-linear) model, the explanatory values increased ostensibly

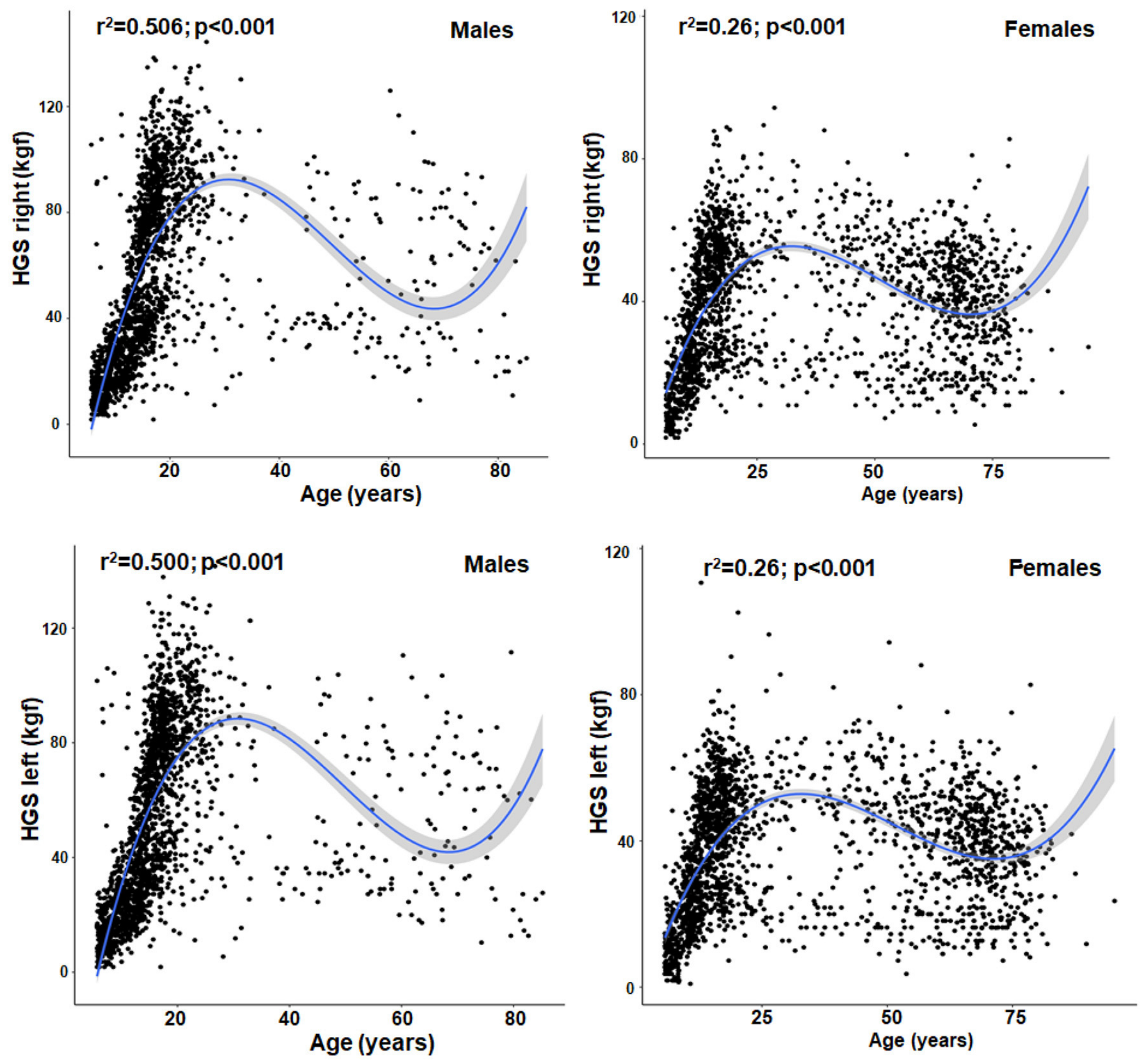

FIGURE 1
Non-linear relationship (cubic) between chronological age with HGS in both hands and both sexes from 6 to 80 years of age.

(in men up to $R^2 = 0.50$ to 0.51 and in women up to 0.26). In the non-linear model generated, the residual standard error (RSE) reflected adequate fit, for example in males (RSE = 11.48 and 11.05), while in females (RSE = 7.55 and 7.34). In general, Figure 1 shows that the cubic (nonlinear) regression model showed a phase of accelerated increase in HGS in both sexes (during childhood, adolescence and young adulthood). Followed by a plateau around the age of 30 years approximately in both sexes (45 kg in men and 28 kg in women), then after the age of 40 years, men begin to experience an accelerated reduction of HGS up to ∼50% at the age of 80 years. While in women a smaller reduction of HGS was observed as age advances (decreasing by ∼37%, approximately).

The HGS percentiles by chronological age and sex can be seen in Table 2 and Figure 2. The percentile distribution was P5, P15, P50, P85, and P95. These values describe HGS patterns that are similar from age 6 to 12 years in both sexes and both hands. However, from the age of 13 years onwards, males present significantly higher levels of HGS ($p < 0.05$) than females until older ages.

Discussion

The first objective of this study was to determine whether a nonlinear relationship model (cubic) could improve the prediction of HGS compared to the linear model by chronological age in a regional population of Chile ranging from 6 to 80 years of age. The results have shown that the nonlinear regression model (cubic) better explains HGS when it is analyzed by chronological age from infancy to senescence.

The cubic relationships observed in this study have evidenced a better explanatory power between age with HGS in both hands and in both sexes (reaching in men up to 51% and in women up to 28%). While, in the linear relationship, the predictive power for both hands showed values of $R^2 = 0.07$ in men and 0.02 in women.

In both cases (for both right and left hand) the curvilinear (i.e., cubic) regression models were superior to linear regression as observed in some recent studies (27, 28). These cubic relationships observed in this study are consistent with the literature, where HGS increases with chronological age during growth and development.

TABLE 2 Percentiles to evaluate HGS from 5 to 80 years according to age range for both sexes.

Age	HGS-RA (kgf)								HGS-LA (kgf)							
	L	M	S	P5	P15	P50	P85	P95	L	M	S	P5	P15	P50	P85	P95
Males																
6	−0.09	5.56	0.62	2.1	3.0	5.6	10.8	16.3	0.41	5.52	0.55	1.8	2.9	5.5	9.2	11.9
7	−0.22	6.89	0.58	2.9	3.9	6.9	13.2	20.2	0.46	7.35	0.52	2.5	4.0	7.3	11.9	15.1
8	0.22	8.49	0.55	3.1	4.6	8.5	14.5	19.3	0.5	9.24	0.49	3.3	5.1	9.2	14.6	18.3
9	0.61	10.26	0.51	3.1	5.4	10.3	16.3	20.3	0.54	11.25	0.47	4.1	6.4	11.2	17.3	21.4
10	0.36	12.13	0.49	4.7	7.0	12.1	19.3	24.5	0.59	13.35	0.44	5.1	7.8	13.4	20.1	24.5
11	0.04	14.43	0.47	6.6	8.9	14.4	23.3	30.7	0.63	15.55	0.42	6.2	9.3	15.5	22.9	27.7
12	0.22	17.6	0.45	7.9	10.8	17.6	27.3	34.7	0.67	17.73	0.40	7.4	10.9	17.7	25.6	30.7
13	0.37	21.75	0.42	9.7	13.5	21.8	32.7	40.4	0.72	19.7	0.39	8.5	12.3	19.7	28	33.2
14	0.51	26.59	0.4	12.0	16.7	26.6	38.7	46.8	0.77	21.33	0.37	9.4	13.5	21.3	29.9	35.2
15	0.89	31.42	0.37	13.0	19.6	31.4	43.7	51.2	0.81	22.55	0.36	10.1	14.5	22.5	31.2	36.6
16	1.10	35.62	0.34	14.8	22.7	35.6	48	55.2	0.86	23.36	0.35	10.5	15.1	23.4	32.1	37.4
17	1.15	38.79	0.32	17.6	25.7	38.8	51.2	58.3	0.9	23.84	0.35	10.7	15.4	23.8	32.6	37.8
18	1.28	40.75	0.3	18.7	27.4	40.7	52.9	59.7	0.93	24.07	0.35	10.7	15.6	24.1	32.8	38.0
19	1.46	41.51	0.3	17.4	27.4	41.5	53.6	60.2	0.97	24.04	0.35	10.5	15.5	24.0	32.7	37.9
20 a 29	1.38	41.01	0.32	16.4	26.5	41	53.8	60.8	0.99	23.75	0.35	10.1	15.1	23.7	32.4	37.4
30 a 39	1.16	39.19	0.35	15.3	24.5	39.2	53	60.9	1.01	23.19	0.35	9.6	14.7	23.2	31.7	36.6
40 a 49	0.79	36.46	0.39	15.0	22.5	36.5	51.7	61.1	1.03	22.37	0.36	9.1	14.0	22.4	30.6	35.4
50 a 59	0.6	33.3	0.43	13.3	19.8	33.3	49.4	60	1.04	21.33	0.36	8.5	13.3	21.3	29.2	33.8
60 a 69	0.63	30.01	0.47	10.4	16.7	30.0	45.9	56.4	1.04	20.18	0.36	7.9	12.5	20.2	27.7	32.1
>70	0.78	26.69	0.51	6.8	13.5	26.7	41.6	51	1.05	18.99	0.37	7.3	11.7	19	26.1	30.3
Females																
6	−0.12	5.02	0.69	1.7	2.5	5.0	10.6	17.1	0.33	4.7	0.56	1.5	2.5	4.7	8.0	10.5
7	0.25	6.26	0.65	1.8	3.0	6.3	11.7	16.1	0.37	6.46	0.54	2.2	3.5	6.5	10.7	13.8
8	0.11	7.71	0.6	2.7	4.0	7.7	14.1	19.7	0.41	8.25	0.51	3.0	4.6	8.3	13.3	16.9
9	0.48	9.28	0.56	2.8	4.7	9.3	15.5	19.9	0.45	10.14	0.48	3.8	5.8	10.1	15.9	20.0
10	0.38	11.0	0.52	3.9	6.0	11.0	18.0	23.2	0.49	12.13	0.46	4.7	7.1	12.1	18.6	23.0

(Continued)

TABLE 2 (Continued)

Age	HGS-RA (kgf)								HGS-LA (kgf)							
	L	M	S	P5	P15	P50	P85	P95	L	M	S	P5	P15	P50	P85	P95
11	0.13	13.2	0.49	5.6	7.8	13.2	21.7	28.6	0.53	14.2	0.44	5.8	8.5	14.2	21.3	26.1
12	0.15	16.25	0.47	7.2	9.8	16.2	25.9	33.5	0.58	16.25	0.42	6.8	9.9	16.3	23.9	28.9
13	0.35	20.26	0.44	8.9	12.4	20.3	30.8	38.5	0.63	18.08	0.4	7.7	11.2	18.1	26.1	31.3
14	0.51	24.95	0.41	11.0	15.5	24.9	36.5	44.3	0.68	19.57	0.39	8.5	12.3	19.6	27.9	33.1
15	0.86	29.61	0.37	12.3	18.5	29.6	41.3	48.5	0.74	20.68	0.37	9.1	13.1	20.7	29.1	34.4
16	1.11	33.63	0.34	14.0	21.5	33.6	45.3	52.0	0.78	21.43	0.37	9.4	13.6	21.4	29.9	35.2
17	1.17	36.65	0.32	16.5	24.3	36.7	48.3	55.0	0.83	21.9	0.36	9.6	13.9	21.9	30.4	35.6
18	1.28	38.51	0.3	17.5	25.8	38.5	50.1	56.6	0.86	22.15	0.36	9.5	14.0	22.2	30.7	35.9
19	1.39	39.23	0.31	16.6	25.9	39.2	51.0	57.4	0.89	22.18	0.37	9.3	13.9	22.2	30.8	36.0
20 a 29	1.33	38.75	0.33	15.2	24.8	38.8	51.2	58.0	0.91	21.98	0.37	9.0	13.7	22	30.6	35.7
30 a 39	1.17	37.02	0.36	13.7	22.8	37.0	50.4	58.0	0.93	21.56	0.38	8.6	13.3	21.6	30.1	35.2
40 a 49	0.81	34.41	0.4	13.6	20.8	34.4	49.1	58.1	0.93	20.88	0.38	8.1	12.7	20.9	29.3	34.3
50 a 59	0.61	31.35	0.44	12.2	18.4	31.4	46.8	57.0	0.93	19.94	0.39	7.6	12.0	19.9	28.1	32.9
60 a 69	0.61	28.14	0.48	9.6	15.6	28.1	43.5	53.7	0.92	18.82	0.39	7.0	11.3	18.8	26.6	31.3
>70	0.72	24.89	0.52	6.5	12.5	24.9	39.3	48.6	0.91	17.63	0.4	6.5	10.5	17.6	25.0	29.5

P, percentile; HGS, Handgrip strength; RA, Right arm; LA, Left arm.

10.3389/fpubh.2022.1072684

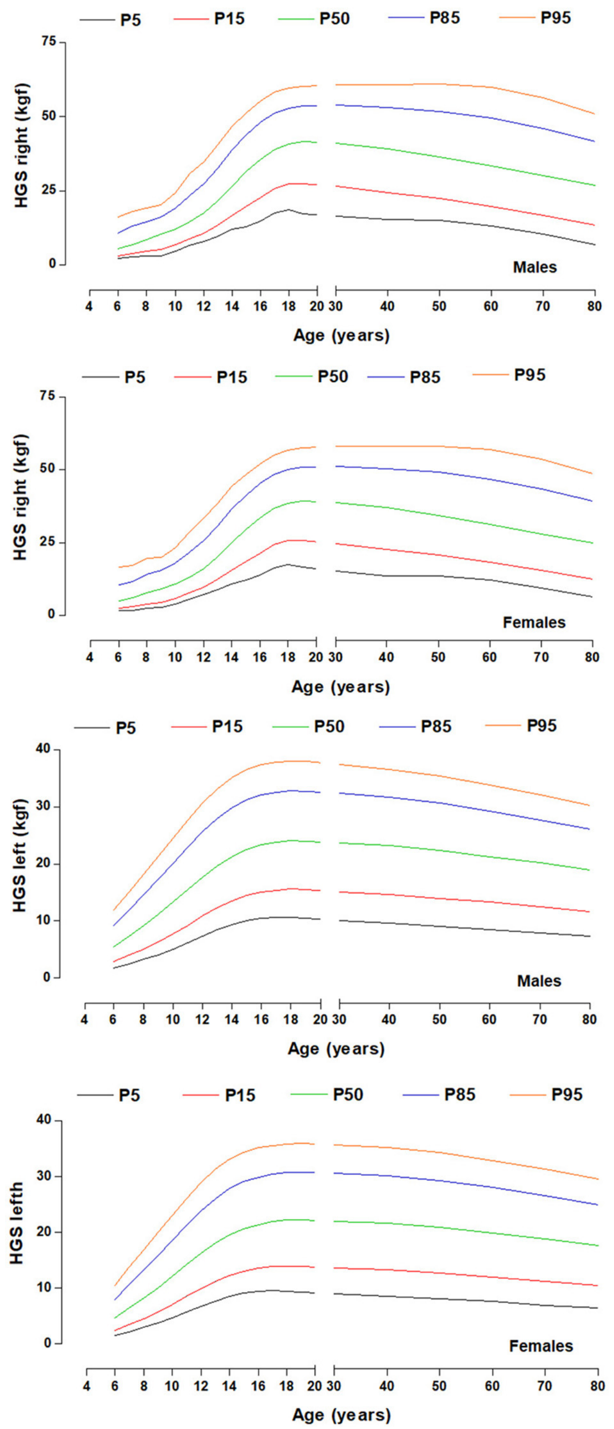

FIGURE 2
HGS percentiles by chronological age for both sexes and both hands.

HGS reaches a plateau around age thirty (12, 29) and declines after age forty (10, 30) and fifty (28, 29), as age advances.

In essence, the predictive power of HGS improves when analyzed from a nonlinear relationship, as demonstrated in this study. Although several studies have used linear relationships between age and anthropometric parameters with HGS in various populations around the world (31–34). Therefore, future studies should take into account that to analyze HGS across the lifespan should consider that the cubic model can be a valuable tool to analyze upper limb muscle fitness trajectories.

Consequently, given that HGS is an indicator of general strength at all ages and stages of life, this study set out as a second objective to develop referential percentiles according to age and sex ranges.

The HGS percentiles as a function of chronological age proposed in this study should be interpreted using specific reference ranges according to geographic region and ethnicity (16). These proposed tools for the Maule region of Chile can be used to assess and monitor muscle strength from infancy to senescence.

In fact, regardless of the country and/or geographic region, the proposed references serve to identify individuals with low performance, to identify those in need of intervention, to follow up high-performing subjects as part of intervention programs (35). As well as to promote occupational therapy (13), physical education classes (12), and to identify frailty phenotypes and healthy aging across the lifespan (6).

In general, the cut-off points adopted in this study for HGS considered as abnormally low is <p5. These values were suggested by some studies (11, 36) where they highlight an early detection of decreased isometric muscle strength. Percentiles p5 to p15 can be interpreted with a low level of HGS and between p15 to p85 as adequate and >p85 as elevated HGS. Other studies have also pragmatically suggested 2SD below the mean maximum sex value (10, 37).

In general, reference values, by chronological age are a valuable tool to be considered as routine measures, both in clinical and epidemiological contexts. In fact, several international studies have used HGS as a prognostic marker of mortality in children, adolescents (38), in middle-aged people (39), and as indicators of frailty and sarcopenia in older adults (40).

This study has some limitations that have to do with the cross-sectional design used in this study, given that the results obtained preclude inferring causal relationships. In addition, data on muscle pathologies, muscle strength values of the lower extremities, including fat-free mass and bone mineral density values, were not collected. This information would have allowed a broader analysis and discussion of the results. Therefore, future studies should take these aspects into account.

Notwithstanding the above, we emphasize that one of the main strengths of the study is the size of the sample and the probabilistic selection, since the results obtained can be generalized to other geographic regions of Chile. These results can also serve as a baseline for future secular trend studies, as well as for short-term comparisons with other national and international studies. It can also serve professionals and researchers in the area as guidelines for clinical and epidemiological use and decision making. Furthermore, its use and application can enrich the International Classification of Functioning, Disability and Health [ICF] (41) in disciplines and sectors such as education and transportation, health and community services, respectively. Calculations can be made through the following link: http://www.reidebihu.net/hgs_infancy_senesce.php.

Conclusion

In conclusion, this study demonstrated that there is a nonlinear relationship between chronological age and HGS from infancy to senescence. This cubic relationship allows us to observe a phase of accelerated increase in HGS during childhood and adolescence, until reaching a plateau around 30 years of age in both sexes, and consequently, a decrease in HGS from 40 years of age onwards, being more accelerated in men than in women. Furthermore, the proposed percentiles can serve as a guide for assessing and monitoring upper extremity muscle strength levels, as well as for surveillance, and in the planning of intervention programs at all stages of life.

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 human participants were reviewed and approved by the UA 238-2014. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

CU-A, FA-V, LC, and RV collected the data. MC-B, RG-C, MA, and ER participated on the conception and design of the study. MC-B, RG-C, JM, JS, and CT analyzed the data. All authors participated in the interpretation of the results, drafted and revised the manuscript, and approved the final revision of the manuscript.

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.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Bimali I, Opsana R, Jeebika S. Normative reference values on handgrip strength among healthy adults of Dhulikhel, Nepal: a cross-sectional study. *J Family Med Primary Care.* (2020) 9:310–4. doi: 10.4103/jfmpc.jfmpc_785_19

2. Carson RG. Get a grip: individual variations in grip strength are a marker of brain health. *Neurobiol Aging.* (2018) 71:189–222. doi: 10.1016/j.neurobiolaging.2018.07.023

3. Lu ZL, Wang TR, Qiao YQ, Zheng Q, Sun Y, Lu JT, et al. Handgrip strength index predicts nutritional status as a complement to body mass index in Crohn's disease. *J Crohns Colitis.* (2016) 10:1395–400. doi: 10.1093/ecco-jcc/jjw121

4. Cooper R, Kuh D, Cooper C, Gale CR, Lawlor DA, Matthews F, et al. Objective measures of physical capability and subsequent health: a systematic review. *Age Ageing.* (2011) 40:14–23. doi: 10.1093/ageing/afq117

5. Leong DP, Teo KK, Rangarajan S, Lopez-Jaramillo P, Avezum A, Orlandini A, et al. Prospective urban rural epidemiology (PURE) study investigators. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet.* (2015) 386:266–73. doi: 10.1016/S0140-6736(14)62000-6

6. Martin-Ruiz C, Von Zglinicki T. Biomarkers of healthy ageing: expectations and validation. *Proc Nutr Soc.* (2014) 73:422–9. doi: 10.1017/S0029665114000147

7. Steiber N. Strong or weak handgrip? NORMATIVE reference values for the german population across the life course stratified by sex, age, and body height. *PLoS ONE.* (2016) 11:e0163917. doi: 10.1371/journal.pone.0163917

8. Beaudart C, Rolland Y, Cruz-Jentoft A, Bauer JM, Sieber C, et al. (2019). Assessment of muscle function and physical performance in daily clinical practice. *Calcif Tissue Int.* (2019) 105, 1–14. doi: 10.1007/s00223-019-00545-w

9. Hoffmann MD, Colley RC, Doyon CY, Wong SL, Tomkinson GR, Lang JJ, et al. Normative-referenced percentile values for physical fitness among Canadians. *Health Rep.* (2019) 30:14–22. doi: 10.25318/82-003-x201901000002-eng

10. Dodds RM, Syddall HE, Cooper R, Benzeval M, Deary IJ, Dennison EM, et al. Grip strength across the life course: normative data from twelve British studies. *PLoS ONE.* (2014) 9:e113637. doi: 10.1371/journal.pone.0113637

11. Wong SL. Grip strength reference values for Canadians aged 6 to 79: Canadian health measures survey, 2007 to 2013. *Health Rep19.* (2016) 3–10.

12. Perna FM, Coa K, Troiano RP, Lawman HG, Wang CY, Li Y, et al. Muscular grip strength estimates of the u.s. population from the national health and nutrition examination survey 2011-2012. *J Strength Cond Res.* (2016) 30:867–74. doi: 10.1519/JSC.0000000000001104

13. Bohannon RW, Wang YC, Yen SC, Grogan KA. Handgrip strength: a comparison of values obtained from the NHANES and NIH toolbox studies. *Am J Occup Ther.* (2019) 73:7302205080p1–9. doi: 10.5014/ajot.2019.029538

14. Centers for Disease Control and Prevention. *National Health and Nutrition Examination Survey (NHANES): Muscle Strength Procedures Manual.* Atlanta. (2011). Available online at: https://wwwn.cdc.gov/nchs/data/nhanes/2011-2012/manuals/Muscle_Strength_Proc_Manual.pdf (accessed September 20, 2022).

15. Ramírez-Vélez R, Rincón-Pabón D, Correa-Bautista JE, García-Hermoso A, Izquierdo M. Handgrip strength: Normative reference values in males and females aged 6-64 Years old in a Colombian population. *Clin Nutr ESPEN.* (2021) 44:379–86. doi: 10.1016/j.clnesp.2021.05.009

16. Leong DP, Teo KK, Rangarajan S, Kutty VR, Lanas F, Hui C. Reference ranges of handgrip strength from 125, 462. healthy adults in 21 countries: a prospective urban rural epidemiologic (PURE) study. *J Cachexia Sarcopenia Muscle.* (2016) 7:535–46. doi: 10.1002/jcsm.12112

17. Angst F, Drerup S, Werle S, Herren DB, Simmen BR, Goldhahn J, et al. Prediction of grip and key pinch strength in 978 healthy subjects. *BMC Musculoskeletal Disorder.* (2010) 11:94. doi: 10.1186/1471-2474-11-94

18. Qiu Z, Wang W, Tan Y, He M, Wang L, Li Y, et al. Associations of grip strength with retinal and choroidal thickness in patients with type 2 diabetes mellitus without retinopathy: a cross-sectional study. *BMJ Open.* (2020) 19:10.e036782. doi: 10.1136/bmjopen-2020-036782

19. Cossio-Bolaños M, Vidal-Espinoza R, Fuentes-Lopez J, Castelli Correia de Campos LF, Andruske CL, Urra-Albornoz C, et al. Reference values for bone density and bone mineral content from 5 to 80 years old in a province of Chile. *PeerJ.* (2022) 23:e13092. doi: 10.7717/peerj.13092

20. United Nations Development Programme (UNDP). *Human Development Report 2019. Beyond Income, Beyond Averages, Beyond Today: Inequalities In Human Development in the 21st Century.* UNDP (2019). Available online at: http://hdr.undp.org/sites/default/files/hdr2019.pdf (accessed August 20, 2022).

21. Ministerio de DESARROLLO SOCIAL CHILE. *Ministerio de DESARROLLO SOCIAL CHILE (MDS) and Informe de Desarrollo Social.* (2018). Available online at: http://www.desarrollosocialyfamilia.gob.cl/storage/docs/Informe_de_Desarrollo_Social_2018.pdf (accessed December 18, 2020).

22. Ross WD, Marfell-Jones MJ. Kinanthropometry. In: MacDougall JD, Wenger HA, Geeny HJ, editor. *Physiological Testing of Elite Athlete, Vol 223* (London: Human Kinetics), p. 308–14 (1991).

23. Oh S, Ahn J, Nam KU, Paeng JY, Hong J. Frankfort horizontal plane is an appropriate three-dimensinal reference in the evaluation of clinical and skeletal cant. *J Korean Assoc Oral Maxillo Surg.* (2013) 39:71–6. doi: 10.5125/jkaoms.2013.39.2.71

24. Richards LG, Olson B, Palmiter-Thomas P. How forearm position affects grip strength. *Am J Occup Ther.* (1996) 50:133–8. doi: 10.5014/ajot.50.2.133

25. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ.* (2000) 320:1240–3. doi: 10.1136/bmj.320.7244.1240

26. Pan H, Cole TJ. LMS Chartmaker. (2006). Available online at: http://www.healthforallchildren.co.uk (accessed March 28, 2015).

27. Hwang J, Lee J, Lee KS. A deep learning-based method for grip strength prediction: comparison of multilayer perceptron and polynomial regression approaches. *PLoS ONE.* (2021) 16:e0246870. doi: 10.1371/journal.pone.0246870

28. Alcazar J, Aagaard P, Haddock B, Kamper RS, Hansen SK, Prescott E, et al. Assessment of functional sit-to-stand muscle power: cross-sectional trajectories across the lifespan. *Exp Gerontol.* (2021) 152:111448. doi: 10.1016/j.exger.2021.111448

29. Nahhas RW, Choh AC, Lee M, Cameron Chumlea M, Duren DL, Siervogel RM, et al. Bayesian longitudinal plateau model of adult grip strength. *Am J Hum Biol.* (2010) 22:648–56. doi: 10.1002/ajhb.21057

30. Metter EJ, Conwit R, Tobin J, Fozard JL. Age-associated loss of power and strength in the upper extremities in women and men. *J Gerontol A Biol Sci Med Sci.* (1997) 52:B267–76. doi: 10.1093/gerona/52A.5.B267

31. Sartorio A, Lafortuna CL, Pogliaghi S, Trecate L. The impact of gender, body dimension and body composition on hand-grip strength in healthy children. *J Endocrinol Invest.* (2002) 25:431–5. doi: 10.1007/BF03344033

32. Visnapuu M, Jurimae T. Handgrip Strength and Hand Dimensions in Young Handball and Basketball Players. *J Strength Condition Res.* (2007) 21:923–9. doi: 10.1519/00124278-200708000-00045

33. Chandrasekaran B, Ghosh A, Prasad C, Krishnan K. Age and anthropometric traits predict handgrip strength in healthy normals. *J Hand Microsurg.* (2010) 2:58–61. doi: 10.1007/s12593-010-0015-6

34. Amaral CA, Amaral T, Monteiro G, Vasconcellos M, Portela MC. Hand grip strength: reference values for adults and elderly people of Rio Branco, Acre, Brazil. *PLoS ONE.* (2019) 14:e0211452. doi: 10.1371/journal.pone.0211452

35. Hoare DG, Warr CR. Talent identification and women's soccer: an Australian experience. *J Sports Sci.* (2000) 18:751–8. doi: 10.1080/02640410050120122

36. Spruit MA, Sillen MJ, Groenen MT, Wouters, EF, Franssen FM. New normative values for handgrip strength: Results from the UK Biobank. *J Am Med Dir Assoc.* (2013) 14:775.e5–11. doi: 10.1016/j.jamda.2013.06.013

37. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the european working group on sarcopenia in older people. *Age Ageing.* (2010) 39:412–23. doi: 10.1093/ageing/afq034

38. Ortega FB, Silventoinen K, Tynelius P, Rasmussen F. Muscular strength in male adolescents and premature death: cohort study of one million participants. *BMJ.* (2012) 20:345. doi: 10.1136/bmj.e7279

39. Henriksson H, Henriksson P, Tynelius P, Ortega FB. Muscular weakness in adolescence is associated with disability 30 years later: a population-based cohort study of 1, 2 million men. *Br J Sports Med.* (2019) 53:1221–30. doi: 10.1136/bjsports-2017-098723

40. Ong HL, Abdin E, Chua BY, Zhang Y, Seow E, Vaingankar JA, et al. Hand-grip strength among older adults in Singapore: a comparison with international norms and associative factors. *BMC Geriatr.* (2017) 17:176. doi: 10.1186/s12877-017-0565-6

41. World Health Organization. *International Classification of Functioning, Disability and Health (ICF).* Geneva: World Health Organization (2001).

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 28 February 2023
DOI 10.3389/fpubh.2023.1087248

OPEN ACCESS

EDITED BY
Marco Carlos Uchida,
State University of Campinas, Brazil

REVIEWED BY
Rossana Gomez-Campos,
Catholic University of the Maule, Chile
Shirko Ahmadi,
Montreal University, Canada
David Hollar,
Mercer University School of Medicine,
United States

*CORRESPONDENCE
Qi Guo
✉ guoqijp@gmail.com

†These authors have contributed equally to this work and share first authorship

SPECIALTY SECTION
This article was submitted to Aging and Public Health, a section of the journal Frontiers in Public Health

RECEIVED 02 November 2022
ACCEPTED 09 February 2023
PUBLISHED 28 February 2023

CITATION
Chen X, Han P, Zhang K, Liang Z, Yu C, Lu N, Shen Z, Chang F, Fang X and Guo Q (2023) Physical performance and muscle strength rather than muscle mass are predictor of all-cause mortality in hemodialysis patients. *Front. Public Health* 11:1087248. doi: 10.3389/fpubh.2023.1087248

Physical performance and muscle strength rather than muscle mass are predictor of all-cause mortality in hemodialysis patients

Xiaoyu Chen[1†], Peipei Han[1†], Kun Zhang[2†], Zhenwen Liang[1], Chen Yu[2], Ningtao Lu[1], Zhouyue Shen[1], Fengyan Chang[1], Xin Fang[1] and Qi Guo[1,3*]

[1]Department of Rehabilitation Medicine, Shanghai University of Medicine and Health Sciences Affiliated Zhoupu Hospital, Shanghai, China, [2]Department of Nephrology, Tongji Hospital, School of Medicine, Tongji University, Shanghai, China, [3]Department of Rehabilitation Medicine, School of Health, Fujian Medical University, Fuzhou, China

Objectives: Patients undergoing maintenance hemodialysis usually suffer a high burden of poor functional status. The aim of this study was to investigate the association between muscle mass, muscle strength as well as physical performance with all-cause mortality in hemodialysis patients.

Methods: 923 hemodialysis patients (565 men, mean aged 61.3 ± 12.7 years) were included from eight facilities in Tianjin and Shanghai of China from 2019 to 2021. Muscle mass was evaluated by skeletal muscle index (SMI) and muscle strength was assessed by handgrip strength. Different measures of physical performance were measured *via* gait speed, Timed Up and Go Test (TUGT) and short physical performance battery (SPPB). Cox proportional hazards regression models were used to determine the adjusted hazard ratios (HRs) of mortality with 95% confidence intervals (95% CIs) for baseline muscle mass, muscle strength and different measures of physical performance. Additionally, the area under the Receiver Operating Characteristic (ROC) curves were constructed to determine which index is a better predictor of mortality.

Results: During a median follow-up of 14 (12–17 months), 79 (8.6%) patients died. Using the Cox regression analysis, we founded that muscle strength and physical performance rather than muscle mass were significantly negatively associated with mortality. The C-index for different measures of physical performance in predicting mortality were 0.709 for SPPB, 0.7 for TUGT and 0.678 for gait speed, respectively. The C-index for muscle strength was 0.635, and the ability of prediction was significantly lower than the physical performance.

Conclusions: Physical performance seems to a better indicator of mortality than muscle mass and strength in hemodialysis patients. Simple measures of physical performance may be appropriately used as a screening tool targeting high-risk hemodialysis patients for the prevention of mortality.

KEYWORDS

hemodialysis, muscle mass, muscle strength, physical performance, all-cause mortality

Introduction

The prevalence of patients with end-stage renal disease (ESRD) is increasing rapidly, which has been a major public health problem in most countries (1, 2). Despite considerable improvement in dialysis modalities and patient care, hemodialysis patients still have an exceedingly higher mortality rate compared to the general population (3). The potential contributors to the poor survival status might be older age, comorbidities, malnutrition, underdialysis and decreased physical function (4, 5). It is reported that poor functional status is strongly related to advanced risks of adverse events in hemodialysis patients (6–8). Therefore, there is growing interest in finding effective and practical tests that can be used as screening tools to identify early populations that may benefit from targeted interventions.

Sarcopenia is a clinical disorder defined as loss of skeletal muscle mass and low muscle strength and/or physical performance (9). It's worth noting that muscle strength is not entirely dependent on muscle mass, and two elements may disassociate. With increasing age, muscle strength decreases at a rate greater than the rate of loss of muscle mass, even when muscle mass is maintained or increased (10, 11). As a result, there is a great interest in correctly distinguishing between the loss of muscle mass with muscle strength. Indeed, this is particularly important because treatments to maintain or increase muscle mass or muscle strength are not necessarily the same (12). Skeletal muscle plays a key role in metabolic function, facilitating glucose uptake and storage, and is related to physical performance. Recent studies suggest that muscle strength and physical performance were associated with mortality in hemodialysis patients (13–15).

However, they did not comprehensively take into account the various domains of physical performance indicators but only focused on one or two domains of physical performance, such as gait speed. Thus, it remains unclear whether or to what extent physical performance indicators are more independently associated to mortality in hemodialysis patients. In addition, several studies showed that higher muscle mass was independently associated with reduced risks of all-cause mortality in hemodialysis patients (16, 17), but previous findings regarding the relationship between the muscle mass and mortality have been discrepant (8, 18). Thus, more evidence is required to explore the associations between muscle mass, muscle strength and physical performance with mortality.

The purpose of this study was to identify the relationships between muscle mass, muscle strength and physical performance with mortality in patients on hemodialysis. Additionally, we aimed to examine which measure(s) was/were the most prominent in this relationship and could, accordingly, be relevant to be used in the clinical screening of hemodialysis patients. A broad understanding and addressing this are important for health care providers and policy makers in response to huge health care challenges.

Methods

Participants and study design

This is a multicenter study including hemodialysis patients from eight hemodialysis centers in Tianjin and Shanghai between December 2019 and April 2021 at baseline. Patients were eligible to participate if they were over 18 years of age, had received maintenance hemodialysis for at least 3 months and were able to provide informed consent. Exclusion criteria was described as follows: (1) unable to measure the body composition; (2) inability to perform the handgrip strength test or the physical performance test; (3) patients with visual impairment or hearing impairment difficulties; (4) unable to communicate with researchers or provide informed consent. The final study sample comprised 923 subjects (Figure 1). All patients provided informed consent prior to enrollment in the study. This study was approved by the Ethics Committee of Shanghai University of Medicine and Health Sciences.

Baseline variable

All patients were invited to a face-to-face interview to answer a standardized questionnaire. Socio-demographic characteristics (including age, gender, post-dialysis weight, dialysis vintage and education level), health behaviors (including smoking and drinking) and condition of chronic diseases were considered as covariates. The short form of the International Physical Activity Questionnaire (IPAQ) was used to assess the physical activity (19). Comorbidity was evaluated by the Charlson comorbidity index (20). All blood samples were drawn pre-dialysis. Details of measurement methods have been described in our recent study (21, 22).

Assessment of muscle mass

Bioelectrical impedance analysis (BIA) (InBody S10; Biospace, Seoul, Korea) was used to measure muscle mass in the pre-dialysis period (23). Patients were placed in a supine position at least 10 min before assessment. Muscle mass was evaluated as the skeletal muscle index (SMI), calculated as the relative skeletal muscle mass index divided by the square of height (9).

Assessment of muscle strength

A dynamometer was used to assess the muscle strength on the non-fistula prior to a dialysis session (GRIP-D; Takei Ltd, Niigata, Japan). Patients were asked to make maximum effort twice, and the result of the strongest handgrip strength was used in the analysis. For patients with indwelling dialysis catheters, we tested handgrip strength with the dominant hand.

Evaluation of physical performance

Physical performance was measured *via* gait speed, Timed Up and Go Test (TUGT) and short physical performance battery (SPPB). We used the four-meter walking test to assess the gait

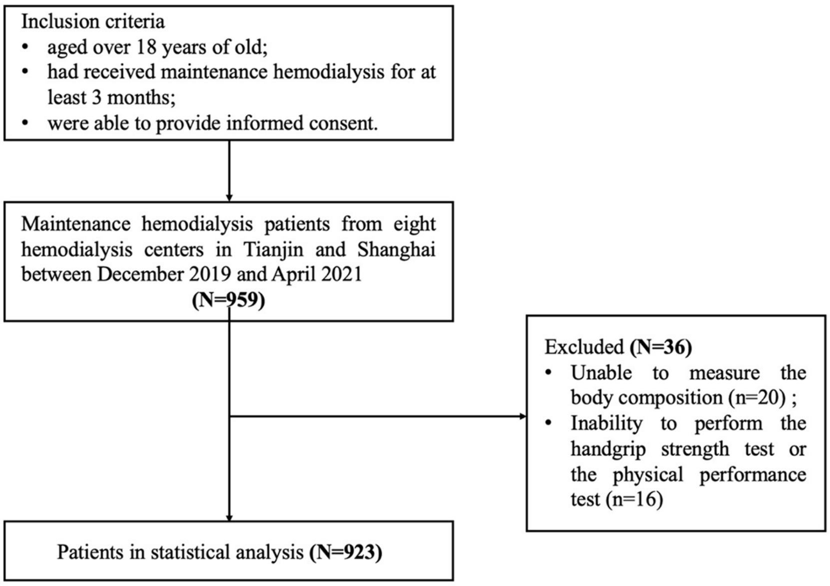

FIGURE 1
Flowchart of study participants.

speed. Patients were asked to stand and walk a distance of eight meters at a normal gait speed, and the time taken for the middle four meters was recorded. The patient was allowed to use a walking aid device (24). TUGT required a person to stand up from a chair, then walk 3 m, turn around, walk back and sit down again (25). The SPPB consists of three sequential tests that assess semi-tandem and tandem balance test, gait speed, and 5-sit-to-stand test. The total score ranges from 0 to 12 points, and 12 showing the best physical function performance to 0 showing inability to do the tests (26). All these physical performance tests were performed before a dialysis session.

Statistical analyses

Baseline characteristics and clinical parameters are expressed as the means ± standard deviations (SDs) or as the numbers of patients and percentages. Analysis of independent t-test and chi-square test were used to compare variables between patients alive and deceased. Cox regression analyses are used to explore the association between muscle mass, muscle strength and physical performance with mortality, presented as hazard ratios with 95% confidence intervals. Kaplan-Meier curves were generated to assess the probabilities of the patient outcomes according to categorical of SPPB, and the Cox proportional hazards model was used for further multivariate adjustments with possible confounders including age, sex, BMI, IPAQ, Kt/v, albumin, hemoglobin, smoking, fall history, depression, malnutrition, and Charlson comorbidity index. The C -index was defined as the area under the ROC curves between individual measurement predictive probabilities for mortality. We further used C-index to identify the physical performance best correlated with all-cause mortality. Statistical analyses were performed using IBM SPSS Statistics v26.0 (SPSS Inc., Chicago, Illinois, United States). $P < 0.05$ was considered to indicate statistical significance.

Results

Baseline characteristics

The baseline characteristics of the study patients were presented in Table 1. Among the 923 patients (565 men), the mean age was 61.3 ±12.7 years. The median dialysis vintage was 45.12 months (range 22.19–92.80 months), and the mean BMI was 23.34 ± 3.82 kg/m^2. Deceased patients were significantly older, and they tend to fall, depressed, malnourished and smoke ($P < 0.05$). Furthermore, BMI, IPAQ, handgrip strength, gait speed, TUGT, SPPB, hemoglobin levels, albumin levels and Kt/v were significantly lower in deceased patients than in patients alive ($P < 0.05$).

Physical performance is associated with poor survival

During a median follow-up of 14 months (10th percentile-90th percentile, 12–17 months), 79 patients (8.6%) died. The associations between muscle strength and different measurements of physical performance and mortality are presented in Table 2. After adjustments for potential confounders (age, sex, BMI, IPAQ, Kt/v, albumin, hemoglobin, smoking, fall history, depression, malnutrition, and Charlson comorbidity index), handgrip strength (HR = 0.96, 95% CI 0.92–0.99), gait speed (HR = 0.40, 0.18–0.92), TUGT (HR = 1.03, 1.01–1.04) were significantly associated with

TABLE 1 Baseline characteristics of study participants according to the presence of mortality.

Characteristics	Total ($n = 923$)	Alive ($n = 844$)	Deceased ($n = 79$)	*P* value
Age (y)	61.3 ± 12.7	60.8 ± 12.7	67.0 ± 11.3	<0.001
Male (%)	565 (61.2)	512 (60.7)	53 (67.1)	0.262
Dry weight (kg)	62.95 ± 12.88	63.18 ± 12.70	60.46 ± 14.48	0.072
BMI (kg/m^2)	23.34 ± 3.82	23.44 ± 3.78	22.25 ± 4.10	0.008
Vintage (months)	45.12 (22.19, 92.80)	45.83 (23.13, 94.80)	39.2 (17.37, 70.13)	0.087
IPAQ (Met-min/wk)	1,386 (594, 3,066)	1,386 (693, 3,273)	660 (0, 1,533)	<0.001
Education (%)				0.062
Less than high school	214 (23.2)	189 (22.4)	25 (31.6)	
High school or higher education	709 (76.8)	655 (77.6)	54 (68.4)	
Drinking (%)	11 (1.2)	11 (1.3)	0 (0.0)	0.421
Smoking (%)	200 (21.7)	180 (21.3)	20 (25.3)	<0.001
SMI (kg/m^2)	7.00 ± 1.21	7.02 ± 1.20	6.77 ± 1.35	0.077
Handgrip strength (kg)	24.81 ± 8.80	25.17 ± 8.74	20.93 ± 8.53	<0.001
Gait speed (m/s)	0.97 ± 0.31	0.99 ± 0.29	0.79 ± 0.36	<0.001
TUGT(s)	10.26 ± 7.90	9.76 ± 6.51	15.56 ± 15.77	<0.001
SPPB	9.57 ± 2.96	9.80 ± 2.73	7.05 ± 4.04	<0.001
Fall history (%)	329 (35.6)	288 (34.1)	41 (51.9)	0.002
Depression (%)	388 (42.0)	340 (40.3)	48 (60.8)	<0.001
Malnutrition (%)	252 (27.3)	214 (25.4)	38 (48.1)	<0.001
Number of medications (*n*)	4.49 ± 2.45	4.46 ± 2.44	4.72 ± 2.55	0.371
Charlson comorbidity index	3.87 ± 1.72	3.80 ± 1.71	4.58 ± 1.66	<0.001
Laboratory parameters				
Hemoglobin (g/dL)	110.78 ± 16.29	111.25 ± 15.96	105.79 ± 18.92	0.004
Albumin (g/L)	39.41 ± 3.61	39.59 ± 3.44	37.47 ± 4.66	<0.001
PTH (pg/dL)	356.86 ± 329.28	361.83 ± 330.38	300.76 ± 313.36	0.129
Calcium (mg/dL)	2.28 ± 0.26	2.27 ± 0.26	2.31 ± 0.31	0.270
Phosphorus (mg/dL)	1.93 ± 0.65	1.94 ± 0.64	1.88 ± 0.81	0.449
Kt/v	1.36 ± 0.33	1.37 ± 0.33	1.27 ± 0.29	0.013

BMI, body mass index; Kt/v, fractional clearance index for urea; SMI, skeletal muscle index; TUGT, timed up and go test; SPPB, Short physical performance battery; MIS, Mini Nutritional Assessment-Short Form; IPAQ, international physical activity questionnaire; Met-min/wk, metabolic equivalent task minutes per week; PTH, parathyroid hormone.

depressive symptoms. In the adjusted Cox regression model by SPPB categories, patients with very low (score 0–3) had significantly higher risks of death (HR = 3.98, 1.99–7.95). Survival curves of patients by SPPB categories are shown in Figure 2. Survival curves differed significantly at the log-rank test ($P < 0.001$).

Predictive values of physical performance measurements for mortality

With regard to model discrimination, the C-index of the physical performance (C-index for TUGT: 0.678; SPPB: 0.709) were significantly higher than the muscle strength (C-index for handgrip strength: 0.635) (TUGT vs. handgrip strength: $P = 0.046$; SPPB vs. handgrip strength: $P = 0.020$), and there was no significant between the handgrip strength and gait speed (C-index for handgrip strength: 0.635; gait speed: 0.678; $P = 0.195$, Table 3). However, there was no significant difference among the different measurements of physical performance in the values of C-index for mortality.

Discussion

This prospective cohort study demonstrated the influence of muscle strength and physical performance on the mortality

TABLE 2 Cox regression model for the physical performance indexes as a predictor for the risk of mortality.

Variables	Hazard ratio (95% CI)			
	Crude	*P*	Adjusted Model	*P*
SMI	0.83 (0.69, 1.01)	0.058	0.86 (0.66, 1.14)	0.297
Handgrip strength	0.94 (0.92, 0.97)	<0.001	0.96 (0.92, 0.99)	0.040
Gait speed	0.13 (0.07, 0.26)	<0.001	0.40 (0.18, 0.92)	0.031
TUGT	1.04 (1.03, 1.05)	<0.001	1.03 (1.01, 1.04)	0.001
SPPB				
Very low (0–3) ($n = 58$)	8.70 (4.93, 15.36)	<0.001	3.98 (1.99, 7.95)	<0.001
Low (4–6) ($n = 84$)	3.03 (1.55, 5.92)	0.001	1.61 (0.76, 3.41)	0.210
Moderate (7–9) ($n = 188$)	1.83 (1.01, 3.23)	0.046	1.32 (0.69, 2.51)	0.398
Good (10–12) ($n = 593$)	1		1	

Adjusted model: Adjusted for age, sex, BMI, IPAQ, smoking, falling history, depression, malnutrition, Charlson comorbidity index, hemoglobin, albumin and Kt/V. SMI, skeletal muscle index; TUGT, timed up and go test; SPPB, Short physical performance battery; BMI, body mass index; Kt/v, fractional clearance index for urea; IPAQ, international physical activity questionnaire.

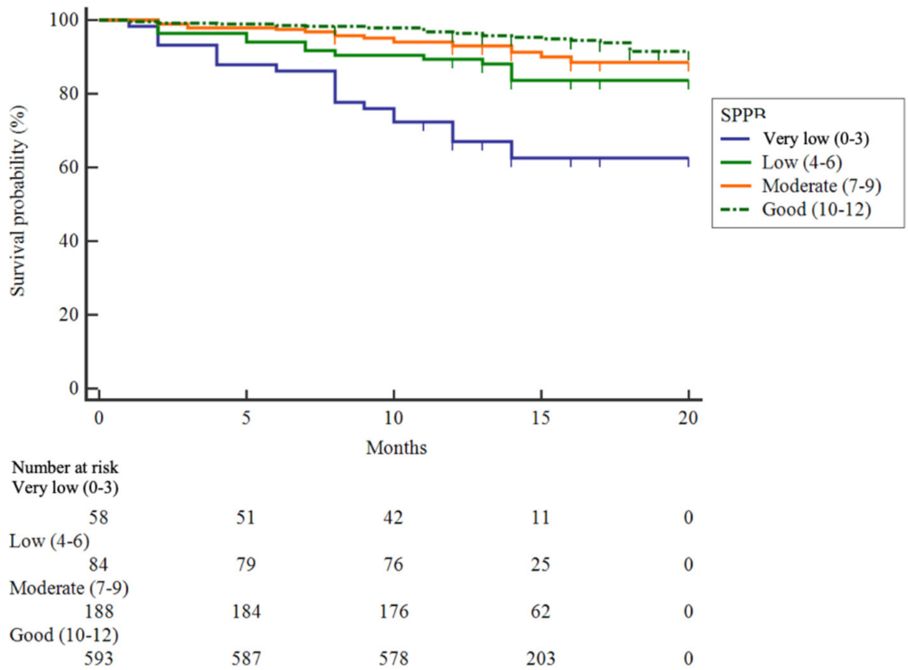

FIGURE 2
Kaplan Meier survival curves for all-cause mortality according to SPPB.

TABLE 3 Predictive values of muscle strength and physical performance measurements for mortality according to the C-index.

Variables	C-index	SE	*P*		
Handgrip strength	0.635 (0.603, 0.666)	0.0329	Ref		
Gait speed	0.678 (0.646, 0.708)	0.0332	0.195	Ref	
TUGT	0.700 (0.669, 0.729)	0.0314	0.046	0.293	Ref
SPPB	0.709 (0.679, 0.738)	0.0317	0.020	0.121	0.637

TUGT, timed up and go test; SPPB, Short physical performance battery.

risk in patients on maintenance hemodialysis, and supports the physical performance had superior prognostic discrimination for mortality, which deserved as an effective, costless and easily feasible screening strategy in this population. In contrast, no association was observed between muscle mass and mortality.

In line with our findings, recent studies suggest that muscle strength and physical performance were associated with mortality in hemodialysis patients (13, 14). These studies didn't comprehensively take into account the various domains of physical performance indicators but only focused on one or two domains of physical performance, such as gait speed. Our study also identified that very low physical performance in the SPPB, as well as gait speed and TUGT, were associated with lower survival and a higher risk of death. In addition, we observed that there was no association between muscle mass and mortality in our study, which was consistent with previous studies (8, 18). However, conflicting results have also been reported. Yajima et al. (16) and Fukasawa et al. (17) demonstrated that higher muscle mass was independently associated with reduced risks of all-cause mortality in hemodialysis patients. The main reasons for the differences are geographical differences and small population samples. In their study, the sample sizes were 162 and 81 respectively, which were significantly lower than the sample sizes of this study. Recent study has shown a strong association between sarcopenia and mortality in patients undergoing hemodialysis (27), so the association between muscle mass, one of the primary diagnostic factors for sarcopenia, and mortality needs to be further confirmed in the future.

Although the clinical relevance of muscle strength and physical performance as predictors of mortality in hemodialysis patients has been documented in previous studies, to date there have been no direct comparisons of the two tests. Interestingly, our results suggest that physical performance had superior prognostic discrimination for mortality than muscle strength. The possible reason may be that muscle function of lower extremities might be more important than that of the upper extremities regarding the patients' adverse outcomes. Previous research reported a discrepancy in upper and lower strength in a CKD cohort study (28), and other studies also revealed that muscle function in the lower extremities but not in the upper extremities was related to overall physical performance (29), suggesting the clinical importance of lower extremity performance. Furthermore, Johansen et al. found that physical performance such as gait speed declined frequently while handgrip strength didn't change over time among the hemodialysis patients (30). In that study, physical performance was the strongest predictor of mortality, which is similar to our results. Thus, we believe that monitor physical performance has the potential to be a valuable tool for continuous risk stratification of hemodialysis population.

Regarding the prognostic discrimination of different physical performance indicators for mortality, although SPPB showed the highest C index, it was not significantly different from gait speed and TUGT. The SPPB is an easy-to-apply instrument that includes balance, gait and lower strength, and has been used to evaluate the level of physical performance in different settings (31, 32). Our results show that patients with very low (score 0–3) by SPPB categories had significantly higher risks of death (HR = 3.98, 1.99–7.95). The cutoff points could help to identify hemodialysis with a higher risk of death at an early stage, given the easy applicability of the SPPB. Of note, SPPB includes three subtests, which would also take longer time to test than gait speed and TUGT. In the future, we need to consider whether isolated gait speed and TUGT would be useful to establish the predictive power for mortality, because there are advantages regarding time and costs to performing one test in an isolated manner compared to the entire SPPB.

Our study has several strengths. This is a multicenter study that comprehensively consider the association of muscle mass, muscle strength and various domains of physical performance indicators with mortality in hemodialysis population. In addition, most recognized confounders were taken into account into Cox regression models to analyze the independent association of physical performance and mortality in this study. Despite extensive efforts to curb study limitations, some limitations of this study should be considered. There is a concern about selection bias because patients who were incapable of performing the muscle strength and physical performance tests were excluded from our study. Second, our study was limited to Chinese patients on hemodialysis, thereby limiting the generalizability of our findings to the broader international hemodialysis population.

Conclusion

Our study suggest that muscle strength and physical performance rather than muscle mass were significantly associated with all-cause mortality in hemodialysis patients. Furthermore, physical performance had superior prognostic discrimination for mortality than muscle strength, which is effective, costless and easily feasible screening strategy for better patient assessment and individualized care.

