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Aging-related sarcopenia and frailty: prevalence, risk factors and prediction models

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Published in
Frontiers in Public Health

ISSN 1664-8714
ISBN 978-2-8325-5950-5
DOI 10.3389/978-2-8325-5950-5

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Citation

Liu, X., Hou, L., Alif, S. M., eds. (2025). *Aging-related sarcopenia and frailty: prevalence, risk factors and prediction models*. Lausanne: Frontiers Media SA. doi: 10.3389/978-2-8325-5950-5

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frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 24 January 2024
DOI 10.3389/fpubh.2023.1285226

OPEN ACCESS

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RECEIVED 29 August 2023
ACCEPTED 30 November 2023
PUBLISHED 24 January 2024

CITATION
Wang M, Deng X, Chen H, Diao Y, Liu C, Gao J, Tang X, Li X, Liu Y and Duan J (2024) Frailty mediated the association between tooth loss and mortality in the oldest old individuals: a cohort study. *Front. Public Health* 11:1285226. doi: 10.3389/fpubh.2023.1285226

Frailty mediated the association between tooth loss and mortality in the oldest old individuals: a cohort study

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Introduction: Tooth loss is associated with increased mortality risk; however, the mechanism underlying this is still not clear. The objective of this study was to explore whether frailty mediates the association between tooth loss and mortality risk among the oldest old individuals.

Methods: The participants were followed up from 1998 to 2018 in the Chinese Longitudinal Healthy Longevity Survey (CLHLS). Frailty was constructed following a standard procedure. Mortality, frailty, and tooth loss were