Data availability statement

The datasets presented in this article are not readily available because our database is still expanding. All the multi-center hemodialysis centers have signed the data confidentiality agreement, so we are very sorry that we cannot upload it to the public database. But if you have any questions about the data, please write to us, and we will be happy to answer them for you. Requests to access the datasets should be directed to QG, guoqijp@gmail.com.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of Shanghai University of Medicine and Health Sciences. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the individual(s) and minor(s)' legal guardian/next of kin, for the publication of any potentially identifiable images or data included in this article.

Author contributions

Study concept and design: XC, PH, and KZ. Acquisition, analysis, and interpretation of data: NL, ZS, FC, and XF. Drafting of the work: XC and PH. Critical revision of the manuscript: ZL, CY, and QG. All authors contributed to the article and approved the submitted version.

Funding

This work was supported by the funding of Capacity Building project of Local Colleges of Shanghai Science and Technology Commission (23010502800), Shanghai Sailing Program (22YF1417900), and Clinical Trial Incubation Program from Tongji Hospital of Tongji University [ITJ (ZD) 1808].

Acknowledgments

We are grateful to all the medical staff at the multi-center dialysis for their generous technical assistance and guidance. We also thank all the study participants for their kind participation and cooperation.

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.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Saran R, Robinson B, Abbott KC, Agodoa LYC, Bragg-Gresham J, Balkrishnan R, et al. US renal data system 2018 annual data report: epidemiology of kidney disease in the United States. *Am J Kidney Dis.* (2019) 73:A7–8. doi: 10.1053/j.ajkd.2019.01.001

2. Jin DC, Yun SR, Lee SW, Han SW, Kim W, Park J, et al. Current characteristics of dialysis therapy in Korea: 2016 registry data focusing on diabetic patients. *Kidney Res Clin Pract.* (2018) 37:20–9. doi: 10.23876/j.krcp.2018.37.1.20

3. Choi H, Kim M, Kim H, Pyo Lee J, Lee J, Tak Park J, et al. Excess mortality among patients on dialysis: comparison with the general population in Korea. *Kidney Res Clin Pract.* (2014) 33:89–94. doi: 10.1016/j.krcp.2014.04.001

4. Kutner NG, Zhang R, Huang Y, Painter P. Gait speed and mortality, hospitalization, and functional status change among hemodialysis patients: a US renal data system special study. *Am J Kidney Dis.* (2015) 66:297–304. doi: 10.1053/j.ajkd.2015.01.024

5. Tong J, Liu M, Li H, Luo Z, Zhong X, Huang J, et al. Mortality and associated risk factors in dialysis patients with cardiovascular disease. *Kidney Blood Press Res.* (2016) 41:479–87. doi: 10.1159/000443449

6. Delgado C, Shieh S, Grimes B, Chertow GM, Dalrymple LS, Kaysen GA, et al. Association of self-reported frailty with falls and fractures among patients new to dialysis. *Am J Nephrol.* (2015) 42:134–40. doi: 10.1159/000439000

7. Shimoda T, Matsuzawa R, Yoneki K, Harada M, Watanabe T, Yoshida A, et al. Combined contribution of reduced functional mobility, muscle weakness, and low serum albumin in prediction of all-cause mortality in hemodialysis patients: a retrospective cohort study. *J Ren Nutr.* (2018) 28:302–8. doi: 10.1053/j.jrn.2017.12.012

8. Isoyama N, Qureshi AR, Avesani CM, Lindholm B, Barany P, Heimburger O, et al. Comparative associations of muscle mass and muscle strength with mortality in dialysis patients. *Clin J Am Soc Nephrol.* (2014) 9:1720–8. doi: 10.2215/CJN.10261013

9. Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K, et al. Asian working group for sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc.* (2020) 21:300–7. doi: 10.1016/j.jamda.2019.12.012

10. Goodpaster BH, Park SW, Harris TB, Kritchevsky SB, Nevitt M, Schwartz AV, et al. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. *J Gerontol A Biol Sci Med Sci.* (2006) 61:1059–64. doi: 10.1093/gerona/61.10.1059

11. Hughes VA, Frontera WR, Wood M, Evans WJ, Dallal GE, Roubenoff R, et al. Longitudinal muscle strength changes in older adults: influence of muscle mass, physical activity, and health. *J Gerontol A Biol Sci Med Sci.* (2001) 56:B209–217. doi: 10.1093/gerona/56.5.B209

12. Manini TM, Clark BC. Dynapenia and aging: an update. *J Gerontol A Biol Sci Med Sci.* (2012) 67:28–40. doi: 10.1093/gerona/glr010

13. Lee YH, Kim JS, Jung SW, Hwang HS, Moon JY, Jeong KH, et al. Gait speed and handgrip strength as predictors of all-cause mortality and cardiovascular events in hemodialysis patients. *BMC Nephrol.* (2020) 21:166. doi: 10.1186/s12882-020-01831-8

14. Valenzuela PL, Cobo F, Diez-Vega I, Sanchez-Hernandez R, Pedrero-Chamizo R, Verde-Rello Z, et al. Physical performance, plasma S-klotho, and all-cause mortality in elderly dialysis patients: a prospective cohort study. *Exp Gerontol.* (2019) 122:123–8. doi: 10.1016/j.exger.2019.05.003

15. Vanden Wyngaert K, Van Biesen W, Eloot S, Van Craenenbroeck AH, Calders P, Holvoet E. The importance of physical performance in the assessment of patients on haemodialysis: a survival analysis. *PLoS ONE.* (2022) 17:e0268115. doi: 10.1371/journal.pone.0268115

16. Yajima T, Arao M, Yajima K, Takahashi H, Yasuda K. The associations of fat tissue and muscle mass indices with all-cause mortality in patients undergoing hemodialysis. *PLoS ONE.* (2019) 14:e0211988. doi: 10.1371/journal.pone.0211988

17. Fukasawa H, Kaneko M, Niwa H, Matsuyama T, Yasuda H, Kumagai H, et al. Lower thigh muscle mass is associated with all-cause and cardiovascular mortality in elderly hemodialysis patients. *Eur J Clin Nutr.* (2017) 71:64–9. doi: 10.1038/ejcn.2016.186

18. Kittiskulnam P, Chertow GM, Carrero JJ, Delgado C, Kaysen GA, Johansen KL. Sarcopenia and its individual criteria are associated, in part, with mortality among patients on hemodialysis. *Kidney Int.* (2017) 92:238–47. doi: 10.1016/j.kint.2017.01.024

19. Bassett DR. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc.* (2003) 35:1396. doi: 10.1249/01.MSS.0000078923.96621.1D

20. Liu H, Song B, Jin J, Liu Y, Wen X, Cheng S, et al. Length of Stay, Hospital costs and mortality associated with comorbidity according to the charlson comorbidity index in immobile patients after ischemic stroke in China: a national study. *Int J Health Policy Manag.* (2021) 11:1780–7. doi: 10.34172/ijhpm.2021.79

21. Chen X, Han P, Song P, Zhao Y, Zhang H, Niu J, et al. Mediating effects of malnutrition on the relationship between depressive symptoms clusters and muscle function rather than muscle mass in older hemodialysis patients. *J Nutr Health Aging.* (2022) 26:461–8. doi: 10.1007/s12603-022-1778-8

22. Zhao Y, Song P, Zhang H, Chen X, Han P, Xie D, et al. Mediating effect of gait speed on the relationship between ankle-brachial index and mild cognitive impairment in hemodialysis patients. *Semin Dial.* (2022) 2022:1–8. doi: 10.1111/sdi.13089

23. Marcelli D, Usvyat LA, Kotanko P, Bayh I, Canaud B, Etter M, et al. Body composition and survival in dialysis patients: results from an international cohort study. *Clin J Am Soc Nephrol.* (2015) 10:1192–200. doi: 10.2215/CJN.08550814

24. Wang X, Ma Y, Wang J, Han P, Dong R, Kang L, et al. Mobility and muscle strength together are more strongly correlated with falls in suburb-dwelling older chinese. *Sci Rep.* (2016) 6:25420. doi: 10.1038/srep25420

25. Shimada H, Suzuki T, Suzukawa M, Makizako H, Doi T, Yoshida D, et al. Performance-based assessments and demand for personal care in older Japanese people: a cross-sectional study. *BMJ Open.* (2013) 3:424. doi: 10.1136/bmjopen-2012-002424

26. Silva CFR, Goncalves Ohara D, Pena Matos A, Nunes Pinto ACP, Sousa Pegorari M. Short physical performance battery as a predictor of mortality in community-dwelling older adults: a longitudinal study in the Brazilian Amazon region. *PeerJ.* (2022) 10:e13630. doi: 10.7717/peerj.13630

27. Kitamura A, Seino S, Abe T, Nofuji Y, Yokoyama Y, Amano H, et al. Sarcopenia: prevalence, associated factors, and the risk of mortality and disability in Japanese older adults. *J Cachexia Sarcopenia Muscle.* (2021) 12:30–8. doi: 10.1002/jcsm.12651

28. Roshanravan B, Robinson-Cohen C, Patel KV, Ayers E, Littman AJ, de Boer IH, et al. Association between physical performance and all-cause mortality in CKD. *J Am Soc Nephrol.* (2013) 24:822–30. doi: 10.1681/ASN.2012070702

29. Harris-Love MO, Benson K, Leasure E, Adams B, McIntosh V. The influence of upper and lower extremity strength on performance-based sarcopenia assessment tests. *J Funct Morphol Kinesiol.* (2018) 3:4. doi: 10.3390/jfmk3040053

30. Johansen KL, Delgado C, Kaysen GA, Chertow GM, Chiang J, Dalrymple LS, et al. Frailty among patients receiving hemodialysis: evolution of components and associations with mortality. *J Gerontol A Biol Sci Med Sci.* (2019) 74:380–6. doi: 10.1093/gerona/gly206

31. Treacy D, Hassett L. The short physical performance battery. *J Physiother.* (2018) 64:61. doi: 10.1016/j.jphys.2017.04.002

32. de Fatima Ribeiro Silva C, Ohara DG, Matos AP, Pinto A, Pegorari MS. Short physical performance battery as a measure of physical performance and mortality predictor in older adults: a comprehensive literature review. *Int J Environ Res Public Health.* (2021) 18:612. doi: 10.3390/ijerph182010612

frontiers | Frontiers in Public Health

TYPE Review
PUBLISHED 08 March 2023
DOI 10.3389/fpubh.2023.1106458

Check for updates

OPEN ACCESS

EDITED BY
Ricardo Aurélio Carvalho Sampaio,
Federal University of Sergipe, Brazil

REVIEWED BY
Ricardo Macedo,
Federal University of Alagoas, Brazil
Shirin Djalalinia,
Ministry of Health and Medical Education, Iran

*CORRESPONDENCE
Jing Tao
✉ taojing01@fjtcm.edu.cn

SPECIALTY SECTION
This article was submitted to Aging and Public Health, a section of the journal Frontiers in Public Health

RECEIVED 23 November 2022
ACCEPTED 17 February 2023
PUBLISHED 08 March 2023

CITATION
Xiang Q, Hu Y, Zheng J, Liu W and Tao J (2023) Research hotspots and trends of exercise for sarcopenia: A bibliometric analysis. *Front. Public Health* 11:1106458. doi: 10.3389/fpubh.2023.1106458

Research hotspots and trends of exercise for sarcopenia: A bibliometric analysis

Qing Xiang[1], Yue Hu[2], Jiaqi Zheng[2], Weilin Liu[1] and Jing Tao[1]*

[1]Rehabilitation Technology Innovation Center by Joint Collaboration of Ministry of Education and Fujian Province, Fujian University of Traditional Chinese Medicine, Fuzhou, China, [2]College of Rehabilitation Medicine, Fujian University of Traditional Chinese Medicine, Fuzhou, China

Exercise is an effective method for the prevention and treatment of sarcopenia, which can improve skeletal muscle mass, strength and physical function in individuals with sarcopenia to varying degrees. Moreover, exercise has an important role in improving ability to perform daily activities and quality of life on sarcopenia. In this study, articles and review articles on exercise interventions for sarcopenia from January 2003 to July 2022 were retrieved from the Web of Science core collection. Then, the number of annual publications, journal/cited journal, country, institution, author/cited author, references and keywords were analyzed using CiteSpace 6.1.R2. A total of 5,507 publications were collected and the number of publications increasing each year. Experimental Gerontology was the most productive journal and the most cited journal was J GERONTOL A-BIOL. The United States of America was the most influential country with the largest number of publications and centrality. Maastricht University in the Netherlands is the most productive institution. The author VAN LOON LJC has the highest ranking in terms of publications and CRUZ-JENTOFT A is ranked first in terms of cited authors. The most frequently occurring keywords in the field of exercise interventions for sarcopenia are "skeletal muscle," "exercise," "body composition," "strength," and "older adult"; the keyword "elderly men" showed the strongest explosive intensity. The keywords formed 6 clusters, namely "skeletal muscle," "muscle strength," "heart failure," "muscle protein synthesis," "insulin resistance" and "high-intensity interval training." In conclusion, this study demonstrates a new perspective on the current state of research and trends in exercise interventions for sarcopenia over the past 20 years *via* the visualization software CiteSpace. It may help researchers to identify potential collaborators and partner institutions, hotspots and research frontiers in the field of exercise interventions for sarcopenia.

KEYWORDS

sarcopenia, exercise, skeletal muscle, bibliometric analysis, CiteSpace

1. Introduction

Sarcopenia is defined as age-related loss of muscle mass, plus low muscle strength, and/or low physical performance by the Asian Working Group for Sarcopenia (AWGS) (1). With the increasing aging of the global population, sarcopenia has become a common disease in the elderly, which not only increases the risk of falls, disability and death (2), but is also associated with a significantly higher risk of cardiovascular disease (3, 4). Sarcopenia seriously impair the physical health and quality of life of the elderly. Therefore, it is necessary to find and develop low-cost, easily accessible rehabilitation methods for sarcopenia. However, there are no effective therapeutic drugs for sarcopenia (5) and exercise plays an important role in its prevention and treatment. Physical activity is one of the recommendations for the management of sarcopenia, which was given by the International clinical Practice Guidelines for Sarcopenia in 2018 (6). The commonly used exercise methods include resistance exercise, aerobic exercise, combination of resistance and aerobic exercise, balance training, flexibility training and other auxiliary exercise methods. These exercises have a positive effect on increasing muscle mass and strength in patients with sarcopenia. These exercises have a positive effect on increasing muscle mass and strength in people with sarcopenia.

Therefore, it is necessary to conduct a comprehensive summary of the research about exercise interventions for sarcopenia. This study used the visualization software CiteSpace to analyze 5,507 retrieved records from January 2003 to July 2022 related to exercise interventions for sarcopenia. Based on a visual bibliometric analysis of the literature from the perspectives of the number of annual publications, countries, institutions, authors, keywords and citations, show the current status and development trend of exercise interventions for sarcopenia. The purpose of this study is to provide a reference for future research about exercise interventions for sarcopenia.

2. Materials and methods

2.1. Database selection

In this study, the Web of Science (WOS) core collection was selected as the data source. Web of Science, as a high-quality digital literature resource database, has been accepted by many researchers. Furthermore, the Web of Science Core Collection has a rigorous selection process based on law of Bradford and includes only the most important scholarly journals in each subject area. Web of Science core collection is regarded as the most suitable database for bibliometric analysis (7).

2.2. Search strategy

The search strategy we used was entering the search expression: Topic = (sarcopenia) AND Topic = ("exercise" OR "training" OR "sport" OR "movement" OR "motion") in the Web of Science core collection. The scope of topic search includes the following fields: title, abstracts, author keywords, and keywords plus. At the time of retrieval, the publication date of the literature was unrestricted. The retrieval date was July 24, 2022. The literature type was selected as article and review article, and the language chose English. Finally, we obtained a total of 5,507 publications related to exercise interventions for sarcopenia.

2.3. Data standardization

All bibliometric records of the 5,507 retrieved literature were downloaded as "full records and cited references" from SCIE. Microsoft Excel 2021 (Microsoft Corporation, Redmond, WA, USA) and CiteSpace 6.1.R2 (Drexel University, Philadelphia, PA, USA) were used to standardize, analyze, and visualize the records.

All records need to be standardized before the bibliometric analysis. Above all, CiteSpace was used to remove the potential duplicate records. Since different names may appear for specific authors or institutions and lead to computational errors, we manually screened the names of identified authors and institutions with high publication volumes and merged the information after confirming that it came from the same author or institution.

2.4. Bibliometric analysis

Descriptive analyses of bibliometric indicators, including the annual number of publications, journals, countries, authors and keywords were analyzed in Microsoft Excel 2021.

In this study, CiteSpace was used to draw the knowledge maps, and the co-occurrence network maps of annual publications, journals, countries, institutions, authors, references and keywords were constructed. CiteSpace is a Java-based application, developed by Professor Chaomei Chen, which visualizes interrelationships between scientific articles according to their co-citation patterns (8, 9). The visual knowledge maps display the networks as the commonly seen types of node-and-link diagrams. Nodes in different networks can represent different elements, such as country, author, institution and keyword. The size of the node, which generally indicates the frequency of citation or appearance, and the different colors of the nodes indicate different years. The warmer the color, the more recent the year, and the cooler the color, the more distant the year. Links between nodes indicate collaboration or co-occurrence or co-referencing relationships. The purple ring represents centrality, and nodes with high centrality (>0.1) are usually considered as key points or turning points in a specific domain. The version of the software is constantly updated, and the version used in this study is 6.1.R2 (64-bit).

3. Results

3.1. Analysis of annual publications

There are 5,507 records related to exercise interventions for sarcopenia in the Web of Science core collection. The number of publications displayed by year is shown in Figure 1. From the figure, we can see the literature in this field was first published in 2003, and the number of publications has increased year by year. The number of publications in 2022 is only counted from January to July, but it is predicted that the number of publications in 2022 will also show an upward trend. From 2003 to 2013, the number of publications was small, but the overall trend was on the rise, indicating that the research related to exercise interventions for sarcopenia gradually attracted the attention of researchers during this period. After 2013, the number of publications increased rapidly, indicating that the research in this field has been highly valued by researchers at this stage, and exercise rehabilitation has become the focus of sarcopenia.

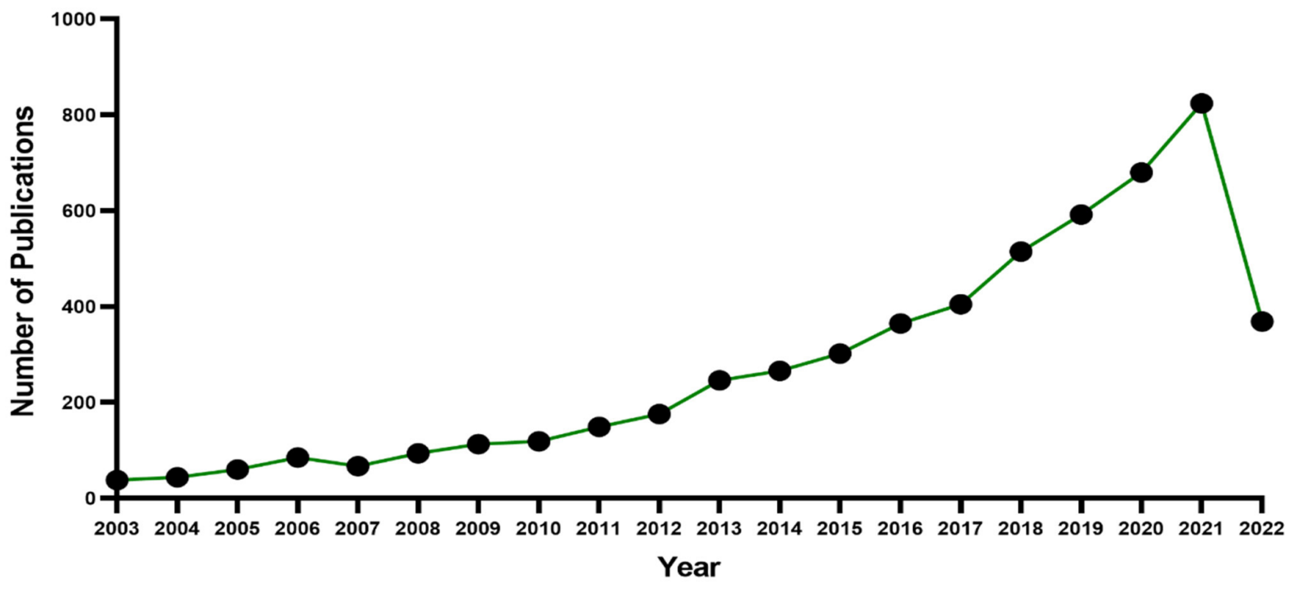

FIGURE 1
Annual number of published articles from 2003 to 2022.

TABLE 1 Top five most productive journals related to exercise interventions for sarcopenia.

Rank	Publication	Journal	IF[a]
1	225	Experimental Gerontology	4.253
2	191	Nutrients	6.706
3	121	Journal of Cachexia Sarcopenia and Muscle	12.063
4	115	PLoS ONE	3.752
5	85	Journals of Gerontology Series A-Biological Sciences and Medical Sciences	6.591

[a]IF, impact factor; IF in category according to Journal Citation Reports (2021).

3.2. Analysis of journals and cited journals

The top five journals with the largest number of published exercise interventions for sarcopenia studies are listed in Table 1. Among these five journals, Experimental Gerontology, Journals of Gerontology Series A-Biological Sciences and Medical Sciences are geriatrics journals. Journal of Cachexia Sarcopenia and Muscle is a journal named sarcopenia. Nutrients and PLoS ONE are general journals.

Moreover, the cited journal map was generated by CiteSpace (Figure 2), yielding 1,166 nodes and 11,707 links. The nodes in the map represent journals, and links between nodes represent co-citation relationships. As can be seen from the figure, there is no purple ring in these nodes, indicating that the centrality of these cited journals is not high, and ANNSURG with the highest centrality is only 0.05. The top 10 journals related to exercise interventions for sarcopenia are listed in Table 2.

3.3. Analysis of countries

To understand which countries are most prominent in the field of exercise interventions for sarcopenia, we used CiteSpace to generate a country map (Figure 3). The 5,507 records were published in 84 countries, and the top five countries of publications are listed in Table 3. The United States of America was the country with the largest number of publications, accounting for about a third of the articles (1,619). Japan and England ranked second and third, respectively, followed by China and Italy.

As shown in Figure 3, the nodes represent countries, and the purple rings indicated the centrality of the literature. The top five countries in centrality are Australia (0.27), Spain (0.2), England (0.19), USA (0.17), and France (0.13). The United States of America has an advantage in numbers, while Australia has an advantage in importance. In the following years, exercise interventions for sarcopenia has attracted increasing attention in Asian countries such as China and South Korea.

3.4. Distribution of institutions

Among the 607 institutions with the highest attention in the field of exercise interventions for sarcopenia, the top 5 institutions are all comprehensive universities (Figure 4). They are Maastricht University, University of Florida, University of Melbourne, Tufts

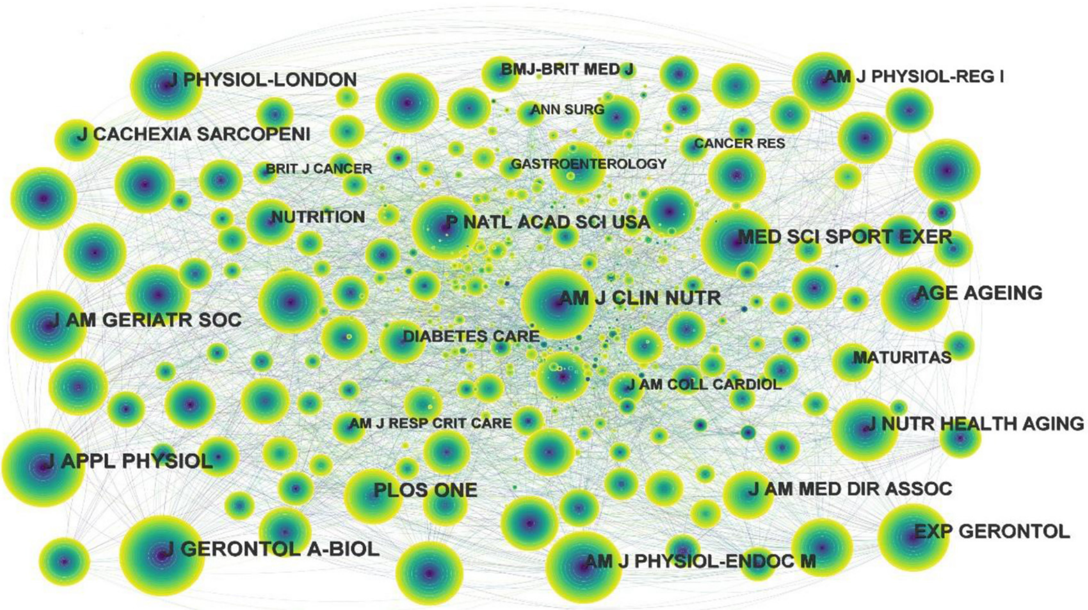

FIGURE 2
Map of cited journals for exercise interventions for sarcopenia from 2003 to 2022.

TABLE 2 Top 10 cited journals related to exercise interventions for sarcopenia.

Rank	Frequency	Cited journal
1	3,433	J Gerontol A-Biol
2	3,059	J Appl Physiol
3	2,418	J Am Geriatr Soc
4	2,363	Age Aging
5	2,351	PLoS ONE
6	2,214	Am J Clin Nutr
7	1,966	Med Sci Sport Exer
8	1,931	Exp Gerontol
9	1,798	Am J Physiol-Endoc M
10	1,778	J Am Med Dir Assoc

University, and McMaster University. The only two universities with centrality >1 were Tufts University (0.12) and the University of Florida (0.1). The number of publications and centrality analysis show that the main research institutions in this field are Tufts University and the University of Florida, which form the core of the complex cooperative network. Tufts previous research focused on sarcopenia diagnosis, nutrition and exercise interventions, body composition, and osteoporosis combined with sarcopenia. In recent years, however, Tufts has shifted its focus to the role of gut microbiota on muscle mass and strength in sarcopenia. The exercise interventions for sarcopenia research at the University of Florida mainly involves the combination with chronic diseases, inflammation, mitochondrial function, oxidative stress and so on.

3.5. Analysis of authors and cited authors

The authors of the 5,507 records were analyzed, and 1,019 nodes and 3,517 links were obtained (Figure 5), indicating that 5,507 articles were published by 1,019 authors. The top five authors were VAN LOON LJC (53), PHILLIPS SM (37), EMANUELE MARZETTI (36), VON HAEHLING S (35), and ANKER SD (34). The research focus of VAN LOON LJC and PHILLIPS SM is similar, mainly focusing on the effects of exercise (10), protein supplementation on muscle protein synthesis (11–15) and muscle strength (16) in sarcopenia. PHILLIPS SM mainly focuses on nutritional supplements in support of resistance exercise to sarcopenia (17–20). EMANUELE MARZETTI not only focused on physical activity and exercise (21), but also analyzed biomarkers of frailty and sarcopenia to provide a reference for the diagnosis and detection of sarcopenia (22–24). VON HAEHLING S focuses on sarcopenia and cachexia caused by heart failure (25–28).

The map of cited authors is shown in Figure 6. CRUZ-JENTOFT A had the highest citation counts (1,878), followed by JANSSEN I, MORLEY J, BAUMGARTNER R, and VISSER M (Table 4). Figure 6 shows that there is no purple ring, indicating that the centrality of cited authors are all <0.1.

3.6. Analysis of cited references

Figure 7 is the cited reference co-citation map, yielding 1,618 nodes and 8,483 links. The two most frequently cited references are those published by CRUZ-JENTOFT A in 2019 and 2010, respectively (29, 30). These two articles detail the consensus on definition and diagnosis for sarcopenia of the European Working Group on Sarcopenia in Older People (EWGSOP) in 2019 and

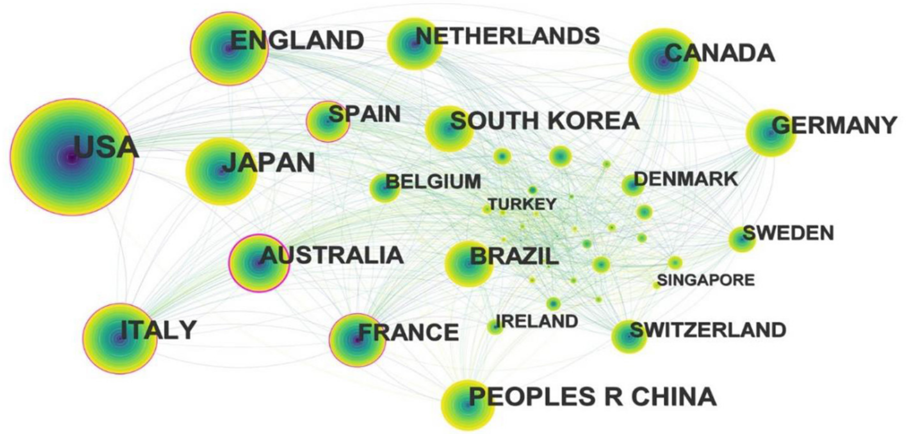

FIGURE 3
Map of countries for exercise interventions for sarcopenia from 2003 to 2022.

TABLE 3 Top five countries in the number of publications related to exercise interventions for sarcopenia.

Rank	Publications	Country	Earliest publication year
1	1,619	USA	2003
2	612	Japan	2003
3	501	England	2004
4	489	Peoples R China	2005
5	465	Italy	2003

2010. The third and fourth cited references detail the consensus on the diagnosis and treatment for sarcopenia of the Asian Working Group for Sarcopenia (AWGS), which was published by Liang-Kung Chen et al. in 2014 and 2020, respectively (1, 31). The fifth cited references was the expert consensus on the definition, prevalence, etiology and outcome for sarcopenia of the International Working Group on Sarcopenia published by Fielding R in 2011 (32). It can be seen that there is no unified definition and diagnostic criteria for sarcopenia at present, furthermore they are constantly updated. Different countries and regions may choose different diagnostic criteria. However, these working groups provide information on the definition, diagnosis and intervention of sarcopenia, which is a valuable reference for researchers engaged in sarcopenia.

The article published by Koopman R in 2009, with a centrality of 0.17, ranked first in cited references, which expounded the relationship between aging, exercise and muscle protein metabolism (33). This article pointed out that aging is accompanied by a steady loss of skeletal muscle mass and strength, age-related skeletal muscle mass loss due to interruptions of skeletal muscle protein turnover adjust to imbalances between muscle protein synthesis and degradation.

We also performed cluster analysis on the cited references to clarify the topic and time distribution of these cited references (Figure 8). In this clustering map, the Q value is 0.6939 and S value is 0.8654, indicating than the clustering effect is valid and the credibility is high. A color region in the clustering map represents a topic. As can be seen from the color in the map, the topics of cited references focus on "resistance training," "apoptosis, mitochondria," "skeletal muscle," "protein," "amino acid," "heart failure," "cirrhosis," "proteomics," "monoclonal antibody," and "machine learning."

3.7. Analysis of keywords

It was considered that the increased frequency of keywords can reflect hot topics, and burst keywords which are cited frequently over a period of time could indicate frontier topics. We generated the network map of keywords, yielding 768 nodes and 9,176 links (Figure 9). A total of 768 research keywords were identified in the field of exercise interventions for sarcopenia, which reveals the hottest topics. According to the frequency and centrality of keywords (Table 5), it can be seen that the hot keywords are "sarcopenia," "skeletal muscle," "exercise," "body composition," "strength," "older adult," "physical activity," "mass" and "resistance exercise," while "resistance exercise" has a high frequency and centrality. The strength and mass of skeletal muscle are the focus of attention in sarcopenia. Therefore, the ultimate goal of any intervention is to improve the strength and mass of skeletal muscle, in order to improve the physical function of sarcopenia. Exercise is the most commonly used, easy to achieve, and effective method of sarcopenia rehabilitation. Resistance exercise is the most commonly used in the clinic, which has a significant effect on increasing the mass and strength of skeletal muscle.

The top 25 keywords with the strongest burst were obtained by time series burst detection of highly cited keywords (Figure 10). Among these keywords, "elderly men," "young," "age," "men," "old rat" are subjects of exercise rehabilitation studies for sarcopenia, "growth factors," "protein synthesis," "messenger rna," "hypertrophy," "growth hormone," "satellite cell," "necrosis factor

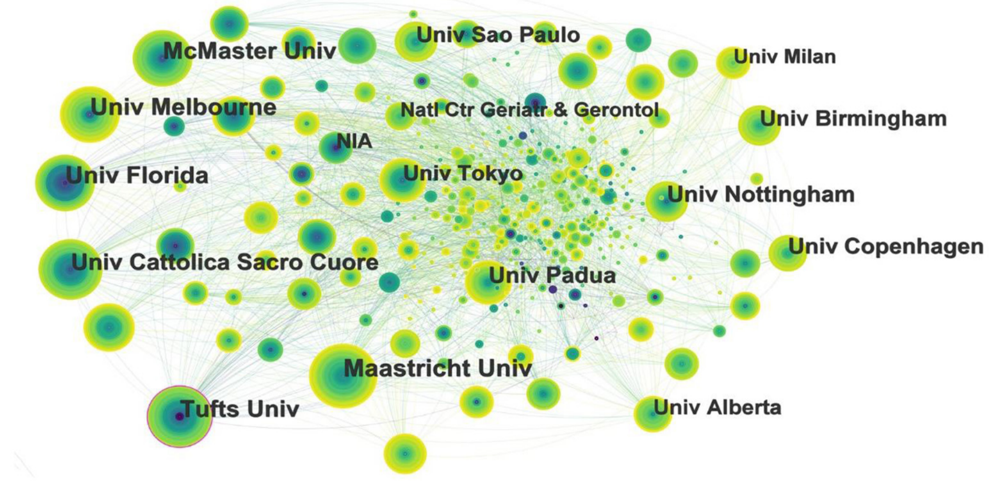

FIGURE 4
Map of institutions researching exercise interventions for sarcopenia from 2003 to 2022.

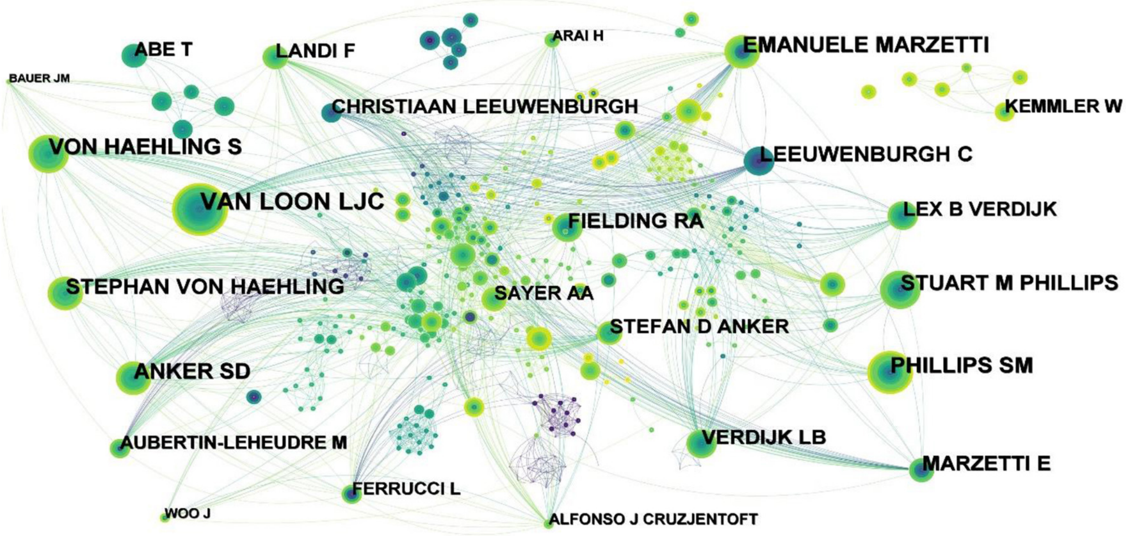

FIGURE 5
Map of authors related to exercise interventions for sarcopenia from 2003 to 2022.

alpha," "necrosis factor alpha," "igf i," "myosin heavy chain," "caloric restriction," "essential amino acid" are the key research directions. The keyword "elderly men," which emerged since 2003, showed the strongest citation burst of 27.33. The second most hot word was "growth factor" with strength of 21.68.

The most recent burst keywords were "Asian working group" and "consensus." "Asian working group" means the Asian Working Group for Sarcopenia. In 2019, the Asian Working Group for Sarcopenia released the latest expert consensus on the diagnosis and treatment of sarcopenia (1), the highlight of which is that medical institutions at different levels should adopt different diagnostic strategies. The expert consensus also give detailed diagnosis and treatment methods for sarcopenia. At the same time, the diagnostic threshold is also updated, which is more operable.

Cluster analysis and summary of these keywords can provide a more intuitive understanding of the current Research Topics related to exercise rehabilitation of sarcopenia (Figure 11). After clustering, the *Q*-value is 0.3397 and the *S*-value is 0.669, indicating that clustering is appropriate and meaningful. A total of six clusters were generated to reflect the hot trends, and they are "skeletal muscle," "muscle strength," "heart failure," "muscle protein synthesis," "insulin resistance" and "high-intensity interval training." From the timeline view (Figure 12), "insulin resistance" and "high-intensity interval training" are the latest studies, while "skeletal muscle" and "muscle strength" appear earlier.

10.3389/fpubh.2023.1106458

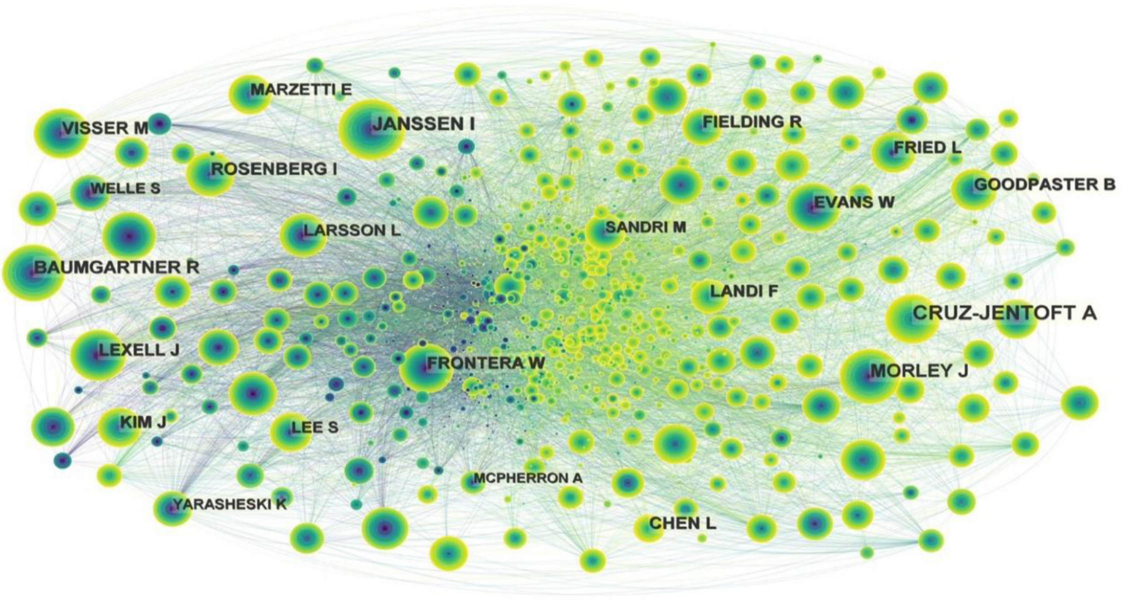

FIGURE 6
Map of cited authors related to exercise interventions for sarcopenia from 2003 to 2022.

TABLE 4 Top five frequency and centrality of cited authors.

Rank	Frequency	Author	Rank	Centrality	Author
1	1,878	Cruz-Jentoft A	1	0.05	Fielding R
2	1,107	Janssen I	2	0.05	Yarasheski K
3	820	Morley J	3	0.05	Bhasin S
4	781	Baumgartner R	4	0.05	Mcpherron A
5	588	Visser M	5	0.04	Marzetti E

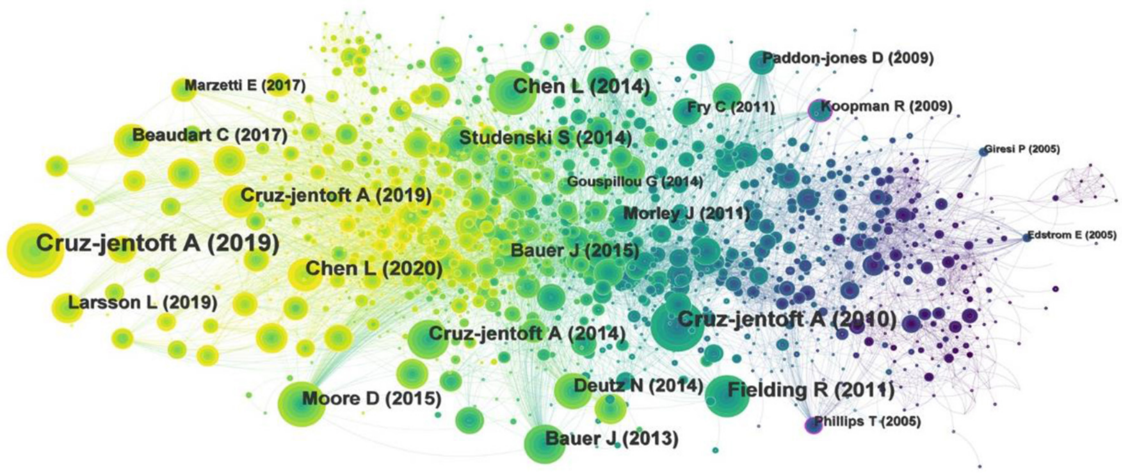

FIGURE 7
Map of cited references for exercise interventions for sarcopenia from 2003 to 2022.

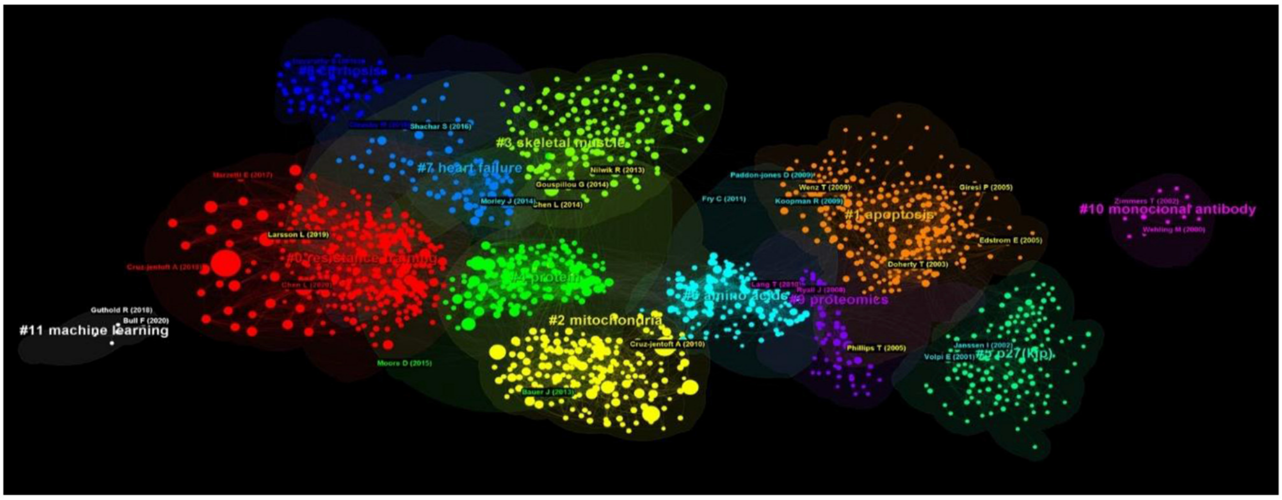

FIGURE 8
The clustering map of cited references related to exercise interventions for sarcopenia from 2003 to 2022.

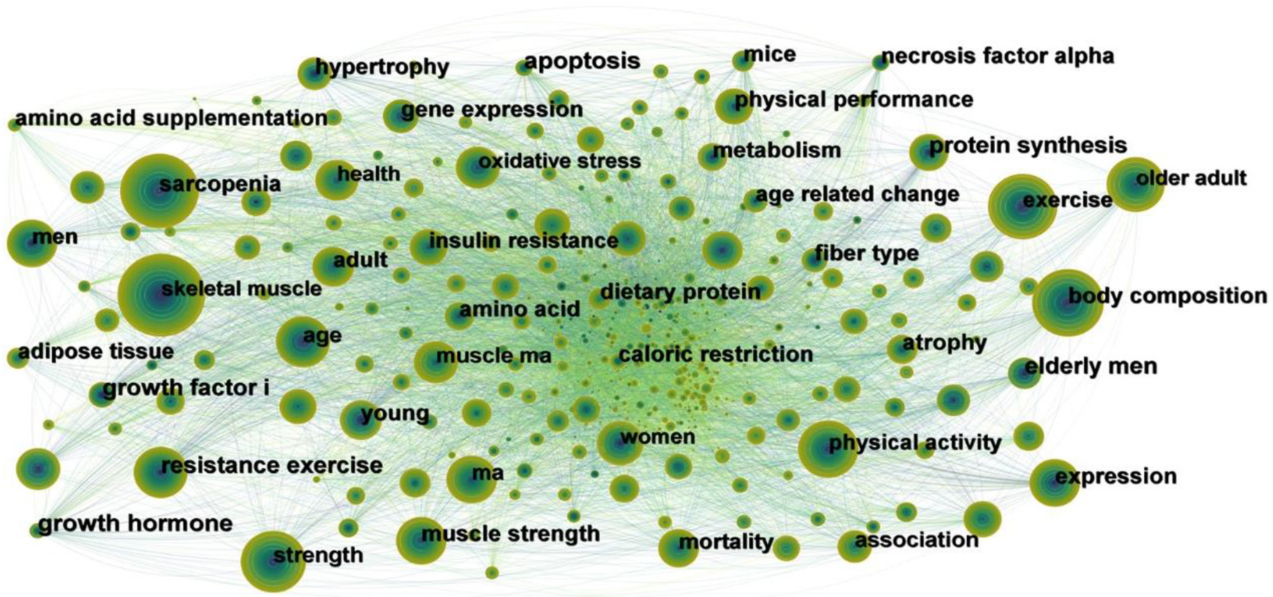

FIGURE 9
Map of keywords to exercise interventions for sarcopenia from 2003 to 2022.

4. Discussion

4.1. General knowledge structure in exercise interventions for sarcopenia research

Exercise is a significant rehabilitation method for sarcopenia, which has received wide attention and is the key research direction of sarcopenia. Exercise rehabilitation has the advantages of easy operation and personalized exercise prescription. In this study, 5,507 records on exercise interventions for sarcopenia from January 2003 to July 2022 were retrieved from the Web of Science core collection. Based on the bibliometrics analysis of CiteSpace, we have clarified the spatial and temporal distribution and research hotspots of exercise interventions for sarcopenia. In the past 20 years, publications related to exercise interventions for sarcopenia have grown rapidly. In this study, the Journal of Experimental Gerontology published the most articles (225), and J GERONTOL A-BIOL was the biggest cited (3,433). The countries and institutions that carry out exercise interventions for sarcopenia research had relatively close cooperation. Generally, the United States of America, Australia, and some other European

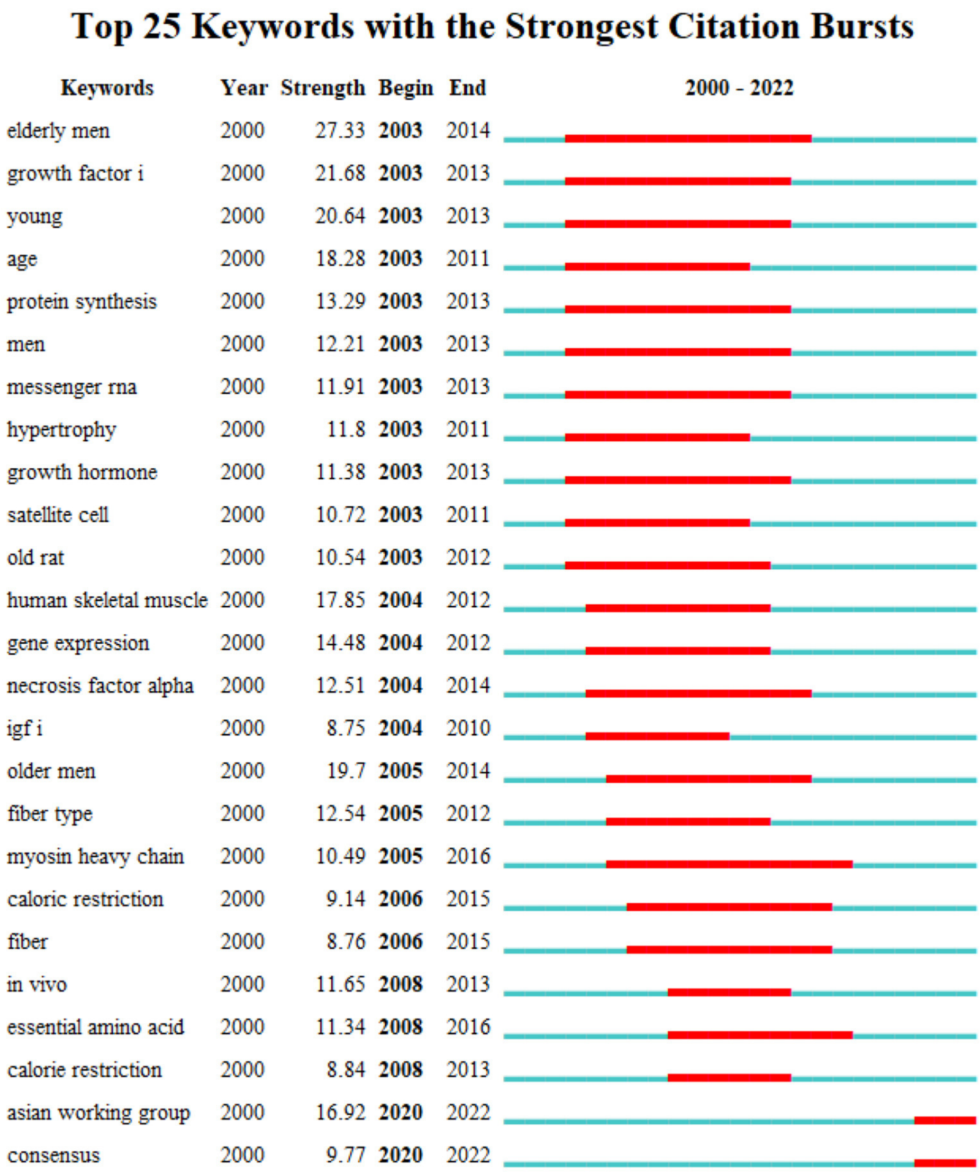

FIGURE 10
Top 25 keywords with the strongest citation burst.

countries, with a high publication rate and centrality, all developed countries, were leading the field of exercise interventions for sarcopenia. The most productive institution was Maastricht University in the Netherlands. A total of 1,019 authors from different countries conducted studies on exercise interventions for sarcopenia. Of these authors, VAN LOON LJC was the most productive author, while CRUZ-JENTOFT A ranked first among cited authors. The cited reference with the highest centrality was a review, which focuses on the relationship between aging, exercise and muscle protein metabolism, published by Koopman R in 2009. Cluster analysis of the cited literature show that the most recently cited hot topics, respectively, were "resistance training," "apoptosis, mitochondria," "skeletal muscle," "protein," "amino acid," "heart failure," "cirrhosis," "proteomics," "monoclonal antibody," and "machine learning."

The hot keywords in the field of exercise interventions for sarcopenia are "sarcopenia," "skeletal muscle," "exercise," "body composition," "strength," "older adult," "physical activity," "mass," and "resistance exercise." The keyword "elderly men" showed the strongest citation burst, and the second outbreak word was "growth factor." A total of six clusters were formed, which, respectively, were "skeletal muscle," "muscle strength," "heart failure," "muscle protein synthesis," "insulin resistance" and "high-intensity interval training." The keywords of "growth factors," "protein synthesis," "messenger rna," "hypertrophy," "growth hormone," "satellite cell," necrosis factor alpha," "necrosis factor alpha," "igf i," "myosin heavy chain," "caloric restriction," "essential amino acid," suggest the mechanisms or targets of exercise interventions for sarcopenia.

TABLE 5 Top 10 frequency and centrality of keywords to exercise interventions for sarcopenia.

Rank	Frequency	Keyword	Rank	Centrality	Keyword
1	1,692	Sarcopenia	1	0.05	Growth factor
2	1,544	Skeletal muscle	2	0.04	Growth hormone
3	1,020	exercise	3	0.04	Apoptosis
4	898	Body composition	4	0.04	Caloric restriction
5	719	Strength	5	0.04	Necrosis factor alpha
6	685	Older adult	6	0.03	Resistance exercise
7	627	Physical activity	7	0.03	Insulin resistance
8	485	Mass	8	0.03	Young
9	474	Resistance exercise	9	0.03	Protein synthesis
10	433	Muscle strength	10	0.03	Age related change

4.2. Main types of exercise for sarcopenia rehabilitation

Exercise therapy is an effective method to prevent and treat sarcopenia (34–39). The commonly used exercise methods include resistance exercise, aerobic exercise, combination of resistance and aerobic exercise, and other auxiliary exercise methods. The keyword related-information in this study shows that resistance exercise is the most commonly used.

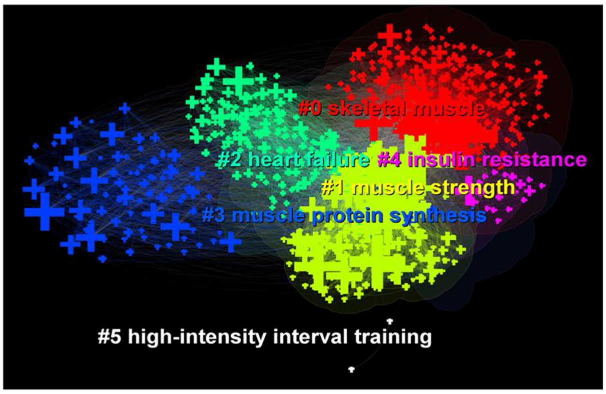

FIGURE 11
The clustering map of keywords related to exercise interventions for sarcopenia.

4.2.1. Resistance exercise

Resistance exercise as an effective way to enhance skeletal muscle protein synthesis, stimulate muscle hypertrophy and improve muscle strength, is the best-recommended exercise for sarcopenia (40–44). The resistance overcome during resistance exercise can be constant or incremental, which can be chosen according to the actual situation of the individuals. The types of exercises include weight lifting, seated leg lifts, static squats against the wall, stretching elastic bands, etc. For individuals with severe sarcopenia, rehabilitation equipment is often used to assist in training. The most recommended rehabilitation program for elderly participants with sarcopenia is at least 8 weeks, 3–4 times per week, actions at intensities of 40–60% of 1-repetition maximum, and for the untrained elderly, the exercise dose can be reduced to 2–3 times per week (45).

4.2.2. Aerobic exercise

Although aerobic exercise cannot stimulate muscle hypertrophy, it can enhance muscle endurance level and muscle contraction capacity by effectively inhibiting the expression of apoptotic factors, improving cell mitochondrial quality and enhancing the activity of metabolic enzymes, thus maintaining muscle function and improving cardiorespiratory endurance (46). Aerobic exercise for about 30 min a day, 3 times a week, for more than 5 months can significantly improve the symptoms and prognosis of sarcopenia (37). Common aerobic exercises include walking, brisk walking, jogging, cycling, swimming, dancing, tai chi, setting-up exercise and some small-ball sports, etc. Participants can choose according to their own situation and interest. Aerobic exercise should start with low-intensity exercise (40% of maximum heart rate), lasting 5–10 min per day; medium intensity (50–60% of maximum heart rate), at least 10 min per time, 5 days per week; high intensity (>60% of maximum heart rate), at least 20–30 min per time, at least 3 days per week (47).

4.2.3. Combination of resistance and aerobic exercise

Resistance exercise can significantly increase muscle mass and strength, but the effect of improving cardiopulmonary endurance is not significant. Aerobic exercise can effectively improve cardiopulmonary endurance, but the improvement of muscle function is limited. Furthermore, the single exercise mode is easy to produce muscle fatigue, lack of fun, and it is difficult for participants to adhere for a long time. Therefore, multi-component exercise is often used clinically to intervene in participants with sarcopenia, such as moderate resistance training, aerobic + resistance training, resistance + balance + gait training and resistance training + outdoor activities, etc. The multi-exercise

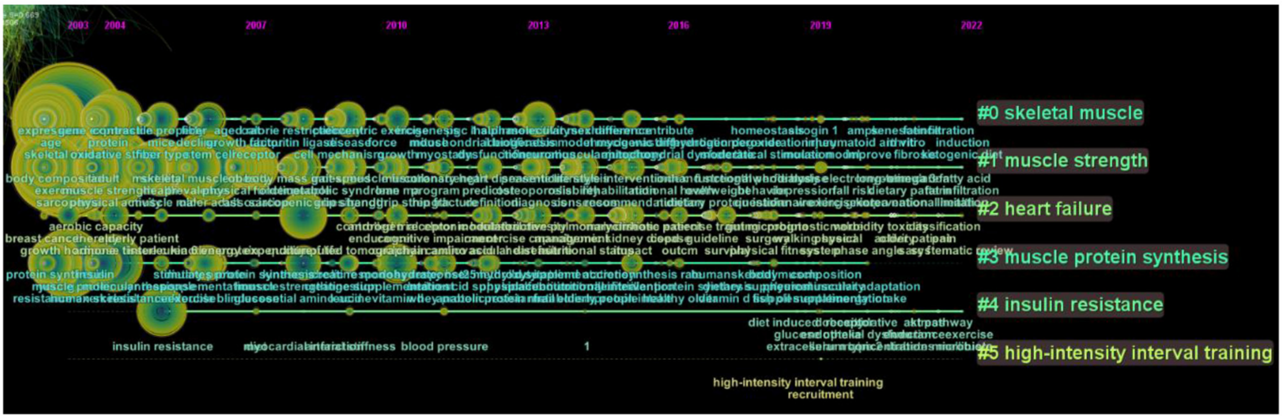

FIGURE 12
The timeline view of keywords related to exercise interventions for sarcopenia.

approach is not only effective, but also more stimulating to participants' interest in exercise (44, 48).

4.2.4. Other auxiliary exercise

Participants with sarcopenia have a gradual loss of balance ability and postural control disorders, which become important factors leading to fall and poor physical flexibility (49, 50). Therefore, it is recommended that older adults perform balance training, such as cross-pacing and tai chi (51), more than three times a week as a way to reduce the risk of falls. At the same time, a cumulative total of at least 2 weeks of flexibility training should be conducted each month, with a moderate to light dose of 10 min each time, including the neck, shoulders, kinesiology, knees and other joint parts (52). For elderly people who are constrained by physical conditions or unwilling to carry out dynamic exercise training, whole body vibration therapy can be used to stimulate the muscles, which can also achieve desired results (53–55). In addition, participants with sarcopenia should try to reduce sedentary and bed-ridden in daily life, and should increase the frequency of daily activities, such as gardening, traveling, housework, shopping, climbing stairs, etc., which can play a role in exercising limb strength.

In this study, six clusters were obtained after cluster analysis of keywords. One of the keywords was high-intensity interval training (HIIT), which has attracted much attention in recent years. Multimodal HIIT has a combination of aerobic and anaerobic performance effects, and has significant effects on improving muscle strength and muscle endurance. HIIT also produce beneficial effects on cardiorespiratory fitness, physical fitness, muscle strength, cardiac contractile function, mitochondrial citrate synthase activity, and lowering blood triglyceride and glucose levels in older adults (56). However, it is worth mentioning that HIIT, as a high-intensity exercise mode, should only be performed by participants with sarcopenia after a systematic physical assessment to determine the appropriate exercise dose. Currently, there are no studies directly targeting participants with sarcopenia for high-intensity interval training due to safety reasons (57).

In addition, the results of several studies confirm that exercise combined with nutritional supplementation is the best choice for the rehabilitation of sarcopenia. Supplementation with protein, amino acids, vitamin D and other nutrients along with exercise intervention can promote muscle protein synthesis, muscle cell proliferation and differentiation, significantly delaying muscle aging (19, 58–61).

4.3. Future trends

Timeline view analysis and burst detection methods were used to identify cutting-edge content and reveal future trends. From Figure 12, we found that heart failure, muscle protein synthesis, insulin resistance, and high-intensity interval training are the hot spots of research in recent years. With the emergence of diversified exercises and their good results in the rehabilitation of sarcopenia, researchers are increasingly concerned about the mechanism of action and safety of exercise for sarcopenia. Sarcopenia was a common condition in participants with heart failure, and heart failure can induce sarcopenia. Therefore, early detection of sarcopenia and appropriate interventions are important in heart failure (62–64). The aim of exercise interventions for sarcopenia is to improve muscle mass and strength. The analysis of timeline view revealed that protein synthesis and insulin resistance are closely related to muscle mass and strength, which provides a direction to study the mechanism of exercise interventions for sarcopenia.

4.4. Strengths and limitations

This study summarized the hotspots and research trends of exercise for sarcopenia, and provided a meaningful reference for the research in this field. However, this study also has some limitations. Firstly, we only analyzed data from the Web of Science core collection. Searches are not selected in PubMed, Scopus, or other databases. Second, the literature contains papers in English only; the status of research on exercise interventions for sarcopenia in other language nations is not possible to determine. Lastly, the number of citations and centrality of articles may vary if the search is conducted at different time periods. Therefore, this study only represents the hotspots in the last 20 years.

5. Conclusion

This study uses the visualization software CiteSpace to identify potential collaborators and partner institutions, hot topics and new perspectives on research frontiers in the research of exercise interventions for sarcopenia. Bibliometric analysis of the literature shows that exercise, as the most significant intervention, remains the most cutting-edge and critical component in the rehabilitation of sarcopenia. Looking for scientific, effective and safe exercise prescriptions will be the focus of future research. In conclusion, our study provided a comprehensive landscape of the development and identified the key features of exercise interventions for sarcopenia over the past 20 years. This may provide a direction for the exploration and development of exercise interventions for sarcopenia.

Author contributions

QX contributed to conception and design of the study and obtaining funding for the study, and wrote the first draft of the manuscript. YH and JZ contributed to data collection and analysis. WL and JT contributed to manuscript revision. All authors contributed to manuscript revision, read, and approved the submitted version.

Funding

This work was supported by the project of Rehabilitation Technology Innovation Center by Joint Collaboration of Ministry of Education and Fujian Province grant number X2022003-Collaboration, school management project of Fujian University of Traditional Chinese Medicine grant number X2020017, and basic science research promotion project of Fujian University of Traditional Chinese Medicine grant number XJC2022005.

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.

Publisher's note

References

1. Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K, et al. Asian working group for sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc.* (2020) 21:300–7. doi: 10.1016/j.jamda.2019.12.012

2. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *Lancet.* (2019) 393:2636–46. doi: 10.1016/S0140-6736(19)31138-9

3. Gao K, Cao LF, Ma WZ, Gao YJ, Luo MS, Zhu J, et al. Association between sarcopenia and cardiovascular disease among middle-aged and older adults: Findings from the China health and retirement longitudinal study. *EClinicalMedicine.* (2022) 44:101264. doi: 10.1016/j.eclinm.2021.101264

4. Sasaki KI, Fukumoto Y. Sarcopenia as a comorbidity of cardiovascular disease. *J Cardiol.* (2022) 79:596–604. doi: 10.1016/j.jjcc.2021.10.013

5. Hardee JP, Lynch GS. Current pharmacotherapies for sarcopenia. *Expert Opin Pharmacother.* (2019) 20:1645–57. doi: 10.1080/14656566.2019.1622093

6. Dent E, Morley JE, Cruz-Jentoft AJ, Arai H, Kritchevsky SB, Guralnik J, et al. International Clinical Practice Guidelines for Sarcopenia (ICFSR): screening, diagnosis and management. *J Nutr Health Aging.* (2018) 22:1148–61. doi: 10.1007/s12603-018-1139-9

7. AlRyalat S, Malkawi LW, Momani SM. Comparing bibliometric analysis using PubMed, scopus, and web of science databases. *J Vis Exp.* (2019) 152:e58494. doi: 10.3791/58494

8. Chen C, Chen Y. Searching for clinical evidence in CiteSpace. *AMIA Annu Symp Proc.* (2005) 121–5.

9. Synnestvedt MB, Chen C, Holmes JH. CiteSpace II: visualization and knowledge discovery in bibliographic databases. *AMIA Annu Symp Proc.* (2005) 724–8.

10. Shad BJ, Wallis G, van Loon LJ, Thompson JL. Exercise prescription for the older population: the interactions between physical activity, sedentary time, and adequate nutrition in maintaining musculoskeletal health. *Maturitas.* (2016) 93:78–82. doi: 10.1016/j.maturitas.2016.05.016

11. Snijders T, Verdijk LB, van Loon LJ. The impact of sarcopenia and exercise training on skeletal muscle satellite cells. *Ageing Res Rev.* (2009) 8:328–38. doi: 10.1016/j.arr.2009.05.003

12. Devries MC, Phillips SM. Supplemental protein in support of muscle mass and health: advantage whey. *J Food Sci.* (2015) 80(Suppl. 1):A8–15. doi: 10.1111/1750-3841.12802

13. Fuchs CJ, Hermans W, Holwerda AM, Smeets J, Senden JM, van Kranenburg J, et al. Branched-chain amino acid and branched-chain ketoacid ingestion increases muscle protein synthesis rates *in vivo* in older adults: a double-blind, randomized trial. *Am J Clin Nutr.* (2019) 110:862–72. doi: 10.1093/ajcn/nqz120

14. Holwerda AM, Paulussen K, Overkamp M, Goessens J, Kramer IF, Wodzig W, et al. Dose-dependent increases in whole-body net protein balance and dietary protein-derived amino acid incorporation into myofibrillar protein during recovery from resistance exercise in older men. *J Nutr.* (2019) 149:221–30. doi: 10.1093/jn/nxy263

15. Nunes EA, Colenso-Semple L, McKellar SR, Yau T, Ali MU, Fitzpatrick-Lewis D, et al. Systematic review and meta-analysis of protein intake to support muscle mass and function in healthy adults. *J Cachexia Sarcopenia Muscle.* (2022) 13:795–810. doi: 10.1002/jcsm.12922

16. Tieland M, Franssen R, Dullemeijer C, van Dronkelaar C, Kyung KH, Ispoglou T, et al. The impact of dietary protein or amino acid supplementation on muscle mass and strength in elderly people: individual participant data and meta-analysis of RCT's. *J Nutr Health Aging.* (2017) 21:994–1001. doi: 10.1007/s12603-017-0896-1

17. Devries MC, Phillips SM. Creatine supplementation during resistance training in older adults-a meta-analysis. *Med Sci Sports Exerc.* (2014) 46:1194–203. doi: 10.1249/MSS.0000000000000220

18. Phillips SM. Nutritional supplements in support of resistance exercise to counter age-related sarcopenia. *Adv Nutr.* (2015) 6:452–60. doi: 10.3945/an.115.008367

19. McKendry J, Currier BS, Lim C, Mcleod JC, Thomas A, Phillips SM. Nutritional supplements to support resistance exercise in countering the sarcopenia of aging. *Nutrients.* (2020) 12:2057. doi: 10.3390/nu12072057

20. McKendry J, Stokes T, Mcleod JC, Phillips SM. Resistance exercise, aging, disuse, and muscle protein metabolism. *Compr Physiol.* (2021) 11:2249–78. doi: 10.1002/cphy.c200029

21. Marzetti E, Calvani R, Tosato M, Cesari M, Di Bari M, Cherubini A, et al. Physical activity and exercise as countermeasures to physical frailty and sarcopenia. *Aging Clin Exp Res.* (2017) 29:35–42. doi: 10.1007/s40520-016-0705-4

22. Tosato M, Marzetti E, Cesari M, Savera G, Miller RR, Bernabei R, et al. Measurement of muscle mass in sarcopenia: from imaging to biochemical markers. *Aging Clin Exp Res.* (2017) 29:19–27. doi: 10.1007/s40520-016-0717-0

23. Calvani R, Picca A, Marini F, Biancolillo A, Gervasoni J, Persichilli S, et al. Identification of biomarkers for physical frailty and sarcopenia through a new multi-marker approach: results from the BIOSPHERE study. *Geroscience.* (2021) 43:727–40. doi: 10.1007/s11357-020-00197-x

24. Picca A, Coelho-Junior HJ, Calvani R, Marzetti E, Vetrano DL. Biomarkers shared by frailty and sarcopenia in older adults: a systematic review and meta-analysis. *Ageing Res Rev.* (2022) 73:101530. doi: 10.1016/j.arr.2021.101530

25. von Haehling S. The wasting continuum in heart failure: from sarcopenia to cachexia. *Proc Nutr Soc.* (2015) 74:367–77. doi: 10.1017/S0029665115002438

26. von Haehling S, Ebner N, Dos SM, Springer J, Anker SD. Muscle wasting and cachexia in heart failure: mechanisms and therapies. *Nat Rev Cardiol.* (2017) 14:323–41. doi: 10.1038/nrcardio.2017.51

27. Saitoh M, Ebner N, von Haehling S, Anker SD, Springer J. Therapeutic considerations of sarcopenia in heart failure patients. *Expert Rev Cardiovasc Ther.* (2018) 16:133–42. doi: 10.1080/14779072.2018.1424542

28. von Haehling S. Muscle wasting and sarcopenia in heart failure: a brief overview of the current literature. *ESC Heart Fail.* (2018) 5:1074–82. doi: 10.1002/ehf2.12388

29. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on Sarcopenia in Older People. *Age Ageing.* (2010) 39:412–23. doi: 10.1093/ageing/afq034

30. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyere O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing.* (2019) 48:16–31. doi: 10.1093/ageing/afy169

31. Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. *J Am Med Dir Assoc.* (2014) 15:95–101. doi: 10.1016/j.jamda.2013.11.025

32. Fielding RA, Vellas B, Evans WJ, Bhasin S, Morley JE, Newman AB, et al. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. *J Am Med Dir Assoc.* (2011) 12:249–56. doi: 10.1016/j.jamda.2011.01.003

33. Koopman R, van Loon LJ. Aging, exercise, and muscle protein metabolism. *J Appl Physiol.* (2009) 106:2040–8. doi: 10.1152/japplphysiol.91551.2008

34. Phu S, Boersma D, Duque G. Exercise and sarcopenia. *J Clin Densitom.* (2015) 18:488–92. doi: 10.1016/j.jocd.2015.04.011

35. Beckwee D, Delaere A, Aelbrecht S, Baert V, Beaudart C, Bruyere O, et al. Exercise interventions for the prevention and treatment of sarcopenia. A systematic umbrella review. *J Nutr Health Aging.* (2019) 23:494–502. doi: 10.1007/s12603-019-1196-8

36. de Mello R, Dalla CR, Gioscia J, Moriguchi EH. Effects of physical exercise programs on sarcopenia management, dynapenia, and physical performance in the elderly: a systematic review of randomized clinical trials. *J Aging Res.* (2019) 2019:1959486. doi: 10.1155/2019/1959486

37. Nascimento CM, Ingles M, Salvador-Pascual A, Cominetti MR, Gomez-Cabrera MC, Vina J. Sarcopenia, frailty and their prevention by exercise. *Free Radic Biol Med.* (2019) 132:42–9. doi: 10.1016/j.freeradbiomed.2018.08.035

38. Moore SA, Hrisos N, Errington L, Rochester L, Rodgers H, Witham M, et al. Exercise as a treatment for sarcopenia: an umbrella review of systematic review evidence. *Physiotherapy.* (2020) 107:189–201. doi: 10.1016/j.physio.2019.08.005

39. Tsekoura M, Billis E, Kastrinis A, Katsoulaki M, Fousekis K, Tsepis E, et al. The effects of exercise in patients with sarcopenia. *Adv Exp Med Biol.* (2021) 1337:281–90. doi: 10.1007/978-3-030-78771-4_31

40. Giallauria F, Cittadini A, Smart NA, Vigorito C. Resistance training and sarcopenia. *Monaldi Arch Chest Dis.* (2016) 84:738. doi: 10.4081/monaldi.2015.738

41. Chen N, He X, Feng Y, Ainsworth BE, Liu Y. Effects of resistance training in healthy older people with sarcopenia: a systematic review and meta-analysis of randomized controlled trials. *Eur Rev Aging Phys Act.* (2021) 18:23. doi: 10.1186/s11556-021-00277-7

42. Cannataro R, Cione E, Bonilla DA, Cerullo G, Angelini F, D'Antona G. Strength training in elderly: An useful tool against sarcopenia. *Front Sports Act Living.* (2022) 4:950949. doi: 10.3389/fspor.2022.950949

43. Mende E, Moeinnia N, Schaller N, Weiss M, Haller B, et al. Progressive machine-based resistance training for prevention and treatment of sarcopenia in the oldest old: a systematic review and meta-analysis. *Exp Gerontol.* (2022) 163:111767. doi: 10.1016/j.exger.2022.111767

44. Wang H, Huang WY, Zhao Y. Efficacy of exercise on muscle function and physical performance in older adults with sarcopenia: an updated systematic review and meta-analysis. *Int J Environ Res Public Health.* (2022) 19:8212. doi: 10.3390/ijerph19138212

45. Silva NL, Oliveira RB, Fleck SJ, Leon AC, Farinatti P. Influence of strength training variables on strength gains in adults over 55 years-old: a meta-analysis of dose-response relationships. *J Sci Med Sport.* (2014) 17:337–44. doi: 10.1016/j.jsams.2013.05.009

46. Ziaaldini MM, Marzetti E, Picca A, Murlasits Z. Biochemical pathways of sarcopenia and their modulation by physical exercise: a narrative review. *Front Med.* (2017) 4:167. doi: 10.3389/fmed.2017.00167

47. Chodzko-Zajko WJ, Proctor DN, Fiatarone SM, Minson CT, Nigg CR, Salem GJ, et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Med Sci Sports Exerc.* (2009) 41:1510–30. doi: 10.1249/MSS.0b013e3181a0c95c

48. Negm AM, Lee J, Hamidian R, Jones CA, Khadaroo RG. Management of sarcopenia: a network meta-analysis of randomized controlled trials. *J Am Med Dir Assoc.* (2022) 23:707–14. doi: 10.1016/j.jamda.2022.01.057

49. Cawthon PM. Assessment of lean mass and physical performance in sarcopenia. *J Clin Densitom.* (2015) 18:467–71. doi: 10.1016/j.jocd.2015.05.063

50. Meng NH, Li CI, Liu CS, Lin WY, Lin CH, Chang CK, et al. Sarcopenia defined by combining height- and weight-adjusted skeletal muscle indices is closely associated with poor physical performance. *J Aging Phys Act.* (2015) 23:597–606. doi: 10.1123/japa.2014-0036

51. Huang CY, Mayer PK, Wu MY, Liu DH, Wu PC, Yen HR. The effect of Tai Chi in elderly individuals with sarcopenia and frailty: a systematic review and meta-analysis of randomized controlled trials. *Ageing Res Rev.* (2022) 82:101747. doi: 10.1016/j.arr.2022.101747

52. Nelson ME, Rejeski WJ, Blair SN, Duncan PW, Judge JO, King AC, et al. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc.* (2007) 39:1435–45. doi: 10.1249/mss.0b013e3180616aa2

53. Wei N, Pang MY, Ng SS, Ng GY. Optimal frequency/time combination of whole body vibration training for developing physical performance of people with sarcopenia: a randomized controlled trial. *Clin Rehabil.* (2017) 31:1313–21. doi: 10.1177/0269215517698835

54. Chang SF, Lin PC, Yang RS, Yang RJ. The preliminary effect of whole-body vibration intervention on improving the skeletal muscle mass index, physical fitness, and quality of life among older people with sarcopenia. *BMC Geriatr.* (2018) 18:17. doi: 10.1186/s12877-018-0712-8

55. Wu S, Ning HT, Xiao SM, Hu MY, Wu XY, Deng HW, et al. Effects of vibration therapy on muscle mass, muscle strength and physical function in older adults with sarcopenia: a systematic review and meta-analysis. *Eur Rev Aging Phys Act.* (2020) 17:14 doi: 10.1186/s11556-020-00247-5

56. Wu ZJ, Wang ZY, Gao HE, Zhou XF, Li FH. Impact of high-intensity interval training on cardiorespiratory fitness, body composition, physical fitness, and metabolic parameters in older adults: a meta-analysis of randomized controlled trials. *Exp Gerontol.* (2021) 150:111345. doi: 10.1016/j.exger.2021.111345

57. Liu QQ, Xie WQ, Luo YX, Li YD, Huang WH, Wu YX, et al. High intensity interval training: a potential method for treating sarcopenia. *Clin Interv Aging.* (2022) 17:857–72. doi: 10.2147/CIA.S366245

58. Zhu LY, Chan R, Kwok T, Cheng KC, Ha A, Woo J. Effects of exercise and nutrition supplementation in community-dwelling older Chinese people with sarcopenia: a randomized controlled trial. *Age Ageing.* (2019) 48:220–8. doi: 10.1093/ageing/afy179

59. Banerjee A, Marotta F, Sriramulu S, Chabria Y, Hari S, Catanzaro R, et al. Beyond physical exercise: the role of nutrition, gut microbiota and nutraceutical supplementation in reducing age-related sarcopenia. *Curr Aging Sci.* (2021) 14:94–104. doi: 10.2174/1874609814666210203090458

60. Wu PY, Huang KS, Chen KM, Chou CP, Tu YK. Exercise, nutrition, and combined exercise and nutrition in older adults with sarcopenia: a systematic review and network meta-analysis. *Maturitas.* (2021) 145:38–48. doi: 10.1016/j.maturitas.2020.12.009

61. Kakehi S, Wakabayashi H, Inuma H, Inose T, Shioya M, Aoyama Y, et al. Rehabilitation nutrition and exercise therapy for sarcopenia. *World J Mens Health.* (2022) 40:1–10. doi: 10.5534/wjmh.200190

62. Curcio F, Testa G, Liguori I, Papillo M, Flocco V, Panicara V, et al. Sarcopenia and heart failure. *Nutrients.* (2020) 12:211. doi: 10.3390/nu12010211

63. Lena A, Anker MS, Springer J. Muscle wasting and sarcopenia in heart failure-the current state of science. *Int J Mol Sci.* (2020) 21:6549. doi: 10.3390/ijms21186549

64. Zhang Y, Zhang J, Ni W, Yuan X, Zhang H, Li P, et al. Sarcopenia in heart failure: a systematic review and meta-analysis. *ESC Heart Fail.* (2021) 8:1007–17. doi: 10.1002/ehf2.13255

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 13 March 2023
DOI 10.3389/fpubh.2023.1081843

OPEN ACCESS

EDITED BY
Priscila Yukari Sewo Sampaio,
Federal University of Sergipe, Brazil

REVIEWED BY
Mara Carsote,
Carol Davila University of Medicine and Pharmacy, Romania
Shirin Djalalinia,
Ministry of Health and Medical Education, Iran

*CORRESPONDENCE
Cheng Huang
✉ chenghuang_scu@163.com

†These authors have contributed equally to this work and share first authorship

SPECIALTY SECTION
This article was submitted to Aging and Public Health, a section of the journal Frontiers in Public Health

RECEIVED 01 November 2022
ACCEPTED 21 February 2023
PUBLISHED 13 March 2023

CITATION
Liu Q, You J, Zhong M, Wu Z, Geng Y and Huang C (2023) Hemoglobin level is negatively associated with sarcopenia and its components in Chinese aged 60 and above. *Front. Public Health* 11:1081843. doi: 10.3389/fpubh.2023.1081843

Hemoglobin level is negatively associated with sarcopenia and its components in Chinese aged 60 and above

Qiaoling Liu[1†], Jiuhong You[2†], Min Zhong[3], Zhigang Wu[4], Yunjie Geng[5] and Cheng Huang[2,6*]

[1]School of Cardiovascular and Metabolic Health, University of Glasgow, Glasgow, United Kingdom, [2]Department of Rehabilitation Medicine, West China Hospital, Sichuan University, Chengdu, Sichuan, China, [3]Department of Geriatric Neurology, Affiliated Brain Hospital of Nanjing Medical University, Nanjing, Jiangsu, China, [4]Department of Chemistry, Southern University of Science and Technology, Shenzhen, Guangdong, China, [5]Research Institute of Statistical Sciences, National Bureau of Statistics, Beijing, China, [6]Key Laboratory of Rehabilitation Medicine in Sichuan Province, West China Hospital, Sichuan University, Chengdu, Sichuan, China

Introduction: Sarcopenia and low hemoglobin level are common in older adults. Few studies have evaluated the association between hemoglobin level and sarcopenia and with inconsistent findings. The multifaceted effects of sarcopenia on the human body and the high prevalence of anemia in the Chinese population make it necessary to explore the association between the two.

Methods: Using the China Health and Retirement Longitudinal Study (CHARLS), we explored the association between hemoglobin with sarcopenia and its components in the Chinese population aged 60 and above. Multivariate logistic and Cox proportional hazards models were constructed to examine the association of hemoglobin level with sarcopenia and sarcopenia components in individuals aged 60 years or above. The subgroup analysis covered residence, body mass index level, drinking status, and smoking status were conducted. The possible difference of associations between sexes was also explored.

Results: With a total of 3,055 people, the hemoglobin concentration in people without sarcopenia, possible sarcopenia, and sarcopenia are 14.34 ± 2.22, 14.64 ± 2.27, and 13.58 ± 2.02 g/dl, respectively. Cross-sectional analysis showed strong evidence that hemoglobin was negatively associated with sarcopenia [Odds Ratio (OR) = 0.95, 95% Confidence Interval (CI): 0.90–0.99] and low height-adjusted appendicular skeletal muscle mass (OR = 0.91, 95% CI: 0.86–0.97). On average, a per 1 g/dl higher hemoglobin level was associated with 5% lower odds of sarcopenia (OR = 0.95, 95% CI: 0.90–0.98). The cohort study of 1,022 people demonstrated a statistically significant negative association of hemoglobin level with low physical performance [Hazard Ratio (HR) = 0.92, 95% CI: 0.85–0.99], merely with sarcopenia (HR = 0.92, 95% CI: 0.84–1.00) and skeletal muscle mass (HR = 0.95, 95% CI: 0.80–1.00). Sex-specific analysis suggested hemoglobin's association with sarcopenia, muscle mass, and physical performance in all sexes, with weaker magnitudes in females. Hemoglobin in urban residents and people with high body mass index (BMI) has a larger magnitude of the negative association with sarcopenia.

Discussion: Hemoglobin level associates with sarcopenia, muscle mass, and physical performance in the Chinese population aged 60 and above, with sex-specific, residence-specific, and BMI-specific effects.

KEYWORDS
China, adult, aging, hemoglobin, sarcopenia, epidemiology

Introduction

Sarcopenia is a syndrome of progressive loss of muscle mass, strength, and physiological function of the muscles as people age. It associates with mortality and a decline in physical function. The physical and functional decline associated with sarcopenia can have serious negative impacts on an individual's quality of life. People suffering from sarcopenia often experience reduced independence, which can lead to feelings of isolation and depression (1). Additionally, they are more likely to suffer from chronic illnesses, such as type 2 diabetes mellitus and heart failure, which can further reduce their quality of life (2, 3).

The prevalence of sarcopenia in older Asian individuals ranges between 2.5 and 45.7% (4). In China, this number is between 8.9 and 38.8% (5). The seventh national population census in 2020 showed that the proportion of people aged 60 years and above in China is 18.7%, a total of 260 million people (6). Risk factors related to sarcopenia, such as obesity and diabetes mellitus, have an upward trend (7, 8). These findings suggested that China has a large vulnerable population, together with a high prevalence of sarcopenia. The lack of awareness of sarcopenia in clinical practitioners further casts shadows on healthy aging (9).

Anemia is a recognized risk factor for fatigue, mortality, and decreased functional capacity in elder individuals (10). The Chinese population has a high prevalence of anemia with considerable geographic differences. In middle and eastern China, the all-age anemia prevalence is 13.4%, and this value is 34% in western China (11, 12). In the Chinese population aged over 60 and above, the age-adjusted prevalence of anemia varies from 8.5 to 35.4% (13). In Asian people, anemia is negatively associated with handgrip strength, muscle mass, and physical performance (14–16), all of which are components in sarcopenia diagnosis.

Hemoglobin is the well-established way that clinical practitioners establish the diagnosis of anemia. As anemia is associated with sarcopenia, it can be assumed that a low level of hemoglobin may associate with sarcopenia (17). Insufficient hemoglobin can affect the oxygen delivery to skeletal muscle, and negatively impact muscle strength, as observed in people with chronic hypoxia (18). Anemia is also positively associated with multiple inflammatory markers, which may affect muscle mass and physical performance in a negative way (18). A few studies have proposed that hemoglobin was positively associated with muscle strength and physical function (17, 19). Even so, these studies have mostly been with small-size samples (17), cross-sectional design (20, 21), or applied sarcopenia diagnosis criteria which is unsuitable in Asian populations (22).

Alerted by the insufficient clinical awareness of sarcopenia, the large Chinese population vulnerable to anemia and low hemoglobin, and the possible mechanism between hemoglobin and sarcopenia components, the association between hemoglobin and sarcopenia in Chinese population should be thoroughly explored. To the best of our knowledge, no large-scale studies of the Chinese population have elucidated the association of hemoglobin level with sarcopenia and its components using guidelines tailored for the Chinese. Therefore, we used a nationally representative, population-based survey [the China Health and Retirement Longitudinal Study (CHARLS)] to explore the aforementioned associations, with the aim of bridging the knowledge gap.

Methods

Study population

The CHARLS is a national, population-based survey focusing on Chinese aged 45 years and above. A total of 450 representative communities from 28 provinces were selected using a multistep probability sampling strategy (23). The first survey was started in 2011, and participants were followed every 2 years. A total of 17,705 respondents were interviewed in 2011, 18,605 respondents were interviewed in 2013, and 21,095 people were interviewed in 2015. Because biomarker and blood tests were only conducted in 2011 and 2015, data from these years were used. The inclusion criteria were (1) individuals aged 60 years or above in 2011; (2) available data regarding sarcopenia status; and (3) the possession of blood test data in 2011. People missing demographic or health information were excluded.

This study contained two sub-studies. (1) A cross-sectional analysis of the CHARLS 2011 population. Of the total of 17,705 participants, 14,650 people were excluded because of missing blood test data ($n = 8{,}293$), no sarcopenia relevant data ($n = 2{,}341$), no demographic or health information ($n = 808$), and ages below 60 years ($n = 3{,}208$). A total of 3,055 participants remained for the analysis. (2) In the cohort analysis, we further excluded 831 people who had either possible sarcopenia or sarcopenia in 2011 and removed 1,202 participants who had no sarcopenia data in 2015; thus, constructed a cohort of 1,022 people.

The Institutional Review Board at Peking University approved CHARLS (approval number: IRB00001052-11014 for biomarker collection; IRB00001052-11015 for main household survey including anthropometrics), and all of the participants were required to provide written informed consent before joining CHARLS.

Assessment of sarcopenia and its components

The first expert consensus on sarcopenia in Chinese population (5) was published in 2021. The Chinese consensus highly considered the guideline issued by the Asian Working Group for Sarcopenia (AWGS) and recommended the use of its cutoff values for sarcopenia diagnosis in Chinese population (24). Participants' sarcopenia status was assessed by three components: appendicular skeletal muscle mass (ASM), muscle strength, and physical performance.

The ASM was estimated using a validated equation derived from Chinese adults (25). The equation has been applied in research which has similar study populations as that of our study (26, 27). The equation is:

$$ASM = 0.193^{*}weight(inkg) + 0.107^{*}height(incm) - 4.157^{*}sex(Male = 1, Female = 2) - 0.037^{*}age(inyear) - 2.631$$

Participants' height and weight were measured using a stadiometer and a digital floor scale, respectively, to the nearest

0.1 cm and 0.1 kg. The ASM derived from the abovementioned equation is consistent with the result from dual X-ray absorptiometry (DXA) (25). In clinical practice, DXA requires specialized radiology equipment and experienced physicians to ensure testing accuracy. Bioelectrical impedance analysis (BIA) is a less expensive assessment technology and requires no specialists to perform. Both DXA and BIA are recommended for muscle mass evaluation, and their results are interchangeable (24, 28). BIA criteria were used in this study to make findings applicable in a more generalized setting. Low muscle mass was defined as a height-adjusted muscle mass (ASM/Height^2) <7.0 kg/m^2 for males and below 5.7 kg/m^2 for females (5).

Muscle strength was measured *via* handgrip strength, which was evaluated by asking participants to hold the dynamometer at a right angle (90°) and squeeze a YuejianTM WL-1000 dynamometer (Nantong Yuejian Physical Measurement Instrument Co., Ltd., Nantong, China) two times in each hand as hard as possible. The maximum reading was used for the sarcopenia diagnosis. The cutoff points for low muscle strength were 28 kg for males and 18 kg for females. CHARLS used a 5-time chair stand test to evaluate physical performance. The cutoff value of low physical performance was a test time $\geq$ 12 s for all sexes (29).

Possible sarcopenia was defined as either low muscle strength or low physical performance without low muscle mass. Sarcopenia was diagnosed when low muscle mass plus either low muscle strength or low physical performance was identified. Severe sarcopenia was defined as the co-existence of low muscle mass, low muscle strength, and low physical performance. As only 166 (5.43%) participants had severe sarcopenia at baseline, severe sarcopenia was merged into sarcopenia to avoid sparse data bias (30). Participants were categorized into no sarcopenia ($n = 1{,}618$), possible sarcopenia ($n = 726$), and sarcopenia ($n = 711$).

Blood sample collection and analysis

The CHARLS project collaborated with the Chinese Center for Disease Control and Prevention (China CDC) to collect and process blood samples. Three tubes of blood were collected from each participant. One tube was immediately stored at 4°C and transported to the nearest CDC center or health center for complete blood count; the median time from collection to analysis was 97 min. The other two tubes were stored at −80°C for bioassay analysis at a national certified lab at Capital Medical University (31). Cystatin C is a protein associated with muscle mass in some chronic disease patients (32). In the CHARLS project, it was measured using a particle-enhanced turbimetric assay with a detection range of 0.5–8.0 mg/L.

Covariates

CHARLS participants were interviewed using a computer-aided structured questionnaire. Demographic information, such as age, sex, socioeconomic level, and urban/rural residence, was collected. Socioeconomic level was collected from the participants' self-evaluation scale. Health status and functioning data, including smoking, drinking, body mass index (BMI), blood pressure, and diagnoses of hypertension/dyslipidemia/diabetes/kidney disease/heart failure/rheumatism, were collected. A participant was identified as a patient with the abovementioned diseases if the participant had been diagnosed by physicians or was on medication at the time of interview. Hypertension was defined as systolic blood pressure $\geq$ 140 mmHg and/or diastolic pressure $\geq$ 90 mmHg or if the participant was on medications by the time of the interview. Diabetes was identified if the participant was on antidiabetic agents or had plasma glucose $\geq$ 200 mg/dl. BMI was categorized into underweight (below 18.5 kg/m^2), normal weight (18.5–23.9 kg/m^2), and overweight or obese (24 kg/m^2 and above).

Statistical analysis

Continuous data were presented as the mean with standard deviation (SD) or median with interquartile range (IQR). Categorical data are presented as *n* (%). The baseline data of all 6,263 participants were summarized and stratified by their sarcopenia status in the baseline year 2011. Comparisons of baseline characteristics among the groups were conducted using the Kruskal–Wallis test. Logistic regression was then performed to identify the association of hemoglobin with sarcopenia and with sarcopenia components (ASM, muscle strength, and physical performance).

All the abovementioned associations were then evaluated in a cohort analysis. As the sarcopenia test was conducted on the day of the interview, the follow-up period was defined as the interval between the interview day in 2011 and the interview day in 2015. Schoenfeld's residuals showed no violation of the proportional hazards assumption ($P = 0.44$). Cox proportional hazard models were used to calculate hazard ratios (HRs) with 95% confidence intervals (CIs). The sex-specific association was then explored. Finally, analyses were conducted in the following subgroups: residence, BMI level, drinking, and smoking. All the analyses were performed using STATA 16.0/MP (StataCorp, USA). A two-sided *P*-value $<$ 0.05 was considered to be statistically significant.

Results

Baseline statistics of the study population

The baseline statistics of the study population are presented in Table 1, as stratified by sarcopenia status in the baseline year. In the total of 3,055 participants, the prevalence of sarcopenia was 23.27%, and the prevalence of possible sarcopenia was 23.76%. Sarcopenia was more common in people of higher age, females, rural residents, unmarried people, less educated people, low socioeconomic level people, and people with low BMI/arthritis/rheumatism. People with higher cystatin C and lower hemoglobin were more commonly found to have sarcopenia (Table 1).

TABLE 1 Baseline characteristics of 3,055 CHARLS participants, stratified by their sarcopenia status in year 2011.

Characteristics	No sarcopenia	Possible sarcopenia	Sarcopenia
Number of people, *n* (row %)	1,618 (52.96)	726 (23.76)	711 (23.27)
Age (year), mean (SD)	66.75 (5.48)	68.28 (6.10)	71.84 (6.81)
Male, *n* (%)	909 (56.18)	401 (55.23)	262 (36.85)
Urban residence, *n* (%)	575 (35.54)	270 (37.19)	191 (26.86)
Married, *n* (%)	1,360 (84.05)	597 (82.23)	504 (70.89)
Smoking, *n* (%)	743 (45.92)	335 (46.14)	253 (35.58)
Drinking, *n* (%)	583 (36.03)	199 (27.41)	177 (24.89)
Educational level, *n* (%)			
No formal education	482 (29.79)	263 (36.23)	398 (55.98)
Primary	788 (48.70)	349 (48.07)	268 (37.69)
Secondary	313 (19.34)	109 (15.01)	44 (6.19)
Tertiary and above	35 (2.16)	5 (0.69)	1 (0.14)
Socioeconomic level, *n* (%)			
Above average	50 (3.09)	25 (3.44)	20 (2.81)
Average	893 (55.19)	386 (53.17)	355 (49.93)
Relatively poor	501 (30.96)	219 (30.17)	210 (29.54)
Poor	174 (10.75)	96 (13.22)	126 (17.72)
BMI (kg/m^2), mean (SD)	22.98 (3.70)	25.24 (3.40)	19.90 (2.19)
Systolic blood pressure (mmHg), mean (SD)	134.59 (22.11)	138.06 (22.33)	136.07 (25.07)
Diastolic blood pressure (mmHg), mean (SD)	74.85 (11.45)	76.27 (11.86)	73.02 (12.23)
Comorbidities, *n* (%)			
Hypertension	467 (28.86)	306 (42.15)	181 (25.46)
Dyslipidemia	164 (10.14)	98 (13.50)	46 (6.47)
Diabetes	99 (6.12)	68 (9.37)	26 (3.66)
Kidney disease	101 (6.24)	67 (9.23)	35 (4.92)
Heart disease	224 (13.84)	139 (19.15)	116 (16.32)
Arthritis or rheumatism	569 (35.17)	301 (41.46)	306 (43.04)
Cystatin C (mg/l), mean (SD)	1.08 (0.27)	1.11 (0.29)	1.16 (0.34)
Hemoglobin (g/dl), mean (SD)	14.34 (2.22)	14.64 (2.27)	13.58 (2.02)
Sarcopenia components, mean (SD)			
Height-adjusted ASM (kg/m^2)	6.68 (1.13)	7.10 (0.86)	5.57 (0.91)
Handgrip strength (kg)	33.02 (8.34)	28.20 (9.07)	23.34 (7.68)
Five-time chair stand time (s)	9.16 (1.76)	15.42 (6.20)	14.97 (5.33)

% was shown as column percentage unless otherwise specified.
ASM, appendicular skeletal muscle mass; BMI, body mass index; SD, standard deviation.

Cross-sectional analysis of the association of hemoglobin with sarcopenia and its components

After adjustments for demographic factors, a very significant association ($P < 0.001$) was found between hemoglobin and sarcopenia. This association was not significantly changed ($P = 0.04$) with further adjustments for health-related factors. On average, a per 1 g/dl higher hemoglobin level was associated with 5% lower odds of sarcopenia (OR = 0.95, 95% CI: 0.90–0.98) (Table 2).

Among sarcopenia components, a statistical association was found between hemoglobin and low height-adjusted ASM. On average, a per 1 g/dl elevated hemoglobin level was associated with 9% lower odds of having low height-adjusted ASM (OR = 0.91, 95% CI: 0.86–0.97). It should be noted that although no statistical

TABLE 2 Cross-sectional associations among hemoglobin, sarcopenia, and sarcopenia components in baseline year 2011.

	Model 1[a]		Model 2[b]		Model 3[c]	
	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value
Sarcopenia						
Hemoglobin	0.89 (0.85–0.93)	<0.001	0.94 (0.90–0.99)	0.02	0.95 (0.90–0.99)	0.04
COMPONENT OF SARCOPENIA						
Low height-adjusted ASM						
Hemoglobin	0.85 (0.82–0.89)	<0.001	0.90 (0.86–0.95)	<0.001	0.91 (0.86–0.97)	0.002
Low muscle strength						
Hemoglobin	0.94 (0.90–0.99)	0.02	0.96 (0.91–1.01)	0.08	0.96 (0.92–1.01)	0.16
Low physical performance						
Hemoglobin	1.03 (0.99–1.07)	0.11	1.02 (0.99–1.06)	0.19	1.02 (0.99–1.06)	0.22

ASM, appendicular skeletal muscle mass; CI, confidence interval; OR, odds ratio.
[a] Adjusted for sex, age, residence.
[b] Adjusted as Model 1 with further adjustments for marital status, socioeconomic level, education, smoking, drinking, body mass index.
[c] Adjusted as Model 2 with further adjustment for systolic blood pressure, diastolic blood pressure, hypertension, dyslipidemia, chronic kidney disease, heart disease, arthritis or rheumatism, cystatin C.

significance ($P = 0.16$) was found in the association between hemoglobin and muscle strength, the upper 95% CI is close to 1.00. No evidence ($P = 0.22$) between hemoglobin and low physical performance was found.

Cohort analysis of the association of hemoglobin with sarcopenia and its components

A total of 1,022 people who had no sarcopenia in 2011 were followed up to 2015; 165 people (13.41%) were diagnosed with sarcopenia, with an incidence rate of 336.61 per 10,000 person-years.

After adjusting for multiple covariates, consistent evidence was found between baseline hemoglobin and sarcopenia (HR = 0.92, 95% CI: 0.84–1.00), low height-adjusted ASM (HR = 0.95, 95% CI: 0.90–1.00), and low physical performance (HR = 0.92, 95% CI: 0.85–0.99). No association between hemoglobin and low muscle strength was observed (Table 3).

Due to the difference in the cutoff value of sarcopenia criteria between sexes, the sex-specific association between baseline hemoglobin and sarcopenia was explored. In males, hemoglobin was associated with sarcopenia, and a per 1 g/dl increase in hemoglobin was associated with a 10% lower rate of sarcopenia (HR = 0.90, 95% CI: 0.83–0.99). Hemoglobin in males was also statistically associated with low height-adjusted ASM (HR = 0.92, 95% CI: 0.89–0.96) and with low physical performance (HR = 0.91, 95% CI: 0.85–0.97). In females, hemoglobin was found to be marginally associated with sarcopenia (HR = 0.92, 95% CI: 0.84–1.00) and with low height-adjusted ASM (HR = 0.96, 95% CI: 0.93–1.00); strong evidence of association was also found in low physical performance (HR = 0.92, 95% CI: 0.86–0.99). Hemoglobin was not evidently associated with low muscle strength in all sexes (Supplementary Table S1).

Subgroup analysis for baseline hemoglobin and its association with sarcopenia

Figure 1 showed that the association between hemoglobin and sarcopenia was stronger in urban residents (HR = 0.89, 95% CI: 0.80–0.98). Among people of different BMI levels, the hemoglobin-sarcopenia association was stronger in people with higher BMI levels. In the overweight/obese group, a per 1 g/dl higher hemoglobin was associated with a 20% lower hazard rate of sarcopenia (HR = 0.80, 95% CI: 0.72–0.89), with very strong evidence ($P < 0.001$). No evidence was found in underweight people. The hemoglobin-sarcopenia association was similar in people with various drinking and smoking statuses (Figure 1).

Discussion

In this study, the cross-sectional analysis demonstrated hemoglobin in Chinese individuals aged 60 and above was negatively associated with sarcopenia and low height-adjusted ASM. The cohort study showed that in the general population, hemoglobin was negatively associated with sarcopenia, low muscle mass, and low physical performance. In both sexes, hemoglobin was negatively associated with sarcopenia, low muscle mass, and physical performance, although the magnitude of association varies. No evidence of the association between hemoglobin and muscle strength was found. Subgroup analyses demonstrated that urban residents and people with higher BMI levels had a large magnitude of hemoglobin-sarcopenia association.

TABLE 3 Longitudinal associations among baseline hemoglobin level, sarcopenia, and sarcopenia components, 2011–2015.

	Model 1[a]		Model 2[b]		Model 3[c]	
	HR (95%CI)	*P*-value	HR (95%CI)	*P*-value	HR (95%CI)	*P*-value
Sarcopenia						
Hemoglobin	0.87 (0.79–0.95)	0.003	0.92 (0.84–1.01)	0.08	0.92 (0.84–1.00)	0.05
COMPONENT OF SARCOPENIA						
Low Height-adjusted ASM						
Hemoglobin	0.90 (0.85–0.95)	<0.001	0.94 (0.89–1.00)	0.04	0.95 (0.90–1.00)	0.05
Low muscle strength						
Hemoglobin	0.94 (0.87–1.03)	0.17	0.97 (0.89–1.06)	0.52	0.98 (0.90–1.06)	0.60
Low physical performance						
Hemoglobin	0.92 (0.83–0.99)	0.04	0.92 (0.85–0.99)	0.03	0.92 (0.85–0.99)	0.03

ASM, appendicular skeletal muscle mass; CI, confidence interval; HR, hazard ratio.
[a] Adjusted for sex, age, residence.
[b] Adjusted as Model 1 with further adjustments for marital status, socioeconomic level, education, smoking, drinking, body mass index.
[c] Adjusted as Model 2 with further adjustment for systolic blood pressure, diastolic blood pressure, hypertension, dyslipidemia, chronic kidney disease, heart disease, arthritis or rheumatism, cystatin C.

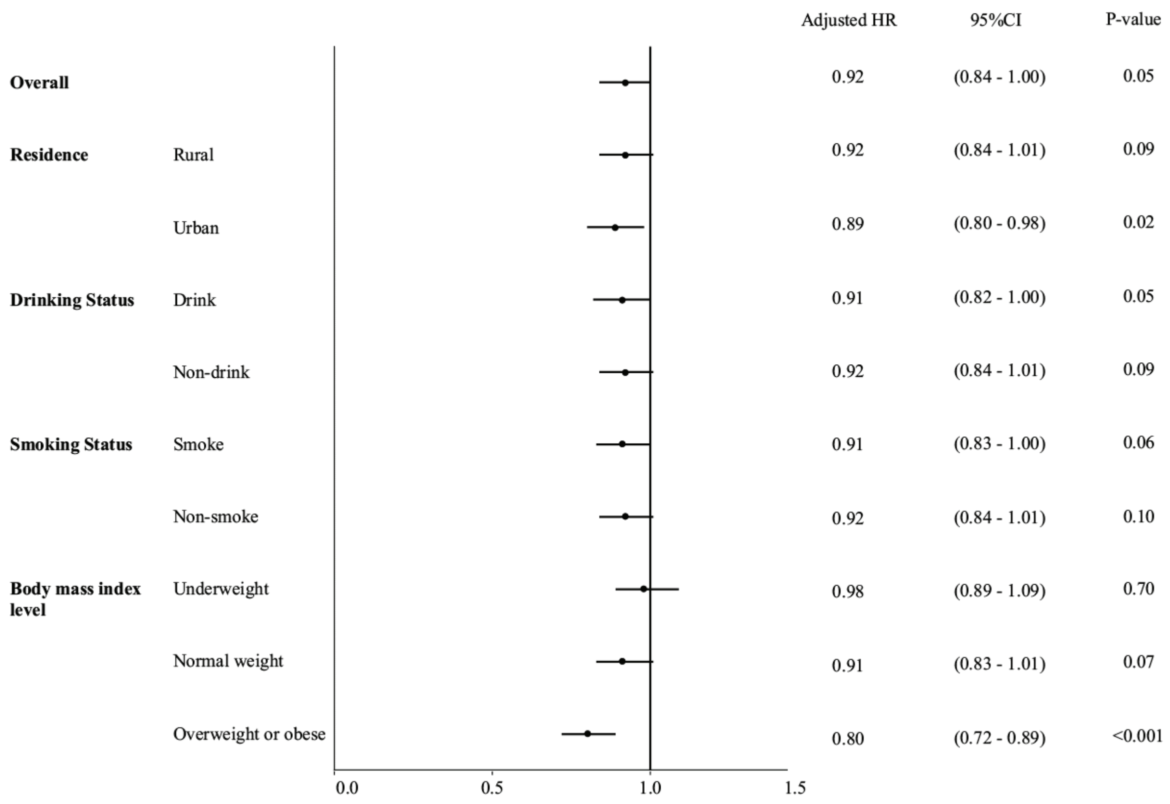

FIGURE 1
Forest plot for multivariable Cox regression results to show the sex-specific association between hemoglobin and sarcopenia, stratified by residence, body mass index level, drinking status, and smoking status.

The overall prevalence of sarcopenia in the study population was 13.41%, with a higher prevalence in females, similar to other studies on Chinese population (33, 34). Our findings were largely consistent with several previous studies (18, 21). However, there were still some discrepancies in this field. A cross-sectional study on a Taiwanese population demonstrated that hemoglobin was only associated with physical performance and muscle strength, not with sarcopenia or muscle mass (17). Erythropoietin receptors are expressed in human skeletal muscle (35). Skeletal muscle mass is independently associated with body responsiveness to erythropoietin stimulating agents (36). It is fairly possible that insufficient skeletal muscle led to decreased hemoglobin production, caused a reverse causality that could not be ruled out in a cross-sectional design and biased the result in that Taiwanese study.

There is a paucity of longitudinal research on hemoglobin and its association with sarcopenia, and there is even more scarce research on sex-specific associations. Along with aging, the decline in serum testosterone in males is associated with compromised hematopoiesis, further inhibiting hemoglobin production (37–39). The decline in hemoglobin in men usually starts in their 30s, whereas hemoglobin in women is slightly increased after menopause before starting to decline in their 60s (40). In the study population, the hemoglobin level in the oldest quartile of males (mean age: 77.5 years) was on average 92.5% of that in the youngest quartile (mean age: 61.5 years); in females, the mean hemoglobin in the oldest quartile (mean age: 77.4 years) was 96.4% of that in the youngest quartile (mean age: 61 years). The above relatively smaller decline in hemoglobin in females as compared to males may explain the sex-specific differences in the magnitude of the association of hemoglobin with sarcopenia, ASM, and physical performance.

This study did not find evidence of the association of hemoglobin with muscle strength in either the cross-sectional or cohort analyses. This finding was consistent with a study on older individuals (41). Yet, another study demonstrated hemoglobin was associated with handgrip strength in older individuals (42). It is possible the higher average age of the participants (over 75 years) and the different sample selections of the above study may justify the conflicting results.

In the cohort study, we found a consistent association of hemoglobin with physical performance. The current research on the association between hemoglobin and physical performance remains controversial. Studies using Functional Independence Measure (43) demonstrated the association of hemoglobin with physical function and performance. A systematic review of fifteen randomized clinical trials and five observational studies reported a negative association between hemoglobin and fatigue but not with physical function (44). We solely evaluated physical performance by the 5-time chair stand test without the gait speed test, and thus the evaluation may not fully reflect the participants' actual physical performance. The CHARLS gait speed test was set at a 2.5 m distance, which was much shorter than the recommended six meters (24). The validity of the 2.5 m distance is unclear, although the 3-meter, 6-meter, and longer distance gait speed tests have been validated (45, 46). As participants were more capable of completing a shorter distance, the 2.5 m test may likely overestimate the gait speed. Only 41.90% of people had both chair stand test and gait speed test records. Statistically significant differences in height, weight, and handgrip strength were found between individuals with gait speed records and those without. Using people with available gait speed in this study will heavily limit the sample size and may bias the study result.

Urban residents and obese/overweight people had a larger magnitude of hemoglobin-sarcopenia association; the underlying mechanism accounting for the larger magnitude remains unclear. Urban residents are known to have higher hemoglobin levels than rural residents (47), and a higher BMI level has an inverse association with hemoglobin in older Chinese people (48). It may be possible that there is a threshold, and only an over-threshold hemoglobin level is associated with sarcopenia. An in-depth analysis of urban/rural residents and people of different BMI groups is needed to further explore the abovementioned findings.

From a perspective of primary prevention and public health, increasing hemoglobin levels in people aged 60 and above can be better achieved through a multidisciplinary approach. Providing access to nutrient-dense foods that are rich in iron, vitamin B12, and folic acid. Older adults may have a reduced appetite or difficulty chewing, so it is important to provide meals that are easy to prepare, chew, and digest. In addition to dietary changes, regular exercise can help increase hemoglobin levels while strengthening muscle and improving physical performance. Low-impact aerobic activities such as walking, swimming, and biking may help increase circulation and promote healthy oxygen levels in the body. Moderate strength training can also help increase hemoglobin levels and build muscle strength to prevent sarcopenia (49). Excessive alcohol intake (over 2 alcoholic drinks/day) should be restricted as they can lead to a decrease in hemoglobin levels (50). It should consider the unique needs and challenges older adults face when designing interventions and involve healthcare providers, community organizations, and family caregivers in the process.

Despite all the efforts made in this study, there were several limitations. First, the core element of our research, the ASM, was calculated using a validated formula instead of BIA/DXA methods. Admittedly, using the formula may impair the generalization of our findings in non-Chinese population. However, this is unavoidable because our study was a secondary research using existing data. Considering the scale and representativeness of CHARLS, along with the consistence in our findings, we believe that this study makes its contribution to solving the urgent public health issue brought by sarcopenia. Readers are advised to be aware of the possible bias of ASM evaluation. Second, gait speed is an indicator of the overall health of the elderly (51). Without adjusting gait speed, our findings may be biased toward the null. Third, confounding factors, such as inflammatory biomarkers and dietary patterns, were not adjusted due to data availability. All this can confound the results. Finally, selection bias, including volunteer bias, should be considered when interpreting our results.

To conclude, our study demonstrated that hemoglobin level is negatively associated with sarcopenia in the Chinese population aged 60 and above. Males, urban residents, and people with a high BMI have a larger magnitude of the negative association between hemoglobin level and sarcopenia. Along with the high prevalence of sarcopenia and an aging society, our findings may generate meaningful implications for preventing sarcopenia and promoting healthy aging in China.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: https://charls.pku.edu.cn/.

Ethics statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The Institutional Review Board at Peking University approved CHARLS (approval number: IRB00001052-11014 for biomarker collection; IRB00001052-11015 for main household survey including anthropometrics), and all of the participants were required to provide written informed consent before joining CHARLS. Data were fully anonymized and it is impossible to re-identify any participants.

Author contributions

QL and CH conceived the protocol. QL, JY, MZ, ZW, and YG contributed to the analysis and interpretation of data. QL and JY drafted the manuscript. QL critically revised the manuscript. All authors agree to be fully accountable for ensuring the integrity and accuracy of the work and read and approved the final manuscript.

Funding

This research was supported by 1·3·5 project for disciplines of excellence–Clinical Research Incubation Project, West China Hospital, Sichuan University (2021HXFH063).

Acknowledgments

This study was based on the baseline of the China Health and Retirement Longitudinal Study (CHARLS). Authors would like to thank the CHARLS research team, field staff, and all the CHARLS participants for their time and efforts.

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.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1081843/full#supplementary-material

References

1. 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) 13:128–44. doi: 10.1002/jcsm.12908

2. Mesinovic J, Zengin A, De Courten B, Ebeling PR, Scott D. Sarcopenia and type 2 diabetes mellitus: a bidirectional relationship. *Diabetes Metab Syndr Obes.* (2019) 12:1057–72. doi: 10.2147/DMSO.S186600

3. Zhang Y, Zhang J, Ni W, Yuan X, Zhang H, Li P, et al. Sarcopenia in heart failure: a systematic review and meta-analysis. *ESC Heart Failure.* (2021) 8:1007–17. doi: 10.1002/ehf2.13255

4. Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, et al. Sarcopenia in Asia: consensus report of the Asian working group for sarcopenia. *J Am Med Dir Assoc.* (2014) 15:95–101. doi: 10.1016/j.jamda.2013.11.025

5. Liu J, Ding Q, Zhou B, Liu X, Liu J, Liu Y, et al. Chinese expert consensus on diagnosis and treatment for elderly with sarcopenia. *Chin J Geriatr.* (2021) 40:943–52. doi: 10.3760/cma.j.issn.0254-9026.2021.08.001

6. Akimov AV, Gemueva KA, Semenova NK. The seventh population census in the PRC: results and prospects of the country's demographic development. *Her Russ Acad Sci.* (2021) 91:724–35. doi: 10.1134/S1019331621060083

7. Ma S, Xi B, Yang L, Sun J, Zhao M, Bovet P. Trends in the prevalence of overweight, obesity, and abdominal obesity among Chinese adults between 1993 and 2015. *Int J Obes.* (2021) 45:427–37. doi: 10.1038/s41366-020-00698-x

8. Tyrovolas S, Koyanagi A, Olaya B, Ayuso-Mateos JL, Miret M, Chatterji S, et al. Factors associated with skeletal muscle mass, sarcopenia, and sarcopenic obesity in older adults: a multi-continent study. *J Cachexia Sarcopenia Muscle.* (2016) 7:312–21. doi: 10.1002/jcsm.12076

9. Marzetti E, Calvani R, Tosato M, Cesari M, Di Bari M, Cherubini A, et al. Sarcopenia: an overview. *Aging Clin Exp Res.* (2017) 29:11–7. doi: 10.1007/s40520-016-0704-5

10. Denny SD, Kuchibhatla MN, Cohen HJ. Impact of anemia on mortality, cognition, and function in community-dwelling elderly. *Am J Med.* (2006) 119:327–34. doi: 10.1016/j.amjmed.2005.08.027

11. Li L, Luo R, Medina A, Rozelle S. The prevalence of anemia in central and eastern China: evidence from the China health and nutrition survey. *Southeast Asian J Trop Med Public Health.* (2015) 46:306–21.

12. Luo R, Wang X, Zhang L, Liu C, Shi Y, Miller G, et al. High anemia prevalence in western China. *Southeast Asian J Trop Med Public Health.* (2011) 42:1204–13.

13. Wang Y, Ping YJ, Jin HY, Ge N, Wu C. Prevalence and health correlates of anaemia among community-dwelling Chinese older adults: the China Health and Retirement Longitudinal Study. *BMJ Open.* (2020) 10:e038147. doi: 10.1136/bmjopen-2020-038147

14. Sutandyo N, Rinaldi I, Sari NK, Winston K. Prevalence of anemia and factors associated with handgrip strength in Indonesian elderly population. *Cureus.* (2022) 14:e25290. doi: 10.7759/cureus.25290

15. Moon J-H, Kong M-H, Kim H-J. Relationship between low muscle mass and anemia in Korean elderly men: using the Korea National Health and Nutrition Examination Survey (KNHANES IV–V). *J Clin Gerontol Geriatr.* (2015) 6:115–9. doi: 10.1016/j.jcgg.2015.03.007

16. Lee CT, Chen MZ, Yip CYC, Yap ES, Lee SY, Merchant RA. Prevalence of anemia and its association with frailty, physical function and cognition in community-dwelling older adults: findings from the HOPE study. *J Nutr Health Aging.* (2021) 25:679–87. doi: 10.1007/s12603-021-1625-3

17. Tseng SH, Lee WJ, Peng LN, Lin MH, Chen LK. Associations between hemoglobin levels and sarcopenia and its components: results from the I-Lan longitudinal study. *Exp Gerontol.* (2021) 150:111379. doi: 10.1016/j.exger.2021.111379

18. Cesari M, Penninx BWJH, Lauretani F, Russo CR, Carter C, Bandinelli S, et al. Hemoglobin levels and skeletal muscle: results from the InCHIANTI study. *J Gerontol Ser A.* (2004) 59:M249–M54. doi: 10.1093/gerona/59.3.M249

19. Aung KC, Feng L, Yap KB, Sitoh YY, Leong IY, Ng TP. Serum albumin and hemoglobin are associated with physical function in community-living older persons in Singapore. *J Nutr Health Aging.* (2011) 15:877–82. doi: 10.1007/s12603-011-0120-7

20. Hai S, Cao L, Wang H, Zhou J, Liu P, Yang Y, et al. Association between sarcopenia and nutritional status and physical activity among community-dwelling Chinese adults aged 60 years and older. *Geriatr Gerontol Int.* (2017) 17:1959–66. doi: 10.1111/ggi.13001

21. Wu X, Li X, Xu M, Zhang Z, He L, Li Y. Sarcopenia prevalence and associated factors among older Chinese population: findings from the China Health and retirement longitudinal study. *PLoS ONE.* (2021) 16:e0247617. doi: 10.1371/journal.pone.0247617

22. Hirani V, Naganathan V, Blyth F, Le Couteur DG, Seibel MJ, Waite LM, et al. Low hemoglobin concentrations are associated with sarcopenia, physical performance, and disability in older Australian men in cross-sectional and longitudinal analysis: the concord health and ageing in men project. *J Gerontol A.* (2016) 71:1667–75. doi: 10.1093/gerona/glw055

23. Zhao Y, Hu Y, Smith JP, Strauss J, Yang G. Cohort profile: the China health and retirement longitudinal study (CHARLS). *Int J Epidemiol.* (2014) 43:61–8. doi: 10.1093/ije/dys203

24. Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K, et al. Asian working group for sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc.* (2020) 21:300–7.e2. doi: 10.1016/j.jamda.2019.12.012

25. Wen X, Wang M, Jiang CM, Zhang YM. Anthropometric equation for estimation of appendicular skeletal muscle mass in Chinese adults. *Asia Pac J Clin Nutr.* (2011) 20:551–6.

26. Hu X, Zhang L, Wang H, Hao Q, Dong B, Yang M. Malnutrition-sarcopenia syndrome predicts mortality in hospitalized older patients. *Sci Rep.* (2017) 7:3171. doi: 10.1038/s41598-017-03388-3

27. Yang M, Hu X, Wang H, Zhang L, Hao Q, Dong B. Sarcopenia predicts readmission and mortality in elderly patients in acute care wards: a prospective study. *J Cachexia Sarcopenia Muscle.* (2017) 8:251–8. doi: 10.1002/jcsm.12163

28. Achamrah N, Colange G, Delay J, Rimbert A, Folope V, Petit A, et al. Comparison of body composition assessment by DXA and BIA according to the body mass index: a retrospective study on 3655 measures. *PLoS ONE.* (2018) 13:e0200465. doi: 10.1371/journal.pone.0200465

29. Zuo M, Gan C, Liu T, Tang J, Dai J, Hu X. Physical predictors of cognitive function in individuals with hypertension: evidence from the CHARLS basline survey. *West J Nurs Res.* (2019) 41:592–614. doi: 10.1177/0193945918770794

30. Greenland S, Mansournia MA, Altman DG. Sparse data bias: a problem hiding in plain sight. *BMJ.* (2016) 352:i1981. doi: 10.1136/bmj.i1981

31. Zhao Y, Crimmins E, Hu P, Hu Y, Ge T, Kim JK, et al. *China Health and Retirement Longitudinal Study 2011-2012 National Baseline Blood Data User's Guide.* China Center for Economic Research, Peking University (2014). Available from: https://charls.pku.edu.cn/wenjian/xuejianshujuyonghushiyongshouce.pdf (accessed October 15, 2022).

32. Ivey-Miranda JB, Inker LA, Griffin M, Rao V, Maulion C, Turner JM, et al. Cystatin C and muscle mass in patients with heart failure. *J Card Fail.* (2021) 27:48–56. doi: 10.1016/j.cardfail.2020.07.013

33. Gao L, Jiang J, Yang M, Hao Q, Luo L, Dong B. Prevalence of sarcopenia and associated factors in Chinese community-dwelling elderly: comparison between rural and urban areas. *J Am Med Dir Assoc.* (2015) 16:1003.e1–e6. doi: 10.1016/j.jamda.2015.07.020

34. Liu X, Hou L, Xia X, Liu Y, Zuo Z, Zhang Y, et al. Prevalence of sarcopenia in multi ethnics adults and the association with cognitive impairment: findings from West-China health and aging trend study. *BMC Geriatr.* (2020) 20:63. doi: 10.1186/s12877-020-1468-5

35. Rundqvist H, Rullman E, Sundberg CJ, Fischer H, Eisleitner K, Stahlberg M, et al. Activation of the erythropoietin receptor in human skeletal muscle. *Eur J Endocrinol.* (2009) 161:427–34. doi: 10.1530/EJE-09-0342

36. Takata T, Mae Y, Yamada K, Taniguchi S, Hamada S, Yamamoto M, et al. Skeletal muscle mass is associated with erythropoietin response in hemodialysis patients. *BMC Nephrol.* (2021) 22:134. doi: 10.1186/s12882-021-02346-6

37. Zirkin BR, Tenover JL. Aging and declining testosterone: past, present, and hopes for the future. *J Androl.* (2012) 33:1111–8. doi: 10.2164/jandrol.112.017160

38. Ellegala DB, Alden TD, Couture DE, Vance ML, Maartens NF, Laws ER. Anemia, testosterone, and pituitary adenoma in men. *J Neurosurg.* (2003) 98:974–7. doi: 10.3171/jns.2003.98.5.0974

39. Wittert GA, Chapman IM, Haren MT, Mackintosh S, Coates P, Morley JE. Oral testosterone supplementation increases muscle and decreases fat mass in healthy elderly males with low-normal gonadal status. *J Gerontol A Biol Sci Med Sci.* (2003) 58:618–25. doi: 10.1093/gerona/58.7.M618

40. Jorgensen JM, Crespo-Bellido M, Dewey KG. Variation in hemoglobin across the life cycle and between males and females. *Ann N Y Acad Sci.* (2019) 1450:105–25. doi: 10.1111/nyas.14096

41. Ferrari M, Manea L, Anton K, Bruzzone P, Meneghello M, Zamboni F, et al. Anemia and hemoglobin serum levels are associated with exercise capacity and quality of life in chronic obstructive pulmonary disease. *BMC Pulm Med.* (2015) 15:58. doi: 10.1186/s12890-015-0050-y

42. Penninx BW, Pahor M, Cesari M, Corsi AM, Woodman RC, Bandinelli S, et al. Anemia is associated with disability and decreased physical performance and muscle strength in the elderly. *J Am Geriatr Soc.* (2004) 52:719–24. doi: 10.1111/j.1532-5415.2004.52208.x

43. Yoshimura Y, Wakabayashi H, Shiraishi A, Nagano F, Bise T, Shimazu S. Hemoglobin improvement is positively associated with functional outcomes in stroke patients with anemia. *J Stroke Cerebrovasc Dis.* (2021) 30:105453. doi: 10.1016/j.jstrokecerebrovasdis.2020.105453

44. Guedes M, Guetter CR, Erbano LHO, Palone AG, Zee J, Robinson BM, et al. Physical health-related quality of life at higher achieved hemoglobin levels among chronic kidney disease patients: a systematic review and meta-analysis. *BMC Nephrol.* (2020) 21:259. doi: 10.1186/s12882-020-01912-8

45. Lyons JG, Heeren T, Stuver SO, Fredman L. Assessing the agreement between 3-meter and 6-meter walk tests in 136 community-dwelling older adults. *J Aging Health.* (2015) 27:594–605. doi: 10.1177/0898264314556987

46. Kim HJ, Park I, Lee HJ, Lee O. The reliability and validity of gait speed with different walking pace and distances against general health, physical function, and chronic disease in aged adults. *J Exerc Nutrition Biochem.* (2016) 20:46–50. doi: 10.20463/jenb.2016.09.20.3.7

47. Li M, Hu Y, Mao D, Wang R, Chen J, Li W, et al. Prevalence of anemia among Chinese rural residents. *Nutrients.* (2017) 9:192. doi: 10.3390/nu9030192

48. Ni W, Yuan X, Sun Y, Zhang H, Zhang Y, Xu J. Anaemia and associated factors among older adults in an urban district in China: a large-scale cross-sectional study. *BMJ Open.* (2022) 12:e056100. doi: 10.1136/bmjopen-2021-056100

49. Hu M, Lin W. Effects of exercise training on red blood cell production: implications for anemia. *Acta Haematol.* (2012) 127:156–64. doi: 10.1159/000335620

50. Ioannou GN, Dominitz JA, Weiss NS, Heagerty PJ, Kowdley KV. The effect of alcohol consumption on the prevalence of iron overload, iron deficiency, and iron deficiency anemia. *Gastroenterology.* (2004) 126:1293–301. doi: 10.1053/j.gastro.2004.01.020

51. Pirker W, Katzenschlager R. Gait disorders in adults and the elderly. *Wien Klin Wochenschr.* (2017) 129:81–95. doi: 10.1007/s00508-016-1096-4

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 23 March 2023
DOI 10.3389/fpubh.2023.1113255

OPEN ACCESS

EDITED BY
Hidenori Arai,
National Center for Geriatrics and Gerontology (NCGG), Japan

REVIEWED BY
Takeshi Nakagawa,
National Center for Geriatrics and Gerontology (NCGG), Japan
Soham Al Snih,
University of Texas Medical Branch at Galveston, United States
Kuntjoro Harimurti,
University of Indonesia, Indonesia

*CORRESPONDENCE
Shuichi Obuchi
✉ obuchipc@tmig.or.jp

SPECIALTY SECTION
This article was submitted to Aging and Public Health, a section of the journal Frontiers in Public Health

RECEIVED 01 December 2022
ACCEPTED 06 March 2023
PUBLISHED 23 March 2023

CITATION
Takahashi J, Kawai H, Ejiri M, Fujiwara Y, Hirano H, Sasai H, Ihara K, Ishii K, Oka K and Obuchi S (2023) Activity diversity is associated with the prevention of frailty in community-dwelling older adults: The Otassha Study. *Front. Public Health* 11:1113255. doi: 10.3389/fpubh.2023.1113255

Activity diversity is associated with the prevention of frailty in community-dwelling older adults: The Otassha Study

Junta Takahashi[1,2], Hisashi Kawai[1], Manami Ejiri[1], Yoshinori Fujiwara[1], Hirohiko Hirano[1], Hiroyuki Sasai[1], Kazushige Ihara[3], Kaori Ishii[4], Koichiro Oka[4] and Shuichi Obuchi[1]*

[1]Research Team for Human Care, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan, [2]Graduate School of Sport Sciences, Waseda University, Tokorozawa, Saitama, Japan, [3]Department of Social Medicine, Hirosaki University Graduate School of Medicine, Aomori, Japan, [4]Faculty of Sport Sciences, Waseda University, Tokorozawa, Saitama, Japan

Introduction: A prior study showed an association between diversity in daily activities (type, frequency, evenness) and frailty in older adults. However, the causality of this relationship is unclear. Therefore, this study aimed to clarify the relationship between activity diversity and frailty through a 2-year longitudinal study conducted among community-dwelling older adults.

Methods: We evaluated data from the 2018 and 2020 waves of the Otassha Study. Frailty was assessed using the Cardiovascular Health Study criteria, with pre-frail and frail participants defined as frail and the other participants categorized into the robust group. We enrolled a total of 207 participants who were not frail at baseline. Activity type, frequency, and evenness scores were calculated using an Activity Diversity Questionnaire. The association between each activity diversity score and the incidence of frailty was evaluated using logistic regression modeling (each diversity score was entered the model after Z-transformation).

Results: Of the 207 enrolled participants (median age, 73 years; age range, 65–91 years; 60.4% women), 64 (30.9%) had incident frailty during the follow-up period. A logistic regression analysis adjusting for sociodemographic and psychosomatic factors revealed odds ratios for activity type and evenness scores of 0.64 and 0.61, respectively ($P < 0.05$). These factors were significantly associated with the incidence of frailty.

Discussion: Activity type and evenness (except frequency) within daily activities were predictors of frailty during 2 years of follow-up. Engagement in diverse activities appears to be more effective in preventing frailty than does engagement in a few activities.

KEYWORDS

frailty, older adults, longitudinal study, activity, diversity

1. Introduction

In developed countries, the burden of nursing care due to aging has become a major social problem, and extending healthy life expectancy is of urgent concern (1, 2). A decline in physical and mental functioning due to aging causes a decline in activities of daily living (ADL) and individuals' overall quality of life. Moreover, it burdens their families and the national medical care system as a whole (2).

Frailty is defined as an age-associated syndrome presenting as decreased reserve and resistance to stressors that cause vulnerability to adverse health outcomes (3). It is an important public health issue of increasing concern due to the global aging of the population (4). Previous studies have reported that frailty is associated with various health problems, including impairments in ADL, falls, institutionalization, hospitalization, and mortality risk (5). However, frailty has been reported to be reversible (4). Moreover, it might be possible to extend healthy life expectancy in at-risk individuals through appropriate interventions.

Factors have been reported to be associated with frailty, including sociodemographic, medical, physiological, and lifestyle factors (6, 7). In particular, lifestyle factors are modifiable and have attracted many researchers' attention. Previous studies have focused on daily activities, including physical, cultural, intellectual, and social activities. Daily activities have been reported to be associated with frailty in prior studies (8, 9). Although these studies examined associations between specific daily activity types and frailty, they did not evaluate daily activities comprehensively. As daily life consists of various activities, it is necessary to comprehensively consider these activities in terms of diversity and examine the association between the diversity of daily activities and frailty.

Several studies have examined associations between activity diversity and health outcomes. Menec (10) and Lee HY et al. (11) defined activity diversity as number of "types" of activities and reported that those who engaged in more types of activities had better cognitive function, less depression, and lower mortality rates. Verghese et al. (12) and Kesavayuth et al. (13) defined activity diversity as "frequency" of activities and reported that those who engaged in more frequency of activities were associated with better cognitive functioning and lower risk of dementia. In addition, Lee S et al. (14) defined activity diversity as "evenness" of engagement in activities over a week and reported that those who engaged in more evenness of activities had better mental health. The above studies have demonstrated that older adults who engage in diverse activities in their lives have better health conditions. However, few studies have examined their relationship with frailty.

In our previous study, we developed the Activity Diversity Questionnaire (ADQ), which is a questionnaire that assesses the implementation of 20 activities of daily living, including physical, intellectual, and social activities (15, 16). Then, we defined activity diversity as the type, frequency, and evenness of daily activities and conducted a cross-sectional study to examine the relationship between activity diversity and frailty in older adults. The results showed that activity diversity scores (including type, frequency, and evenness scores) were independently associated with frailty (17). However, this was a cross-sectional study, and the causal relationship between activity diversity and frailty was unclear.

The current study investigated the association between activity diversity scores and the incidence of frailty in community-dwelling older adults in a 2-year longitudinal cohort study aiming to clarify the causal factors in the association between activity diversity and frailty.

2. Materials and methods

2.1. Study design and participants

We conducted a 2-year longitudinal study using data from the Otassha Study cohorts. The Otassha Study cohorts is conducted among older adults aged 65 years or older living in nine areas of Itabashi Ward, Tokyo, except for those residing in nursing homes. Comprehensive health checkup surveys, consisting of a mail survey part and a venue survey part, are conducted in September and October every year (18, 19).

We enrolled individuals who participated in the 2018 survey. Individuals with frail or pre-frail at the time of the 2018 survey and those with missing data on outcomes or important covariates were excluded from the current study. In addition, individuals with cardiac disease or stroke in the past 6 months and with blood pressure above the reference value (systolic blood pressure ≥180 mmHg, diastolic blood pressure ≥100 mmHg) were also excluded as grip strength (the evaluation of which is required in the assessment of frailty) was not measured. All participants had been fully informed about the study (procedures, benefits, and drawbacks) and had provided their written informed consent prior to participation. This study was approved by the Ethics Committee of the Tokyo Metropolitan Institute of Gerontology (approval number: 2018–16) and was conducted in accordance with the principles of the Declaration of Helsinki.

2.2. Assessment of frailty

Frailty was assessed in the 2018 and 2020 surveys using the five items in the Japanese version of the Cardiovascular Health Study (J-CHS) criteria (20): weight loss, low activity, exhaustion, weakness, and slowness. Weight loss was defined as a loss of 2–3 kg or more in the past 6 months. Low activity was indicated by a negative response to both of the following items: "Do you engage in moderate levels of physical exercise or sports aimed at health?" "Do you engage in low levels of physical exercise aimed at health?" Exhaustion was indicated by a positive response to the following item: "(In the last 2 weeks) I have felt tired for no particular reason." Weakness was indicated by a grip strength of <26 kg for men and <18 kg for women. Slowness was indicated by a usual gait speed of 1.0 m/s or less. Weight loss, low activity, and exhaustion were assessed in a mailed survey using a self-administered questionnaire, whereas grip strength and gait speed were measured at the survey site. Grip strength was measured twice using a hand dynamometer (Smedley-type hand dynamometer, Yagami, Nagoya, Japan). The strongest grip value of the two tests was considered for the analysis. Usual gait speed was obtained using a stopwatch to measure the time necessary to walk a 5-m walkway with 3-m acceleration and deceleration areas placed before and after the walkway. Walking speed was measured once. Those who met three or more of the above criteria were considered frail. Those who met one or two criteria were designated as pre-frail. Participants who were frail or pre-frail at baseline were excluded from the current study. Finally, those who developed pre-frailty or frailty during the 2-year follow-up period were allocated to the frail group and the rest to the robust group.

2.3. Assessment of activity diversity

Activity diversity was assessed using the Activity Diversity Questionnaire (ADQ) administered during the 2018 survey (10). The ADQ is a self-administered questionnaire that assesses 20 daily activities (see Supplementary Table 1). This questionnaire has been reported to have good reliability and validity within prior research (15). The 20 questionnaire items were preceded by the question: "How often did you engage in these activities in the last week?" The responses to the items were scored from 0 to 3, where 0 = "rarely," 1 = "1–2 times a week," 2 = "once every 2 days," and 3 = "almost every day." Activity diversity was defined as daily activities' type, frequency, and evenness (17). Scores for type, frequency, and evenness were calculated as follows. Type scores were calculated as the total number of activity types the individuals engaged in at least once a week; these scores could range from 0 to 20. Frequency scores were calculated by summing the frequency of engagement within the 20 activities (score range, 0–60). Evenness scores were calculated according to Shannon's entropy formula (21), as indicated by the following equation:

$$\textit{Evenness score} = -\left(\frac{1}{\log m}\right)\sum_{i=1}^{m} P_i \left(\log P_i\right)$$

Where m represents the total number of activities ($m = 20$), i represents each activity, and P_i represents the proportion of each implemented activity. Evenness scores could range from 0 to 1, with higher scores indicating wide-ranging and even engagement in daily activities across the 20 evaluated items.

2.4. Covariates

Age, sex, the number of chronic diseases (stroke, heart disease, chronic obstructive pulmonary disease, chronic kidney disease, cancer, diabetes), subjective financial status (sufficient to live on, not sufficient to live on), and family structure (living with others, living alone) were examined as sociodemographic factors. In addition, physical and mental functioning were assessed using body mass index (BMI; <18.5, 18.5–25.0, and >25.0 kg/m^2), Mini-Mental State Examination (MMSE) (22), and the World Health Organization-Five Wellbeing Index (WHO-5) (23, 24). Subjective financial status and family structure were assessed through a mailed survey, whereas the other covariates were assessed at the survey site in 2018.

2.5. Statistical analysis

Differences in medical and demographic characteristics between the robust and incident frail groups were examined using t-tests and χ^2 tests. Logistic regression analysis was performed to examine associations between activity diversity and the incidence of frailty, with the presence or absence of frailty as the dependent variable. To evaluate these associations, we implemented the following models: (i) a crude model, in which each of the three indicators of activity diversity (type, frequency, and evenness scores) were entered as independent variables; (ii) Model 1, in which sociodemographic factors were added as covariates to the crude model; and (iii) Model 2, in which physical and mental functioning factors were added to Model 1. The three indicators of activity diversity (type, frequency, and evenness score) were strongly correlated [type score vs. frequency score: $r = 0.79$ ($p < 0.001$), type score vs. evenness score: $r = 0.98$ ($p < 0.001$), and frequency score vs. evenness score: $r = 0.85$ ($p < 0.001$)], respectively. Due to multicollinearity issues, each indicator was not put into the model simultaneously. In the logistic regression analyses, the three indicators of activity diversity were standardized *via* Z-transformation to compare the odds ratios (ORs). Moreover, a power analysis was conducted using the G*Power software (25). Based on prior studies, the OR of the standardized activity diversity indicators with respect to the incidence of frailty or pre-frailty during study follow-up was presumed to be 1.5 (17). In contrast, the predicted incidence of frailty or pre-frailty was presumed to be 0.34 (26). Given an α of 0.05 and a targeted statistical power of 0.80, the minimum target sample size necessary within this study was $n = 179$.

We performed the following two supplementary analyses to examine the effects of those who were lost to follow-up and missing values. First, we compared medical and demographic characteristics at the baseline survey between the participants enrolled in the final analysis ($n = 207$) and those lost to follow-up ($n = 119$) using t-tests and χ-square tests. In addition, to ensure the robustness of the data in this study, missing value imputation was conducted supplementally using the multiple imputation method. The results with missing value imputation and the results from the complete case analysis were compared. Missing value imputation was performed on data from those who participated in both the 2018 and 2020 surveys ($n = 456$). Missing values were found in J-CHS criteria item [e.g., weight loss ($n = 25$), weakness ($n = 47$), slowness ($n = 2$) and low activity ($n = 1$)], subjective financial status ($n = 34$), family structure ($n = 4$) and MMSE ($n = 1$). Multiple imputation was performed using an iterative Markov chain Monte Carlo method (27). The number of imputed data sets was set to 100 (28), and logistic regression analysis was performed on the association between activity diversity and the occurrence of frailty, as in the main analysis. Since the missing value imputation was conducted as a supplementary analysis, only the results of the complete case analysis are shown in the main text.

The statistical significance level was set to a threshold of $P < 0.05$. All statistical analyses were conducted using IBM SPSS statistical software (version 28, IBM Corp. Armonk, NY, USA).

3. Results

The 2018 wave of the study included 769 participants, of whom 443 were excluded from the current secondary analysis due to the

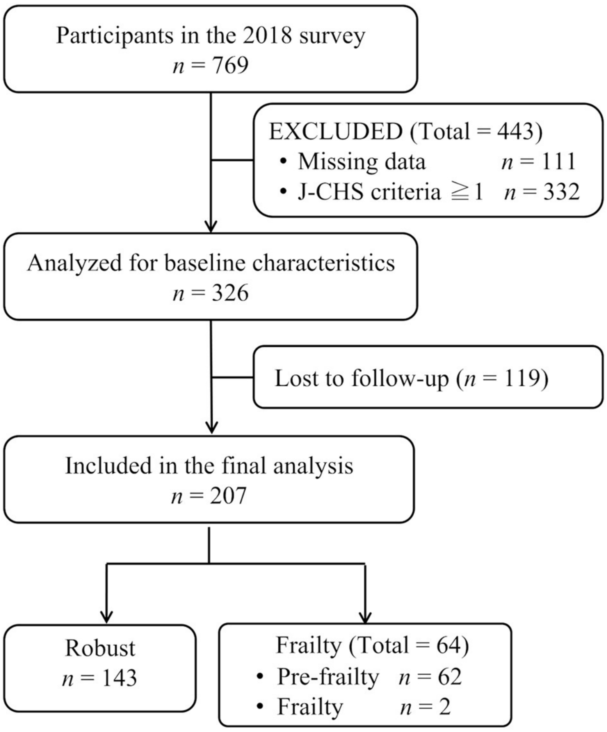

FIGURE 1
Flow chart of participant enrollment. J-CHS, Japanese version of the Cardiovascular Health Study.

aforementioned exclusion criteria (missing data, 111; frail or pre-frail status, 332). One hundred nineteen participants were lost to follow-up as of the 2020 study wave. The final analysis included 207 participants [median age, 73 years; range, 65–89 years; 125 (60.4%) women]. Of the enrolled participants, there were 143 (69.1%) participants in the robust group as of the end of the study follow-up period and 64 (30.9%; pre-frail: $n = 62$, frail: $n = 2$) participants in the frail group (Figure 1).

Of the participants enrolled in the final analysis, 150 (72.5%) had an appropriate (normal) BMI (18.5–24.9 kg/m^2). The mean MMSE score was 29.0 [standard deviation (SD) = 1.4]. The mean WHO-5 score was 18.5 (SD = 3.8). The evaluated activity type, frequency, and evenness scores were 11.2 (SD = 2.3), 24.4 (SD = 5.1), and 0.77 (SD = 0.07), respectively (Table 1). Type scores [robust vs. frail; 11.4 (SD = 2.2) vs. 10.6 (SD = 2.5), $P = 0.015$] and evenness scores [0.78 (SD = 0.07) vs. 0.75 (SD = 0.08), $P=0.015$] were lower in the frail group than in the robust group. There were no significant differences between the two groups with respect to the other evaluated items.

A comparison of medical and demographic characteristics between the participants enrolled in the final analysis ($n = 207$) and those lost to follow-up ($n = 119$) are shown in Supplementary Table 2. Compared with the participants included in the final analysis, those who were lost to follow-up were significantly younger (final analysis vs. lost to follow-up, 72.8 (SD = 5.4) years vs. 71.2 (SD = 6.2) years, $P = 0.013$). No significant differences were observed with respect to the other evaluated items.

The results of logistic regression modeling showed that standardized type and evenness scores were significantly associated with the incidence of frailty in the crude model. This association was maintained after adjusting for all covariates specified within Models 1 and 2. The ORs for standardized type and evenness scores were ∼0.6, indicating a similar degree of association with the incidence of frailty. Conversely, no significant associations were found for frequency scores within any model (crude model, Model 1, Model 2; Table 2).

When examining the association between activity diversity and the occurrence of frailty at 2 years in the data set with missing value imputation, a significant association was found between the type and evenness scores. On the other hand, the frequency score was not significantly associated with frailty (Supplementary Table 3). These results were similar to those of the main analysis using the complete case analysis method; therefore, only the results of the complete case analysis method are presented in the main text.

4. Discussion

The present study investigated associations between activity diversity and the incidence of frailty in community-dwelling older adults through a 2-year longitudinal study. Type and evenness scores were significantly associated with the incidence of frailty, even after adjusting for covariates such as sociodemographic variables and physical and mental functioning evaluations. While several prior studies have examined the association between frailty and specific daily activities (8, 9), few studies have focused on diversity in daily activities. To the best of our knowledge, this study is the first to show that activity diversity is a predictor of frailty, revealing the importance of maintaining and increasing the diversity of daily activities in older adults to prevent frailty.

The median age of the participants enrolled in this study was 73 years. Nevertheless, the percentage of participants with a normal BMI (18.5–24.9 kg/m^2) was 75.8%, and the average scores for the MMSE and WHO-5 evaluations were 29.0 and 18.5, respectively. These findings indicate that the physical and mental functioning of these older participants was superior to that of participants evaluated in other cohort studies (23, 29–31). During the follow-up period, only two individuals became newly frail (vs. pre-frail) in this study (4.8 new cases per 1,000 person-years). This incidence of frailty was lower than that reported in a prior investigation (12.0 new cases per 1,000 person-years) (32). Thus, healthier older adults could have been recruited for this study due to the survey being conducted at a venue. Moreover, those with a deteriorated health condition (who were thus at a high risk of frailty) may have dropped out of the study during follow-up. However, it is important finding that even among these healthy older adults with a low risk of frailty, an independent association was found between activity diversity and the incidence of frailty (defined as frailty or pre-frailty). Although activity type and evenness scores at baseline were significantly lower in the frail group than in the robust group, the two groups were not significantly different with respect to the other evaluated characteristics. This suggests the importance of activity diversity in preventing frailty.

TABLE 1 Comparison of participants' medical and demographic characteristics in the 2018 survey.

Variable	All $n = 207$		Frailty status				P-value
			Robust group $n = 143$		Frailty group $n = 64$		
Age, years, median (range)	73	(65–89)	72	(65–89)	73	(65–84)	0.733
Women, *n* (%)	125	(60.4)	90	(62.9)	35	(54.7)	0.262
Number of chronic diseases, *n* (%)							0.222
0	110	(53.1)	81	(56.6)	29	(45.3)	
1	66	(31.9)	44	(30.8)	22	(34.4)	
2+	31	(15.0)	18	(12.6)	13	(20.3)	
Subjective financial status, *n* (%)							0.067
Sufficient to live on	189	(91.3)	134	(93.7)	55	(85.9)	
Not sufficient to live on	18	(8.7)	9	(6.3)	9	(14.1)	
Family structure, *n* (%)							0.111
Living with others	157	(75.8)	113	(79.0)	44	(68.8)	
Living alone	50	(24.2)	30	(21.0)	20	(31.3)	
BMI, kg/m^2, *n* (%)							0.106
18.5–24.9	150	(72.5)	109	(76.2)	41	(64.1)	
<18.5	14	(6.8)	10	(7.0)	4	(6.3)	
≥25.0	43	(20.8)	24	(16.8)	19	(29.7)	
MMSE, mean (SD)	29.0	(1.4)	29.1	(1.3)	28.9	(1.4)	0.352
WHO-5, mean (SD)	18.5	(3.8)	18.7	(3.8)	18.0	(4.0)	0.203
Type score, mean (SD)	11.2	(2.3)	11.4	(2.2)	10.6	(2.5)	0.015
Frequency score, mean (SD)	24.4	(5.1)	24.8	(5.1)	23.6	(5.3)	0.144
Evenness score, mean (SD)	0.77	(0.07)	0.78	(0.07)	0.75	(0.08)	0.015

BMI, body mass index; MMSE, Mini-Mental State Examination; SD, standard deviation; WHO-5, World Health Organization-Five Wellbeing Index.

TABLE 2 Results of logistic regression analyses with respect to the association between activity diversity and the incidence of frailty.

Variable	Crude model			Model 1			Model 2		
	OR	(95% CI)	P-value	OR	(95% CI)	P-value	OR	(95% CI)	P-value
Standardized type scores	0.66	(0.47–0.93)	0.017	0.64	(0.45–0.91)	0.014	0.64	(0.44–0.92)	0.018
Standardized frequency scores	0.78	(0.56–1.09)	0.144	0.76	(0.54–1.07)	0.117	0.76	(0.53–1.09)	0.130
Standardized evenness scores	0.64	(0.44–0.92)	0.017	0.61	(0.41–0.90)	0.014	0.61	(0.40–0.91)	0.017

BMI, body mass index; CI, confidence interval; MMSE, Mini-Mental State Examination; OR, odds ratio; WHO-5, World Health Organization-Five WellBeing Index.
Crude model: Standardized type scores, standardized frequency scores, and standardized evenness scores were entered as independent variables.
Model 1: Adjusted for age, sex, the number of chronic diseases, perceived financial status, and family structure.
Model 2: Adjusted for the covariates in Model 1, plus BMI, MMSE, and WHO-5 scores.

Logistic regression analysis demonstrated that both type and evenness scores were significantly associated with the incidence of frailty even after adjusting for all covariates, suggesting the importance of implementing more activities evenly. Seino et al. (33) investigated the association between the occurrence of functional disability and three healthy habits (moderate-to-vigorous-intensity physical activity, dietary variety, and social interaction). Their results showed that the risk of functional disability was reduced by 28% in those who had one type of habit, 49% in those who had two types of habits, and 62% in those who had all three types of habits compared to those who did nothing, suggesting that having a multidimensional lifestyle is important for the health of older adults. Ngandu et al. (34) examined the effect of a Multidimensional Lifestyle Improvement Intervention combining exercise, nutritional guidance, cognitive training, and social participation on cognitive function in the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER). They reported that the multidimensional approach to lifestyle was effective in reducing cognitive impairment. This, therefore, suggests that multidimensional lifestyle has positive impacts on health of older adults. Our findings showed that type and evenness scores were significantly associated with the occurrence of frailty. This suggests that those who engaged in more types of activities evenly were more likely to have a multidimensional lifestyle, and this may have been effective in preventing the occurrence of frailty. On the other hand, frequency scores showed no significant association with the incidence of frailty in the current study. Frequency scores were evaluated as the sum of the frequency of each activity; if the frequency of even one activity was high, the overall frequency score was high. Therefore, a high-frequency score does not necessarily indicate the implementation of multidimensional activities and may not be associated with the incidence of frailty (in contrast to the other two evaluated scores). In addition, the type score and evenness score were highly correlated ($r = 0.98$). This may be because the evenness score weights each activity according to the proportion of each implemented activity, but is also greatly influenced by the number of types of activities, which may have approximated the type score. The current operationalizations failed to empirically distinguish the two concepts, i.e., type and evenness. The two scores are theoretically distinct but methodologically not distinct. Therefore, it may be necessary to consider a new methodology for evenness indicator that is separated from the effects of number of types.

This study had some limitations. First, many participants were lost to follow-up ($n = 119$) or had missing data ($n = 111$). If the causes of dropout were related to the development of flailty, the bias due to lost to follow-up may have influenced the results of this study. The item with the highest amount of missing data was weight loss ($n = 85$, a sub-item of the J-CHS criteria), followed by subjective financial status ($n = 58$). The missing data was considerable, as information was obtained through a mailed survey. However, comparing the baseline characteristics of the participants included in the final analysis and those lost to follow-up showed only a significant difference in age. No significant differences in physical and mental functioning were observed. Furthermore, the analysis was also performed for the dataset with missing data imputation, and the results were similar to those of the main analysis. These results suggest a slight bias due to loss of follow-up and missing data. Moreover, we did not evaluate the amount of physical activity. A decreased amount of activity may affect the association between activity diversity and the incidence of frailty. Thus, it is necessary to simultaneously evaluate activity diversity and the amount of physical activity. Future studies enrolling more participants and intervention studies aimed at maintaining and improving activity diversity in older adults are warranted to confirm the findings of this investigation.

In conclusion, we found that activity type and evenness scores concerning daily activities were significantly associated with the incidence of frailty during a 2-year follow-up period, even after adjusting for a range of covariates. These results indicate the importance of diversity in daily activities (i.e., performing many types of daily activities evenly) to prevent frailty. Furthermore, our findings demonstrate the need for future efforts to maintain and improve the diversity of daily activities in older adults.

Data availability statement

The datasets presented in this article are not readily available because of ethical and privacy restrictions. Requests to access the datasets should be directed to obuchipc@tmig.or.jp.

Ethics statement

The studies involving human participants were reviewed and approved by Ethics Committee of the Tokyo Metropolitan Institute of Gerontology. The patients/participants provided their written informed consent to participate in this study.

Author contributions

JT: formal analysis, investigation, and writing—original draft. HK: methodology, validation, investigation, resources, data curation, writing—review and editing, project administration, and funding acquisition. ME: project administration and investigation. YF, HH, HS, and KIh: investigation, resources, and funding acquisition. KIs: methodology. KO: supervision and methodology. SO: conceptualization, resources, supervision, and funding acquisition. All authors contributed to the article and approved the submitted version.

Funding

This work was supported by the Japan Society for the Promotion of Science KAKENHI (grant number: 20K19664) and Research Funding for Longevity Sciences from the National Center for Geriatrics and Gerontology, Japan (grant numbers: 28–30 and 29–42). The funding agencies played no role in the study design, collection, analysis, interpretation of the data, report writing, or the decision to submit the article for publication.

Acknowledgments

We are grateful to the local authorities of Itabashi Ward and the individuals who participated in this study.

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.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1113255/full#supplementary-material

References

1. Hosokawa R, Ojima T, Myojin T, Aida J, Kondo K, Kondo N. Associations between healthcare resources and healthy life expectancy: a descriptive study across secondary medical areas in Japan. *Int J Environ Res Public Health.* (2020) 17:6301. doi: 10.3390/ijerph17176301

2. Kyu HH, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet.* (2018) 392:1859–922. doi: 10.1016/S0140-6736(18)32335-3

3. Buchner DM, Wagner EH. Preventing frail health. *Clin Geriatr Med.* (1992) 8:1–17. doi: 10.1016/S0749-0690(18)30494-4

4. Cesari M, Prince M, Thiyagarajan JA, De Carvalho IA, Bernabei R, Chan P, et al. Frailty: an emerging public health priority. *J Am Med Dir Assoc.* (2016) 17:188–92. doi: 10.1016/j.jamda.2015.12.016

5. Vermeiren S, Vella-Azzopardi R, Beckwée D, Habbig AK, Scafoglieri A, Jansen B, et al. Frailty and the prediction of negative health outcomes: a meta-analysis. *J Am Med Dir Assoc.* (2016) 17:1163.e1–1163.e17. doi: 10.1016/j.jamda.2016.09.010

6. Feng Z, Lugtenberg M, Franse C, Fang X, Hu S, Jin C, et al. Risk factors and protective factors associated with incident or increase of frailty among community-dwelling older adults: a systematic review of longitudinal studies. *PLoS ONE.* (2017) 12:e0178383. doi: 10.1371/journal.pone.0178383

7. Hoogendijk EO, Afilalo J, Ensrud KE, Kowal P, Onder G, Fried LP. Frailty: implications for clinical practice and public health. *Lancet.* (2019) 394:1365–75. doi: 10.1016/S0140-6736(19)31786-6

8. Abe T, Nofuji Y, Seino S, Murayama H, Yoshida Y, Tanigaki T, et al. Healthy lifestyle behaviors and transitions in frailty status among independent community-dwelling older adults: the Yabu cohort study. *Maturitas.* (2020) 136:54–9. doi: 10.1016/j.maturitas.2020.04.007

9. Poli S, Cella A, Puntoni M, Musacchio C, Pomata M, Torriglia D. et at. Frailty is associated with socioeconomic and lifestyle factors in community-dwelling older subjects. *Aging Clin Exp Res.* (2017) 29:721–8. doi: 10.1007/s40520-016-0623-5

10. Menec V. The relation between everyday activities and successful aging: a 6- year longitudinal study. *J Gerontol B Psychol Sci Soc Sci.* (2003) 58:S74–82. doi: 10.1093/geronb/58.2.S74

11. Lee HY Yu CP, Wu CD, Pan WC. The effect of leisure activity diversity and exercise time on the prevention of depression in the middle-aged and elderly residents of Taiwan. *IJERPH.* (2018) 15:654. doi: 10.3390/ijerph15040654

12. Verghese J, Lipton RB, Katz MJ, Hall CB, Derby CA, Kuslansky G, et al. Leisure activities and the risk of dementia in the elderly. *N Engl J Med.* (2003) 348:2508–16. doi: 10.1056/NEJMoa022252

13. Kesavayuth D, Liang Y, Zikos V. An active lifestyle and cognitive function: Evidence from China. *J Econ Ageing.* (2018) 12:183–91. doi: 10.1016/j.jeoa.2018.05.001

14. Lee S, Koffer RE, Sprague BN, Charles ST, Ram N, Almeida DM. Activity diversity and its associations with psychological well-being across adulthood. *J Gerontol B Psychol Sci Soc Sci.* (2018) 73:985–95. doi: 10.1093/geronb/gbw118

15. Takahashi J, Kawai H, Suzuki H, Fujiwara Y, Watanabe Y, Hirano H, et al. Reliability and validity of the activity diversity questionnaire for older adults in Japan. *Int J Environ Res Public Health.* (2020) 17:2384. doi: 10.3390/ijerph17072384

16. Yildirim C, Tekgul B, Tonak HA. Psychometric properties of the Turkish version of the activity diversity questionnaire for older adults. *Exp Aging Res.* (2022) 14:1–14. doi: 10.1080/0361073X.2022.2133294

17. Takahashi J, Kawai H, Fujiwara Y, Watanabe Y, Hirano H, Kim H, et al. Association between activity diversity and frailty among community-dwelling older Japanese: a cross-sectional study. *Arch Gerontol Geriatr.* (2021) 95:104377. doi: 10.1016/j.archger.2021.104377

18. Kawai H, Ihara K, Kera T, Hirano H, Fujiwara Y, Tanaka M, et al. Association between statin use and physical function among community-dwelling older Japanese adults. *Geriatr Gerontol Int.* (2018) 18:623–30. doi: 10.1111/ggi.13228

19. Kera T, Kawai H, Hirano H, Kojima M, Watanabe Y, Fujiwara Y, et al. Comparison of body composition and physical and cognitive function between older Japanese adults with no diabetes, prediabetes and diabetes: a cross-sectional study in community-dwelling Japanese older people. *Geriatr Gerontol Int.* (2018) 18:1031–7. doi: 10.1111/ggi.13301

20. Satake S, Shimada H, Yamada M, Kim H, Yoshida H, Gondo Y, et al. Prevalence of frailty among community-dwellers and outpatients in Japan as defined by the Japanese version of the cardiovascular Health Study criteria. *Geriatr Gerontol Int.* (2017) 17:2629–34. doi: 10.1111/ggi.13129

21. Shannon CE. A mathematical theory of communication. *Bell Syst Tech J.* (1948) 27:623–56. doi: 10.1002/j.1538-7305.1948.tb00917.x

22. O'Bryant SE, Humphreys JD, Smith GE, Ivnik RJ, Graff-Radford NR, Petersen RC, et al. Detecting dementia with the mini-mental state examination in highly educated individuals. *Arch Neurol.* (2008) 65:963–7. doi: 10.1001/archneur.65.7.963

23. Awata S, Bech P, Koizumi Y, Seki T, Kuriyama S, Hozawa A. et al. Validity and utility of the Japanese version of the WHO-Five Well-Being Index in the context of detecting suicidal ideation in older community residents. *Int Psychogeriatr.* (2007) 19:77–88. doi: 10.1017/S1041610206004212

24. Bech P, Gudex C, Johansen KS. The WHO (Ten) wellbeing index: validation in diabetes. *Psychother Psychosom.* (1996) 65:183–90. doi: 10.1159/000289073

25. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods.* (2007) 39:175–91. doi: 10.3758/BF03193146

26. Jazbar J, Locatelli I, Kos M. The association between medication or alcohol use and the incidence of frailty: a retrospective cohort study. *BMC Geriatr.* (2021) 21:25. doi: 10.1186/s12877-020-01969-y

27. IBM Corp. *IBM SPSS Missing Values 28.* Avaliable online at: https://www.ibm.com/docs/SSLVMB_28.0.0/pdf/IBM_SPSS_Missing_Values.pdf (accessed October 28, 2022).

28. Royston P, White IR. Multiple imputation by chained equations (MICE): implementation in stata. *J Stat Softw.* (2011) 45:1–20. doi: 10.18637/jss.v045.i04

29. Kugimiya Y, Ueda T, Watanabe Y, Takano T, Edahiro A, Awata S, et al. Relationship between mild cognitive decline and oral motor functions in metropolitan community-dwelling older Japanese: the takashimadaira study. *Arch Gerontol Geriatr.* (2019) 81:53–8. doi: 10.1016/j.archger.2018.11.008

30. Seino S, Shinkai S, Iijima K, Obuchi S, Fujiwara Y, Yoshida H, et al. Reference values and age differences in body composition of community-dwelling older Japanese men and women: a pooled analysis of four cohort studies. *PLoS ONE.* (2015) 10:e0131975. doi: 10.1371/journal.pone.0131975

31. Taniguchi Y, Kitamura A, Murayama H, Amano H, Shinozaki T, Yokota I, et al. Mini-Mental State Examination score trajectories and incident disabling dementia among community-dwelling older Japanese adults. *Geriatr Gerontol Int.* (2017) 17:1928–35. doi: 10.1111/ggi.12996

32. Ofori-Asenso R, Chin KL, Mazidi M, Zomer E, Ilomaki J, Zullo AR, et al. Global incidence of frailty and prefrailty among community-dwelling older adults: a systematic review and meta-analysis. *JAMA Netw Open.* (2019) 2:e198398. doi: 10.1001/jamanetworkopen.2019.8398

33. Seino S, Nofuji Y, Yokoyama Y, Abe T, Nishi M, Yamashita M, et al. Combined impacts of physical activity, dietary variety, and social interaction on incident functional disability in older Japanese adults. *J Epidemiol.* (2021). doi: 10.2188/jea.JE20210392

34. Ngandu T, Lehtisalo J, Solomon A, Levälahti E, Ahtiluoto S, Antikainen R, et al. A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring vs. control to prevent cognitive decline in at-risk older people (Finger): a randomised controlled trial. *Lancet.* (2015) 385:2255–63. doi: 10.1016/S0140-6736(15)60461-5

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 04 April 2023
DOI 10.3389/fpubh.2023.1148404

Check for updates

OPEN ACCESS

EDITED BY
Marco Carlos Uchida,
State University of Campinas, Brazil

REVIEWED BY
Shuangling Xiu,
Xuanwu Hospital, Capital Medical University, China
Milan Chang Gudjonsson,
Icelandic Gerontological Research Institute, Iceland
Stefan Löfler,
Ludwig Boltzmann Institute for Rehabilitation Research, Austria

*CORRESPONDENCE
Takahisa Ohta
✉ otakahisa@tmigmuscle.onmicrosoft.com

SPECIALTY SECTION
This article was submitted to Aging and Public Health, a section of the journal Frontiers in Public Health

RECEIVED 20 January 2023
ACCEPTED 14 March 2023
PUBLISHED 04 April 2023

CITATION
Ohta T, Sasai H, Osuka Y, Kojima N, Abe T, Yamashita M, Obuchi SP, Ishizaki T, Fujiwara Y, Awata S, Toba K and IRIDE Cohort Study Investigators (2023) Age- and sex-specific associations between sarcopenia severity and poor cognitive function among community-dwelling older adults in Japan: The IRIDE Cohort Study.
Front. Public Health 11:1148404.
doi: 10.3389/fpubh.2023.1148404

Age- and sex-specific associations between sarcopenia severity and poor cognitive function among community-dwelling older adults in Japan: The IRIDE Cohort Study

Takahisa Ohta[1]*, Hiroyuki Sasai[2], Yosuke Osuka[2,3], Narumi Kojima[2], Takumi Abe[4], Mari Yamashita[1], Shuichi P. Obuchi[5], Tatsuro Ishizaki[5], Yoshinori Fujiwara[1,4], Shuichi Awata[1,6], Kenji Toba[1,6] and IRIDE Cohort Study Investigators

[1]Integrated Research Initiative for Living Well With Dementia, Tokyo Metropolitan Institute for Geriatrics and Gerontology, Tokyo, Japan, [2]Research Team for Promoting Independence and Mental Health, Tokyo Metropolitan Institute for Geriatrics and Gerontology, Tokyo, Japan, [3]Department of Frailty Research, Center for Gerontology and Social Science, Research Institute, National Center for Geriatrics and Gerontology, Obu, Japan, [4]Research Team for Social Participation and Community Health, Tokyo Metropolitan Institute for Geriatrics and Gerontology, Tokyo, Japan, [5]Human Care Research Team, Tokyo Metropolitan Institute for Geriatrics and Gerontology, Tokyo, Japan, [6]Tokyo Metropolitan Institute for Geriatrics and Gerontology, Tokyo, Japan

Introduction: This study examined whether the association between sarcopenia severity and cognitive function differed according to sex and age in community-dwelling older adults in Japan.

Methods: This is a cross-sectional study of older adults (age ≥ 65 years) consisting of five regional cohorts integrated as the Integrated Research Initiative for Living Well with Dementia (IRIDE) Cohort Study. Sarcopenia severity was determined based on the Asian Working Group for Sarcopenia 2019, which assessed grip strength, walking speed, and skeletal muscle mass index. Poor cognitive function was defined as a Mini-Mental State Examination score of ≤ 23. Odds ratios (ORs) and 95% confidence intervals (CIs) for poor cognitive function were calculated by sex and age group (65–74 and ≥75 years) using binomial logistic regression models, which were adjusted for age, educational attainment, history of non-communicable diseases, smoking and drinking habits, living alone, frequency of going outdoors, exercise habits, and depressive symptom.

Results: Of the 8,180 participants, 6,426 (1,157 men aged 65–74 and 1,063 men aged 75 or older; 2,281 women aged 65–74 and 1,925 women aged 75 or older) were analyzed. The prevalence ratio of sarcopenia and severe sarcopenia were 309 (13.9%) and 92 (4.1%) among men and 559 (13.3%) and 166 (3.7%) among women, respectively. A total of 127 (5.8%) men and 161 (3.9%) women had a poor cognitive function. Setting non-sarcopenia as a reference, the adjusted ORs (95% CI) of poor cognitive function were 2.20 (1.54, 3.15) for sarcopenia and 3.56 (2.20, 5.71) for severe sarcopenia. A similar trend was observed in analyses stratified by sex and age, with linear associations (*P* for trend <0.05) in both categories. Furthermore, there was a significant interaction (*P* < 0.05) between sex and sarcopenia severity, indicating a stronger linear association of sarcopenia severity with poor cognitive function in women compared with men.

Discussion and conclusion: Sarcopenia severity was linearly associated with poor cognitive function in adults aged ≥ 65 years, with a stronger association in women compared with men.

KEYWORDS

sarcopenia, cognitive function, poor cognitive function, Asian Working Group for Sarcopenia 2019, sarcopenia severity

Introduction

Cognitive decline leading to dementia or mild cognitive impairment (MCI) is characterized by decreased memory, language, and executive function abilities. The number of dementia patients worldwide is projected to reach 78 million by 2030 and 139 million by 2050 (1). In addition, the number of dementia patients in the super-aged society of Japan is estimated to reach 7.4 million in 2030 and 8.5 million in 2060 (2). Therefore, examining the factors that may lead to poor cognitive function is essential.

Risk factors of poor cognitive function include genetic, psychological, and environmental factors, such as physical inactivity (3). Physical inactivity increases the risk of cognitive decline resulting from cardiovascular disease (4), and promotes the accumulation of amyloid-β and tau proteins specific to Alzheimer's disease (5). In contrast, myokines, such as brain-derived neurotrophic factor (BDNF), are secreted by muscle cells with the contraction of skeletal muscles in regular exercise. These myokines cross the blood-brain barrier and promote further BDNF production in the brain. This, in turn, promotes improved neurogenesis, memory, and learning, suggesting that myokines may be effective in improving cognitive function (5, 6). Therefore, since physical activity is closely related to skeletal muscle performance (7), the quantity, quality, and function of skeletal muscle may substantially impact cognitive function.

From an epidemiological perspective, the association between sarcopenia and MCI has been reported in numerous observational studies and systematic reviews (8–10). Sarcopenia is defined as an age-related decline in skeletal muscle mass, muscle strength, and physical function, with decreased physical activity and poor nutrition as risk factors (11). As evidence suggests a close relationship between reduced muscle mass and strength and neuroinflammatory responses in the cerebrum, many individuals with sarcopenia may experience a cognitive decline (12, 13). However, the associations between sarcopenia and cognitive function may be controversial due to methodological issues such as insufficient sample sizes, and no consistent conclusions have been obtained (8, 9). In addition, the relationship between sex- and age-related sarcopenia and cognitive function in Japan's super-aged society, particularly with regard to cognitive decline in severely physically impaired sarcopenic individuals, has not been examined, and these findings may serve as a guideline for the realization of healthy longevity.

This study aimed to examine the association between sarcopenia and cognitive function, and its specificity by sex and age, in a large sample of community-dwelling older Japanese adults. These findings may provide a valid basis for detecting cognitive decline according to skeletal muscle characteristics in older populations.

Methods

Study design and participants

This study analyzed cross-sectional data from the Integrated Research Initiative for Living Well With Dementia Cohort Study (IRIDE-CS) conducted by the Tokyo Metropolitan Institute of Gerontology (14). The IRIDE-CS included five cohorts of community-dwelling older adults (≥65 years) from the Otassha Study (n = 3,426), Takashimadaira Study (n = 2,053), Septuagenarians, Octogenarians, Nonagenarians Investigation with Centenarians (SONIC) Study (n = 567), Hatoyama Study (n = 742), and Kusatsu Longitudinal Study on Aging (n = 1,392). Each cohort is an ongoing longitudinal study with its own recruitment methods (15–19). A total of 8,180 older adults were included in the IRIDE-CS.

All participants were informed about the aims and protocols of each cohort study as well as the IRIDE-CS, and written informed consent was obtained. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committee of the Tokyo Metropolitan Institute for Geriatrics and Gerontology (R21–28).

Assessment of sarcopenia

Sarcopenia status was based on lean mass, muscle strength, and physical function, and was defined according to the criteria established by the 2019 Asian Working Group for Sarcopenia (AWGS) (11). Lean mass was assessed using direct segmental multi-frequency bioelectrical impedance analysis (InBody S10, Biospace, Seoul, Korea for Takashimadaira cohort, InBody 720 analyzer, InBody Co., Ltd., Seoul, Korea for the other cohorts). Low muscle mass was defined as a skeletal muscle mass index of <7.0 kg/m^2 for men and <5.7 kg/m^2 for women. Low muscle strength was defined as handgrip strength of 28 kg for men and < 18 kg for women. Handgrip strength was assessed with Takei 5401 Digital Dynamometer (Takei, Japan). Low physical function was defined as a 5-m gait speed of <1.0 m/s for both sexes. Sarcopenia was defined as low muscle mass, and either low muscle strength or low physical function. Severe sarcopenia was defined as low muscle mass and strength as well as low physical function.

Definition of poor cognitive function

Cognitive function was assessed using the Mini-Mental State Examination, which assessed the following: time registration, place registration, immediate and delayed recall of three words, mathematical calculation, object naming, sentence recall, three levels of verbal commands, written commands, sentence writing, and pentagon drawing (20). The cutoff for MMSE was set at 24 points, at which substantial hippocampal atrophy may be detected (21).

Assessment of covariates

Information on the history of non-communicable diseases (hypertension, diabetes, dyslipidemia, and stroke) was obtained using a questionnaire with yes/no answers in self-reported form and interview. Data on smoking status (never/past/current), drinking status (never/past/current), educational attainment (years), frequency of going outdoors (days per week) (<1, 1–2, 3–6, 7), exercise habits (days per week; <1, 1–4, >4), and depressive symptoms [Geriatric Depression Scale-15 (GDS-15)] were also obtained (22).

Statistical analysis

Participants were divided by sex and age (65–74 and ≥ 75 years). Continuous variables, which performed normality tests, were expressed as means (standard deviations) or median [interquartile range], and categorical variables were expressed as numbers and percentages.

The association between sarcopenia severity and poor cognitive function was evaluated using binary logistic regression analyses. Multivariable odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using non-sarcopenia as a reference after adjusting for age, educational attainment, smoking and drinking status, cohort categories, living alone, history of non-communicable diseases (hypertension, diabetes, dyslipidemia, and stroke), GDS-15 scores, frequency of going outdoors, and exercise habits. Sex- and age-stratified analyses were also performed. In addition, the linearity association was tested by entering sarcopenia severity as a continuous variable in a regression model. Finally, to test whether sex differences in the association between sarcopenia severity and cognitive function existed, an interaction term (sex*sarcopenia severity) was created and added to the multivariate model for analysis.

Data were analyzed using SPSS Statistics version 25.0 (IBM Corporation, Armonk, NY, USA), and statistical significance was set at $p < 0.05$.

Results

Some of the SONIC and Takashimadaira studies were excluded from the analysis because sarcopenia could not be determined (e.g., missing body composition and gait function). In addition, those with missing MMSE scores ($n = 91$) and sarcopenia status ($n = 404$) were excluded. In total, 6,426 participants were included in the analysis (Figure 1).

The characteristics of the cohort [mean age (min-max): 72.9 (65–95) years] are shown in Table 1. The prevalence of sarcopenia was 13.9% for men and 13.3% for women. The prevalence of severe sarcopenia was 4.2% for men and 3.9% for women. Poor cognitive function was observed in 270 participants (4.2%), with a higher prevalence in men (5.7%) compared with in women (3.4%). Educational attainment was higher in men than in women and decreased with sarcopenia severity in both sexes.

There was a positive association between sarcopenia severity and poor cognitive function (P for trend <0.001). The multivariable OR (95% CIs) for poor cognitive function was 2.19 (1.54, 3.13) for individuals with sarcopenia and 3.43 (2.14, 5.49) for those with severe sarcopenia (Table 2).

The sex- and age-stratified analyses showed that prevalence of poor cognitive function was higher in the older age group than in the younger age group for both sexes. Additionally, the prevalence of poor cognitive function was higher in men (57.2%) than that in women (34.0%) and higher in older category (86.5% for men and 59.7% for women). Multivariate analyses showed a positive association between sarcopenia severity and poor cognitive function in both sexes and age-category. Its association was stronger in women than men (p for interaction; <0.001) between sex and sarcopenia severity in both age groups.

Discussion

This study investigated the association between sarcopenia severity and poor cognitive function according to sex and age among community-dwelling older adults in Japan. There was a linear relationship between sarcopenia severity and poor cognitive function across different sex and age categories and was most clearly reflected in the older age group. Additionally, this association was stronger in women compared with men. These findings indicate that the association between sarcopenia severity, or skeletal muscle health, and cognitive function is clearer for women than for men. Additionally, these results suggest that skeletal muscle mass and function and motor control may be closely associated with cognitive function and, through related behavior change, may serve as a method for preventing MCI and dementia.

Systematic reviews and meta-analyses have reported an association between sarcopenia and cognitive impairment, but the heterogeneity is high and inconclusive (8, 9). Our results showed that severe sarcopenia was associated with a higher risk of poor cognitive function than sarcopenia and non-sarcopenia in both sexes and age categories, consistent with a previous study demonstrating a strong association between poor physical function and cognitive impairment (23). Therefore, not only muscle mass, but also muscle strength and gait function may contribute to cognitive function. The role of skeletal muscle as an endocrine organ includes the secretion of myokines with its contraction in exercise. For instance, physical activity and exercise stimulate BDNF expression in the hippocampus, a brain region responsible for memory and learning (24). This association is widely recognized as muscle-brain crosstalk, and quantitative and qualitative (neurological) aspects of skeletal muscle are closely

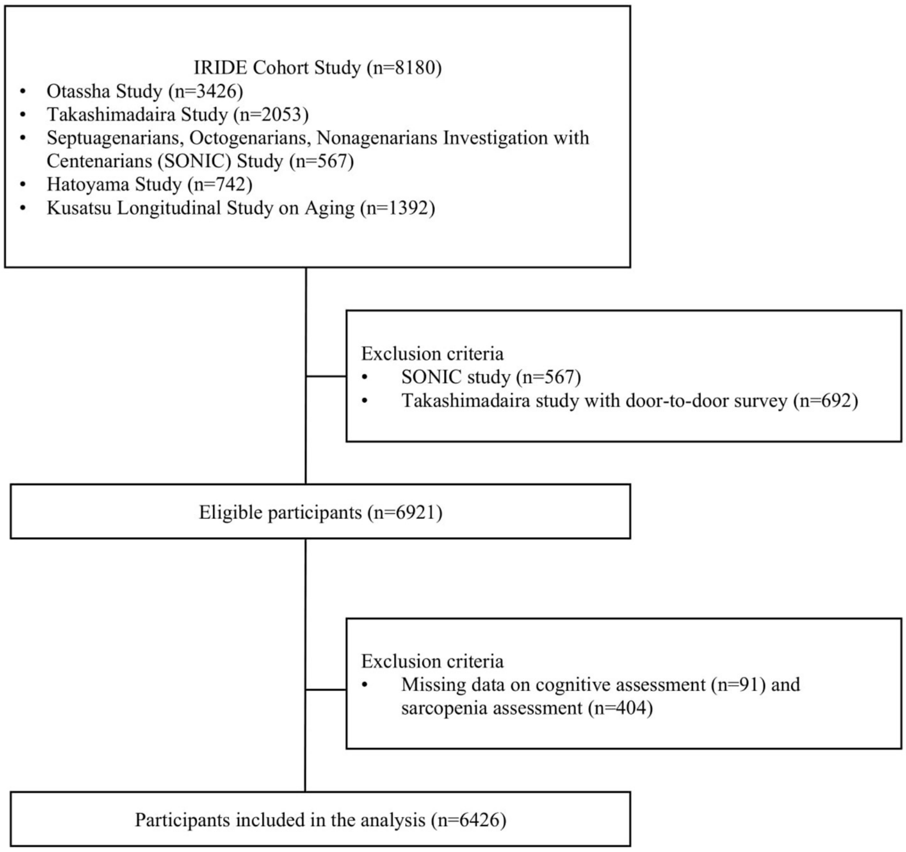

FIGURE 1
Flowchart of participant selection.

related to poor cognitive function (6, 25). Indeed, aerobic and resistance exercise interventions have been shown to be effective in improving cognitive function, regardless of cognitive status (26). Other possibilities include an increased fear of falling and injury due to reduced skeletal muscle function, which may result in a shift away from social participation and a decline in cognitive function (27). Alternatively, the progression of sarcopenia could lead to vascular cognitive dysfunction *via* exacerbation of metabolic diseases (28). Therefore, further longitudinal studies from multiple perspectives on the relationship between sarcopenia and cognitive function are needed.

The detailed mechanisms for the sex differences in the effects of sarcopenia severity on cognitive function are unclear, although they may be related to biological differences between men and women, such as differences in brain volume (29, 30), sex hormones (31), and body composition and physical performance (31). In particular, brain volume is related to brain reserve and is known to be one of the factors contributing to sex differences in cognitive decline (32). It has also been shown that elevated inflammatory markers (e.g., interleukin-6 and C-reactive protein) associated with reduced skeletal muscle mass are particularly noticeable in women (33). These may be one factor explaining the possible strong association between sarcopenia severity and poor cognitive decline in women than in men (29).

Moreover, the correlation between sarcopenia and poor cognitive function may be due to inflammation, oxidative stress, and abnormal hormone secretion (34). These conditions affect skeletal muscle and brain health and may contribute to brain atrophy in neurodegenerative diseases (35). In addition, inflammatory biomarkers, such as tumor necrosis factor-α, interleukin-6, and C-reactive protein, are associated with physical function and medial temporal lobe atrophy (36, 37). Therefore, future longitudinal studies should be conducted to ascertain whether inflammatory markers mediate the association between sarcopenia and poor cognitive function.

We clearly demonstrated linear association between sarcopenia severity and poor cognitive function according to sex and age categories. This can be attainable due to larger sample size than that of previous studies and systematic reviews. However, there are several noteworthy limitations. First, the study's cross-sectional and observational nature prevented the determination of causal relationships between sarcopenia and poor cognitive function. Second, although the model adjusted for potential confounding factors, unmeasured confounders may have affected the association, including dietary habits, and genetic factors. Third, the voluntary nature of participation in health checkups may have led to selection bias, where the individuals who underwent checkups tended to have higher health literacy levels, and those who did not might have had additional health

TABLE 1 Characteristics of the cohort according to the severity of sarcopenia.

	Overall (n = 6,426)	Men (n = 2,220) Sarcopenia status			Women (n = 4,206) Sarcopenia status		
		Non-sarcopenia (n = 1,819, 81.9%)	Sarcopenia (n = 309, 13.9%)	Severe sarcopenia (n = 92, 4.2%)	Non-sarcopenia (n = 3,481, 82.8%)	Sarcopenia (n = 559, 13.3%)	Severe sarcopenia (n = 166, 3.9%)
Age, years	74 [9]	73 [10]	79 [7]	83 [6]	73 [9]	78 [8]	80 [8]
65–74	3,438 (53.5)	1,078 (59.3)	70 (22.7)	9 (9.8)	2,081 (59.8)	180 (32.2)	20 (12.0)
≥75	2,988 (46.5)	741 (40.7)	239 (77.3)	83 (90.2)	1,400 (40.2)	379 (67.8)	146 (88.0)
MMSE, score	29 [3]	29 [2]	28 [4]	27 [4]	29 [2]	28 [2]	27 [4]
Poor cognitive function, yes	270 (4.2)	74 (4.1)	34 (11.0)	19 (20.7)	75 (2.2)	35 (6.3)	33 (19.9)
Past medical history							
Hypertension	2,849 (44.3)	880 (48.4)	145 (46.9)	49 (53.3)	1,439 (41.3)	249 (44.5)	87 (52.4)
Diabetes	811 (12.6)	322 (17.7)	62 (20.1)	20 (21.7)	328 (9.4)	57 (10.2)	22 (13.3)
Dyslipidemia	2,257 (35.1)	510 (28.0)	78 (25.2)	22 (23.9)	1,373 (39.4)	227 (40.6)	47 (28.3)
Stroke	377 (5.9)	154 (8.5)	23 (7.4)	16 (17.4)	137 (3.9)	32 (5.7)	15 (9.0)
Smoking							
Current	624 (9.7)	312 (17.2)	54 (17.5)	13 (14.1)	201 (5.8)	35 (6.3)	9 (5.4)
Past	1,623 (25.3)	968 (53.2)	162 (52.4)	52 (56.5)	370 (10.6)	52 (9.3)	19 (11.4)
Never	4,065 (63.3)	505 (27.8)	89 (28.8)	23 (25.0)	2,865 (82.3)	459 (82.1)	124 (74.7)
Alcohol consumption							
Current	2,844 (44.3)	1,190 (65.4)	173 (56.0)	34 (37.0)	1,265 (36.3)	143 (25.6)	39 (23.5)
Past	518 (8.1)	172 (9.5)	54 (17.5)	20 (21.7)	206 (5.9)	50 (8.9)	16 (9.6)
Never	2,881 (44.8)	393 (21.6)	66 (21.4)	29 (31.5)	1,955 (56.2)	341 (61.0)	97 (58.4)
Educational attainment, years	12 [4]	12 [4]	12 [7]	12 [7]	12 [3]	12 [3]	11 [3]
GDS-15, score	2 [3]	2 [3]	3 [5]	4 [4]	2 [3]	3 [5]	4 [4]
Depressive symptoms, n	1,244 (19.4)	313 (17.2)	96 (31.4)	30 (32.6)	568 (16.3)	180 (32.2)	57 (34.3)
Frequency of going outdoors (days per week)							
<1	39 (0.6)	12 (0.7)	3 (1.0)	3 (3.3)	12 (0.3)	3 (0.5)	6 (3.6)
1–2	192 (3.0)	49 (2.7)	13 (4.2)	8 (8.7)	67 (1.9)	34 (6.1)	21 (12.7)
3–6	1,269 (19.7)	310 (17.0)	78 (25.2)	26 (28.3)	665 (19.1)	148 (26.5)	42 (25.3)
7	4,902 (76.3)	1,445 (79.4)	213 (68.9)	52 (56.5)	2,727 (78.3)	370 (66.2)	95 (57.2)
Exercise habits (days per week)							
<1	888 (13.8)	246 (13.5)	41 (13.3)	13 (14.1)	471 (13.5)	89 (15.9)	28 (16.9)
1–4	5,068 (78.9)	1,380 (75.9)	237 (76.7)	65 (70.7)	2,842 (81.6)	427 (76.4)	117 (70.5)
>4	86 (1.3)	49 (2.7)	2 (0.6)	1 (1.1)	30 (0.9)	2 (0.4)	2 (1.2)

Data are means (standard deviations) or median [interquartile range], or numbers (percentages).
MMSE, Mini-mental State Examination; GDS, Geriatric Depression Scale-15.
Depressive symptoms were defined as a GDS ≥ 5.

10.3389/fpubh.2023.1148404

TABLE 2 Sex-stratified odds ratios (95% confidence intervals) of poor cognitive function according to sarcopenia status and gender.

	Age-stratified	Number of cases (%)		Sarcopenia	Severe sarcopenia	*P* for trend	Interaction between sex and sarcopenia severity
All participants (*n* = 6,426)		270 (4.2)	Unadjusted	3.16 (2.37, 4.21)	9.91 (7.11, 13.81)	<0.001	
			Age-adjusted	2.05 (1.52, 2.77)	4.50 (3.12, 6.51)	<0.001	
			Multivariate[†]	2.19 (1.54, 3.13)	3.43 (2.14, 5.49)	<0.001	
Men	Total cohort (*n* = 2,220)	127 (5.7)	Unadjusted	2.92 (1.91, 4.46)	6.14 (3.52, 9.74)	<0.001	
			Age-adjusted	1.93 (1.22, 3.06)	2.80 (1.48, 5.30)	<0.001	
			Multivariate*	2.00 (1.14, 3.51)	2.78 (1.24, 6.23)	0.003	
	65–74 years (*n* = 1,157)	35 (3.0)	Age-adjusted	5.12 (2.16, 12.12)	4.71 (0.55, 40.02)	0.002	
			Multivariate*	3.74 (1.03, 13.60)	18.27 (1.29, 259.69)	0.007	
	≥75 years (*n* = 1,083)	92 (8.7)	Age-adjusted	1.45 (0.87, 2.42)	2.70 (1.42, 5.13)	0.005	
			Multivariate*	1.73 (0.92, 3.24)	2.41 (1.02, 5.70)	0.021	0.001
Women	Total cohort (*n* = 4,206)	143 (3.4)	Unadjusted	3.37 (2.28, 4.96)	13.50 (8.88, 20.52)	<0.001	
			Age-adjusted	2.00 (1.31, 3.07)	5.36 (3.26, 8.79)	<0.001	0.001
			Multivariate*	2.36 (1.48, 3.76)	4.18 (2.31, 7.56)	<0.001	<0.001
	65–74 years (*n* = 2,281)	28 (1.2)	Age-adjusted	3.05 (1.22, 7.63)	13.97 (3.75, 51.98)	<0.001	
			Multivariate*	3.57 (1.29, 9.88)	15.68 (2.97, 82.93)	0.001	
	≥75 years (*n* = 1,925)	115 (6.0)	Age-adjusted	1.99 (1.27, 3.10)	5.15 (3.16, 8.41)	<0.001	
			Multivariate*	2.04 (1.21, 3.44)	3.57 (1.87, 6.80)	<0.001	

The odds ratios and 95% confidence intervals were calculated using non-sarcopenia as a reference in each model.
[†]Adjusted for sex, age, educational attainment, smoking status, drinking status, cohort categories, living alone, history of non-communicable diseases (hypertension, diabetes, dyslipidemia, and stroke), geriatric depressive symptom (GDS ≥ 5), frequency of going outdoors, and exercise habits.
*, † minus sex.

10.3389/fpubh.2023.1148404

conditions or lower health literacy levels. Finally, poor cognitive function was assessed using the MMSE, and a cutoff with high sensitivity and specificity for MCI was applied. However, the MMSE is not necessarily valid for diagnosing dementia or MCI. Therefore, some participants with poor cognitive function may have been misclassified. Future studies should incorporate methods higher sensitivity levels for monitoring cognitive outcomes during examinations.

Conclusion

In conclusion, sarcopenia severity was linearly associated with poor cognitive function among community-dwelling older adults in Japan, and this association was stronger in women compared with men. Further studies should examine the longitudinal relationship between sarcopenia and poor cognitive function, including the onset of MCI and dementia.

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 human participants were reviewed and approved by the Research Ethics Committee of the Tokyo Metropolitan Institute for Geriatrics and Gerontology. The patients/participants provided their written informed consent to participate in this study.

Author contributions

TO designed the study, analyzed the data, and wrote the manuscript. HS, YO, NK, TA, MY, SO, TI, YF, SA, and IRIDE Cohort Study Investigators collected the data and revised the manuscript. KT supervised the project. All authors critically revised the manuscript for important intellectual content and approved the version to be published.

Funding

This research was supported by a grant from the Integrated Research Initiative for Living Well With Dementia from Tokyo Metropolitan Government.

Acknowledgments

We thank the participants and staff of the Tokyo Metropolitan Institute of Gerontology and Editage (www.editage.com) for English language editing.

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.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1148404/full#supplementary-material

References

1. WHO. *Dementia*. Available online at: https://www.who.int/news-room/fact-sheets/detail/dementia (accessed November 2, 2022).

2. Cabinet Office Site. *Annual Report on the Aging Society*. (2017). Available online at: https://www8.cao.go.jp/kourei/english/annualreport/2017/pdf/c1-2-1.pdf (accessed November 2, 2022).

3. Petersen RC, Caracciolo B, Brayne C, Gauthier S, Jelic V, Fratiglioni L. Mild cognitive impairment: A concept in evolution. *J Intern Med.* (2014) 275:214–28. doi: 10.1111/joim.12190

4. Nuzum H, Stickel A, Corona M, Zeller M, Melrose RJ, Wilkins SS. Potential benefits of physical activity in MCI and dementia. *Behav Neurol.* (2020) 2020:7807856. doi: 10.1155/2020/7807856

5. Brown BM, Peiffer J, Rainey-Smith SR. Exploring the relationship between physical activity, beta-amyloid and tau: A narrative review. *Ageing Res Rev.* (2019) 50:9–18. doi: 10.1016/j.arr.2019.01.003

6. Pedersen BK. Physical activity and muscle–brain crosstalk. *Nat Rev Endocrinol.* (2019) 15:383–92. doi: 10.1038/s41574-019-0174-x

7. Ramsey KA, Rojer AGM, D'Andrea L, Otten RHJ, Heymans MW, Trappenburg MC, et al. The association of objectively measured physical activity and sedentary behavior with skeletal muscle strength and muscle power in older adults: A systematic review and meta-analysis. *Ageing Res Rev.* (2021) 67:101266. doi: 10.1016/j.arr.2021.101266

8. Peng TC, Chen WL, Wu LW, Chang YW, Kao TW. Sarcopenia and cognitive impairment: A systematic review and meta-analysis. *Clin Nutr.* (2020) 39:2695–701. doi: 10.1016/j.clnu.2019.12.014

9. Cabett Cipolli G, Sanches Yassuda M, Aprahamian I. Sarcopenia is associated with cognitive impairment in older adults: A systematic review and meta-analysis. *J Nutr Health Aging.* (2019) 23:525–31. doi: 10.1007/s12603-019-1188-8

10. Chen X, Cao M, Liu M, Liu S, Zhao Z, Chen H. Association between sarcopenia and cognitive impairment in the older people: A meta-analysis. *Eur Geriatr Med.* (2022) 22:1. doi: 10.1007/s41999-022-00661-1

11. Chen L, Woo J, Assantachai P, Auyeung T, Chou M, Iijima K, et al. Asian working group for sarcopenia : 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc.* (2020) 21:300–7. doi: 10.1016/j.jamda.2019.12.012

12. Bradburn S, Murgatroyd C, Ray N. Neuroinflammation in mild cognitive impairment and Alzheimer's disease: A meta-analysis. *Ageing Res Rev.* (2019) 50:1–8. doi: 10.1016/j.arr.2019.01.002

13. Nagase T, Tohda C. Skeletal muscle atrophy-induced hemopexin accelerates onset of cognitive impairment in Alzheimer's disease. *J Cachexia Sarcopenia Muscle.* (2021) 12:2199–210. doi: 10.1002/jcsm.12830

14. Abe T, Kitamura A, Yamashita M, Kim H, Obuchi SP, Ishizaki T, et al. Simple screening models for cognitive impairment in community settings: The IRIDE Cohort Study. *Geriatr Gerontol Int.* (2022) 22:292–7. doi: 10.1111/ggi.14360

15. Shoji S, Yoshida H, Fujiwara Y, Amano H, Fukaya T, Ri S, et al. A 10-year community intervention for disability prevention and its effect on healthy aging in Kusatsu town. *Nihon Koshu Eisei Zasshi.* (2013) 60:596–605. doi: 10.11236/JPH.60.9_596

16. Murayama H, Nishi M, Shimizu Y, Kim MJ, Yoshida H, Amano H, et al. The hatoyama cohort study: Design and profile of participants at baseline. *J Epidemiol.* (2012) 22:551–8. doi: 10.2188/jea.JE20120015

17. Miura Y, Hashii N, Tsumoto H, Takakura D, Ohta Y, Abe Y, et al. Change in N-glycosylation of plasma proteins in Japanese semisupercentenarians. *PLoS ONE.* (2015) 10:142645. doi: 10.1371/journal.pone.0142645

18. Kera T, Kawai H, Yoshida H, Hirano H, Kojima M, Fujiwara Y, et al. Physical and psychological characteristics of the community-dwelling elderly with heart disease. *Nihon Koshu Eisei Zasshi.* (2017) 64:3–13. doi: 10.11236/JPH.64.1_3

19. Taniguchi Y, Watanabe Y, Osuka Y, Kitamura A, Seino S, Kim H, et al. Characteristics for gait parameters of community-dwelling elderly Japanese with lower cognitive function. *PLoS ONE.* (2019) 14:212646. doi: 10.1371/journal.pone.0212646

20. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* (1975) 12:162–7. doi: 10.1016/0022-3956(75)90026-6

21. Sakurai R, Kim Y, Inagaki H, Tokumaru AM, Sakurai K, Shimoji K, et al. MMSE cutoff discriminates hippocampal atrophy: Neural evidence for the cutoff of 24 points. *J Am Geriatr Soc.* (2021) 69:839–41. doi: 10.1111/jgs.17010

22. Shah A, Herbert R, Lewis' S, Mahendran R, Platt J, Bhattacharyya B. Screening for depression among acutely ill geriatric inpatients with a short geriatric depression scale. *Age Ageing.* (1997) 26:217–21. doi: 10.1093/ageing/26.3.217

23. Ishii H, Makizako H, Doi T, Tsutsumimoto K, Shimada H. Associations of skeletal muscle mass, lower-extremity functioning, and cognitive impairment in community-dwelling older people in Japan. *J Nutr Health Aging.* (2019) 23:35–41. doi: 10.1007/s12603-018-1110-9

24. Severinsen MCK, Pedersen BK. Muscle–organ crosstalk: The emerging roles of myokines. *Endocr Rev.* (2020) 41:594–609. doi: 10.1210/endrev/bnaa016

25. Severinsen MCK, Pedersen BK. Muscle-organ crosstalk: the emerging roles of myokines. *Endocr Rev.* (2020) 42:97–9. doi: 10.1210/endrev/bnaa024

26. Northey JM, Cherbuin N, Pumpa KL, Smee DJ, Rattray B. Exercise interventions for cognitive function in adults older than 50: A systematic review with meta-analysis. *Br J Sports Med.* (2018) 52:154–60. doi: 10.1136/bjsports-2016-096587

27. Merchant RA, Chen MZ, Wong BLL, Ng SE, Shirooka H, Lim JY, et al. Relationship between fear of falling, fear-related activity restriction, frailty, and sarcopenia. *J Am Geriatr Soc.* (2020) 68:2602–8. doi: 10.1111/jgs.16719

28. Srikanth V, Sinclair AJ, Hill-Briggs F, Moran C, Biessels GJ. Type 2 diabetes and cognitive dysfunction—Towards effective management of both comorbidities. *Lancet Diabetes Endocrinol.* (2020) 8:535–45. doi: 10.1016/S2213-8587(20)30118-2

29. Levine DA, Gross AL, Briceño EM, Tilton N, Giordani BJ, Sussman JB, et al. Sex differences in cognitive decline among US adults. *J Am Med Assoc Netw Open.* (2021) 4:169. doi: 10.1001/jamanetworkopen.2021.0169

30. Ruigrok ANV, Salimi-Khorshidi G, Lai MC, Baron-Cohen S, Lombardo MV, Tait RJ, et al. A meta-analysis of sex differences in human brain structure. *Neurosci Biobehav Rev.* (2014) 39:34–50. doi: 10.1016/j.neubiorev.2013.12.004

31. Anderson LJ, Liu H, Garcia JM. Sex differences in muscle wasting. *Adv Exp Med Biol.* (2017) 9:153–97. doi: 10.1007/978-3-319-70178-3_9

32. Subramaniapillai S, Almey A, Natasha Rajah M, Einstein G. Sex and gender differences in cognitive and brain reserve: Implications for Alzheimer's disease in women. *Front Neuroendocrinol.* (2021) 60:100879. doi: 10.1016/j.yfrne.2020.100879

33. Canon ME, Crimmins EM. Sex differences in the association between muscle quality, inflammatory markers, and cognitive decline. *J Nutr Health Aging.* (2011) 15:695–8. doi: 10.1007/s12603-011-0340-x

34. Namioka N, Hanyu H, Hirose D, Hatanaka H, Sato T, Shimizu S. Oxidative stress and inflammation are associated with physical frailty in patients with Alzheimer's disease. *Geriatr Gerontol Int.* (2017) 17:913–8. doi: 10.1111/ggi.12804

35. Kilgour AHM, Todd OM, Starr JM. A systematic review of the evidence that brain structure is related to muscle structure and their relationship to brain and m. *BMC Geriatr.* (2014) 14:35. doi: 10.1186/1471-2318-14-85

36. Kamper RS, Alcazar J, Andersen LL, Haddock B, Jørgensen NR, Hovind P, et al. Associations between inflammatory markers, body composition, and physical function: the Copenhagen Sarcopenia Study. *J Cachexia Sarcopenia Muscle.* (2021) 12:1641–52. doi: 10.1002/jcsm.12832

37. Kose Y, Ikenaga M, Yamada Y, Morimura K, Takeda N, Ouma S, et al. Timed Up and Go test, atrophy of medial temporal areas and cognitive functions in community-dwelling older adults with normal cognition and mild cognitive impairment. *Exp Gerontol.* (2016) 85:81–7. doi: 10.1016/j.exger.2016.09.019

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 13 April 2023
DOI 10.3389/fpubh.2023.1073968

Check for updates

OPEN ACCESS

EDITED BY
Luciane Portas Capelo,
Federal University of São Paulo,
Brazil

REVIEWED BY
Mara Carsote,
Carol Davila University of Medicine and Pharmacy,
Romania
Xiang Li,
Tulane University School of Public Health and Tropical Medicine,
United States
Shangmin Chen,
Shantou University,
China

*CORRESPONDENCE
Lige Song
✉ 6songlige@tongji.edu.cn

SPECIALTY SECTION
This article was submitted to Aging and Public Health, a section of the journal Frontiers in Public Health

RECEIVED 19 October 2022
ACCEPTED 21 March 2023
PUBLISHED 13 April 2023

CITATION
Liu Y, Zeng Y, Lu J, Zhang X, Zhang Z, Li H, Liu P, Ma B, Gu Y and Song L (2023) Correlation of hemoglobin with osteoporosis in elderly Chinese population: A cross-sectional study. *Front. Public Health* 11:1073968.
doi: 10.3389/fpubh.2023.1073968

Correlation of hemoglobin with osteoporosis in elderly Chinese population: A cross-sectional study

Yichen Liu[1,2], Yue Zeng[1,2], Jun Lu[3], Xiaoya Zhang[1,2], Zikai Zhang[4], Huijuan Li[1,2], Peipei Liu[1], Bin Ma[5], Yiqun Gu[6] and Lige Song[1,2]*

[1]Department of Endocrinology, Shanghai Tongji Hospital, School of Medicine, Tongji University, Shanghai, China, [2]Institute of Osteoporosis and Metabolic Bone Diseases, School of Medicine, Tongji University, Shanghai, China, [3]Department of Endocrinology and Metabolism, Putuo Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, China, [4]Division of Science and Research, Shanghai Tongji Hospital, School of Medicine, Tongji University, Shanghai, China, [5]Division of Spine, Department of Orthopedics, Shanghai Tongji Hospital, School of Medicine, Tongji University, Shanghai, China, [6]Ganquan Community Health Service Center, Shanghai, China

Introduction: In the elder population, both low hemoglobin (Hb)/anemia and osteoporosis (OP) are highly prevalent. However, the relationship between Hb and OP is still poorly understood. This study was to evaluate the correlation between Hb and OP in Chinese elderly population.

Methods: One thousand and sisty-eight individuals aged 55–85 years were enrolled into this cross-sectional study during June 2019–November 2019. Data on the demographics and clinical characteristics were recorded. Detections of complete blood count, liver/kidney function, glucose metabolism and lipid profile, and thoracolumbar X-ray were performed, and bone mineral density (BMD) at lumbar spine 1–4, femur neck, and total hip was measured by dual-energy X-ray absorptiometry (DXA). Univariate and multivariate linear regression analyses were employed to evaluate the correlation between Hb with BMD T-score. Logistic regression analysis was performed to access the correlation between different Hb levels and the odds ratio (OR) for OP.

Results: Compared with non-OP group, OP patients had lower level of Hb. Univariate linear regression analysis indicated Hb level was positively related to the BMD of lumbar spine 1–4, femur neck and total hip, and this relationship remained after adjusting confounding variables [gender, age, body mass index (BMI), diabetes mellitus (DM) and morphological vertebral fracture]. Logistic regression analysis showed the ORs for OP decreased with the increase of Hb. Compared with the subjects with the lowest quartile of Hb, the OR for OP in the highest quartile group was 0.60 (0.41–0.89) after adjusting for gender, age and BMI, and the OR for OP was 0.62 (0.41–0.92) after further adjustment for gender, age, BMI, DM, and lipid indexes.

Discussion: In conclusion, Lower Hb level is related to lower BMD in the elderly population. However, whether Hb level could be used to predict the risk of OP needs to be further determined in more longitudinal clinical studies.

KEYWORDS

hemoglobin, osteoporosis, bone mineral density, elderly population, Chinese

1. Introduction

Along with the aging of society, osteoporosis (OP) and anemia become more and more popular, which may be related to the prevalence of malnutrition in the aged population (1, 2). OP is a metabolic skeletal disease characterized by the decreased bone mineral density (BMD) and microarchitectural deterioration with increased bone fragility and susceptibility to fractures, which may increase the disability and mortality (3, 4). OP, the most common metabolic bone disorder, brings major burden to the public health and affects an enormous number of people (5). According to the statistics from the International Osteoporosis Foundation (IOF), one in three women and one in five men older than 50 years will experience osteoporotic fracture in their lifetime (6). There are many causes for the decreased BMD in the elder population, including reduction of sex steroid (7), lower insulin-like growth factor-1(IGF-1) (8), inadequate physical activity (9), and improper nutrition status (10). In addition, nutritional deficiency due to reduced dietary intake and/or inadequate absorption of particular nutrients has been identified as an important cause of osteopenia and OP (11).

Hemoglobins (Hbs) are large and complex protein molecules, and the Hb level is related to nutrients from dietary intakes (12). Animal experiments have shown that lower Hb level is related to the impaired bone turnover and poor bone strength (13–15). Dietary iron deficiency in Wistar rats can induce the decrease of Hb concentration, accompanied by decreased serum osteocalcin concentration, bone mineral content, BMD, and mechanical strength of the femur (14). Thalassemia and sickle cell anemia are two hematopoietic disorders. The trabecular bone volume, trabecular number, trabecular thickness, cortical thickness, and cortical area reduce significantly in both heterozygous and homozygous thalassemia mice (th3) (16). These bone abnormalities in thalassemia may be induced by ineffective erythropoiesis, iron overload, chelation, and endocrine dysfunction secondary to iron overload (17, 18). In addition, abnormal bone microarchitectural and biomechanical properties have also been identified in sickle cell anemia mice (19). Comparing to wild-type mice, transgenic sickle cell anemia mice displayed significantly fewer and deteriorated geometry trabeculae, decreased cortical thickness, and lower elastic modulus of the cortical bone (19). These indicate that lower Hb level and anemia are related to the abnormal bone phenotypes in animals.

There is evidence showing that lower Hb level is related to the lower BMD. An Italy population-based study on 950 elderly individuals showed that the individuals with lower Hb levels or anemia had lower bone density on the peripheral quantitative computed tomography (pQCT), especially in the cortical bone (20). Similar results were reported in another Italy study on the elderly population (>75 years) when BMD was detected by ultrasound bone densitometer (21). A Korean cross-sectional study involving 13,127 subjects (>20 years) also showed that Hb level was positively related to the lumbar spine and femoral neck BMD on dual-energy X-ray absorptiometry (DXA) in men (22). Concerning the possible biological mechanisms between Hb and BMD, the bone-derived hormone fibroblast growth factor 23 (FGF-23), mainly produced by osteoblasts and osteocytes, can regulate erythropoiesis and may be an important link between bone metabolism and erythropoiesis (23). Besides, another study proposed that extracellular acidification and oxidative stress under hypoxemia caused by anemia could increase bone resorption and lead to lower BMD (24). Nevertheless, a prospective longitudinal study from United States failed to show the association between Hb level and lumbar spine or total hip BMD in the community-dwelling older individuals (25). Besides BMD, some studies have also focused on the relationship between serum Hb level and fracture risk. A prospective cohort study showed that the increased fracture risk associated with anemia ranged from 7 to 38% across the fracture sites in the United States. postmenopausal women of diverse racial and ethnic backgrounds (26), but some other studies showed the U-shaped relationship between Hb level and hip fracture risk (27).

There were few studies investigating the relationship between Hb and OP in China. A cross-sectional study which included 495 type 2 diabetes mellitus (T2DM) patients showed that Hb levels were associated with the presence of OP in male patients, especially in those with aged 50 years and older (28). Another retrospective study conducted in China demonstrated that the Hb level in the OP group were higher than those without OP, and moreover, BMD was negatively correlated with Hb level in postmenopausal women (29). To further confirm the relationship between Hb level and OP in aged Chinese individuals, we conducted a cross-sectional study with larger samples than the published study.

2. Materials and methods

2.1. Study population

This was a cross-sectional study conducted from June 2019 to November 2019. The participants in this study were recruited from individuals who underwent routine physical examination at Ganquan community and Yichuan community in Putuo District, Shanghai, China. Questionnaire including name, gender, age, birth of data, race, home address, weight, and height was collected during visit. The inclusion criteria were as follows: (1) 55–85 years old; (2) BMI between18.5 and 35.0 kg/m^2; (3) normal liver and renal function; and (4) never use of drugs that can affect bone metabolism such as anti-osteoporotic drugs, glucocorticoid, thyroid hormones, estrogen, and thiazolidinedione. The exclusion criteria were as follows: (1) a history of gastrointestinal surgery; (2) a history of Hb disease (e.g., sickle cell anemia, thalassemia); (3) a history of diseases that can affect Hb levels (e.g., diabetes insipidus and parathyroid storm); (4) a history of major cardiovascular and cerebrovascular diseases; (5) autoimmune diseases; (6) malignant tumors; (7) mental diseases; (8) Non-menopausal women; and (9) with unhealthy lifestyle habits (e.g., addiction to smoking and excessive drinking). A total of 1,068 participants (449 males and 619 females) were recruited into this study. OP was diagnosed according to the AACE/ACE primary osteoporosis guideline (2020) (2). Written informed consent was obtained from each participant. This study was approved by the Ethics Committee of Shanghai Tongji Hospital.

2.2. Demographics and clinical characteristics

Data on demographics including age, height, weight, body mass index (BMI), and clinical characteristics (diseases, medications, etc.) were recorded. Physical examinations were performed by trained medical staffs following standardized procedures.

2.3. Complete blood count and biochemical parameters

Fasting blood samples were obtained and complete blood count [red blood cell (RBC) count, Hb, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and white blood cell (WBC) count] was measured using an automatic blood analyzer (SYSMEX XN3000) immediately. Serum and plasma were stored at −80°C for further automatic biochemical assays, including glucose metabolic indices, lipid profile [triglyceride (TG), total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), and high-density lipoprotein-cholesterol (HDL-C)], and liver and kidney function. All laboratory examinations were performed in Shanghai Tongji Hospital, Shanghai, China. Considering gender difference, patients were divided into four groups according to Hb quartiles as follows: Quartile 1, ≤143.0; Quartile 2, 143.1–151.0; Quartile 3, 151.1–159.6; and Quartile 4, >159.6 g/L for men; and Quartile 1, ≤130.0; Quartile 2, 130.1–137.0; Quartile 3, 137.1–143.0; and Quartile 4, >143.0 g/L for women, separately.

2.4. Thoracolumbar spine X-ray

The radiographs of the spine (standing long-cassette coronal and lateral views) of each individual were evaluated with the Genant visual semi-quantitative method independently by three radiologists. The lateral view should include at least T4 to L5.

2.5. BMD by dual-energy X-ray absorptiometry

Bone mineral density at lumbar spine 1–4, femur neck and total hip were detected by dual-energy X-ray absorptiometry (DXA, HOLOGIC Discovery; coefficient of variation <1%).

2.6. Statistical analysis

Kolmogorov–Smirnov test was used to assess the distribution of continuous variables. Data were expressed as median (interquartile range, IQR) or mean ± SD for continuous variables or as frequency (%) for categorical variables. The differences between continuous variables were examined using the Mann–Whitney U test or Student's *t*-test; categorical variables were tested using the Chi-square test.

Multivariate linear regression model was employed to analyze the association of BMD T-score at each site with clinical characteristics and results from blood examinations. Logistic regression model was used to estimate the odds ratios for OP according to different Hb levels/categories. All analyses were adjusted for gender, age, and BMI (Model 1), and then for gender, age, BMI, and diabetes mellitus (DM; Model 2), and further for gender, age, BMI, DM, TG, TC, LDL-C, and HDL-C. A value of two-sided $p < 0.05$ was considered statistically significant.

3. Results

3.1. Clinical characteristics

The enrolled individuals ($n = 1,068$) were divided into osteoporotic (OP) and non-osteoporotic (non-OP) groups according to the guideline from the IOF (30). Subjects in the OP group had significantly older age (68.81 ± 4.96 vs. 67.81 ± 5.57 years, $p = 0.004$) and lower BMI (23.15 ± 3.88 vs. 24.40 ± 3.47 kg/m^2, $p < 0.001$) when compared with those in the non-OP group. Furthermore, the prevalence of DM was lower (20.54 vs. 30.05%, $p = 0.001$) and the rate of morphological vertebral fracture was higher (78.85 vs. 45.22%, $p < 0.001$) in the OP group as compared to the non-OP group.

Red blood cell count, Hb, and mean corpuscular hemoglobin (MCH) were markedly lower in the OP group than in the non-OP group (4.56 ± 0.51 × 10^{12}/L vs. 4.78 ± 0.50 × 10^{12}/L, $p < 0.001$; 137.68 ± 12.35 vs. 145.40 ± 13.15 g/L, $p < 0.001$ and 30.37 ± 1.83. vs 30.65 ± 1.72 pg., $p = 0.015$). Moreover, as compared to the subjects in the non-OP group, subjects in the OP group had lower fasting plasma glucose (FBG; 5.51 ± 1.28 vs. 5.80 ± 1.45 mmol/L, $p = 0.001$) and higher TC (5.41 ± 1.10 vs. 5.05 ± 1.07 mmol/L, $p < 0.001$), LDL-C (3.11 ± 0.94 vs. 2.90 ± 0.95 mmol/L, $p = 0.001$) and HDL-C (1.51 ± 0.44 vs. 1.33 ± 0.40 mmol/L, $p < 0.001$) but lower TG (1.64 ± 0.93 vs. 1.79 ± 1.20 mmol/L, $p = 0.020$; Table 1).

3.2. Correlation between Hb and BMD T-score on multivariate linear regression analysis

The correlations of clinical parameters (gender, age, BMI, history of DM, and vertebral fracture) and Hb with BMD T-score were analyzed by multivariate linear regression. As compared to males, the gender of female was negatively related to the BMD T-score at lumbar spine 1–4 ($\beta = -1.156$, $p < 0.001$), femur neck ($\beta = -0.494$, $p < 0.001$), and total hip ($\beta = -0.513$, $p < 0.001$). Age was negatively related to the BMD T-score at the femur neck ($\beta = -0.031$, $p < 0.001$) and total hip ($\beta = -0.015$, $p = 0.004$). Moreover, BMI and history of DM were positively related to the BMD T-score at lumbar spine 1–4 ($\beta = 0.083$, $p < 0.001$ and $\beta = 0.409$, $p < 0.001$), femur neck ($\beta = 0.036$, $p < 0.001$ and $\beta = 0.244$, $p < 0.001$), and total hip ($\beta = 0.054$, $p < 0.001$ and $\beta = 0.303$, $p < 0.001$), and fracture history was negatively related to the BMD T-score at femur neck ($\beta = -0.178$, $p = 0.004$) and total hip ($\beta = -0.267$, $p < 0.001$). Most interestingly, Hb level was positively related to the BMD T-score at lumbar spine 1–4 ($\beta = 0.008$, $p = 0.035$), femur neck ($\beta = 0.006$, $p = 0.005$), and total hip ($\beta = 0.007$, $p = 0.007$; Table 2).

3.3. Correlation between complete blood count and BMD T-score

Then, the correlation of complete blood count with BMD T-score was further evaluated after adjusting gender, age, BMI,

TABLE 1 Demographic and clinical characteristics of individual with/without osteoporosis.

Variable	Non-OP group (n=659)	OP Group (n=409)	p value
Gender (men/women)	361/298	88/321	<0.001***
Age (years)	67.81 ± 5.57	68.81 ± 4.96	0.004**
BMI (kg/m^2)	24.40 ± 3.47	23.15 ± 3.88	<0.001***
Diabetes mellitus, n (%)	198 (30.05)	84 (20.54)	0.001**
Vertebral fracture, n (%)	298 (45.22)	321 (78.85)	<0.001***
Complete blood count			
RBC count (×10^{12}/L)	4.78 ± 0.50	4.56 ± 0.51	<0.001***
Hb (g/L)	145.40 ± 13.15	137.68 ± 12.35	<0.001***
MCV (fl)	91.56 ± 6.50	91.15 ± 6.66	0.329
MCH (pg)	30.65 ± 1.72	30.37 ± 1.83	0.015*
MCHC (g/L)	338.00 (321.00–351.00)	336.00 (321.00–348.00)	0.126
WBC count (×10^9/L)	5.75 ± 1.30	5.61 ± 1.41	0.102
Lipid profile			
TG (mmol/L)	1.54 (1.00–2.08)	1.44 (1.00–2.00)	0.034*
TC (mmol/L)	5.05 ± 1.07	5.41 ± 1.10	<0.001***
LDL-C (mmol/L)	2.90 ± 0.95	3.11 ± 0.94	0.001**
HDL-C (mmol/L)	1.23 (1.00–1.55)	1.46 (1.09–1.97)	<0.001***
Liver and kidney function			
AST (U/L)	20.00 (17.00–24.00)	19.00 (17.00–23.00)	0.208
ALT (U/L)	17.00 (14.00–24.00)	16.00 (12.00–21.00)	<0.001***
Serum creatinine (μmol/L)	75.00 (65.00–85.00)	67.00 (59.00–76.00)	<0.001***
Bone mineral density (T-score)			
Lumbar spine (L1–L4)	−0.77 ± 1.25	−2.89 ± 0.90	<0.001***
Femur neck	−1.44 ± 0.69	−2.65 ± 0.60	<0.001***
Total hip	−0.62 ± 0.79	−1.87 ± 0.71	<0.001***

Data are expressed as mean ± SD, median (p25–p75), or number (%).
Non-OP group, participants without OP; OP group, participants with OP; BMI, body mass index; RBC, red blood cell; Hb, hemoglobin; MCV, mean corpuscular volume; MCH, mean corpuscular Hb; MCHC, mean corpuscular Hb concentration; WBC, white blood cell; TG, Triglyceride; TC, Total cholesterol; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; AST, aspartate aminotransferase; and ALT, alanine aminotransferase. *p < 0.05; **p < 0.01; and ***p < 0.001.

history of DM, and blood lipid profile (TG, TC, LDL-C, and HDL-C). In the Model 1, after adjusting gender, age and BMI, RBC count, and Hb level were positively related to the BMD T-score at lumbar spine 1–4 ($\beta = 0.204$, $p = 0.020$ and $\beta = 0.008$, $p = 0.037$), femur neck ($\beta = 0.133$, $p = 0.011$ and $\beta = 0.006$, $p = 0.005$), and total hip ($\beta = 0.132$, $p = 0.023$ and $\beta = 0.007$, $p = 0.006$). Meanwhile, MCV was negatively related to the BMD T-score at total hip ($\beta = -0.010$, $p = 0.018$) and MCHC was positively related to the BMD T-score at total hip ($\beta = 0.007$, $p < 0.001$). After further adjusting for DM (Model 2) and blood lipid profile (Model 3), the positively correlation between Hb and BMD T-score remained (Table 3).

3.4. Relationship of hemoglobin level with odds ratios of OP

In the overall enrolled individuals including men and women, the prevalence of OP in the groups of quartiles 3 and 4 of Hb level was lower than in the group of quartile 1 after adjusting gender, age, BMI, DM, TG, TC, LDL-C, and HDL-C (Table 4), and this was also observed in the groups of quartile 3 and 4 in women and in the group of quartile 3 in men (Table 4). For one SD increase of Hb level, the adjusted OR for OP was 0.73 (0.57–0.92; $p = 0.008$) in women and 0.74 (0.57–0.96; $p = 0.025$) in men (Table 4).

4. Discussion

In the present study, a total of 1,068 individuals were enrolled and our results showed that OP individuals had significantly lower Hb level as compared to non-OP individuals, and the lower Hb level was related to higher OR of OP in the elderly Chinese population.

Currently, a total of 49.3 million women and 10.9 million men in China are estimated to have OP (31). Gender, age, and BMI are the major risk factors of OP. With the increase of age, the bone metabolism is impaired because of lower IGF-1 level (32), unbalanced sex hormones, lack of exercise, and so on (33). Lower BMI has been shown to have a relationship with higher risk of OP (34) which is induced by increased mechanical load on the bone with higher body weight and higher estrogen production in the adipose tissues (35). However, obesity may deteriorate bone because of ectopic adipocyte accumulation in the bone marrow (BM) cavities, and the adipocytes in BM can also release a wide variety of adipokines which may regulate bone remodeling directly or indirectly (36). Moreover, nutritional status and exercise levels can affect the correlation between Hb levels and BMD. Imbalance dietary habit can result in low protein and malnutrition, which can result in inadequate nutritional status and contribute to diseases such as anemia, hypoproteinemia, and low BMD (37). Moreover, physical exercise favors maintenance of bone mineral density during aging (38).

Anemia and OP always occur simultaneously in the elderly population. Some clinical studies have shown the relationship between anemia and risk of OP. One study conducted in Korea indicated a positive relationship between blood cell count and BMD in the healthy postmenopausal women which suggests that blood cell count may serve as a putative marker for estimating BMD (39). Another study on 371 postmenopausal women (including 82 anemic patients) showed that anemia was one of the risk factors for low BMD in the postmenopausal women (40). Moreover, a longitudinal study based on a large nationwide

TABLE 2 Multivariate linear regression analysis of clinical parameters and BMD T-score.

	BMD of lumbar spine (L1-L4; T-score)		BMD of femur neck (T-score)		BMD of total hip (T-score)	
Covariates	β (95% CI)	*p* value	β (95% CI)	*p* value	β (95% CI)	*p* value
Gender						
Male	Reference					
Female	−1.156 (−1.354, −0.959)	<0.001***	−0.494 (−0.611, −0.378)	<0.001***	−0.513 (−0.643, −0.384)	<0.001***
Age	0.001 (−0.015, 0.016)	0.911	−0.031 (−0.040, −0.022)	<0.001***	−0.015 (−0.025, −0.005)	0.004**
BMI	0.083 (0.061, 0.105)	<0.001***	0.036 (0.023, 0.049)	<0.001***	0.054 (0.039, 0.068)	<0.001***
DM						
Non-DM	Reference					
DM	0.409 (0.222, 0.595)	<0.001***	0.244 (0.134, 0.354)	<0.001***	0.303 (0.181, 0.425)	<0.001***
Morphological vertebral fracture						
No fracture	Reference					
Fracture	−0.198 (−0.403, 0.006)	0.057	−0.178 (−0.298, −0.057)	0.004**	−0.267 (−0.402, −0.133)	<0.001***
Hb	0.008 (0.001, 0.015)	0.035*	0.006 (0.002, 0.010)	0.005**	0.007 (0.002, 0.011)	0.007**

BMD, bone mineral density; BMI, body mass index; DM, diabetes mellitus; Hb, hemoglobin; CI, confidence interval. *$p < 0.05$; **$p < 0.01$; and ***$p < 0.001$.

TABLE 3 Correlation between blood indices and BMD T-score at lumbar spine1-4, femur neck, and total hip.

	BMD of lumbar spine (L1–L4; T-score)		BMD of femur neck (T-score)		BMD of total hip (T-score)	
Covariates	β	*p* value	β	*p* value	β	*p* value
Model 1: Adjusting gender, age, and BMI						
RBC count	0.204	0.020*	0.133	0.011*	0.132	0.023*
Hb	0.008	0.037*	0.006	0.005**	0.007	0.006**
MCV	−0.008	0.224	0.000	0.957	−0.010	0.018*
MCH	−0.002	0.935	0.008	0.568	0.024	0.141
MCHC	0.003	0.116	0.001	0.455	0.007	<0.001***
WBC count	−0.001	0.985	−0.006	0.736	0.011	0.583
Model 2: Adjusting gender, age, BMI, and DM						
RBC count	0.190	0.130	0.124	0.017**	0.121	0.036*
Hb	0.008	0.027*	0.006	0.003**	0.007	0.004**
MCV	−0.005	0.405	0.002	0.651	−0.008	0.049*
MCH	0.009	0.715	0.015	0.309	0.032	0.048*
MCHC	0.003	0.128	0.001	0.492	0.006	<0.001***
WBC count	−0.018	0.574	−0.017	0.373	−0.001	0.957
Model 3: Adjusting gender, age, BMI, DM, TG, TC, LDL-C, and HDL-C						
RBC count	0.170	0.058	0.112	0.035*	0.083	0.158
Hb	0.007	0.049*	0.006	0.008**	0.005	0.033*
MCV	−0.007	0.267	0.002	0.550	−0.006	0.153
MCH	0.010	0.679	0.016	0.273	0.035	0.029*
MCHC	0.004	0.050	0.001	0.526	0.006	<0.001***
WBC count	−0.038	0.244	−0.024	0.203	−0.014	0.519

BMD, bone mineral density; RBC, red blood cell; Hb, hemoglobin; MCV, mean corpuscular volume; MCH, mean corpuscular Hb; MCHC, mean corpuscular Hb concentration; and WBC, white blood cell. *$p < 0.05$; **$p < 0.01$; and ***$p < 0.001$.

TABLE 4 Relationship between Hb quartiles and risk of OP after gender stratification and adjustment.

	No. of participants	No. of cases	Model 1		Model 2		Model 3	
			Odds ratio (95% CI)	*p* value	Odds ratio (95% CI)	*p* value	Odds ratio (95% CI)	*p* value
Overall								
Quartile1	256	124	1 (reference)		1 (reference)		1 (reference)	
Quartile 2	281	122	0.84 (0.58–1.22)	0.361	0.84 (0.58–1.21)	0.339	0.83 (0.57–1.20)	0.310
Quartile 3	263	83	0.55 (0.37–0.81)	0.002**	0.54 (0.37–0.78)	0.002**	0.54 (0.36–0.80)	0.002**
Quartile 4	248	78	0.60 (0.41–0.89)	0.012*	0.60 (0.41–0.90)	0.012*	0.62 (0.41–0.92)	0.019*
p for trend				0.001**		0.001**		0.001**
One SD increase			0.75 (0.63–0.88)	0.001**	0.74 (0.63–0.88)	<0.001***	0.75 (0.63–0.89)	0.001**
Men								
Quartile 1	120	30	1 (reference)		1 (reference)		1 (reference)	
Quartile 2	108	22	0.88 (0.46–1.67)	0.695	0.89 (0.46–1.70)	0.716	0.84 (0.44–1.62)	0.603
Quartile 3	110	13	0.45 (0.21–0.94)	0.034*	0.44 (0.21–0.94)	0.034*	0.42 (0.19–0.89)	0.024*
Quartile 4	111	21	0.87 (0.45–1.69)	0.688	0.88 (0.45–1.71)	0.699	0.79 (0.39–1.57)	0.493
p for trend				0.340		0.347		0.225
One SD increase			0.79 (0.62–1.01)	0.057	0.79 (0.61–1.01)	0.059	0.74 (0.57–0.96)	0.025*
Women								
Quartile 1	156	94	1 (reference)		1 (reference)		1 (reference)	
Quartile 2	173	100	0.82 (0.52–1.29)	0.390	0.80 (0.51–1.27)	0.350	0.78 (0.49–1.24)	0.291
Quartile 3	153	70	0.57 (0.36–0.92)	0.020*	0.57 (0.35–0.91)	0.018*	0.57 (0.35–0.92)	0.022*
Quartile 4	137	57	0.50 (0.31–0.81)	0.005**	0.50 (0.31–0.81)	0.005**	0.52 (0.32–0.86)	0.010*
p for trend				0.002**		0.002**		0.004**
One SD increase			0.71 (0.56–0.89)	0.003**	0.70 (0.56–0.89)	0.003**	0.73 (0.57–0.92)	0.008**

Model 1: Adjusted for gender, age, and BMI. Model 2: Adjusted for gender, age, and DM. Model 3: Adjusted for gender, age, BMI, DM, TG, TC, LDL-C, and HDL-C.
CI, confidence interval. *$p < 0.05$; **$p < 0.01$; and ***$p < 0.001$.

population showed that patients with a history of iron deficiency anemia (IDA) had a near two-fold risk for OP (41).

With the increase of age, the decrease of Hb may be caused by the decline of red blood cell production due to hematopoietic dysfunction including reduced regenerative capacity and myeloid-biased differentiation (1, 42), the shortened survival of red blood cells (43), nutritional deficiency, and impaired inflammatory processes (44). However, recent studies also reveal direct connection between bone metabolism and hematopoiesis. Firstly, hematopoiesis origin from bone marrow which facilitates structural support and provides sites for hematopoiesis (45). Secondly, osteoblastic lineage cells, as a part of hematopoietic stem cell niche, have been shown to support bone marrow hematopoietic stem and progenitor cells (HSPCs) in mice (46, 47). Other findings also indicate that bone marrow hematopoietic dysfunction may affect bone metabolism (48), Moreover, chronic hypoxia and its related oxidative stress (49, 50) due to lower Hb level may directly interfere with bone mass and bone metabolism (51).

There were several strengths in the present study. The individuals who had no diseases or did not take drugs which could influence Hb level and bone metabolism were included in this study, and thus the results may be applicable in most elderly subjects. However, there are also some limitations. (1) As a cross-sectional study, the cause-and-effect relationships cannot be fully established and long-term follow-up studies are needed; (2) We did not take into account other factors that may affect the correlation between Hb levels and BMD, such as nutritional status and exercise levels in this study; and (3) Whether the increase of Hb level after nutritional supplementation may delay the bone loss in the elderly population is needed to be determined by more randomized, controlled trials.

5. Conclusion

Serum Hb level is positively related to the bone mass in the elderly Chinese population and the decrease of Hb level may increase the odds ratio of OP. Thus, BMD should be monitored closely in the anemia patients.

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 human participants were reviewed and approved by Ethics Committee of Shanghai Tongji Hospital. The patients/participants provided their written informed consent to participate in this study.

Author contributions

YL designed the work, acquired and analyzed the data, and participated in writing the manuscript. YZ, JL, XZ, ZZ, HL, PL, BM, and YG acquired and analyzed the data and revised the manuscript. LS contributed to the concept and design of the work, and reviewed and revised the manuscript. All authors contributed to the article and approved the submitted version.

Funding

This work was supported by the Shanghai Science and Technology Foundation to LS (19ZR1448600); Project supported by Shanghai Commission of Science and Technology to LS (22Y11904600) and Clinical Research Project of Tongji Hospital of Tongji University to LS [Grant No. ITJ(ZD)1904].

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.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Stauder R, Valent P, Theurl I. Anemia at older age: etiologies, clinical implications, and management. *Blood*. (2018) 131:505–14. doi: 10.1182/blood-2017-07-746446

2. Camacho PM, Petak SM, Binkley N, Diab DL, Eldeiry LS, Farooki A, et al. American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of postmenopausal Osteoporosis-2020 update. *Endocr Pract*. (2020) 26:1–46. doi: 10.4158/GL-2020-0524SUPPL

3. Ensrud KE, Crandall CJ. Osteoporosis. *Ann Intern Med*. (2017) 167:ITC17–32. doi: 10.7326/AITC201708010

4. Wang P, Abdin E, Shafie S, Chong SA, Vaingankar JA, Subramaniam M. Estimation of prevalence of osteoporosis using OSTA and its correlation with sociodemographic factors, disability and comorbidities. *Int J Environ Res Public Health*. (2019) 16. doi: 10.3390/ijerph16132338

5. Rachner TD, Khosla S, Hofbauer LC. Osteoporosis: now and the future. *Lancet*. (2011) 377:1276–87. doi: 10.1016/S0140-6736(10)62349-5

6. Sozen T, Ozisik L, Basaran NC. An overview and management of osteoporosis. *Eur J Rheumatol*. (2017) 4:46–56. doi: 10.5152/eurjrheum.2016.048

7. Farr JN, Rowsey JL, Eckhardt BA, Thicke BS, Fraser DG, Tchkonia T, et al. Independent roles of estrogen deficiency and cellular senescence in the pathogenesis of osteoporosis: evidence in young adult mice and older humans. *J Bone Miner Res*. (2019) 34:1407–18. doi: 10.1002/jbmr.3729

8. Gao ST, Lv ZT, Zhou CK, Mao C, Sheng WB. Association between IGF-1 polymorphisms and risk of osteoporosis in Chinese population: a meta-analysis. *BMC Musculoskelet Disord*. (2018) 19:141. doi: 10.1186/s12891-018-2066-y

9. Pasqualini L, Ministrini S, Lombardini R, Bagaglia F, Paltriccia R, Pippi R, et al. Effects of a 3-month weight-bearing and resistance exercise training on circulating osteogenic cells and bone formation markers in postmenopausal women with low bone mass. *Osteoporos Int*. (2019) 30:797–806. doi: 10.1007/s00198-019-04908-9

10. Fabiani R, Naldini G, Chiavarini M. Dietary patterns in relation to low bone mineral density and fracture risk: a systematic review and meta-analysis. *Adv Nutr*. (2019) 10:219–36. doi: 10.1093/advances/nmy073

11. Mutlu M, Argun M, Kilic E, Saraymen R, Yazar S. Magnesium, zinc and copper status in osteoporotic, osteopenic and normal post-menopausal women. *J Int Med Res*. (2007) 35:692–5. doi: 10.1177/147323000703500514

12. Timmer TC, de Groot R, Rijnhart JJM, Lakerveld J, Brug J, Perenboom CWM, et al. Dietary intake of heme iron is associated with ferritin and hemoglobin levels in Dutch blood donors: results from donor InSight. *Haematologica*. (2020) 105:2400–6. doi: 10.3324/haematol.2019.229450

13. Katsumata S, Katsumata-Tsuboi R, Uehara M, Suzuki K. Severe iron deficiency decreases both bone formation and bone resorption in rats. *J Nutr*. (2009) 139:238–43. doi: 10.3945/jn.108.093757

14. Katsumata S, Tsuboi R, Uehara M, Suzuki K. Dietary iron deficiency decreases serum osteocalcin concentration and bone mineral density in rats. *Biosci Biotechnol Biochem*. (2006) 70:2547–50. doi: 10.1271/bbb.60221

15. Lobo AR, Gaievski EH, Colli C. Hemoglobin regeneration efficiency in anemic rats: effects on bone mineral composition and biomechanical properties. *Biol Trace Elem Res*. (2011) 143:403–11. doi: 10.1007/s12011-010-8871-2

16. Rivella S, May C, Chadburn A, Riviere I, Sadelain M. A novel murine model of Cooley anemia and its rescue by lentiviral-mediated human beta-globin gene transfer. *Blood*. (2003) 101:2932–9. doi: 10.1182/blood-2002-10-3305

17. Vogiatzi MG, Tsay J, Verdelis K, Rivella S, Grady RW, Doty S, et al. Changes in bone microarchitecture and biomechanical properties in the th3 thalassemia mouse are associated with decreased bone turnover and occur during the period of bone accrual. *Calcif Tissue Int*. (2010) 86:484–94. doi: 10.1007/s00223-010-9365-0

18. Garcia-Santos D, Hamdi A, Saxova Z, Fillebeen C, Pantopoulos K, Horvathova M, et al. Inhibition of heme oxygenase ameliorates anemia and reduces iron overload in a beta-thalassemia mouse model. *Blood*. (2018) 131:236–46. doi: 10.1182/blood-2017-07-798728

19. Green M, Akinsami I, Lin A, Banton S, Ghosh S, Chen B, et al. Microarchitectural and mechanical characterization of the sickle bone. *J Mech Behav Biomed Mater*. (2015) 48:220–8. doi: 10.1016/j.jmbbm.2015.04.019

20. Cesari M, Pahor M, Lauretani F, Penninx BWHJ, Bartali B, Russo R, et al. Bone density and hemoglobin levels in older persons: results from the InCHIANTI study. *Osteoporos Int*. (2005) 16:691–9. doi: 10.1007/s00198-004-1739-6

21. Laudisio A, Marzetti E, Pagano F, Bernabei R, Zuccala G. Haemoglobin levels are associated with bone mineral density in the elderly: a population-based study. *Clin Rheumatol*. (2009) 28:145–51. doi: 10.1007/s10067-008-0998-6

22. Oh YH, Moon JH, Cho B. Association between hemoglobin level and bone mineral density in Korean adults. *J Bone Metab*. (2017) 24:161–73. doi: 10.11005/jbm.2017.24.3.161

23. Hannemann A, Nauck M, Volzke H, Weidner H, Platzbecker U, Hofbauer LC, et al. Interactions of anemia, FGF-23, and bone in healthy adults-results from the study of health in Pomerania (SHIP). *J Clin Endocrinol Metab*. (2021) 106:e288–99. doi: 10.1210/clinem/dgaa716

24. Arnett TR, Gibbons DC, Utting JC, Orriss IR, Hoebertz A, Rosendaal M, et al. Hypoxia is a major stimulator of osteoclast formation and bone resorption. *J Cell Physiol*. (2003) 196:2–8. doi: 10.1002/jcp.10321

25. Valderrabano RJ, Buzkova P, Chang PY, Zakai NA, Fink HA, Robbins JA, et al. Association of bone mineral density with hemoglobin and change in hemoglobin among older men and women: the cardiovascular health study. *Bone*. (2019) 120:321–6. doi: 10.1016/j.bone.2018.11.010

26. Chen Z, Thomson CA, Aickin M, Nicholas JS, van Wyck D, Lewis CE, et al. The relationship between incidence of fractures and anemia in older multiethnic women. *J Am Geriatr Soc*. (2010) 58:2337–44. doi: 10.1111/j.1532-5415.2010.03183.x

27. Looker AC. Hemoglobin and hip fracture risk in older non-Hispanic white adults. *Osteoporos Int*. (2014) 25:2389–98. doi: 10.1007/s00198-014-2769-3

28. Ye T, Lu L, Guo L, Liang M. Association between hemoglobin levels and osteoporosis in Chinese patients with type 2 diabetes mellitus: a cross-sectional study. *Diabetes Metab Syndr Obes*. (2022) 15:2803–11. doi: 10.2147/DMSO.S382480

29. Li L, Ge JR, Chen J, Ye YJ, Xu PC, Li JY. Association of bone mineral density with peripheral blood cell counts and hemoglobin in Chinese postmenopausal women: a retrospective study. *Medicine (Baltimore)*. (2020) 99:e20906. doi: 10.1097/MD.0000000000020906

30. Kanis JA, Cooper C, Rizzoli R, Reginster JYScientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF). European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Osteoporos Int*. (2019) 30:3–44. doi: 10.1007/s00198-018-4704-5

31. Zeng Q, Li N, Wang Q, Feng J, Sun D, Zhang Q, et al. The prevalence of osteoporosis in China, a Nationwide, multicenter DXA survey. *J Bone Miner Res*. (2019) 34:1789–97. doi: 10.1002/jbmr.3757

32. Ashpole NM, Herron JC, Mitschelen MC, Farley JA, Logan S, Yan H, et al. IGF-1 regulates vertebral bone aging through sex-specific and time-dependent mechanisms. *J Bone Miner Res*. (2016) 31:443–54. doi: 10.1002/jbmr.2689

33. Ma L, Oei L, Jiang L, Estrada K, Chen H, Wang Z, et al. Association between bone mineral density and type 2 diabetes mellitus: a meta-analysis of observational studies. *Eur J Epidemiol*. (2012) 27:319–32. doi: 10.1007/s10654-012-9674-x

34. Cherukuri L, Kinninger A, Birudaraju D, Lakshmanan S, Li D, Flores F, et al. Effect of body mass index on bone mineral density is age-specific. *Nutr Metab Cardiovasc Dis*. (2021) 31:1767–73. doi: 10.1016/j.numecd.2021.02.027

35. Mazocco L, Chagas P. Association between body mass index and osteoporosis in women from northwestern Rio Grande do Sul. *Rev Bras Reumatol Engl Ed*. (2017) 57:299–305. doi: 10.1016/j.rbr.2016.07.009

36. Muruganandan S, Govindarajan R, Sinal CJ. Bone marrow adipose tissue and skeletal health. *Curr Osteoporos Rep*. (2018) 16:434–42. doi: 10.1007/s11914-018-0451-y

37. Lopes SO, Ribeiro SAV, Morais DC, Miguel EDS, Gusmão LS, Franceschini SDCC, et al. Factors associated with anemia among adults and the elderly family farmers. *Int J Environ Res Public Health*. (2022) 19. doi: 10.3390/ijerph19127371

38. Benedetti MG, Furlini G, Zati A, Letizia MG. The effectiveness of physical exercise on bone density in osteoporotic patients. *Biomed Res Int*. (2018) 2018:1–10. doi: 10.1155/2018/4840531

39. Kim HL, Cho HY, Park IY, Choi JM, Kim M, Jang HJ, et al. The positive association between peripheral blood cell counts and bone mineral density in postmenopausal women. *Yonsei Med J*. (2011) 52:739–45. doi: 10.3349/ymj.2011.52.5.739

40. Korkmaz U, Korkmaz N, Yazici S, Erkan M, Baki AE, Yazici M, et al. Anemia as a risk factor for low bone mineral density in postmenopausal Turkish women. *Eur J Intern Med*. (2012) 23:154–8. doi: 10.1016/j.ejim.2011.11.009

41. Pan ML, Chen LR, Tsao HM, Chen KH. Iron deficiency anemia as a risk factor for osteoporosis in Taiwan: a Nationwide population-based study. *Nutrients*. (2017) 9. doi: 10.3390/nu9060616

42. Kuribayashi W, Oshima M, Itokawa N, Koide S, Nakajima-Takagi Y, Yamashita M, et al. Limited rejuvenation of aged hematopoietic stem cells in young bone marrow niche. *J Exp Med*. (2021) 218. doi: 10.1084/jem.20192283

43. Cappellini MD, Motta I. Anemia in clinical practice-definition and classification: does hemoglobin change with aging? *Semin Hematol*. (2015) 52:261–9. doi: 10.1053/j.seminhematol.2015.07.006

44. Hardy R, Cooper MS. Bone loss in inflammatory disorders. *J Endocrinol*. (2009) 201:309–20. doi: 10.1677/JOE-08-0568

45. Thomsen JS, Jensen MV, Niklassen AS, Ebbesen EN, Bruel A. Age-related changes in vertebral and iliac crest 3D bone microstructure--differences and similarities. *Osteoporos Int*. (2015) 26:219–28. doi: 10.1007/s00198-014-2851-x

46. Calvi LM, Adams GB, Weibrecht KW, Weber JM, Olson DP, Knight MC, et al. Osteoblastic cells regulate the haematopoietic stem cell niche. *Nature*. (2003) 425:841–6. doi: 10.1038/nature02040

47. Zhang J, Niu C, Ye L, Huang H, He X, Tong WG, et al. Identification of the haematopoietic stem cell niche and control of the niche size. *Nature*. (2003) 425:836–41. doi: 10.1038/nature02041

48. Despars G, St-Pierre Y. Bidirectional interactions between bone metabolism and hematopoiesis. *Exp Hematol*. (2011) 39:809–16. doi: 10.1016/j.exphem.2011.04.008

49. Yang Y, Sun Y, Mao WW, Zhang H, Ni B, Jiang L. Oxidative stress induces downregulation of TP53INP2 and suppresses osteogenic differentiation of BMSCs during osteoporosis through the autophagy degradation pathway. *Free Radic Biol Med*. (2021) 166:226–37. doi: 10.1016/j.freeradbiomed.2021.02.025

50. Wauquier F, Leotoing L, Coxam V, Guicheux J, Wittrant Y. Oxidative stress in bone remodelling and disease. *Trends Mol Med*. (2009) 15:468–77. doi: 10.1016/j.molmed.2009.08.004

51. Hannah SS, McFadden S, McNeilly A, McClean C. "take my bone away?" hypoxia and bone: a narrative review. *J Cell Physiol*. (2021) 236:721–40. doi: 10.1002/jcp.29921

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 13 June 2023
DOI 10.3389/fpubh.2023.1197025

Check for updates

OPEN ACCESS

EDITED BY
Ricardo Aurélio Carvalho Sampaio,
Federal University of Sergipe, Brazil

REVIEWED BY
Garyfallia Pepera,
University of Thessaly, Greece
Juliette Hussey,
Trinity College Dublin, Ireland

*CORRESPONDENCE
Andreas Nilsson
✉ andreas.nilsson@oru.se

RECEIVED 30 March 2023
ACCEPTED 22 May 2023
PUBLISHED 13 June 2023

CITATION
Veen J, Edholm P, Rodriguez-Zamora L, Folkesson M, Kadi F and Nilsson A (2023) Adherence to the physical activity guideline beyond the recommended minimum weekly amount: impacts on indicators of physical function in older adults. *Front. Public Health* 11:1197025. doi: 10.3389/fpubh.2023.1197025

Adherence to the physical activity guideline beyond the recommended minimum weekly amount: impacts on indicators of physical function in older adults

Jort Veen, Peter Edholm, Lara Rodriguez-Zamora, Mattias Folkesson, Fawzi Kadi and Andreas Nilsson*

School of Health Sciences, Örebro University, Örebro, Sweden

Introduction: The extent to which additional health benefits of accumulating twice the minimum amount of time in moderate-to-vigorous physical activity (MVPA) affects indicators of physical function in older adults is unclear. Therefore, the aim of the present study was to assess indicators of physical function in older adults who accumulate at least 150 but less than 300min/week of MVPA compared to those accumulating at least 300min/week.

Methods: Indicators of physical function, including handgrip strength, 5 times sit-to-stand test (5-STS), squat jump and 6-min walk test (6MWT) were assessed in a sample of 193 older men (n=71, 67±2years), and women (n=122, 67±2years), who all accumulated at least 150 weekly minutes of MVPA. Time in MVPA was assessed by accelerometry during 1week and engagement in muscle strengthening activities (MSA) was assessed by self-report. Protein intake was assessed by a food-frequency-questionnaire. Participants were classified as physically active (≥150 but <300min of MVPA per week) or as highly physically active (≥300min of MVPA per week).

Results: Factorial analysis of variance revealed that older adults accumulating at least 300min of MVPA per week had a significantly (p<0.05) better 6MWT performance and overall physical function compared to the less active group. These findings remained significant after further adjustment for MSA, sex, waist circumference and protein intake. In contrast, no significant differences in indicators of muscle strength were observed between the two groups.

Discussion: Adherence to twice the recommended minimum amount of weekly MVPA time is related to a better physical function, evidenced by a better walking performance compared to adherence to the minimum weekly amount of MVPA. This finding emphasizes the benefits of accumulating daily MVPA beyond the minimum recommended amount to optimize the ability to perform activities of daily living, thus reducing the burden of physical disability and related health-care costs.

KEYWORDS
exercise, sarcopenia, aging, muscle strength, physical performance, protein intake, six-minute walk test

1. Introduction

The aging process is accompanied by a gradual decline in physical performance including compromised muscle strength, muscle power and aerobic capacity (1–3). These changes lead to a reduced physical function, which in turn may limit older adults' ability to carry out tasks of daily living, reduce their independency and increase the risk of sarcopenia (4, 5).

Major health organizations, including the World Health Organization (WHO), have emphasized the important role of regular physical exercise as a therapeutic tool to delay age-related functional decline and treat functional limitations (6). Therefore, a physically active lifestyle represents a key behavior to maintain physical function by advancing age (7), where engagement in moderate-to-vigorous physical activity (MVPA) is related to better functional health outcomes (8–10). Current PA guidelines for older adults (65+) stipulate engagement in 150–300 weekly minutes of aerobic type PA of at least moderate intensity to promote healthy aging (11). Furthermore, the WHO also indicates that additional health benefits would be achieved by accumulating twice the recommended minimum amount of aerobic type MVPA (300 weekly minutes) (11). Indeed, based on data from two databases the NHS (Nurses' Health Study) and the HPFS (Health Professionals Follow-Up Study) including 116,221 female nurses with an age range between 30 and 76 years, it was shown that adults reporting at least twice the recommended minimum amount of either vigorous intensity PA or moderate intensity PA exhibited a significantly lower mortality risk compared to those reporting less time in PA of any intensity (12). Interestingly, a recent meta-analysis of observational studies including 36,383 participants (mean age: 62.6 years) based on objective assessment of PA using accelerometry reported that higher PA volume are related to a lower risk for premature mortality irrespective of the intensity level (13). Notably, the dose–response relationship between time in MVPA and all-cause mortality did not reveal any further significant risk reduction beyond a daily average amount of 25 min MVPA, which roughly corresponds to the minimum weekly recommended amount of MVPA, i.e., 150 min. Furthermore, using baseline data from the Alberta Caring for Diabetes (ABCD) cohort study including 1948 participants no further benefits on health-related quality of life were denoted between participants accumulating twice the recommended minimum amount of MVPA and those reporting less MVPA time (14). However, as indicated by the authors of that study the lack of statistical power may provide an explanation to the lack of significant differences between those who met baseline recommendations and those who adhered to twice the minimum recommendation (14). Thus, the proposed additional benefit of exceeding recommended minimum amount of MVPA remains a matter of debate and is likely dependent on the health outcome of interest. Currently, the extent to which additional accumulation of twice the minimum amount of MVPA benefits indicators of physical function in older adults is unknown. This is unfortunate given the importance of maintained physical function during the aging process. Additionally, the exploration of the potential benefits of accumulating MVPA time beyond the minimum recommendations would be substantially strengthened by the use of objectively assessed MVPA time, complemented by self-reported information regarding the type of activities performed. Indeed, in addition to the weekly aerobic type MVPA, older adults should engage in muscle-strengthening activities (MSA) at least twice a week (11). Emerging evidence suggests that engagement in MSA is related to a lower risk of sarcopenia (15), lower fall incidence (16), lower prevalence of obesity (17), and lower mortality risk (18). Therefore, adherence to the MSA guideline should be taken into account when investigating the potential benefits of accumulating twice the recommended minimum amount of aerobic type MVPA on indicators of physical function in older adults.

The aim of the present study was to assess physical function in older adults who accumulate at least 150 min/week but less than 300 min/week of MVPA compared to those accumulating at least 300 min/week, while taking into account engagement in MSA, protein intake and central obesity.

2. Materials and methods

2.1. Participants

Seventy-one men (67 ± 2 years) and 122 women (67 ± 2 years) were recruited through local advertisement. Inclusion criteria included the following: adherence to the recommended weekly amount of at least 150 min of MVPA including absence of overt diseases, cardiovascular, diabetes and psychiatric conditions and disability issues regarding immobility. All procedures were conducted according to the principles set by the Declaration of Helsinki and all participants were provided with written information regarding the study and written signed consent was obtained. The study protocol was approved by the regional ethics committee of Uppsala, Sweden (Dnr, 2017/511).

2.2. Anthropometry

All anthropometric measurements were performed by trained personal. Body weight and body height were measured using standardized conditions and following standard procedures (19). Participants arrived at the testing facility between 8:00 a.m. and 9:30 a.m. after an overnight fast. Weight was recorded using a Tanita scale (Tanita MC-780, Tanita Amsterdam, The Netherlands) to the nearest 0.1 kg. Body height was measured using a portable stadiometer (Seca 213, Hamburg, Germany) to the nearest 0.1 cm. Waist circumference (WC) was measured to the nearest 0.1 cm at the midpoint between the iliac crest and lower costal margin in a standing position (19) using a measuring tape (Seca 201, Hamburg, Germany).

2.3. Physical activity

Daily time spent in MVPA was assessed using the Actigraph GT3x (Actigraph, Pensacola, FL, United States) accelerometer, as previously described (20). All participants were instructed to wear the activity monitor during awake time for seven consecutive days with exception for showering or other water-based activities. The activity monitor was placed at the right hip using an adjustable waste-mounted elastic belt. Participants were instructed not to alter their daily living routines during the measurement period. A minimum of 10 h of daily wear time accumulated during at least 4 days was required for inclusion in further data analysis of physical activity. Accelerometer count cut-point for MVPA was set to >2019 counts per minute according to

Troiano et al. (21). Based on average daily time spent in MVPA, participants were classified as physically active (accumulating ≥150 min but <300 min of MVPA per week) or as highly physically active (accumulating ≥300 min of MVPA per week). Engagement in MSA was assessed using the EPAQ2 questionnaire, which has previously been validated (22). Accordingly, participants reported on duration and frequency of MSA during the last 12 months regarding the following activities: strength training, yoga and qigong types, rhythmic gymnastics, rubber band resistance exercises, water-based gym, group-based workout, DVD-based resistance exercises, core workout, and sit-ups. Participants reporting MSA at least twice a week were classified as adhering to the MSA guideline.

2.4. Protein intake

Daily protein intake was assessed by a validated food frequency questionnaire (FFQ) (23). Daily protein intake was expressed as g protein/kg body weight. Participants with a daily protein intake of at least 1.1 g/BW were classified as meeting recommendations on adequate protein intake in older adults (24).

2.5. Physical function

Handgrip strength (expressed in kg/kg body weight) was assessed by standardized procedures using a Jamar handheld dynamometer (Patterson Medical, Warrenville, IL, United States). Handgrip strength was assessed in standing position with elbow flexed 90° and wrist in neutral position. Participants performed 3 maximal attempts separated by 1.5 min of rest, where the highest score was recorded. A five times sit-to-stand test (5-STS; expressed in seconds, s) was performed, whereby participants were instructed to start from a seated position in a chair to a fully upright standing position and to sit down back in the chair. This sequence was repeated five times. The participants were also instructed to place their arms across their chest during the test and to perform this sequence as quickly as possible. Squat jump performance (expressed in N/kg body weight) was assessed on a force platform (Kistler 9,281 B, Kistler Nordic AB, Sweden). Participants started from a static position with knee bent in a 90° angle, with their hands kept on the hip during the jump. Participants performed 3 maximal jumps separated by 1.5 min of rest. The highest recorded maximal ground reaction force during the concentric phase of the squat jump was recorded (25). A six-minute walk test (6MWT, expressed in meters, m) (26) was used to assess functional walking capacity and cardiorespiratory fitness. Participants were instructed to walk as fast as possible along a 50-meter corridor for a period of 6 min. Participants were allowed to rest in case of any discomfort during the 6 MWT. The total distance walked was recorded.

2.6. Physical performance score

A continuous clustered physical performance score (PPS) covering the separate physical function indicators was created. The PPS was derived by first transforming each physical function indicator into sex-specific standardized units (z-scores). Thereafter, the four standardized variables were summed and averaged into one sex-adjusted composite variable, with a mean value of zero and where a positive score indicates a better physical function compared to a negative score. Since longer time to complete the 5STS test indicates a lower physical function, data on 5STS were inverted before creating the PPS.

2.7. Statistical analyses

Data are presented as mean and standard deviation unless otherwise stated. Data were checked for normality using the Kolmogorov–Smirnov normality test and visual inspection. In case of deviations from normality, data were log-transformed to better fit a normal distribution. Differences in physical function indicators between the physically active and highly physically active groups were analyzed using a factorial analysis of variance (ANOVA). All models were adjusted by sex, engagement in MSA and adherence to protein intake guideline. In addition, models analyzing 6MWT and 5-STS performances were further adjusted by waist circumference to account for adiposity level on weight-related exercises. *A priori* power calculation showed that small to moderate effect sizes were detected with a power of ≥80%, when based on our sample size and alpha level set to 0.05. All analyses were conducted using SPSS version 28 (SPSS, Chicago, IL, United States).

3. Results

A total of 193 community-dwelling older men ($n = 71$, 67 ± 2 years), and women ($n = 122$, 67 ± 2 years) were included in the analysis. Forty-eight percent of the participants ($n = 93$) accumulated ≥150 but <300 weekly minutes of MVPA and 52% ($n = 100$) accumulated ≥300 weekly minutes of MVPA. Correspondingly, 27% ($n = 52$) of the participants engaged in MSA for at least twice a week. Thirty-three percent of the participants ($n = 63$) adhered to the protein recommendation of at least 1.1 g/kg/day. Data on anthropometric measurements in physically active and highly physically active older men and women are presented in Table 1. Data on indicators of physical function in the two groups are presented in Table 2.

We first compared clustered PPS between the physically active and highly physically active groups. Factorial ANOVA revealed a significantly higher PPS in the highly physically active compared to physically active group (0.12 ± 0.07 vs. −0.13 ± 0.07, $p < 0.05$).

TABLE 1 Body composition variables in the study sample.

	Physically active		Highly physically active	
	Men (n=35)	Women (n=58)	Men (n=36)	Women (n=64)
Height (cm)	177.0 ± 5.3	164.3 ± 5.9	179.2 ± 6.4	165.6 ± 4.6
Weight (kg)	80.4 ± 12.9	64.6 ± 9.1	79.5 ± 8.9	63.0 ± 9.2
Waist circumference (cm)	95.1 ± 11.1	79.6 ± 8.2	92.3 ± 8.6	78.7 ± 8.9

Data are presented as mean ± SD.

TABLE 2 Indicators of physical performance in the study sample.

	Physically active (n=93)	Highly physically active (n=100)
Squat Jump (N/kg bw)	9.4 ± 2.3	9.8 ± 2.2
Handgrip (kg/kg bw)	0.48 ± 0.1	0.50 ± 0.1
5-STS (s)	10.3 ± 2.0	10.0 ± 2.3
6MWT (m)	631 ± 63	655 ± 62*

Data are presented as mean ± SD. 5-STS, 5-time sit to stand; 6MWT, Six-minute walk test; kg bw, kilogram body weight. *p < 0.05. vs. Physically active.

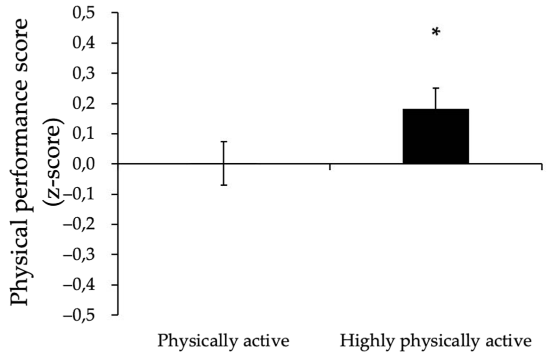

FIGURE 1
Physical performance score (z-score) in physically active and highly physically active older adults. Data are means ± SEM, adjusted for MSA, sex, waist circumference and protein intake. *p<0.05.

Importantly, further adjustments by MSA, sex, WC and protein intake did not change the significance of the results (Figure 1).

Further analysis of each separate indicators of physical function showed that the highly physically active group had a significantly better 6MWT performance (p < 0.05) compared to the less active group (Table 2), which remained evident after adjustment for MSA, sex, WC, and protein intake (664 ± 6.09 m vs. 644 ± 6.46 m, p = 0.01). In contrast, no significant group differences in squat jump, hand grip strength and 5-STS were observed (Table 2).

4. Discussion

The World Health Organization recommends older adults to engage in a minimum of 150 weekly minutes of aerobic type PA of at least moderate intensity, while also advocating the potential health benefits of moving beyond this minimum threshold toward a doubling of the weakly recommended amount of aerobic type MVPA (300 weekly minutes) (11). The scarcity of data addressing potential benefits of accumulating twice the minimum amount of MVPA on health outcomes in older adults may be explained by a generally low PA level in age groups similar to ours, i.e., above 65 years. Moreover, the benefits of doubling the minimum recommended PA amount on indicators of physical function in aging populations have not been previously explored. In the present study we show for the first time that accumulation of ≥300 weekly minutes of MVPA is related to a significantly better physical function, which is driven by a significantly better walking performance in older adults when compared to older adults who accumulate between 150 and 300 min/week.

A recently published large prospective US cohort study showed that adults reporting at least twice the recommended minimum amount of MVPA exhibited a significantly lower mortality risk compared to those with less MVPA time (12). Interestingly, the authors of this study including 116,000 participants aged between 30 and 76 years showed that engaging in twice the amount of either moderate or vigorous intensity PA would result in similar health benefits. In our study, times spent in moderate and vigorous intensity PA were not analyzed separately, hence the impact of PA intensities above the moderate threshold on physical performance outcomes cannot be clarified. Notably, none of the participants in our study accumulated twice the recommended amount of weekly vigorous PA (150 min or more). Therefore, data on PA spent in moderate and vigorous PA were collapsed into one MVPA variable showing that aerobic-type activities of at least moderate intensity, such as brisk walking, is beneficial for cardiorespiratory fitness in older adults, as mirrored by the better 6MWT performance.

The results from our current study expand on the findings from Lee et al. (12) showing that benefits of being physically active beyond the minimum recommended MVPA level also include a better physical function. However, in contrast to the favorable impact on walking performance, no corresponding benefits were observed for any indicator of muscle strength and function. Handgrip strength, a proxy for overall muscle strength commonly used for strength assessment in older adults (27) was similar in the two groups. It may be hypothesized that most activities performed within the MVPA domain were predominantly of aerobic type, which would unlikely elicit significant improvements in forearm muscle flexors (28). Further, although the 5-STS is an established functional test for assessment of functional ability and lower limb strength (29), it may lack sensitivity to detect differences between participants who already adhere to the MVPA guideline. However, we further took advantage of using an instrument with higher sensitivity, a force platform, to determine lower limb strength, which confirmed the lack of beneficial impact of accumulating twice the minimum recommended MVPA amount on lower limb strength. However, we have previously reported (15) that engagement in MSA alongside adherence to the minimum weekly MVPA time is positively related to indicators of muscle strength and function. Thus, it can be speculated that doubling the recommended aerobic type MVPA amount alone would not be sufficient to infer benefits on all dimensions of physical function including muscle strength.

The fact that adherence to the MSA guideline was considered in the statistical analysis strengthens the finding that adherence to twice the recommended MVPA amount is related to better walking performance. Importantly, adherence to MSA guideline should still be encouraged alongside adherence to the aerobic-type guideline for optimal impacts on physical function during aging, as MSA can improve important fall risk factors including strength and flexibility (30). These findings may hold important clinical and public health implications on the ability to perform activities of daily living and reducing the burden of physical disability and related health-care costs during the aging process.

Importantly, the findings from our study are strengthened by the use of both objectively assessed PA and self-reported engagement in MSA. Further, important factors known to impact on physical performance, including sex, protein intake, adiposity level and physical activity type (MSA) were considered in the analysis. It should be noted that for the specific purpose of the present study, only physically active older adults were included, which implies that data on indicators of physical function may not be representative of a larger sample of older adults with sedentary lifestyles. Finally, due to the cross-sectional analysis, causality cannot be determined.

In conclusion, the present study shows that accumulating at least 300 weekly minutes of MVPA is linked to a better walking performance in older adults compared to those just adhering to the minimum weekly amount of MVPA. However, in order to promote maintenance of muscle strength and function, engagement in MSA is likely necessary alongside adherence to the aerobic-type MVPA guideline.

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 human participants were reviewed and approved by the Regional Ethics Committee of Uppsala, Sweden (Dnr, 2017/511). The patients/participants provided their written informed consent to participate in this study.

Author contributions

JV, FK, and AN: conceptualization. JV, PE, FK, and AN: methodology. JV: formal analysis and writing—original draft preparation. JV, PE, LR-Z, MF, FK, and AN: investigation and writing—review and editing. FK, PE, and AN: supervision. FK and AN: project administration. FK: funding acquisition. All authors read and agreed to the published version of the manuscript.

Funding

This research was funded by the EU HORIZON 2020 Research and Innovation Program (Euro-pean Joint Programming Initiative "A healthy diet for a healthy life" "JPI HDHL," the ERA-NET co-fund HDHL-INTIMIC) GA no. 727565 and The Kamprad Family Foundation for Entrepre-neurship, Research and Charity (ref 20210070).

Acknowledgments

We would like to thank Oscar Bergens for his valuable assistance in participant recruitment and collection of data, and other colleagues involved in the research project. We thank the European Commission through the Marie Skłodowska-Curie Actions, Cofunding of Regional, National and International Programs (MSCA COFUND) for supporting one author (JV).

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.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Goodpaster BH, Park SW, Harris TB, Kritchevsky SB, Nevitt M, Schwartz AV, et al. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. *J Gerontol A Biol Sci Med Sci*. (2006) 61:1059–64. doi: 10.1093/gerona/61.10.1059

2. Norheim KL, Hjort Bønløkke J, Samani A, Omland Ø, Madeleine P. The effect of aging on physical performance among elderly manual workers: protocol of a cross-sectional study. *JMIR Res Protoc*. (2017) 6:e226. doi: 10.2196/resprot.8196

3. Hollenberg M, Yang J, Haight TJ, Tager IB. Longitudinal changes in aerobic capacity: implications for concepts of aging. *J Gerontol A Biol Sci Med Sci*. (2006) 61:851–8. doi: 10.1093/gerona/61.8.851

4. Judge JO, Schechtman K, Cress EGroup F. The relationship between physical performance measures and independence in instrumental activities of daily living. *J Am Geriatr Soc*. (1996) 44:1332–41. doi: 10.1111/j.1532-5415.1996.tb01404.x

5. Anton SD, Woods AJ, Ashizawa T, Barb D, Buford TW, Carter CS, et al. Successful aging: advancing the science of physical independence in older adults. *Ageing Res Rev*. (2015) 24:304–27. doi: 10.1016/j.arr.2015.09.005

6. Izquierdo M, Duque G, Morley JE. Physical activity guidelines for older people: knowledge gaps and future directions. *Lancet Healthy Longev*. (2021) 2:e380–3. doi: 10.1016/S2666-7568(21)00079-9

7. Stenholm S, Koster A, Valkeinen H, Patel KV, Bandinelli S, Guralnik JM, et al. Association of physical activity history with physical function and mortality in old age. *J Gerontol Biol Sci Med Sci*. (2016) 71:496–501. doi: 10.1093/gerona/glv111

8. Santos DA, Silva AM, Baptista F, Santos R, Vale S, Mota J, et al. Sedentary behavior and physical activity are independently related to functional fitness in older adults. *Exp Gerontol*. (2012) 47:908–12. doi: 10.1016/j.exger.2012.07.011

9. Chen T, Honda T, Chen S, Narazaki K, Kumagai S. Dose–response association between accelerometer-assessed physical activity and incidence of functional disability in older Japanese adults: a 6-year prospective study. *J Gerontol A Biol Sci Med Sci*. (2020) 75:1763–70. doi: 10.1093/gerona/glaa046

10. Veen J, Montiel-Rojas D, Kadi F, Nilsson A. Effects of reallocating time spent in different physical activity intensities on sarcopenia risk in older adults: an isotemporal substitution analysis. *Biology*. (2022) 11:111. doi: 10.3390/biology11010111

11. World Health Organization. *WHO guidelines on physical activity and sedentary behaviour*. Geneva: World Health Organization (2020).

12. Lee DH, Rezende LFM, Joh H-K, Keum N, Ferrari G, Rey-Lopez JP, et al. Long-term leisure-time physical activity intensity and all-cause and cause-specific mortality: a prospective cohort of US adults. *Circulation*. (2022) 146:523–34. doi: 10.1161/CIRCULATIONAHA.121.058162

13. Ekelund U, Tarp J, Steene-Johannessen J, Hansen BH, Jefferis B, Fagerland MW, et al. Dose-response associations between accelerometry measured physical activity and sedentary time and all cause mortality: systematic review and harmonised meta-analysis. *BMJ*. (2019) 366:l4570. doi: 10.1136/bmj.l4570

14. Thiel DM, Al Sayah F, Vallance JK, Johnson ST, Johnson JA. Association between physical activity and health-related quality of life in adults with type 2 diabetes. *Can J Diabetes*. (2017) 41:58–63. doi: 10.1016/j.jcjd.2016.07.004

15. Veen J, Montiel-Rojas D, Nilsson A, Kadi F. Engagement in muscle-strengthening activities lowers sarcopenia risk in older adults already adhering to the aerobic physical activity guidelines. *Int J Environ Res Public Health*. (2021) 18:989. doi: 10.3390/ijerph18030989

16. Ishigaki E, Ramos LG, Carvalho ES, Lunardi AC. Effectiveness of muscle strengthening and description of protocols for preventing falls in the elderly: a

systematic review. *Brazilian J Phys Ther*. (2014) 18:111–8. doi: 10.1590/S1413-35552012005000148

17. Bennie J.A, Ding D, De Cocker K. Dose-dependent associations of joint aerobic and muscle-strengthening exercise with obesity: a cross-sectional study of 280,605 adults. *J Sport Heal Sci* 12:186–193 (2021), doi: 10.1016/j.jshs.2021.01.002

18. Saeidifard F, Medina-Inojosa JR, West CP, Olson TP, Somers VK, Bonikowske AR, et al. The association of resistance training with mortality: a systematic review and meta-analysis. *Eur J Prev Cardiol*. (2019) 26:1647–65. doi: 10.1177/2047487319850718

19. da Silva VS, Vieira MFS. International Society for the Advancement of Kinanthropometry (ISAK) Global: international accreditation scheme of the competent anthropometrist. *Rev Bras Cineantropometria Desempenho Hum*. (2020) 22:e70517. doi: 10.1590/1980-0037.2020v22e70517

20. Nilsson A, Wåhlin-Larsson B, Kadi F. Physical activity and not sedentary time per se influences on clustered metabolic risk in elderly community-dwelling women. *PLoS One*. (2017) 12:e0175496. doi: 10.1371/journal.pone.0175496

21. Troiano RP, Berrigan D, Dodd KW, Mâsse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. *Med Sci Sports Exerc*. (2008) 40:181–8. doi: 10.1249/mss.0b013e31815a51b3

22. Wareham NJ, Jakes RW, Rennie KL, Mitchell J, Hennings S, Day NE. Validity and repeatability of the EPIC-Norfolk Physical Activity Questionnaire. *Int J Epidemiol*. (2002) 31:168–74. doi: 10.1093/ije/31.1.168

23. Johansson I, Van Guelpen B, Hultdin J, Johansson M, Hallmans G, Stattin P. Validity of food frequency questionnaire estimated intakes of folate and other B vitamins in a region without folic acid fortification. *Eur J Clin Nutr*. (2010) 64:905–13. doi: 10.1038/ejcn.2010.80

24. Bauer J, Biolo G, Cederholm T, Cesari M, Cruz-Jentoft AJ, Morley JE, et al. Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE study group. *J Am Med Dir Assoc*. (2013) 14:542–59. doi: 10.1016/j.jamda.2013.05.021

25. Edholm P, Strandberg E, Kadi F. Lower limb explosive strength capacity in elderly women: effects of resistance training and healthy diet. *J Appl Physiol*. (2017) 123:190–6. doi: 10.1152/japplphysiol.00924.2016

26. ATS. ATS Statement. *Am J Respir Crit Care Med*. (2002) 166:111–7. doi: 10.1164/ajrccm.166.1.at1102

27. Bohannon RW. Grip strength: an indispensable biomarker for older adults. *Clin Interv Aging*. (2019) 14:1681–91. doi: 10.2147/CIA.S194543

28. Hughes DC, Ellefsen S, Baar K. Adaptations to endurance and strength training. *Cold Spring Harb Perspect Med*. (2018) 8:a029769. doi: 10.1101/cshperspect.a029769

29. Bohannon RW, Bubela DJ, Magasi SR, Wang Y-C, Gershon RC. Sit-to-stand test: performance and determinants across the age-span. *Isokinet Exerc Sci*. (2010) 18:235–40. doi: 10.3233/IES-2010-0389

30. Pepera G, Krinta K, Mpea C, Antoniou V, Peristeropoulos A, Dimitriadis Z. Randomized controlled trial of group exercise intervention for fall risk factors reduction in nursing home residents. *Can J Aging*. (2023) 42:328–36. doi: 10.1017/S0714980822000265

frontiers | Frontiers in Public Health

TYPE Clinical Trial
PUBLISHED 21 June 2023
DOI 10.3389/fpubh.2023.1159343

Check for updates

OPEN ACCESS

EDITED BY
Rafael Reimann Baptista,
Pontifical Catholic University of Rio Grande do Sul, Brazil

REVIEWED BY
Luis Henrique Telles Da Rosa,
Federal University of Health Sciences of Porto Alegre, Brazil
Clarissa Biehl Printes,
Pontifical Catholic University of Rio Grande do Sul, Brazil

*CORRESPONDENCE
Luz Albany Arcila Castaño
luz.albany.arcila@gmail.com

†These authors have contributed equally to this work

RECEIVED 05 February 2023
ACCEPTED 25 May 2023
PUBLISHED 21 June 2023

CITATION
Castillo de Lima V, Castaño LAA, Sampaio RAC, Sampaio PYS, Teixeira CVL and Uchida MC (2023) Effect of agility ladder training with a cognitive task (dual task) on physical and cognitive functions: a randomized study. *Front. Public Health* 11:1159343.
doi: 10.3389/fpubh.2023.1159343

Effect of agility ladder training with a cognitive task (dual task) on physical and cognitive functions: a randomized study

Vivian Castillo de Lima[1†], Luz Albany Arcila Castaño[1*†], Ricardo Aurélio Carvalho Sampaio[2], Priscila Yukari Sewo Sampaio[3], Camila Vieira Ligo Teixeira[4] and Marco Carlos Uchida[1]

[1]Laboratory of Applied Kinesiology, Faculty of Physical Education, State University of Campinas, Campinas, Brazil, [2]Department of Physical Education, Federal University of Sergipe, São Cristóvão, Brazil, [3]Department of Occupational Therapy, Federal University of Sergipe, São Cristóvão, Brazil, [4]NIH Biomedical Research Center, University of Maryland, Baltimore, MD, United States

Introduction: Agility training (AT) is used to improve neuromuscular performance and dynamic balance, which are crucial for the physical function of older adults. Activities of daily living, which decrease with age, involve tasks that simultaneously require motor, and cognitive abilities and can be considered dual tasks.

Methods: This study investigates a training program's physical and cognitive effects using an agility ladder on healthy older adults. This program consisted of 30-min sessions twice per week and lasted for 14 weeks. The physical training included four different sequences with progressive difficulty levels, while the cognitive training (CT) included different verbal fluency (VF) tasks for each physical task. Sixteen participants (mean age of 66.9 ± 5.0 years) were allocated to two groups: AT alone (AT) and dual-task training (AT combined with CT [AT + CT]). Assessments were performed before and after 14 weeks of interventions using physical functional tests (e.g., Illinois agility test, five times sit-to-stand test, timed up and go [TUG], and one-leg stand) and cognitive tests (cognitive TUG, verbal fluency, attention, and scenery picture memory test).

Results: After this period, both groups had significant differences in physical performance, muscle power, agility, static and dynamic balance, and short-term memory, whereas only the AT + CT group improved phonological verbal fluency, executive function (TUG combined with a cognitive task), attention (trail-making test-B), and short-term memory (scenery picture memory test).

Conclusion: Indicating that only the group that received direct cognitive training had better enhanced cognitive function.

Clinical trial registration: www.ClinicalTrials.gov, identifier: RBR-7t7gnjk.

KEYWORDS

aging, cognitive function, executive function, dual-task, physical function

Introduction

Aging is associated with neuromuscular, cardiovascular, and central nervous system decline (1) and has been shown to impair physical function and decrease muscle mass, strength, and power (2), leading to functional limitations associated with independence and autonomy reduction, decreasing, consequently, the quality of life in older adults. In this respect, the World Health Organization (WHO) reported that the age-related decrease in neuromuscular and cognitive function limits the execution of multiple tasks, such as walking and talking on the cell phone, or walking and watching traffic lights (3). The performance of multiple tasks may demand a special effort to coordinate and modulate the physical (physical action, e.g., walking) and cognitive task (cognitive action, e.g., attention and executive function), simultaneously. The capacity to modulate these functions is reduced with age. Moreover, functional decline and geriatric syndromes associated with non-communicable diseases reduce the capacity to perform activities of daily living (1, 4).

The modulation of dual tasks or multiple tasks requires divided attention in different actions, physical or cognitive tasks. This modulation may have interfered with gait and postural control, which may cause the risk of falling (3). Therefore, new strategies, and therapies have been developed as aerobic training, stepping training (agility), and resistance training in dual task (physical task + cognitive task, simultaneously), preserving neuromuscular and cognitive function (5–9).

Agility training (AT) is the other physical function that can increase neuromuscular performance and dynamic balance (10). Agility has classically been defined as the simple ability to change direction rapidly. According to Young et al., agility involves a rapid displacing of the center of mass by changing direction or speed when reacting to a stimulus (11). On the other hand, this kind of physical activity was used as a methodology to improve physical function in older adults (12).

Yamada et al. (9) trained older adults during 60 min of rhythmic step exercise (step to multidirectional) with a cognitive task (reaction time and short memory), simultaneously for 24 weeks. This study showed that the program promotes training across different modalities (motor and cognitive functions), leading to improvements in tasks that need more attention, such as walking while performing the cognitive task (i.e., counting numbers aloud in inverse order) (9).

The improvement of divided attention (cognitive and/or physical task) benefits multiple functions, depending on the trained capacities. The physical training program provides physical adaptation (e.g., resistance training improves strength and power muscle), and the cognitive training (CT) program provides cognitive adaptations (e.g., verbal fluency [VF] training improves VF ability) simultaneously (6, 9, 13). Castaño et al. (6) performed resistance exercises in two conditions, with and without a cognitive task. The dual task (resistance exercise + cognitive task, simultaneously) used VF as a cognitive task. After 16 weeks of intervention, the study showed improvements in executive function and physical capacities.

We proposed that agility ladder training with VF (cognitive task) might help improve dual-task abilities (physical and cognitive function, simultaneously). For this reason, the effect of a 14-week exercise program involving AT with and without cognitive tasks on physical and cognitive functions in community-dwelling older adults was evaluated. We hypothesized that physical function would increase in both groups and cognitive function would improve only in the dual-task group.

Materials and methods

Study design

This two-arm, parallel, randomized, controlled trial compared the effects of AT and AT + CT (two groups) on cognitive function and physical performance in community-dwelling older adults without cognitive decline. Participants were recruited through advertisements in public sports areas located in Campinas, state of São Paulo, Brazil. After checking for eligibility, the participants were randomly allocated into the intervention groups using computer-generated random numbers (https://www.randomizer.org). The numbers were generated using "Math. Random" with a complex algorithm that gives the appearance of randomness. The education and literacy of the participants were evaluated through demography questionnaires.

The study was approved by the Research Ethics Committee of the University of Campinas (UNICAMP) (Protocol No. 2479761) and followed the ethical guidelines of the Declaration of Helsinki and Resolution 466/12 of the Brazilian Health Council. Participants were informed about the study procedures and objectives before giving written informed consent.

Eligibility criteria

We included participants aged >60 years old who were cognitively healthy, physically independent, and able to perform the physical function tests.

We excluded subjects who had started a structured physical activity program 2 months before the beginning of the study or participated in other exercise programs during the study period, and individuals with a clinical diagnosis of cardiovascular (e.g., acute myocardial infarction and transient ischemic disease), pulmonary (e.g., emphysema), neurological, psychiatric (e.g., Parkinson's, dementia or Alzheimer's disease), skeletal muscle disorders, and cognitive disorders (MMSE score was used as criteria of exclusion <24). The participants who were absent for more than 10% of the exercise sessions were also excluded from the study analysis.

The Mini-Mental State Examination (MMSE) was used as cognitive screening according to the Brazilian education level (14). The MMSE assesses spatial orientation, short memory, attention, and calculation, as well as the ability to name objects, follow commands, write a sentence, and reproduce a complex drawing (15).

All experimental procedures were conducted at the School of Physical Education of UNICAMP from February 2018 to June 2018.

Interventions

AT and AT + CT were performed twice a week for 14 weeks in two phases: a 2-week familiarization period followed by a 14-week training period. Exercise sessions lasted approximately 30 min, including a 10-min warm-up, a 15-min exercise session (main part), and a 5-min cooldown. All sessions were conducted in groups of two or three people, with a distance of 2 m between the participants

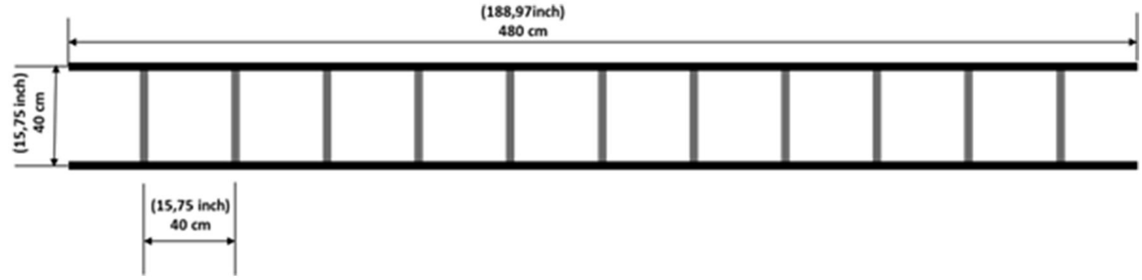

FIGURE 1
Agility ladder with a length of 4.8 m and 12 rungs (40 cm × 40 cm).

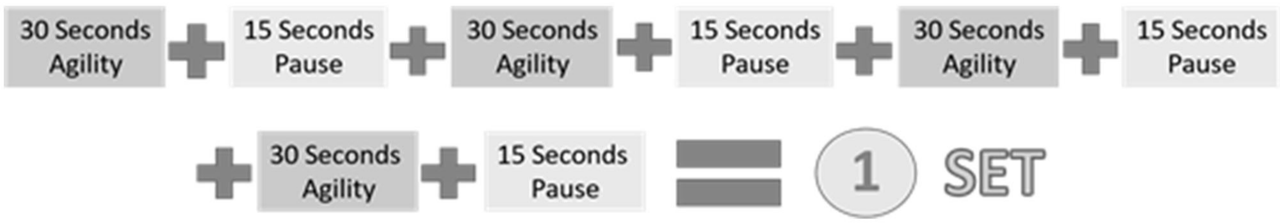

FIGURE 2
Exercise sets. Each exercise session (e.g., sequence A) included four subsets, each with a 30-s exercise period and a 15-s rest.

to avoid training interference. The participants of the AT + CT group were assigned the same cognitive task but in a different order. An agility ladder adapted from sports training was used in exercise sessions (Figure 1). Participants were instructed to step in the squares and not on the rungs and performed all activities under the supervision of an experienced trainer, who had 5 years of experience and supervised all the training sessions.

The familiarization period was designed to adapt participants to the laboratory setting, exercise sequences, and perception of effort (rating of perceived exertion). Participants were instructed to perform each exercise sequence round trip on the agility ladder for 30 s.

The duration of each session was equal for both groups (AT and AT + CT). Participants completed the same exercise sequence during the familiarization period. At week 6, the exercise difficulty was increased by substituting sequences 2A and 3A for 2B and 3B, respectively, and at week 10, difficulty increased by adding 30 s to each sequence (Figure 2). The sequences were considered with different combinations of the foot stepping on the ladder, as previously published by our group members (16).

Participants performed four sequences 1, 2 (2A or 2B), 3 (3A or 3B), and 4 for 30 s each, followed by 15 s of rest (Table 1). The physical exercise (agility ladder) sequence was performed in the same order by both groups (AT and AT + CT). Each session lasted 12 min from weeks 1 to 10 (3 sets to each sequence) and 15 min at weeks 11 and 12 (4 sets to each sequence), and more details were previously published (16).

The AT + CT group performed agility training concurrently with a cognitive task (e.g., VF). The participants were instructed to say aloud as many words of a specific category as possible in each subset. The difficulty level of the cognitive task was increased monthly by changing word categories, from general to specific, while phonemic (e.g., words beginning with vowels letters and consonants) or semantic (e.g., people names, sports, clothes, male names, aquatic sports, and winter clothes) categories were changed in each subset (Table 2). Participants were encouraged to not repeat words in each subset.

Measures

Assessments were performed before (at the baseline) and after the intervention (14 weeks), and each evaluation lasted for 2 days. Physical performance was assessed on the 1st day, and cognitive function was evaluated on the 2nd day.

Physical function

The following physical function tests were performed: (1) Walking speed (WS) at a normal and fast pace, (2) five times sit-to-stand test (5XSTS), (3) timed up and go (TUG), (4) isometric handgrip strength (IHG), (5) one-leg stand (OLS), and (6) Illinois agility test (IAT).

Walking speed

The WS test required walking 12 m at a normal and fast pace. Before the test, both feet remained on the starting line. The stopwatch was started when one foot reached the 1-m line and was stopped when one foot reached the 11-m line. The first and last 1-m

TABLE 1 Training sessions outlook.

Description	Quantity															
Sequences	1				2A or 2B				3A or 3B				4			
Sets	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Duration set (s)	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30
Rest sets (s)	15	15	15	-	15	15	15	-	15	15	15	-	15	15	15	-
Rest sequences (s)	60				60				60				60			

Sequence (combination of the footsteps on the ladder) = 1, 2 (2A or 2B), 3 (3A or 3B).

TABLE 2 Examples of semantic (e.g., 1st set—color and 2nd set—country) and phonological (e.g., 3rd set—M letter and 4th set—R letter) categories used for the verbal fluency test.

Sequence (A)	Time									
	30 Seconds									
1st Set	Green	Blue	Yellow	Red	Orange	Purple	White	Black	Gray	Pink
2nd Set	Brazil	Japan	Argentina	Italy	Colombia	China	Mexico	France	Paraguay	Spain
3rd Set	Mouse	Mini	Max	Math	Make	Map	Made	Medium	Memory	Meet
4th Set	Rule	Run	River	Route	Ring	Ready	Read	Rat	Rain	Right

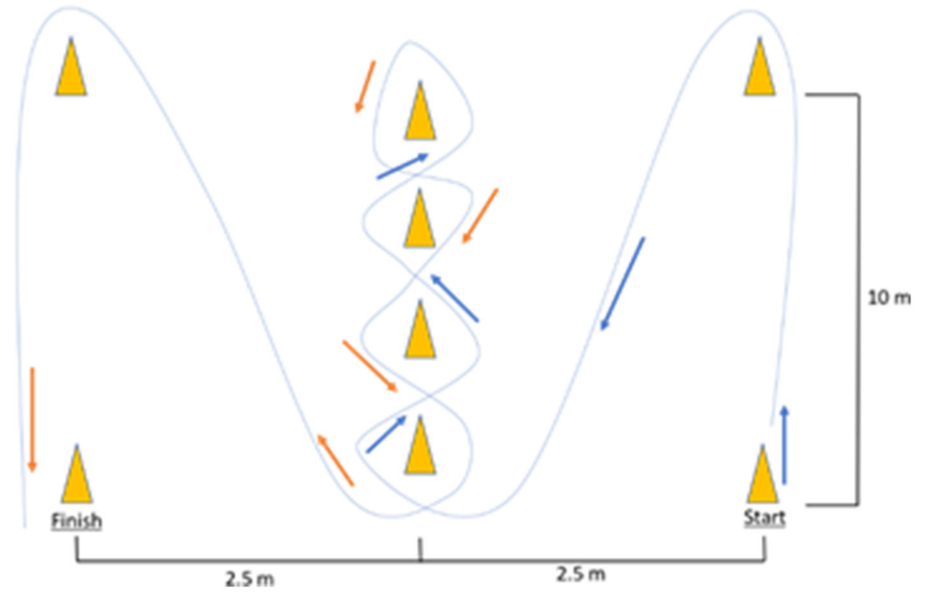

FIGURE 3
Illinois agility test.

stretches were used for acceleration and deceleration, respectively, and therefore were not considered (17). The fastest time of two trials (in m/s) was used for the present analyses.

Five times sit-to-stand test

This test comprises rising from and seating on an armless chair (total height, 87 cm; seat height, 45 cm; seat width, 33 cm) five times as fast as possible with arms crossed in front of the body. A stopwatch (1/100 second accuracy) was started when the participant raised the hip from the chair and stopped when the participant sat down for the fifth time (18).

Timed up and go

Upon hearing the command "go," the participants were required to get up from a chair without using their arms, walk as fast as possible along a 3-m straight line demarcated on the floor, turn around, return to the original position, and sit down on the chair again (19).

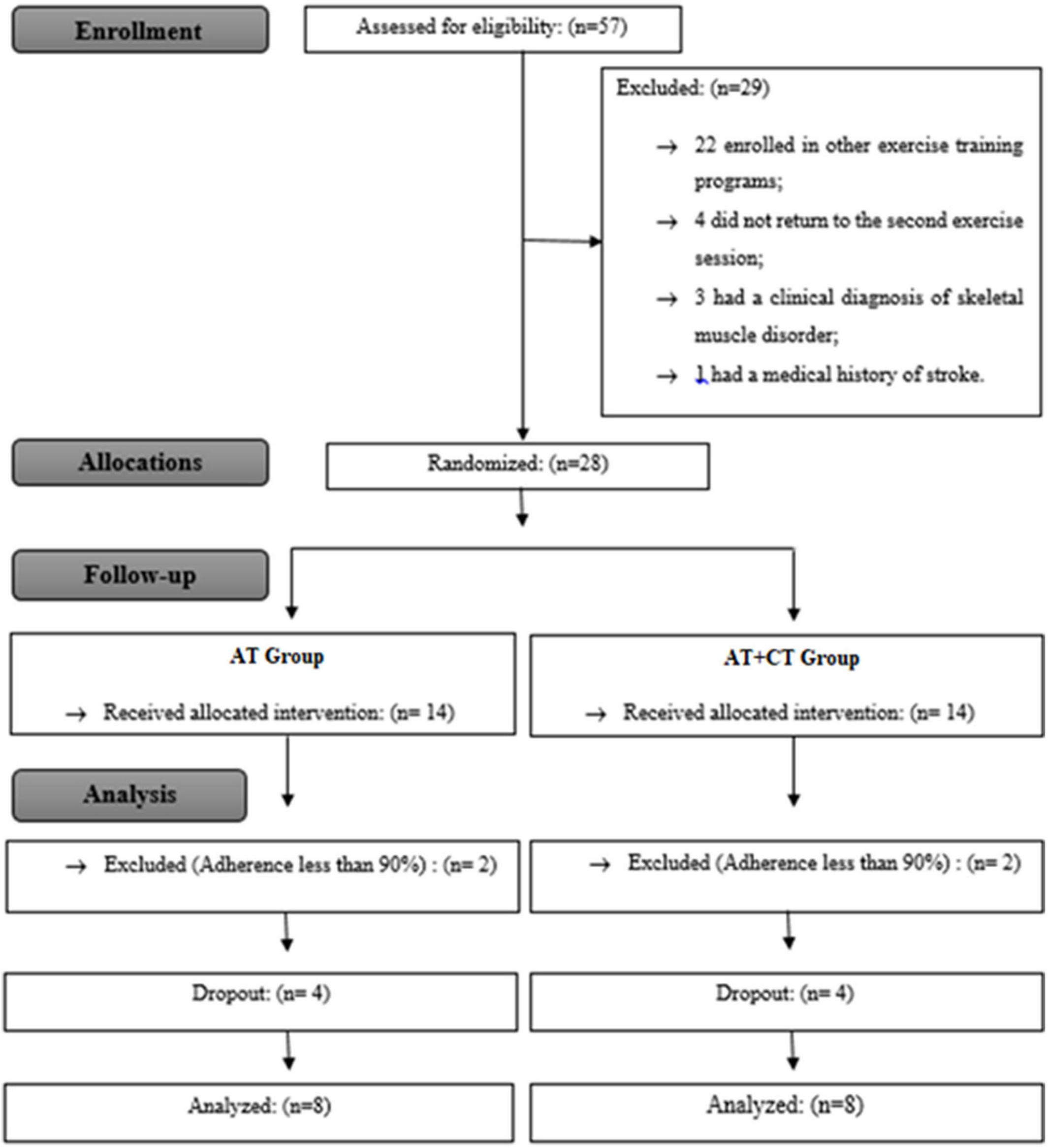

FIGURE 4
Study flowchart: AT, agility training; AT + CT, AT combined with cognitive training.

Isometric handgrip strength

The IHG was measured using a Jamar® dynamometer with participants sitting on a chair with shoulders adducted, elbows flexed at 90° beside the trunk, and wrists in a neutral position. The contralateral arm remained relaxed beside the trunk. The study subjects were asked to squeeze the handgrip as hard as they could for 4 to 6 s using the dominant hand. The highest test–retest reliability for each test was achieved, and 1 min to rest between retests was provided. The mean of three trials was used (20). Relative IHG was calculated by dividing IHG by the BMI.

One-leg stand

This test was performed with participants standing on one foot, the contralateral knee flexed at 90°, arms folded across the chest, and head straight. The stopwatch was started when one foot was raised off the floor and stopped when the foot touched the floor again. The test was performed in both legs, and the highest score was used in the analysis (21).

Illinois agility test

The participant was asked to walk as fast as possible (i.e., move quickly) through obstacles in multiple directions but not run. The course was marked in the corners by four cones (start, finish, and two turning cones) and four central cones spaced 3.3 m apart. The participants were instructed to walk in a straight line from the start line to the first turning cone located 10 m apart and from this site to the first central cone, weave back and forth through the four central cones, and walk from the first central cone to the second turning cone located

TABLE 3 Baseline comparison of both groups characteristics.

Variables	AT (n=8)	AT+CT (n=8)	*p*-value
Age (years)	66.6 ± 5.7	67.1 ± 4.6	0.64
Formal education (years)	12.6 ± 2.0	11.4 ± 4.8	0.96
Male gender (*n*, %)	3 (37.5%)	2 (25.0%)	0.72
Height (cm)	1.6 ± 0.1	1.6 ± 0.1	0.57
Body mass (kg)	70.6 ± 12,7	70.7 ± 7.2	0.87
BMI (kg/m²)	26.8 ± 4.3	26.7 ± 3.0	0.67
MMSE (points)	28.3 ± 1.7	27.2 ± 3.3	0.57

AT, Agility training; BMI, body mass index; CT, Cognitive training; MMSE, Mini-Mental State Examination.

on the far right and from this point to the finish line (22) (Figure 3).

Cognitive function

Cognitive function was assessed using VF (23), dual task, TUG combined with a cognitive task (TUG-cog) (24), trail-making test (TMT) (25), and the scenery picture memory test (SPMT) (26). Below we describe the tests mentioned above:

Verbal fluency test

VF was assessed using phonological and semantic tests. Participants were requested to name as many animals (semantic domain) and words that began with the letter "A" (phonological domain) as possible for 2 min (1 min each). The scores of the VF domains (phonological [VFP] and semantic [VFS]) were calculated as the sum of all the words that were evoked for 1 min (23).

TUG-cog

TUG-cog is a test that evaluates the divided attention, physical function, and cognitive function, simultaneously (walking [TUG test] + VF [cognitive task]). In this study, participants were required to say the names of animals out loud during the execution of TUG (27). Time started when participants got up from the chair and stopped when the participant returned to the chair and sat down. The result is shown in the second part.

Trail-making test

The TMT provides information on visual search, scanning, speed of processing, mental flexibility, and executive functions. The TMT was divided into two parts: TMT-A and TMT-B. TMT-A consisted of drawing a line connecting a sequential set of numbers (1–25), whereas TMT-B consisted of drawing a line connecting sequential numbers (1–13) and letters (A–L) and alternating between numbers and letters (e.g., 1a, 2b, 3c, and 4d). The test should be performed as quickly as possible (28). The final score is the total time spent finishing the connection between letters and numbers.

Scenery picture memory test

This test is based on the memorization of an image, requiring attention and short-term memory. The image of a living room containing 23 objects was drawn on a piece of paper. The participants were instructed to examine the image for 1 min and mention which elements they remembered. The total score corresponded to the number of items recalled (26).

Statistical analysis

Descriptive data were shown as mean ± standard deviation (SD). Continuous variables (age, formal education years, height, BMI, and MMSE scores) were compared using the Mann–Whitney *U*-test. Gender was compared using the chi-square test.

The effect of exercise on the study groups (AT and AT + CT) was analyzed using a two-way analysis of variance (ANOVA). Tukey's *post hoc* tests were used to assess which group or time showed significant differences. Effect size (ES) was calculated using each variable of the post-training score (value) minus the pre-intervention (baseline), and then divided by the pre-intervention (baseline). An ES of 0.00–0.19, 0.20–0.49, 0.50–0.79, and ≥0.80 were considered marginal, small, moderate, and large, respectively (29). Delta was also calculated [(baseline value − post-training value)/baseline value × 100]. ES and delta were calculated for all the variables, and *post hoc* was performed only for variables that presented a difference. The relationship between AT and cognitive test scores after training was assessed using Pearson's correlation. The data were analyzed using Statistical Analysis System version 9.4 for Windows (SAS Institute Inc., Cary, NC, USA). Statistical significance was set at a *p*-value of < 0.05.

Results

A total of 57 older adults were recruited. In total, 27 participants were excluded according to the eligibility criteria, and 28 were randomly allocated into the AT and AT + CT groups. Twelve participants were excluded from the analysis: four had <90% adherence to the training sessions, and we had eight dropouts. Hence, 16 subjects were included in the study and completed the training program (Figure 4).

There were no significant differences between groups in the baseline characteristics, as shown in Table 3.

AT + CT improved the scores of TUG-cog, phonological VF, and SPMT, whereas AT had better scores in SPMT after the training. Only for TUG-cog, ANOVA showed time x group interaction ($p = 0.019$) between AT + CT and AT. For the dual-task training, the cognitive functions improved by approximately 39, 32, and 7% in the tests TUG-cog, phonological VF, and SPMT (short-term memory), respectively. AT enhanced short-term memory,

TABLE 4 Effects of AT and AT+CT on cognitive functions and comparison between groups.

Cognitive domains	AT+CT ($n = 8$)				AT ($n = 8$)				Time × Group	Time	Group
	Pre	Post	ES	Δ%	Pre	Post	ES	Δ%			
TUG-cog (s)	9.5 ± 3.0	5.8 ± 0.5*#	1.4	38.9	7.5 ± 1.1	6.5 ± 1.0	1.0	13.3	0.0196	0.0004	0.2867
TMT-A (s)	47.3 ± 6.1	41.3 ± 13.2	0.5	2.65	37.7 ± 11.6	38.7 ± 10.1	0.1	9.6	0.4765	0.6531	0.1677
TMT-B (s)	130.7 ± 51.3	111.3± 63.2	0.5	18.4	90.4 ± 30.6	84.2 ± 24.8	0.2	6.8	0.1936	0.0937	0.2854
VFP (words/min)	12.4 ± 4.6	16.4 ± 6.6*	0.8	32.2	13.4 ± 2.9	13.8 ± 4.4	0.1	2.98	0.142	0.0514	0.7056
VFS (words/min)	19.7 ± 8.2	19.6 ± 8.4	0.1	0.50	18.9 ± 3.5	19.6 ± 6.1	0.2	3.7	0.8699	0.9022	0.8699
SPMT (points)	16.3 ± 2.7	17.5 ± 3.3*	0.4	7.3	14.9 ± 3.4	17.9 ± 3.2*	1.0	20.1	0.1738	0.0037	0.7354

*Main effect of time (*Post-hoc*), $p \leq 0.05$. #Main effect of group. AT, Agility training; CT, Cognitive training; ES, effect size; SPMT, Scenery Picture Memory Test; TMT-A, Trail Making Test A; TMT-B, Trail Making Test B; SVF, semantic verbal fluency; PVF, phonological verbal fluency.

TABLE 5 Effects of AT and AT+CT on physical function.

Variables	AT ($n = 8$)				Time × Group				Time	Group	
	Pre	Post	ES	Δ (%)	Pre	Post	ES	Δ (%)			
Usual WS (m/s)	1.3 ± 0.1	1.5 ± 0.1*	1.4	15.3	1.3 ± 0.1	1.5 ± 0.2*	1.6	15.3	0.9999	0.0002	0.9999
Fast WS (m/s)	1.8 ± 0.2	1.9 ± 0.2*	0.9	5.5	1.9 ± 0.2	1.9 ± 0.2	0.4	0.0	0.1686	0.0009	0.4942
5XSTS (s)	11.1 ± 2.2	7.9 ± 1.2*	2.0	27.4	10.2 ± 1.9	7.4 ± 1.0*	2.1	28.8	0.6871	0.0001	0.3428
TUG (s)	8.0 ± 1.2	5.8 ± 0.8*	2.4	27.5	7.4 ± 1.2	5.8 ± 0.7*	1.8	21.6	0.4039	0.0001	0.5287
Absolute IHG (kg)	23.9 ± 5.1	28.8 ± 6.3*	0.9	20.5	24.6 ± 9.3	29.5 ± 10*	0.5	19.9	0.9999	0.0002	0.8049
Relative IHG (kg/BMI)	0.9 ± 0.3	1.1 ± 0.3*	0.6	22.2	1.0 ± 0.3	1.1 ± 0.3*	0.4	10	0.6410	0.0002	0.6410
OLS right (s)	15.1 ± 8.9	25.6 ± 8.1	1.3	69.5	17.7 ± 12.2	21.8 ± 10	0.4	23.1	0.3694	0.0467	0.8654
Illinois test (s)	36.5 ± 6.0	31.8 ± 5.0*	0.9	12.8	35.3 ± 5.0	31.3 ± 4.3*	0.9	11.3	0.6148	0.0001	0.7256

*Main effect of time (*Post-hoc*), $p < 0.05$; AT, Agility training; BMI, body mass index; CT, Cognitive training; ES, effect size; IHG, isometric handgrip strength; OLS, One-leg stand; TUG, timed up-and-go test; WS, walking speed; 5XSTS, five-times sit-to-stand test.

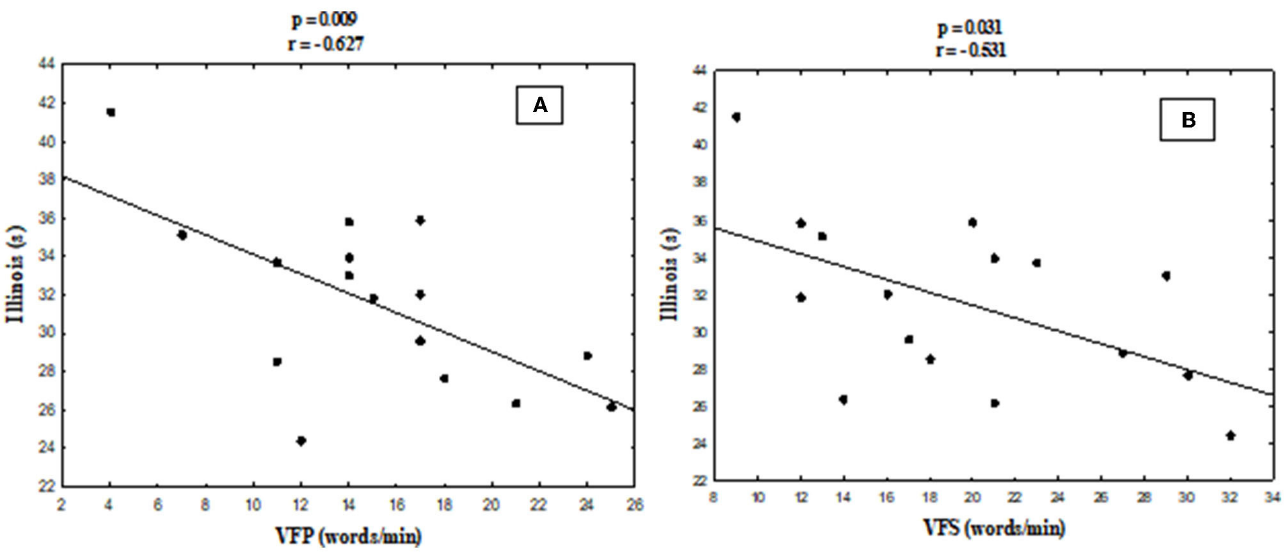

FIGURE 5
Pearson's correlation between the Illinois agility test and phonological **(A)** and semantic **(B)** verbal fluency scores.

which is indicated by an increase of approximately 20% in SPMT (Table 4).

The effects of AT + CT and AT on physical performance are shown in Table 5. The time effect (pre-post) was observed for both intervention groups ($p < 0.05$). AT + CT and AT increased the scores of WS at a normal pace, 5XSTS, TUG, IHG, relative IHG, and IAT. The AT + CT and AT groups improved physical function, with an increase in walking speed at a normal pace [WS Δ(%) 15, 15], power muscle [5XSTS Δ(%) 27, 29], dynamic balance [TUG Δ(%) 27, 22], isometric strength muscle [absolute IHG Δ(%) 21, 20], and agility function [IAT Δ(%) 13, 11], respectively (Table 5).

There was a significant correlation between IAT scores and VFP ($r = -0.627$; $P = 0.009$, $n = 16$) and between IAT scores and VFS ($r = -0.539$; $P = 0.031$, $n = 16$) as seen in Figure 5.

Discussion

The current study investigated the influence of 14-week AT and AT + CT on physical and cognitive functions in community-dwelling older adults. The current study shows that both interventions were beneficial for the physical function (in all the evaluated parameters) of the participants. Moreover, AT + CT had an additional positive effect on cognitive function (executive function and VF) in healthy older adults after 3 months of the intervention program (dual-task training). In addition, there was a positive correlation between agility test scores and VF scores, suggesting that those who performed better in the agility test (Illinois test) may have a high processing speed when evoking words.

Cognitive functions

Cognitive functions showed improvements after the intervention program. TUG-cog scores were significantly higher in the AT + CT group. Previous studies support these results, wherein dual-task intervention (e.g., combined physical activity [PA] and CT) is more beneficial than PA or CT interventions alone (7, 13, 30, 31). Castaño et al. (6) showed that physical activity training for 16 weeks increased physical function. However, the authors showed that the combination of physical and cognitive training improved physical and cognitive function and increased the levels of neurotrophic biomarkers (brain-derived neurotrophic factor) (6). The cognitive functions improvement (e.g., short-term and working memory and executive function) may prevent the risk of cognitive impairment and dementia.

The participants who underwent AT + CT were required to perform VF (pronouncing specific classes of words) jointly with physical coordination tasks (agility training ladder), involving working memory and cognitive flexibility (32). A previous meta-analysis supports this finding and suggests that PA programs for older adults can yield superior cognitive benefits when cognitive tasks are integrated into the programs without interfering with the results of physical function (30).

Cognitive functions (including executive functions and memory) are essential in regulating functional mobility. Several studies have shown that gait abnormalities might precede the diagnosis of cognitive decline, and people showing slower gait during a dual task (e.g., TUG-cog) are more likely to develop cognitive impairment (27, 33). De Melo Borges et al. (27) showed that the greater the cognitive impairment, the worse the TUG-cog performance.

Physical activity can increase some cognitive functions, especially aerobic training, which has been shown to have the most significant impact on the aging brain and cognition compared to other types of physical activity (9, 13). SPMT scores increased in both groups, corroborating the findings in the literature. Although the intensity of aerobic training is essential for cognitive and physical improvements, aerobic training can counter cognitive declines, including memory (34).

Physical function

The present results showed that agility ladder training with/without CT could prevent the loss of muscle power/strength despite the age-related decrease in neuromuscular performance (35, 36). Frailty is associated with decreased strength and physical function (37), and some studies demonstrated that physical activity can improve muscle power/strength and, finally, physical function in older adults (35–37).

The score in the TUG test is associated with the risk of falls in older adults (38). Segev et al. (39) found that a 12-week coordination training decreased the risk of falls in older adults with cardiovascular disease, demonstrating that a fast pace is related to a low risk of falls and better dynamic balance since those abilities are considered the main components of postural control.

The AT is comprised of perception (e.g., the organization, identification, and interpretation of sensory information), cognitive function (e.g., attention, planning, and decision-making), and changes in direction (e.g., sudden starts, stops, and turns, reactive control, and concentric and eccentric contractions) that might enable for integration of sensorimotor, neuromuscular, and cardio-circulatory demands (11, 40). Balance also depends on muscle strength and neuromuscular coordination (41), which may be one of the reasons why the interventions enhanced static and dynamic balance.

It is essential to highlight that AT + CT is low-cost, practical, readily accessible, and easily adapted to specific populations by changing speed and complexity (9). Studies attest to the beneficial effects of DT on executive function, fall prevention, and memory compared with isolated training (9, 42).

Limitations

The limitations of this study include the lack of control and/or CT group and the small sample size, and the latter can potentially decrease statistical power. Despite not having a control group or one group that performed only CT, there was no significant difference between groups at the baseline, and we used their baseline data as control data. Although the sample size can be a limitation to be pointed out, especially regarding statistical power, the results found herein showed that the dual-task activity (physical and cognitive) was able to promote benefit in a greater proportion of the participants than the physical activity alone. It is a potential intervention that needs to be further explored.

Conclusion

We investigated the effects of 14 weeks (two familiarization weeks) of AT and AT + CT on physical and cognitive function in community-dwelling older adults. Both interventions improved muscle power and strength, dynamic balance, agility, and short-term memory, whereas AT + CT showed additional improvements in other cognitive functions. Our results show that AT + CT should be included in physical activity programs for older adults because it is easy to apply, practical, and cost-effective intervention and has benefits for physical and cognitive function together.

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 human participants were reviewed and approved by Institutional Human Research Ethics Committee of the UNICAMP. The patients/participants provided their written informed consent to participate in this study.

Author contributions

VC and MU: conceptualization and project administration. LC and VC: data collection. LC, VC, and MU: formal analysis. VC, PS, RS, and MU: funding acquisition and methodology. LC, VC, and RS: investigation. CT and MU: supervision. LC, MU, and CT: writing—original draft. LC, CT, MU, PS, and RS: writing—reviewing and editing. All authors contributed to the article and approved the submitted version.

Funding

VC received a scholarship from the Coordination for the Improvement of Higher Education Personnel of Brazil (CAPES) (Protocol # 1800789) during this study.

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.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Murman DL. The impact of age on cognition. *Semin Hear.* (2015) 36:111–21. doi: 10.1055/s-0035-1555115

2. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised european consensus on definition and diagnosis. *Age Ageing.* (2018) 48:16–31. doi: 10.1093/ageing/afy169

3. Woollacott M, Shumway-Cook A. Attention and the control of posture and gait: a review of an emerging area of research. *Gait and Posture.* (2002) 16:1–14. doi: 10.1016/S0966-6362(01)00156-4

4. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *Lancet.* (2019) 393:2636–46. doi: 10.1016/S0140-6736(19)31138-9

5. Cassilhas RC, Viana VAR, Grassmann V, Santos RT, Santos RF, Tufik S, et al. The impact of resistance exercise on the cognitive function of the elderly. *Med Sci Sports Exerc.* (2007) 39:1401–7. doi: 10.1249/mss.0b013e318060111f

6. Castaño LAA, de Lima VC, Barbieri JF, de Lucena EGP, Gáspari AF, Arai H, et al. Resistance training combined with cognitive training increases brain derived neurotrophic factor and improves cognitive function in healthy older adults. *Front Psychol.* (2022) 13:3941. doi: 10.3389/fpsyg.2022.870561

7. Damirchi A, Hosseini F, Babaei P. Mental training enhances cognitive function and BDNF more than either physical or combined training in elderly women with MCI: a small-scale study. *Am J Alzheimer Dis Other Dement.* (2018) 33:20–9. doi: 10.1177/1533317517727068

8. Monteiro-Junior RS, Vaghetti CAO, Nascimento OJM, Laks J, Deslandes AC. Exergames: neuroplastic hypothesis about cognitive improvement and biological effects on physical function of institutionalized older persons. *Neural Regener Res.* (2016) 11:201. doi: 10.4103/1673-5374.177709

9. Yamada M, Tanaka B, Nagai K, Aoyama T, Ichihashi N. Rhythmic stepping exercise under cognitive conditions improves fall risk factors in community-dwelling older adults: preliminary results of a cluster-randomized controlled trial. *Aging Mental Health.* (2011) 15:647–53. doi: 10.1080/13607863.2010.551341

10. Robert SK, Cheung CW, Sum Raymond KW. Effects of 6-week agility ladder drills during recess intervention on dynamic balance performance. *J Phys Educ Sport.* (2017) 17:306–11. doi: 10.3791/60468

11. Sheppard J, Young W. Agility literature review: classifications, training and testing. *J Sports Sci.* (2006) 24:919–32. doi: 10.1080/02640410500457109

12. Morat M, Morat T, Zijlstra W, Donath L. Effects of multimodal agility-like exercise training compared to inactive controls and alternative training on physical performance in older adults: a systematic review and meta-analysis. *Eur Rev Aging Phys Activity.* (2021) 18:1–20. doi: 10.1186/s11556-021-00256-y

13. Nishiguchi S, Yamada M, Tanigawa T, Sekiyama K, Kawagoe T, Suzuki M, et al. A 12-week physical and cognitive exercise program can improve cognitive function and neural efficiency in community-dwelling older adults: a randomized controlled trial. *J Am Geriatr Soc.* (2015) 63:1355–1363. doi: 10.1111/jgs.13481

14. Brucki SMD, Nitrini R, Caramelli P, Bertolucci PHF, Okamoto IH. Sugestões Para o Uso Do Mini-Exame Do Estado Mental No Brasil. *Arq Neuropsiquiatr.* (2003) 61:777–781. doi: 10.1590/S0004-282X2003000500014

15. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* (1975) 12:189–98. doi: 10.1016/0022-3956(75)90026-6

16. de Lima VC, Castaño LAA, Boas VV, Uchida MC. A training program using an agility ladder for community-dwelling older adults. *JoVE.* (2020) 157:e60468.

17. Sampaio PYS, Ito E, Sampaio RAC. The association of activity and participation with quality of life between Japanese older adults living in rural and urban areas. *J Clin Gerontol Geriatr.* (2013) 4:51–6. doi: 10.1016/j.jcgg.2012.11.004

18. Buatois S, Miljkovic D, Manckoundia P, Gueguen R, Miget P, Vançon G, et al. Five times sit to stand test is a predictor of recurrent falls in healthy community-living subjects aged 65 and older. *J Am Geriatr Soc.* (2008) 56:1575–7. doi: 10.1111/j.1532-5415.2008.01777.x

19. Podsiadlo D, Richardson S. The timed 'Up and Go': a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc.* (1991) 39:142–8. doi: 10.1111/j.1532-5415.1991.tb01616.x

20. Mathiowetz V, Weber K, Volland G, Kashman N. Reliability and validity of grip and pinch strength evaluations. *J Hand Surg Am.* (1984) 9:222–6. doi: 10.1016/S0363-5023(84)80146-X

21. Briggs RC, Gossman MR, Birch R, Drews JE, Shaddeau SA. Balance performance among noninstitutionalized elderly women. *Phys Ther.* (1989) 69:748–56. doi: 10.1093/ptj/69.9.748

22. Raya MA, Gailey RS, Gaunaurd IA, Jayne DM, Campbell SM, Gagne E, et al. Comparison of three agility tests with male servicemembers: edgren side step test, *t*-test, and Illinois agility test. *J Rehabil Res Dev.* (2013) 50:951–60. doi: 10.1682/JRRD.2012.05.0096

23. Troyer AK, Moscovitch M, Winocur G. Clustering and switching as two components of verbal fluency: evidence from younger and older healthy adults. *Neuropsychology.* (1997) 11:138. doi: 10.1037/0894-4105.11.1.138

24. Coelho-Júnior HJ, Goncalvez IDO, Callado Sanches I, Gonçalves L, Caperuto EC, Uchida MC, et al. Multicomponent exercise improves physical functioning but not cognition and hemodynamic parameters in elderly osteoarthritis patients regardless of hypertension. *Biomed Res Int.* (2018) 2018:3714739. doi: 10.1155/2018/3714739

25. Tischler L, Petermann F. Trail making test (TMT). *Zeitschrift für Psychiatr Psychol Psychother.* (2010) 58:79–81. doi: 10.1024/1661-4747.a000009

26. Takechi H, Dodge HH. Scenery Picture Memory Test: A new type of quick and effective screening test to detect early stage Alzheimer's disease patients. *Geriatr Gerontol Int.* (2010) 10:183–90. doi: 10.1111/j.1447-0594.2009.00576.x

27. De Melo Borges S, Radanovic M, Forlenza OV. Functional mobility in a divided attention task in older adults with cognitive impairment. *J Mot Behav.* (2015) 47:378–85. doi: 10.1080/00222895.2014.998331

28. Tombaugh TN. Trail making test A and B: normative data stratified by age and education. *Arch Clin Neuropsychol.* (2004) 19:203–14. doi: 10.1016/S0887-6177(03)00039-8

29. Cohen J. A power primer. *Curr Dir Psychol Sci.* (1992) 112:155–9. doi: 10.1037/0033-2909.112.1.155

30. Gheysen F, Poppe L, DeSmet A, Swinnen S, Cardon G, De Bourdeaudhuij I, et al. Physical activity to improve cognition in older adults: can physical activity programs enriched with cognitive challenges enhance the effects? A systematic review and meta-analysis. *Int J Behav Nutr Phys Activity.* (2018) 15:1–13. doi: 10.1186/s12966-018-0697-x

31. Law LLF, Barnett F, Yau MK, Gray MA. Effects of combined cognitive and exercise interventions on cognition in older adults with and without cognitive impairment: a systematic review. *Ageing Res Rev.* (2014) 15:61–75. doi: 10.1016/j.arr.2014.02.008

32. Diamond A. Executive Functions. *Ann Rev Clin Psychol.* (2014) 64:135–68. doi: 10.1146/annurev-psych-113011-143750

33. Beauchet O, Allali G, Berrut G, Hommet C, Dubost V, Assal F. Gait analysis in demented subjects: interests and perspectives. *Neuropsychiatr Dis Treatm.* (2008) 4:155–160. doi: 10.2147/NDT.S2070

34. Chapman SB, Aslan S, Spence JS, Defina LF, Keebler MW, Didehbani N, et al. Shorter term aerobic exercise improves brain, cognition, and cardiovascular fitness in aging. *Front Aging Neurosci.* (2013) 5:1–9. doi: 10.3389/fnagi.2013.00075

35. Izquierdo M, Cadore EL. Muscle power training in the institutionalized frail: a new approach to counteracting functional declines and very late-life disability. *Curr Med Res Opin.* (2014) 30:1385–90. doi: 10.1185/03007995.2014.908175

36. Reid KF, Fielding RA. Skeletal muscle power: a critical determinant of physical functioning in older adults. *Exerc Sport Sci Rev.* (2012) 40:4–12. doi: 10.1097/JES.0b013e31823b5f13

37. Sampaio PYS, Sampaio RAC, Júnior HJC, Teixeira LFM, Tessutti VD, Uchida MC, et al. Differences in lifestyle, physical performance and quality of life between frail and robust brazilian community-dwelling elderly women. *Geriatr Gerontol Int.* (2016) 16:829–35. doi: 10.1111/ggi.12562

38. Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the Timed Up and Go Test. *Phys Ther.* (2000) 80:896–903. doi: 10.1093/ptj/80.9.896

39. Segev D, Hellerstein D, Carasso R, Dunsky A. The effect of a stability and coordination training programme on balance in older adults with cardiovascular disease: a randomised exploratory study. *Eur J Cardiov Nurs.* (2019) 18:736–43. doi: 10.1177/1474515119864201

40. Donath L, van Dieën J, Faude O. Exercise-based fall prevention in the elderly: what about agility? *Sports Med.* (2016) 46:143–9. doi: 10.1007/s40279-015-0389-5

41. Ahmad I, Noohu MM, Verma S, Singla D, Hussain ME. Effect of sensorimotor training on balance measures and proprioception among middle and older age adults with diabetic peripheral neuropathy. *Gait Posture.* (2019) 74:114–20. doi: 10.1016/j.gaitpost.2019.08.018

42. Falbo S, Condello G, Capranica L, Forte R, Pesce C. Effects of physical-cognitive dual task training on executive function and gait performance in older adults: a randomized controlled trial. *Biomed Res Int.* (2016) 2016:5812092. doi: 10.1155/2016/5812092

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 08 September 2023
DOI 10.3389/fpubh.2023.1189173

Check for updates

OPEN ACCESS

EDITED BY
Marco Carlos Uchida,
State University of Campinas, Brazil

REVIEWED BY
Woo Jung Kim,
Yonsei University, Republic of Korea
John Tshon Yit Soong,
National University Hospital, Singapore

*CORRESPONDENCE
Su Min
201371@cqmu.edu.cn
Feng Lv
lvfengmazui@sina.cn

†These authors share first authorship

RECEIVED 31 March 2023
ACCEPTED 29 August 2023
PUBLISHED 08 September 2023

CITATION
Chen A, Ren L, Min S, Li P, Wei K, Cao J, Tao Y and Lv F (2023) Analysis of the relationship between body habitus and frailty of community adults in Chongqing: a cross-sectional survey study.
Front. Public Health 11:1189173.
doi: 10.3389/fpubh.2023.1189173

Analysis of the relationship between body habitus and frailty of community adults in Chongqing: a cross-sectional survey study

Aini Chen[1†], Li Ren[2†], Su Min[2*], Ping Li[2], Ke Wei[2], Jun Cao[2], Yi Tao[3] and Feng Lv[2*]

[1]School of Medical, Chongqing Medical University, Chongqing, China, [2]Department of Anesthesiology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China, [3]Department of Phase I Clinical Trial Ward, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China

Objective: Currently, a multitude of studies are underway to investigate the factors affecting the degree of frailty, with a significant focus on the critical role of body mass index (BMI). This study aims to conduct a cross-sectional survey to investigate the multifaceted relationship between multiple body habitus and the factors that influence the degree of frailty.

Methods: A questionnaire survey was conducted among 840 adult residents in Chongqing communities. A total of 723 participants were included in the data analysis, with an effective response rate of 92.0%. Fried's frailty scale was used to classify individuals into fit, pre-frail, or frail. Non-parametric tests and chi-square tests were employed to evaluate the inter-group differences in frailty levels under different influencing factors. Multivariate logistic regression analysis was performed to select the independent variables associated with frailty statistics. According to the results of the parallel line test, ordered or disordered multivariate logistic regression was used to evaluate the impact of a single independent variable on frailty for different variables.

Results: Adult community residents in Chongqing accounted for 29.18 and 5.67% in pre-frailty and frailty, respectively. In multivariate logistic regression analysis, high BMI, and high waist-hip ratio (WHR) were identified as major risk factors for frailty. Furthermore, the process of aging, coupled with moderate to heavy alcohol consumption, active weight loss behavior in the past year, and the presence of comorbidities, emerged as significant contributors to frailty. Conversely, factors such as a positive inclination toward taste, consistent meal timing, habitual breakfast consumption, sound nutritional intake, and the cultivation of healthy dietary practices were recognized as pivotal elements that act as protective factors against frailty.

Conclusion: The integration of both BMI and WHR provides a more comprehensive perspective, effectively capturing the intertwined influence of obesity and sarcopenia on the extent of frailty. To mitigate the risk of community-wide frailty, a multipronged approach is essential, involving the promotion of favorable dietary practices and achieving nutritional equilibrium, diligent management of coexisting medical conditions, moderation in alcohol consumption, and the enhancement of physical functionality.

KEYWORDS
frailty, body mass index, waist-hip ratio, body habitus, community adult

1. Introduction

Frailty is a multifaceted clinical condition that arises with age, characterized by a decline in physiological capabilities across various organ systems, rendering individuals more susceptible to stressors (1). The significance of frailty as a predictor of mortality risk among older adults dwelling in the community has been underscored through an in-depth research (2). A comprehensive meta-analysis encompassing 21 studies conducted in high-income countries revealed that the prevalence of frailty among community-dwelling older adults ranged from 4.0 to 59.1%, with an average prevalence of 10.7% (3). In China, the total prevalence rates of pre-frailty and frailty in community-dwelling older adults are 43 and 10%, respectively (4). Clinical manifestations of frailty include weight loss, muscle atrophy and weakness, diminished endurance, compromised balance and mobility, reduced gait speed, and cognitive impairment (5). Given these considerations, it is imperative to embark on research and interventions targeted at addressing frailty.

Beyond the realm of older adults, certain studies have unveiled the occurrence of frailty across other age groups as well (6, 7). Factors affecting frailty are generally considered to be related to BMI (8), as well as risk factors such as aging, smoking, alcohol consumption, comorbidities, malnutrition, diabetes, cognitive impairment, and history of falls (9). Frailty can be mitigated through engagement in physical activities, exercise regimens, dietary modifications, and modulation of gut microbiota (10–13).

Previous research (14) has shown that sarcopenia (the decline in function accompanied by low muscle mass) is the primary cause of frailty, accounting for 70% of frailty cases. The Asian Working Group for Sarcopenia (AWGS) 2014 consensus has defined sarcopenia as "age-related loss of muscle mass, plus low muscle strength, and/or low physical performance" (15), the European Society for Clinical Nutrition and Metabolism (ESPEN) in association with the European Association for the Study of Obesity (EASO) considers BMI as a screening tool for sarcopenia, highlighting that excessive adiposity in conjunction with diminished skeletal muscle mass or correlated body compartments substantiates the diagnosis of sarcopenia (16). Since sarcopenia is a prominent manifestation and risk factor for frailty, BMI is frequently adopted in studies to prognosticate the extent of frailty. Low BMI has been correlated with an elevated frailty risk (17), while conversely, an elevated BMI might augment the likelihood of frailty (18). Nevertheless, relying solely on BMI might not yield a comprehensive understanding of the degree of frailty. Hence, the incorporation of additional indicators of body habitus, such as waist-hip ratio, body fat percentage, body roundness index, body shape index, etc. Become crucial for defining individual physical characteristics, including physique, general bearing, and body shape (19). These indicators facilitate a more accurate and comprehensive characterization of frail patients. Furthermore, scant exploration has been devoted to the factors that influence body habitus, such as dietary habits and nutritional status. Therefore, this study aimed to explore the relationship between body habitus (BMI and the degree of frailty), potential associations between lifestyle, nutrition, dietary habits, and the degree of frailty [as indicated by waist-hip ratio (WHR), body fat percentage (BFP), body roundness index (BRI), and body shape index (ABSI)] based on a community sample.

2. Materials and methods

2.1. Ethical considerations

This study followed the guidelines for human research in the 2013 revised Declaration of Helsinki. The research protocol was approved by the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University (2023–021) and registered at the Chinese Clinical Trial Registry in 2023 (ChiCTR2300068834). Participation in the survey was entirely voluntary, and prior to the commencement of the survey, written informed consent was obtained from each participant. It was explicitly communicated that the anonymity of all participants would be rigorously upheld.

2.2. Participants and procedure

The present cross-sectional study was carried out in Chongqing (China) from March 1, 2023 to March 7, 2023. To be eligible for participation, individuals had to meet the following inclusion criteria: (1) Possession of a registered household registration or temporary residency permit in Chongqing, with a minimum residency duration of 6 months, excluding those classified as migrant population; (2) Attainment of at least 18 years of age; and (3) Willingness to provide informed consent for participation in the study. In order to ensure the scientific validity of the survey design, a multi-stage random cluster sampling method was employed, taking into account significant aspects such as economic status and demographic variables. This approach aimed to ensure the overall representativeness of the sample by aligning with regional income standards, maintaining a distribution of age and gender akin to the general population in Chongqing, and achieving a balanced geographical distribution. The survey targeted 10 communities within Chongqing, which were selected through a random sampling process. Among 12 street offices, six were chosen at random, and from each selected street office, three communities were randomly picked. The sample size of each community survey was approximately 40 individuals. Ultimately, three street offices were identified for inclusion in the survey. All individuals meeting the inclusion criteria were selected from the designated households until the requisite sample size was attained. The study population encompassed individuals aged 18 or above, inclusive of those aged 18. A total of 720 participants were required in the 10 surveyed communities. Upon obtaining informed consent from the participants, pertinent data was acquired *via* on-site survey questionnaires, which were pre-tested to ensure their validity and reliability. In total, 840 survey questionnaires were distributed, yielding 786 collected responses and an actual response rate of 93.6%. After the exclusion of 61 participants with missing data, the final dataset comprised 723 participants ($n = 723$), resulting in an effective rate of 92.0%.

2.3. Measures

The survey encompassed an assessment of various domains, including socio-demographic information, body habitus, nutritional assessment, dietary habits, Fried's frailty scale, and related domains (Appendix 1). Trained personnel executed all evaluations using standardized methodologies. Before distributing the questionnaire, a panel of 5 experts participated in the discussion and evaluation process for scrutinizing and refining the language, accuracy, order, and fluency of the questions and response options. The evaluation process comprised both individual assessment and group discussion. To obviate mutual influence, the experts remained uninformed about each other's evaluation outcomes. Following the expert evaluation, the questionnaire underwent an initial pre-testing within a small-scale community study, yielding a Cronbach's alpha coefficient of 0.744.

2.3.1. Sociodemographic characteristics

This study thoroughly examined the sociodemographic characteristics of the participants, including age, gender, marital status (single, married, divorced, widowed), education level (primary school and below, junior high school, senior high school, vocational school, undergraduate, graduate and above), occupation (government enterprises, healthcare professionals, self-employed, students, and retired) and personal income (less than ¥1,000, ¥1,000–3,999, ¥4,000–9,999, more than ¥10,000). Smoking status was classified as smoking (continuous or cumulative smoking for 6 months or more) or non-smoking (20). Drinking status was classified as non-drinking, moderate drinking (female ≤1 glass/day for women, male ≤2 glasses/day), or heavy drinking (female >1 glass/day, male >2 glasses/day) (21). Exercise was defined as moderate-intensity activity for ≥150 min/week or high-intensity activity for ≥75 min/week (22). Active weight loss behavior in the past year was defined as a binary variable (yes or no), indicating whether individuals had actively pursued strategies to manage their weight. Comorbidities were defined as self-reported chronic diseases (such as hypertension, diabetes, coronary heart disease, cerebrovascular disease, chronic obstructive pulmonary disease, joint diseases, etc.).

2.3.2. Body habitus

This section comprises nine indicators pertinent to body habitus, including height, weight, waist circumference, hip circumference, BMI, WHR, BFP, BRI, and ABSI.

BRI serves as an index for measuring the distribution of body fat, which considers the mass, distribution, and shape of total fat. BRI is calculated by the ratio of waist circumference to hip circumference. A higher BRI value corresponds to greater fat accumulation around the waist. Notably, BRI stands as a more precise gage of waist fat distribution and the roundness of body shape, characterized by robust practicality and accuracy (23, 24). ABSI, on the other hand, offers a body shape measurement that takes into account body fat distribution and BMI (25). ABSI is calculated based on the ratio of waist circumference to [height raises to 2/3 power times the square root of BMI]. A higher ABSI value implies greater waist fat accumulation relative to height and BMI. Several studies have shown that high ABSI and BRI values are associated with increased risks of cardiovascular disease, diabetes, and cancer (26, 27). Currently, ABSI is incorporated in certain studies for the prediction of health risks and the evaluation of body shape (28). The measurement of all the aforementioned indicators adhered to the standard methods specified by the Chinese Center for Disease Control and Prevention (29). Calibrated weighing scales with a precision of 1,000 grams were employed, height measurements were precise to 1 cm, and the calculation outcomes were recorded to two decimal places.

2.3.3. Nutritional assessment scale

The Short Nutritional Assessment Questionnaire (SNAQ), a concise, succinct, and repeatable survey questionnaire, was utilized for the nutritional appetite assessment (30). SNAQ consists of 4 questions, each with 5 answer options, represented by the letters A through E. The questionnaire's content, along with the scoring criteria, are detailed in Appendix 1. Lower scores denote poorer appetite and an elevated risk of weight loss, with the score range spanning 4 to 20. A score of ≤14 signifies a potential risk of weight loss.

2.3.4. Dietary habits assessment scale

This segment of the questionnaire aligns with the "Chinese Dietary Guidelines for Residents (2016 edition)" (31). The questionnaire consists of 5 questions, and the specific questions and corresponding scoring criteria can be found in Appendix 1. The cumulative score on this scale ranges from 12 to 55 points.

2.3.5. Frailty assessment scale

In this study, frailty measurement was defined using the Fried and colleagues Frailty Assessment Scale (32), a rigorously validated and widely used tool. The assessment model of this scale centers around five criteria: feeling exhausted, physical activity, walk time, grip strength, and weight loss. In instances where a participant is unable to ambulate due to a fracture or injury, their pre-fracture or pre-injury activity level should be reported. Satisfying 1–2 of these criteria indicates pre-frailty while meeting 3 or more criteria signifies frailty.

2.4. Statistics analysis

IBM SPSS Statistics 26.0 (IBM Corporation, Armonk, NY, United States) was used for data analysis. First, descriptive statistics were used to examine the baseline characteristics of the study population. Next, the Kruskal-Wallis H test was used for non-parametric analysis of asymmetric continuous count data, while the chi-square test was used for metric data of continuous normal distribution. These assessments were conducted to discern whether variations existed in the distribution of different frailty degrees across diverse conditions, including body habitus, nutritional status, and dietary habits. Then, multiple logistic regression was performed to identify the most significant frailty-related predictors among variables exhibiting statistical significance. Finally, based on parallel line test results, ordinal or nominal multiple logistic regression analyzes were conducted for each variable with statistical differences to examine the relationship between the specific predictor variable and frailty. In the regression analyzes, all variables considered to be potential confounders were meticulously adjusted. All statistical tests conducted within the model were two-tailed and predicated on a significance level of 0.05.

3. Result

3.1. Participants' sociodemographic characteristics

Table 1 presents the socio-demographic characteristics of the 723 participants. The median age of the sample was 47 years, with a first quartile (Q1) of 29 and a third quartile (Q3) of 67 (SD = 20.217, SE = 0.752). Among the participants, 51.5% were females, while 48.5% were males. Out of the total, 471 individuals (65.1%) were considered healthy, 211 (29.2%) exhibited pre-frailty, and 41 (5.7%) were identified as frail. Regarding occupational distribution, a majority of participants were engaged in company jobs (31.3%) or had retired (34.3%). As for education, 39.6% possessed a college degree. In terms of monthly income, the largest proportion fell within the range of 1,001–3,499 yuan (31.1%). Additionally, 40.1% of the participants were married.

3.2. Comparison of body habitus and influencing factors for frailty

Table 2 demonstrates the comparison and tests conducted between body habitus and levels of frailty. After standardized grouping based on diverse indicators, the populations categorized as frail and pre-frail were primarily concentrated within the overweight population (75.6%). Individuals exhibiting both high and low WHR manifested varying degrees of frailty, with a higher risk of frailty observed in comparison to those with normal WHR. Notably, among individuals with different levels of frailty, BMI, WHR, BRI, and ABSI demonstrated significant inter-group differences ($p < 0.05$), suggesting their potential influence on frailty degree. Moreover, the results indicated significant group variations within the Nutrition Assessment Scale and the Dietary Habits Assessment Scale, as reflected by distinct total scores ($p < 0.05$) among individuals with varying degrees of frailty. Specifically, factors such as the acceptance of food taste, regular daily meals, and regular breakfast may become one of the factors affecting the degree of frailty. Additionally, diverse lifestyles were found to have an impact on the degree of frailty. Variables such as

TABLE 1 Baseline characteristics adjusted for debilitating status (n = 723).

Characteristics		Fit (*n* = 471)		Pre-frail (*n* = 211)		Frail (*n* = 41)		Total (*n* = 723)	
		N	%	*N*	%	N	%	*N*	%
Gender	Female	260	55.2%	94	44.5%	18	43.9%	372	51.5%
	Male	211	44.8%	117	55.5%	23	56.1%	351	48.5%
Age*	Below 29	139	29.5%	19	9.0%	1	2.4%	159	22.0%
	29 ~ 47	140	29.7%	52	24.6%	8	19.5%	200	27.7%
	47 ~ 67	100	21.2%	67	31.8%	11	26.8%	178	24.6%
	Above 67	92	19.5%	73	34.6%	21	51.2%	186	25.7%
Profession	Self-employed	111	23.6%	50	23.7%	5	12.2%	166	23.0%
	Company Enterprise	162	34.4%	55	25.1%	9	21.9%	226	31.3%
	Health Care	39	8.3%	1	0.5%	0	0.0%	40	5.5%
	Student	39	8.3%	4	1.9%	0	0.0%	43	5.9%
	Retiree	120	25.5%	101	47.9%	27	65.9%	248	34.3%
Educational background	Primary school and below	1	0.2%	3	1.4%	2	4.9%	6	0.8%
	Junior high school	95	20.2%	65	30.8%	14	34.1%	174	24.1%
	High School	133	28.2%	57	27.0%	10	24.4%	200	27.7%
	Undergraduate	198	42.0%	75	35.5%	13	31.7%	286	39.6%
	Postgraduate and above	44	9.3%	11	5.2%	2	4.9%	57	7.9%
Monthly incomes (RMB, Yuan)	≤1,000	70	14.9%	36	17.1%	6	14.6%	112	15.5%
	1,001–3,499	52	32.5%	37	26.1%	7	41.5%	96	31.1%
	3,500–9,999	153	11.0%	55	17.5%	17	17.1%	225	13.3%
	≥10,000	117	24.8%	53	25.1%	4	9.8%	174	24.1%
Marital status	Single	194	41.2%	59	28.0%	10	24.4%	263	36.4%
	Married	176	37.4%	96	45.5%	18	43.9%	290	40.1%
	Divorced	81	17.2%	42	19.9%	9	22.0%	132	18.3%
	Widowed	20	4.2%	14	6.6%	4	9.8%	38	5.3%

*Segmentation of age according to the results of the quartiles.

TABLE 2 Descriptive analysis of body habitus and influencing factors.

Independent variable		Fit (*n* = 471)	Pre-Frail (*n* = 211)	Frail (*n* = 41)	Total (*n* = 723)	*P*
		N(%)/Mean (SD)	*N*(%)/Mean (SD)	*N*(%)/Mean (SD)	*N*(%)/Mean (SD)	
Body habitus						
Body mass index (BMI)	Underweight	29 (6.20%)	4 (1.90%)	0 (0.00%)	33 (4.60%)	0.000*
	Normal weight	217 (46.10%)	64 (30.30%)	10 (24.40%)	291 (40.20%)	
	Overweight	225 (47.80%)	143 (67.80%)	31 (75.60%)	399 (55.20%)	
Waist-hip ratio (WHR)	Low	127 (27.00%)	67 (31.80%)	7 (17.10%)	201 (27.80%)	0.010*
	Normal	97 (20.60%)	38 (18.00%)	2 (4.90%)	137 (18.90%)	
	High	247 (52.40%)	106 (50.20%)	32 (78.00%)	385 (53.30%)	
Body fat percentage	Low	1 (0.20%)	3 (1.40%)	0 (0.00%)	4 (0.60%)	0.083*
	Normal	30 (6.40%)	2 (0.90%)	2 (4.90%)	34 (4.70%)	
	High	440 (93.40%)	206 (97.60%)	39 (95.10%)	685 (94.70%)	
Body roundness index (BRI)		3.26 ± 0.62	2.99 ± 0.76	3.08 ± 0.61	3.17 ± 0.68	0.000
A body shape index (ABSI)		0.73 ± 0.11	0.69 ± 0.14	0.72 ± 0.11	0.72 ± 0.12	0.038
Lifestyle						
Age		44.17 ± 19.60	56.22 ± 18.78	63.61 ± 15.60	48.79 ± 20.22	0.000
Smoking**	No	321 (68.20%)	95 (45.00%)	20 (48.80%)	436(60.30%)	0.000
	Yes	150 (31.80%)	116 (55.00%)	21 (51.20%)	287 (39.70%)	
Drinking alcohol***	No	369 (78.30%)	127 (60.20%)	22 (53.70%)	518 (71.60%)	0.000
	Moderate drinking	69 (14.60%)	53 (25.10%)	15 (36.60%)	137 (18.90%)	
	Heavy drinking	33 (7.00%)	31 (14.70%)	4 (9.80%)	68 (9.40%)	
Active weight loss behavior in the past year****	No	416 (88.30%)	177 (83.90%)	31 (75.60%)	624 (86.30%)	0.036
	Yes	55 (11.70%)	34 (16.10%)	10 (24.40%)	99 (13.70%)	
Daily exercise*****	No	183 (38.90%)	83 (39.30%)	18 (43.90%)	284 (39.30%)	0.818
	Yes	288 (61.10%)	128 (60.70%)	23 (56.10%)	439 (60.70%)	
Comorbidities	No	413 (87.70%)	61 (28.90%)	16 (39.00%)	490 (67.80%)	0.000
	Yes	58 (12.30%)	150 (71.10%)	25 (61.00%)	233 (32.20%)	
SNAQ total score		13.42 ± 2.66	12.88 ± 2.87	13.17 ± 2.70	13.35 ± 2.73	0.020
Appetite level		3.44 ± 1.23	3.29 ± 1.32	3.56 ± 1.25	3.4 ± 1.25	0.338
Food taste acceptance		3.4 ± 1.22	3.12 ± 1.23	3.05 ± 1.32	3.3 ± 1.23	0.009
Food intake per meal		3.13 ± 1.15	3.03 ± 1.2	3.1 ± 1.02	3.1 ± 1.16	0.497
Number of meals per day		3.45 ± 0.98	3.44 ± 1.1	3.46 ± 1.03	3.45 ± 1.02	0.971
Dietary habits scale total score		39.12 ± 5.04	38.24 ± 6.96	37.78 ± 5.261	38.79 ± 5.691	0.002
Daily meal situation		1.63 ± 0.48	1.5 ± 0.5	1.39 ± 0.49	1.58 ± 0.49	0.000
Regular breakfast		2.59 ± 0.51	2.4 ± 0.56	2.44 ± 0.55	2.53 ± 0.53	0.000
Eating frequency of staple food		4.13 ± 1.01	3.92 ± 1.23	4.1 ± 0.94	4.07 ± 1.07	0.254
Eating frequency of whole grains		3.1 ± 1.12	3.23 ± 1.35	3.32 ± 1.04	3.15 ± 1.19	0.285
Eating frequency of vegetables		3.71 ± 1.15	3.68 ± 1.22	3.27 ± 1.27	3.68 ± 1.18	0.084
Eating frequency of fruit		3.59 ± 1.19	3.62 ± 1.27	3.54 ± 1.23	3.6 ± 1.21	0.821
Eating frequency of poultry		3.5 ± 1.18	3.53 ± 1.24	3.61 ± 1.12	3.51 ± 1.19	0.855
Eating frequency of meat		3.11 ± 1.28	2.95 ± 1.31	2.85 ± 1.17	3.05 ± 1.29	0.199
Eating frequency of fish and its products		3.27 ± 1.3	3.34 ± 1.31	3.12 ± 1.29	3.28 ± 1.3	0.570
Eating frequency of eggs and its products		3.65 ± 1.13	3.57 ± 1.21	3.34 ± 1.32	3.61 ± 1.17	0.406
Eating frequency of beans and its products		3.44 ± 1.26	3.18 ± 1.32	3.39 ± 1.12	3.36 ± 1.27	0.054
Eating frequency of milk and its products		3.39 ± 1.25	3.33 ± 1.37	3.41 ± 1.22	3.37 ± 1.28	0.946

*Since there is a certain categorical sample size n < 5 for this categorical variable, Fisher's exact test is used. **Smoking: Smoking is defined as continuous or cumulative smoking for 6 months or more. ***Drinking alcohol: Whether it is white wine, beer, wine, or yellow wine, as long as the number of times it is consumed is defined as drinking alcohol, and those who consume it only once on festivals are not considered as drinking alcohol. ****Active weight loss behavior in the past year: It is defined as a binary variable (yes or no), indicating whether individuals had actively pursued strategies to manage their weight. It may not always result in significant weight reduction and can be influenced by various factors. These factors could include medical conditions, medications, and other underlying health conditions. *****Daily exercise: physical activity was defined as ≥150 min/week of moderate-intensity or ≥ 75 min/week of high-intensity physical activity.

smoking, alcohol consumption, active weight loss behavior in the past year, patient age, and the presence of comorbidities were all associated with varying degrees of frailty within different populations.

3.3. Multivariate logistic regression analysis of factors related to different degrees of frailty

Using frailty, pre-frailty, and fitness as dependent variables, we considered the following factors as independent variables: age, smoking, drinking, active weight loss behavior in the past year, comorbidities, BMI, WHR, BRI, ABSI, food taste acceptance score, daily regular meal score, regular breakfast score, total score of Nutrition Assessment Scale and total score of Dietary Habits Scale. Table 3 shows the variables that exhibited statistical significance in the analysis ($p<0.05$). In our study, the application of multivariate logistic regression aims to identify significant contributing factors without establishing linear relationships between variables. This statistical approach is commonly employed in the field (33, 34). owing to its effectiveness in identifying significant predictors among multiple variables. It serves as a valuable tool for assessing associations between various factors and the targeted outcome. The results showed that 11 independent variables were associated with frailty and pre-frailty, including age, moderate and heavy drinking, active weight loss behavior in the last year, comorbidities, BMI, WHR, food taste acceptance score, daily meal score, regular breakfast score, total score of the Short Nutritional Assessment Scale, and total score of the Eating Habits Scale.

3.4. Logistic regression analysis of the single factor and different degrees of frailty

To prevent mutual influence and interference among independent variables, each independent variable was subjected to separate regression analysis. Previously, a parallel lines assumption test was conducted to ensure the parallelism of the response curves of categorical variables in the ordered logistic regression model. This

TABLE 3 Multivariate logistic regression analysis of factors related to different degrees of frailty.

Independent variable		Pre-Frail vs. Fit				Frail vs. Fit			
		OR	95%CI		*P*	OR	95%CI		*P*
			Lower	Upper			Lower	Upper	
Body habitus									
Body mass index (BMI)	Normal weight(ref)								
	Underweight	0.621	0.142	2.712	0.526	2.829E-09	2.829E-09	2.829E-09	0.000
	Overweight	0.615	1.191	0.603	2.351	3.527	1.013	12.286	0.048
Waist-hip ratio (WHR)	Normal(ref)								
	Low	1.073	0.557	2.065	0.833	2.228	0.407	12.189	0.355
	High	1.423	0.783	2.585	0.247	10.265	2.165	48.667	0.003
Body roundness index (BRI)		0.967	0.139	6.748	0.973	5.615	0.206	153.403	0.307
A body shape index (ABSI)		0.030	1.640E-06	554.665	0.485	3.965E-05	1.764E-12	891.252	0.241
Lifestyle									
Age		1.005	0.991	1.019	0.490	1.048	1.024	1.072	0.000
Smoking	No(ref)								
	Yes	0.666	0.419	1.060	0.087	0.689	0.311	1.525	0.358
Drinking alcohol	No(ref)								
	Moderate drinking	1768	1.019	3.066	0.043	3.105	1.336	7.217	0.008
	Heavy drinking	2.189	1.089	4.402	0.028	1.389	0.393	4.911	0.610
Active weight loss behavior in the past year	No(ref)								
	Yes	1.850	1.008	3.394	0.047	2.512	0.971	6.501	0.058
Comorbidity	No(ref)								
	Yes	23.528	13.649	40.556	0.000	8.147	3.347	19.831	0.000
SNAQ total score		1.079	0.968	1.202	0.168	1.240	1.029	1.495	0.024
Food taste acceptance score		0.837	0.671	1.043	0.113	0.692	0.481	0.996	0.047
Dietary habits scale total score		1.063	1.018	1.111	0.006	1.058	0.985	1.138	0.124
Daily meal score		0.614	0.393	0.959	0.032	0.360	0.164	0.788	0.011
Regular breakfast score		0.355	0.234	0.539	0.000	0.553	0.270	1.133	0.106

parallel lines assumption, commonly used in cross-sectional studies (35), signifies that distinct categories of an independent variable maintain a consistent parallel relationship across its entire range. This ensures the reliability of regression models for prediction and interpretation. If the parallel lines assumption is violated ($p < 0.05$), it suggests that the model may not accurately capture the relationships between different categories. This situation can lead to unstable predictive outcomes and compromise the overall reliability of the model. When $p > 0.05$, the response curves of each variable at varying levels of categorical variables exhibit parallelism, which can be analyzed using an ordered logistic regression model (36, 37).

As a result, except for WHR and comorbidities analyzed using unordered logistic regression, all other independent variables can be analyzed using ordered logistic regression. The impact of each independent variable on the degree of frailty was statistically different ($p < 0.05$). The results presented in Tables 4, 5 showed that aging annually increases the log odds value of frailty by 0.035 units (B = 0.035), indicating the significant effect of age on frailty. In terms of body habitus, the degree of frailty increased with increasing BMI values. The coefficient B for the variable “Overweight” with a value of 0.823 (greater than 0) indicates that a positive value signifies an augmented probability ratio of transitioning from lower to higher levels of the dependent variable with an increase in the independent variable. This implies that the degree of frailty is correlated with an elevated BMI. For every unit increase in the BMI value, the odds ratio of transitioning from one level of the dependent variable to the next higher level increases by approximately a factor of 0.823. Individuals with a high WHR had a 6.283-fold increased risk of frailty compared to fitness. Moderate drinking, heavy drinking, and comorbidities, as factors influencing body habitus, all increased the relative probability of frailty (B > 0). Conversely, the relative probability of frailty decreased (B < 0) with each unit increase in active weight loss behavior in the past year, food taste acceptance score, daily meal score, regular breakfast score, simple nutritional assessment scale total score, and dietary habit scale total score. Comorbidity significantly increased the odds of frailty (OR = 11.126) and pre-frailty (OR = 17.510) when compared to the healthy population, and these results were statistically significant ($p < 0.01$).

TABLE 4 Univariate ordinal logistic regression.

Independent variable		*B*	95%CI		*P*
			Lower	Upper	
Age		0.035	0.027	0.043	0.000
Drinking alcohol	No(ref)				
	Moderate drinking	0.918	0.543	1.293	0.000
	Heavy drinking	0.886	0.389	1.383	0.000
Active weight loss behavior in the past year	No(ref)				
	Yes	0.508	0.089	0.927	0.018
Body mass index (BMI)	Normal weight(ref)				
	Underweight	−0.921	−2.004	0.163	0.096
	Overweight	0.832	0.496	1.149	0.000
SNAQ total score		−0.061	−0.116	−0.006	0.031
Food taste acceptance score		−0.188	−0.311	−0.066	0.003
Dietary habits scale total score		−0.029	−0.056	−0.002	0.035
Daily meal score		−0.639	−0.945	−0.333	0.000
Regular breakfast score		−0.599	−0.883	−0.315	0.000

4. Discussion

In previous studies, discussions on frailty mainly centered on the older adult population (38, 39). The present study conducted a comprehensive analysis of adult community residents for the first time. The outcomes unveiled a frailty prevalence rate of 5.67% and a pre-frailty prevalence rate of 29.18%, which were consistent with findings from numerous previous studies (40, 41). Moreover, this research delved into body habitus indicators beyond the confines of BMI, opting for a more accurate and comprehensive evaluation through multiple indicators such as WHR, body fat percentage, BRI, and weight index. This multifaceted approach enables a more comprehensive grasp of the relationships between factors such as fat mass, central obesity, and frailty.

In this study, Fried’s frailty scale (32), also known as the phenotype model (42), was utilized as the tool for screening and grading frailty. As the most widely employed method for assessing frailty, this questionnaire adeptly and swiftly portrays participants’ physical frailty statuses. Additionally, it exhibits a robust correlation with BMI and other body habitus indicators, rendering it the most appropriate method for assessing frailty within the scope of this cross-sectional study (43). Although the Fried frailty scale was initially designed for individuals aged 65 and older, recent research has indicated that it maintains a high level of accuracy when applied to the assessment of frailty in the middle-aged population (44). In contrast, the commonly used clinical frailty scale (CFS) (45) and frailty index (FI) (46) lack comprehensive evaluation criteria pertaining to body habitus. Consequently, these tools possess certain limitations when evaluating frailty across diverse body habitus profiles. The CFS primarily assesses frailty based on mobility status, while the FI lacks standardized criteria for variable inclusion. Researchers determine variable inclusion based on their study objectives and available health indicators, leading to variations in the number of variables (ranging from 30 to 70), and the corresponding threshold values (47–49), and researchers from different countries have developed their own versions of the FI. Hence, these two commonly used assessment tools inherently carry limitations that render them unsuitable for the present study.

Nutritional status was evaluated using the Simplified Nutritional Appetite Questionnaire (SNAQ) (50), which encompasses several indicators such as appetite, hunger, and sensory perception. This questionnaire embraces high reliability, sensitivity, and predictability, enabling it to effectively reflect the nutritional status of the population and predict the risk of malnutrition. To evaluate dietary habits, the China Food Guide Pagoda (2016 version) (31) and multiple references were consulted, covering various types of food and frequency of consumption, providing a comprehensive reflection of participants’ dietary preferences and dietary balance.

TABLE 5 Univariate multinomial logistic regression.

Independent variable		Pre-Frail vs. Fit				Frail vs. Fit			
		OR	95%CI		*P*	OR	95%CI		*P*
			Lower	Upper			Lower	Upper	
Comorbidities	No(ref)								
	Yes	17.510	11.677	26.256	0.000	11.126	5.608	22.073	0.000
Waist-hip ratio (WHR)	Normal(ref)								
	Low	1.347	0.835	2.171	0.222	2.673	0.543	13.115	0.227
	High	1.095	0.706	1.699	0.684	6.283	1.477	26.726	0.013

The findings of this study reaffirmed previously identified risk factors for frailty, including age, alcohol consumption, and comorbidities (4, 9, 14). In comparison to individuals classified as fit, those categorized as frail or pre-frail were older and more likely to engage in moderate or heavy drinking and suffer from comorbidities. Prior research has indicated that exercise can mitigate the risk of frailty and enhance physiological function in older adults (51). However, in this study, 56.10% of frail participants and 60.70% of pre-frail participants reported engaging in regular exercise. This suggests that the manner, frequency, and intensity of their exercise may not be sufficient to effectively prevent or delay frailty. Furthermore, these results imply that the cause of frailty may extend beyond merely insufficient exercise, encompassing other factors such as age, health status, dietary habits, and medication usage.

In the present study, the relationship between BMI and frailty did not fully align with the findings of previous research. According to one study (52), there is a U-shaped association between BMI and frailty, suggesting that both high and low BMI values increase the likelihood of frailty. In our study, overweight individuals had a higher incidence of frailty, but the statistical association between low BMI value and frailty was not fully confirmed. Several factors could contribute to this outcome. Firstly, due to the high prevalence of obesity in China (53), our study had limited representation of individuals with low BMI and instead, had a greater prevalence of overnutrition and high BMI. This trend is consistent with previous research conducted within Chinese communities (54). Moreover, this discrepancy might be explicable through the mechanisms of frailty. Sarcopenia, the key contributor to frailty, primarily involves a decline in muscle mass within the body (55). However, for participants with lower BMI values, the reduction in BMI might not be entirely attributed to the loss of muscle mass; it could also involve loss of fat or calcium (56, 57). Similarly, a high BMI does not necessarily signify muscle gain but may be a sign of fat gain and muscle loss. Numerous studies have highlighted the risk of synergistic complications of sarcopenia and obesity in aging populations (58). Therefore, if frailty is described solely from the perspective of BMI as in previous studies, the relationship between sarcopenia and frailty may not be adequately substantiated. Our study encompassed various body habitus indicators, and both BMI and WHR demonstrated statistical significance. As a descriptive index for waist and hip circumference, WHR can better reflect the distribution of muscle and fat in different parts of the body. It effectively highlights unfavorable fat accumulation around the abdomen and is also easier to calculate than BMI (59). Several studies have demonstrated that the WHR is a more effective predictor of mortality and the incidence of certain diseases in middle-aged and older adults compared to BMI. It has also been adopted as an indicator of health and the presence of significant health risks (60, 61). Our results confirmed that high WHR independently increased the risk of current community frailty. This finding suggests that, in the context of Chinese community populations, low BMI or low WHR no longer constitute major factors in frailty development. Instead, high BMI and high WHR are more closely associated with frailty progression. Furthermore, we propose that WHR can offer a more accurate depiction of the relationship between frailty and sarcopenia compared to BMI. Individuals with high WHR are more likely to shift from fitness to frailty, implying an overlap between our physical condition characterized by high waist fat and low hip circumference fat, and the clinical manifestations of sarcopenia. Unlike BMI, which solely considers height and weight, WHR takes into account critical factors of sarcopenia: muscle mass and fat mass. It is worth noting that the formula for calculating WHR considers gender differences, which is particularly important since females are more susceptible to frailty (3, 62, 63). This gender-specific aspect is often overlooked when calculating BMI. In conclusion, the assessment of frailty can be enhanced by considering multiple body habitus indicators, such as WHR and BMI, to achieve more accurate and comprehensive results.

The absence of a significant correlation between body fat percentage (BFP) and frailty status, as observed in Table 2, presents an intriguing finding. This finding aligns with previous research that has highlighted inconsistencies and even reversals in the significance of WHR and BFP (64). BFP serves as an indicator of the proportion of total body weight attributed to adipose tissue, essentially representing the overall adiposity of the body. While an elevated body fat percentage may indicate a higher overall fat content, it fails to provide insights into the distribution of fat within specific anatomical regions. In the context of our study, the lack of a significant association between body fat percentage and frailty status suggests that the overall fat content might have a relatively minor impact on frailty. Conversely, WHR is regarded as a more refined measure, reflecting the proportion of abdominal fat within the total body fat composition. Elevated WHR is often indicative of abdominal obesity, which has a strong association with various health concerns and displays a significant relationship with frailty status (65). Our study confirms this perspective, underscoring that WHR could be more sensitive than BFP in assessing frailty status, or alternatively, the abdominal fat distribution might play a more pivotal role in determining frailty status. Furthermore, studies have indicated that Asians tend to possess a higher proportion of visceral fat compared to Europeans, which provides an additional perspective to explain the significant WHR result and the non-significant BFP finding in our study (66, 67).

This study also covered some relevant factors affecting body habitus, including lifestyle, nutritional status, and dietary habits. The scoring outcomes of the questionnaire imply that a regimen of regular eating, daily breakfast consumption, high acceptance of food taste, a balanced diet, and adequate nutrition can collectively lower the relative likelihood of developing frailty. This suggests that favorable dietary habits can contribute to weight management, maintaining health status, and diminishing the risk of frailty (68, 69). Additionally, some literature has suggested a relationship between frailty and malnutrition (70–72). Malnutrition has been identified as the primary risk factor for frailty among community-dwelling older adults (73), which has a greater impact on the frailty of the population (70).

5. Limitation

Although we selected the most suitable frailty assessment scale for our study, there is currently no frailty scale available that encompasses all age groups. Hence, there might be some bias in the assessment of frailty among the younger population. In terms of sample selection and collection, this study was limited to community populations in urban areas of China. While we have made considerable efforts to ensure sample representativeness, achieving a 100% representation of the overall situation is challenging. Moreover, factors such as rural areas and ethnicity should be taken into consideration. Additionally, the sample size gathered for some indicators remains moderate. Despite our efforts to rule out collinearity, this might result in some inevitable errors in the outcomes, such as wider confidence intervals. In future investigations, we intend to explore the possibility of employing a multi-center or longitudinal research approach, thereby broadening the spectrum and comprehensiveness of the sample. Furthermore, the percentage of body fat was calculated during the measurement process, without using instruments for obtaining highly accurate results. To enhance the accuracy of body composition measurement, we aim to employ more comprehensive and precise measurement methods. Finally, since our study was cross-sectional in nature, we did not conduct subgroup analyzes of frailty status across different populations or genders. Further research is needed to explore the interplay and influence of BMI and other contributing factors.

6. Conclusion

This cross-sectional analysis elucidated the relationship between body habitus and frailty in community-dwelling adults. The study also incorporated pertinent influencing factors such as lifestyle, nutritional status, and dietary habits. The results demonstrated that compared to previous studies solely focused on BMI, a comprehensive evaluation of body habitus involving BMI, WHR, BFP, BRI, ABSI, and other indicators can provide a more thorough and accurate reflection of the influence of body size and obesity on frailty severity. Furthermore, this approach can help explain the mechanisms underlying frailty caused by sarcopenia, thereby aiding in predicting changes in the prevalence of adult frailty within communities. By fostering good dietary habits, achieving nutritional balance, managing comorbidities, and reducing alcohol consumption, the risk of community frailty can be significantly mitigated. These findings offer novel insights into targeted prevention and even reversal of frailty.

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 First Affiliated Hospital of Chongqing Medical University (2023–021) and the Chinese Clinical Trial Registry in 2023 (ChiCTR2300068834). 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

AC, FL, and SM conceived the presented idea, developed the framework, and wrote the manuscript. AC, LR, and KW were involved in the data collection. YT and PL provided critical feedback and contributed to the final version. All authors contributed to the article and approved the submitted version.

Funding

This research was funded by Chongqing Social Science Planning Project (2021PY27); Chongqing Graduate Joint Training Base (lpjd202204); Chongqing Medical University Future Medical Youth Innovation Team Development Support Plan (W0006).

Acknowledgments

We thank all the participants for participating in this study.

Conflict of interest

All 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.

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1189173/full#supplementary-material

References

1. Dent E, Martin FC, Bergman H, Woo J, Romero-Ortuno R, Walston JD. Management of frailty: opportunities, challenges, and future directions. *Lancet*. (2019) 394:1376–86. doi: 10.1016/S0140-6736(19)31785-4

2. Fan J, Yu C, Guo Y, Bian Z, Sun Z, Yang L, et al. Frailty index and all-cause and cause-specific mortality in Chinese adults: a prospective cohort study. *Lancet Public Health*. (2020) 5:e650–60. doi: 10.1016/S2468-2667(20)30113-4

3. Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: A systematic review. *J Am Geriatr Soc*. (2012) 60:1487–92. doi: 10.1111/j.1532-5415.2012.04054.x

4. He B, Ma Y, Wang C, Jiang M, Geng C, Chang X, et al. Prevalence and risk factors for frailty among community-dwelling older people in China: A systematic review and Meta-analysis. *J Nutr Health Aging*. (2019) 23:442–50. doi: 10.1007/s12603-019-1179-9

5. Rockwood K, Hogan DB, MacKnight C. Conceptualisation and measurement of frailty in elderly people. *Drugs Aging*. (2000) 17:295–302. doi: 10.2165/00002512-200017040-00005

6. Jayanama K, Theou O, Godin J, Mayo A, Cahill L, Rockwood K. Relationship of body mass index with frailty and all-cause mortality among middle-aged and older adults. *BMC Med*. (2022) 20:404. doi: 10.1186/s12916-022-02596-7

7. Santos-Eggimann B, Cuénoud P, Spagnoli J, Junod J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. *J Gerontol A Biol Sci Med Sci*. (2009) 64:675–81. doi: 10.1093/gerona/glp012

8. Hubbard RE, Lang IA, Llewellyn DJ, Rockwood K. Frailty, body mass index, and abdominal obesity in older people. *J Gerontol A Biol Sci Med Sci*. (2010) 65:377–81. doi: 10.1093/gerona/glp186

9. Wang X, Hu J, Wu D. Risk factors for frailty in older adults. *Medicine (Baltimore)*. (2022) 101:e30169–9. doi: 10.1097/MD.0000000000030169

10. Harper C, Gopalan V, Goh J. Exercise rescues mitochondrial coupling in aged skeletal muscle: a comparison of different modalities in preventing sarcopenia. *J Transl Med*. (2021) 19:71. doi: 10.1186/s12967-021-02737-1

11. Jayanama K, Theou O, Godin J, Cahill L, Shivappa N, Hébert JR, et al. Relationship between diet quality scores and the risk of frailty and mortality in adults across a wide age spectrum. *BMC Med*. (2021) 19:64. doi: 10.1186/s12916-021-01918-5

12. Ghosh TS, Rampelli S, Jeffery IB, Santoro A, Neto M, Capri M, et al. Mediterranean diet intervention alters the gut microbiome in older people reducing frailty and improving health status: the NU-AGE 1-year dietary intervention across five European countries. *Gut*. (2020) 69:1218–28. doi: 10.1136/gutjnl-2019-319654

13. Almeida HM, Sardeli AV, Conway J, Duggal NA, Cavaglieri CR. Comparison between frail and non-frail older adults' gut microbiota: A systematic review and meta-analysis. *Ageing Res Rev*. (2022) 82:101773. doi: 10.1016/j.arr.2022.101773

14. Mijnarends DM, Schols JMGA, Meijers JMM, Tan FES, Verlaan S, Luiking YC, et al. Instruments to assess sarcopenia and physical frailty in older people living in a community (care) setting: similarities and discrepancies. *J Am Med Dir Assoc*. (2015) 16:301–8. doi: 10.1016/j.jamda.2014.11.011

15. Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K, et al. Asian working Group for Sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc*. (2020) 21:300–307.e2. doi: 10.1016/j.jamda.2019.12.012

16. Donini LM, Busetto L, Bischoff SC, Cederholm T, Ballesteros-Pomar MD, Batsis JA, et al. Definition and diagnostic criteria for Sarcopenic obesity: ESPEN and EASO consensus statement. *Obes Facts*. (2022) 15:321–35. doi: 10.1159/000521241

17. Xu L, Zhang J, Shen S, Hong X, Zeng X, Yang Y, et al. Association between body composition and frailty in elder inpatients. *Clin Interv Aging*. (2020) 15:313–20. doi: 10.2147/CIA.S243211

18. Yuan L, Chang M, Wang J. Abdominal obesity, body mass index and the risk of frailty in community-dwelling older adults: a systematic review and meta-analysis. *Age Ageing*. (2021) 50:1118–28. doi: 10.1093/ageing/afab039

19. Zinn SL. *Body size and habitus. Clinical methods: The history, physical, and laboratory examinations. 3rd* ed. Boston: Butterworths (1990).

20. National Health Interview Survey. (2023). Available at: https://www.cdc.gov/nchs/nhis/index.htm.

21. World Health Organization. *Global strategy to reduce the harmful use of alcohol*. Geneva: World Health Organization (2010). 38 p.

22. World Health Organization. *Global recommendations on physical activity for healt*. Geneva: World Health Organization (2010). 56 p.

23. Tian T, Zhang J, Zhu Q, Xie W, Wang Y, Dai Y. Predicting value of five anthropometric measures in metabolic syndrome among Jiangsu Province, China. *BMC Public Health*. (2020) 20:1317. doi: 10.1186/s12889-020-09423-9

24. Zhang J, Fang L, Qiu L, Huang L, Zhu W, Yu Y. Comparison of the ability to identify arterial stiffness between two new anthropometric indices and classical obesity indices in Chinese adults. *Atherosclerosis*. (2017) 263:263–71. doi: 10.1016/j.atherosclerosis.2017.06.031

25. Christakoudi S, Tsilidis KK, Muller DC, Freisling H, Weiderpass E, Overvad K, et al. A body shape index (ABSI) achieves better mortality risk stratification than alternative indices of abdominal obesity: results from a large European cohort. *Sci Rep*. (2020) 10:14541. doi: 10.1038/s41598-020-71302-5

26. Calderón-García JF, Roncero-Martín R, Rico-Martín S, de Nicolás-Jiménez JM, López-Espuela F, Santano-Mogena E, et al. Effectiveness of body roundness index (BRI) and a body shape index (ABSI) in predicting hypertension: A systematic review and Meta-analysis of observational studies. *Int J Environ Res Public Health*. (2021) 18:11607. doi: 10.3390/ijerph182111607

27. Lee X, Gao Y, Zhang Y, Feng Y, Gao L, Wang A, et al. Comparison of 10 obesity-related indices for predicting hypertension based on ROC analysis in Chinese adults. *Front Public Health*. (2022) 202:10–1. doi: 10.1016/j.puhe.2021.01.009

28. Krakauer NY, Krakauer JC. Untangling waist circumference and hip circumference from body mass index with a body shape index, hip index, and anthropometric risk Indicator. *Metab Syndr Relat Disord*. (2018) 16:160–5. doi: 10.1089/met.2017.0166

29. Chinese Center for Disease Control and Prevention. *Anthropometric methods for population health monitoring*. (2015). Available at: https://www.chinacdc.cn/jkzt/yyhspws/xzdc/201501/t20150116_109924.html.

30. Kruizenga HM, Seidell JC, De Vet HCW, Wierdsma NJ, Van Bokhorst–de van der Schueren MAE. Development and validation of a hospital screening tool for malnutrition: the short nutritional assessment questionnaire (SNAQ©). *Clin Nutr*. (2005) 24:75–82. doi: 10.1016/j.clnu.2004.07.015

31. Dietary Guidelines for Chinese Residents. (2016). Available at: http://dg.cnsoc.org/article/2016b.html.

32. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol*. (2001) 56:M146–57. doi: 10.1093/gerona/56.3.M146

33. Vakrinou A, Murphy E, Sisodiya SM, Vivekananda U, Balestrini S. Risk factors and outcome of hyperammonaemia in people with epilepsy. *J Neurol*. (2022) 269:6395–405. doi: 10.1007/s00415-022-11304-7

34. Liang J, Wang L, Song S, Dong M, Xu Y, Zuo X, et al. Quality and audience engagement of Takotsubo syndrome–related videos on TikTok: content analysis. *J Med Internet Res*. (2022) 24:e39360. doi: 10.2196/39360

35. Campillo JT, Hemilembolo MC, Pion SDS, Lebredonchel E, Dupasquier V, Boullé C, et al. Association between blood Loa loa microfilarial density and proteinuria levels in a rural area of the republic of Congo (the MorLo project): a population-based cross-sectional study. *Lancet Microb*. (2023) 2023:142. doi: 10.1016/S2666-5247(23)00142-8

36. Kasza J, Wolfe R. Interpretation of commonly used statistical regression models. *Respirology*. (2014) 19:14–21. doi: 10.1111/resp.12221

37. Zhao DX, Gootee E, Johansen MC. Atrial cardiopathy is associated with cerebral microbleeds in ischemic stroke patients. *Front Neurol*. (2022) 13:982926. doi: 10.3389/fneur.2022.982926

38. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet*. (2013) 381:752–62. doi: 10.1016/S0140-6736(12)62167-9

39. Rockwood K, Fox RA, Stolee P, Robertson D, Beattie BL. Frailty in elderly people: an evolving concept. CMAJ. *Can Med Assoc J*. (1994) 150:489–95.

40. O'Caoimh R, Sezgin D, O'Donovan MR, Molloy DW, Clegg A, Rockwood K, et al. Prevalence of frailty in 62 countries across the world: a systematic review and meta-analysis of population-level studies. *Age Ageing*. (2021) 50:96–104. doi: 10.1093/ageing/afaa219

41. Tian P, Yang N, Hao Q, Peng Z. A systematic review of the prevalence of frailty in the elderly in China. *Chin J Evid Based Med*. (2019) 19:656–64. doi: 10.1007/s12603-019-1179-9

42. Li G, Thabane L, Papaioannou A, Ioannidis G, Levine MAH, Adachi JD. An overview of osteoporosis and frailty in the elderly. *BMC Musculoskelet Disord*. (2017) 18:46. doi: 10.1186/s12891-017-1403-x

43. Picca A, Coelho-Junior HJ, Calvani R, Marzetti E, Vetrano DL. Biomarkers shared by frailty and sarcopenia in older adults: A systematic review and meta-analysis. *Ageing Res Rev*. (2022) 73:101530. doi: 10.1016/j.arr.2021.101530

44. Wu S, Yang Z, Liu S, Zhang Q, Zhang S, Zhu S. Frailty status and risk of irritable bowel syndrome in middle-aged and older adults: a large-scale prospective cohort study. *EClinicalMedicine*. (2023) 56:101807. doi: 10.1016/j.eclinm.2022.101807

45. Sternberg SA, Schwartz AW, Karunananthan S, Bergman H, Mark CA. The identification of frailty: A systematic literature review. *J Am Geriatr Soc*. (2011) 59:2129–38. doi: 10.1111/j.1532-5415.2011.03597.x

46. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. *Sci World J*. 1:323–36. doi: 10.1100/tsw.2001.58

47. Mitnitski A, Song X, Skoog I, Broe G, Cox JL, Grunfeld E, et al. Relative fitness and frailty of elderly men and women in developed countries and their relationship with mortality. *J Am Geriatr Soc*. (2005) 53:2184–9. doi: 10.1111/j.1532-5415.2005.00506.x

48. Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A standard procedure for creating a frailty index. *BMC Geriatr*. (2008) 8:24. doi: 10.1186/1471-2318-8-24

49. Davis DHJ, Rockwood MRH, Mitnitski AB, Rockwood K. Impairments in mobility and balance in relation to frailty. *Arch Gerontol Geriatr*. (2011) 53:79–83. doi: 10.1016/j.archger.2010.06.013

50. Lau S, Pek K, Chew J, Lim JP, Ismail NH, Ding YY, et al. The simplified nutritional appetite questionnaire (SNAQ) as a screening tool for risk of malnutrition: optimal cutoff, factor structure, and validation in healthy community-dwelling older adults. *Nutrients*. (2020) 12:2885. doi: 10.3390/nu12092885

51. Sadjapong U, Yodkeeree S, Sungkarat S, Siviroj P. Multicomponent exercise program reduces frailty and inflammatory biomarkers and improves physical performance in community-dwelling older adults: A randomized controlled trial. *Int J Environ Res Public Health*. (2020) 17:3760. doi: 10.3390/ijerph17113760

52. Rietman ML, van der A DL, van Oostrom SH, Picavet HSJ, Dollé MET, van Steeg H, et al. The association between BMI and different frailty domains: A U-shaped curve? *J Nutr Health Aging*. (2018) 22:8–15. doi: 10.1007/s12603-016-0854-3

53. World Obesity Federation. *World Obesity Atlas* (2023). Available at: https://www.worldobesity.org/resources/resource-library/world-obesity-atlas-2023.

54. Pan XF, Wang L, Pan A. Epidemiology and determinants of obesity in China. *Lancet Diabetes Endocrinol*. (2021) 9:373–92. doi: 10.1016/S2213-8587(21)00045-0

55. Cooper C, Fielding R, Visser M, van Loon LJ, Rolland Y, Orwoll E, et al. Tools in the assessment of sarcopenia. *Calcif Tissue Int*. (2013) 93:201–10. doi: 10.1007/s00223-013-9757-z

56. Newman AB, Kupelian V, Visser M, Simonsick E, Goodpaster B, Nevitt M, et al. Sarcopenia: alternative definitions and associations with lower extremity function. *J Am Geriatr Soc*. (2003) 51:1602–9. doi: 10.1046/j.1532-5415.2003.51534.x

57. Feingold KR. Obesity and dyslipidemia. Feingold KR, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, *Endotext*. South Dartmouth, MA: MDText COM, Inc. (2020).

58. Batsis JA, Villareal DT. Sarcopenic obesity in older adults: aetiology, epidemiology and treatment strategies. *Nat Rev Endocrinol*. (2018) 14:513–37. doi: 10.1038/s41574-018-0062-9

59. Haufs MG, Z-llner YF. Waist-hip ratio more appropriate than body mass index. *Dtsch Arztebl Int*. (2020) 117:659–9. doi: 10.3238/arztebl.2020.0659a

60. Price GM, Uauy R, Breeze E, Bulpitt CJ, Fletcher AE. Weight, shape, and mortality risk in older persons: elevated waist-hip ratio, not high body mass index, is associated with a greater risk of death. *Am J Clin Nutr*. (2006) 84:449–60. doi: 10.1093/ajcn/84.2.449

61. Yusuf S, Hawken S, Ôunpuu S, Bautista L, Franzosi MG, Commerford P, et al. Obesity and the risk of myocardial infarction in 27 000 participants from 52 countries: a case-control study. *Lancet*. (2005) 366:1640–9. doi: 10.1016/S0140-6736(05)67663-5

62. Choi J, Ahn A, Kim S, Won CW. Global prevalence of physical frailty by Fried's criteria in community-dwelling elderly with National Population-Based Surveys. *J Am Med Dir Assoc*. (2015) 16:548–50. doi: 10.1016/j.jamda.2015.02.004

63. Almohaisen N, Gittins M, Todd C, Sremanakova J, Sowerbutts AM, Aldossari A, et al. Prevalence of undernutrition, frailty and sarcopenia in community-dwelling people aged 50 years and above: systematic review and Meta-analysis. *Nutrients*. (2022) 14:1537. doi: 10.3390/nu14081537

64. Xia L, Dong F, Gong H, Xu G, Wang K, Liu F, et al. Association between indices of body composition and abnormal metabolic phenotype in Normal-weight Chinese adults. *Int J Environ Res Public Health*. (2017) 14:391. doi: 10.3390/ijerph14040391

65. Haapanen MJ, Mikkola TM, Kortelainen L, Jylhävä J, Wasenius NS, Kajantie E, et al. Body composition in late midlife as a predictor of accelerated age-associated deficit-accumulation from late midlife into old age: A longitudinal birth cohort study. *J Gerontol A Biol Sci Med Sci*. 78:980–7. doi: 10.1093/gerona/glac233

66. Nazare JA, Smith JD, Borel AL, Haffner SM, Balkau B, Ross R, et al. Ethnic influences on the relations between abdominal subcutaneous and visceral adiposity, liver fat, and cardiometabolic risk profile: the international study of prediction of intra-abdominal adiposity and its relationship with Cardiometabolic risk/intra-abdominal adiposity. *Am J Clin Nutr*. (2012) 96:714–26. doi: 10.3945/ajcn.112.035758

67. Lear SA, Humphries KH, Kohli S, Birmingham CL. The use of BMI and waist circumference as surrogates of body fat differs by ethnicity. *Obesity*. (2007) 15:2817–24. doi: 10.1038/oby.2007.334

68. Yang J, Wang A, Shang L, Sun C, Jia X, Hou L, et al. Study on the association between dietary habits, patterns and frailty of the elderly: A cross-sectional survey from communities in China. *Clin Interv Aging*. (2022) 17:1527–38. doi: 10.2147/CIA.S378138

69. Osuka Y, Kojima N, Yoshida Y, Kim M, Won CW, Suzuki T, et al. Exercise and/or dietary varieties and incidence of frailty in community-dwelling older women: A 2-year cohort study. *J Nutr Health Aging*. (2019) 23:425–30. doi: 10.1007/s12603-019-1166-1

70. Wei K, Nyunt MSZ, Gao Q, Wee SL, Ng TP. Frailty and malnutrition: related and distinct syndrome prevalence and association among community-dwelling older adults: Singapore longitudinal ageing studies. *J Am Med Dir Assoc*. (2017) 18:1019–28. doi: 10.1016/j.jamda.2017.06.017

71. Sieber CC. Malnutrition and sarcopenia. *Aging Clin Exp Res*. (2019) 31:793–8. doi: 10.1007/s40520-019-01170-1

72. Roberts S, Collins P, Rattray M. Identifying and managing malnutrition, frailty and sarcopenia in the community: A narrative review. *Nutrients*. (2021) 13:2316. doi: 10.3390/nu13072316

73. Chang SF. Frailty is a major related factor for at risk of malnutrition in community-dwelling older adults. *J Nurs Scholarsh*. (2017) 49:63–72. doi: 10.1111/jnu.12258

Frontiers in
Public Health

Explores and addresses today's fast-moving healthcare challenges

One of the most cited journals in its field, which promotes discussion around inter-sectoral public health challenges spanning health promotion to climate change, transportation, environmental change and even species diversity.

Discover the latest Research Topics

See more →

Frontiers

Avenue du Tribunal-Fédéral 34
1005 Lausanne, Switzerland
frontiersin.org

Contact us

+41 (0)21 510 17 00
frontiersin.org/about/contact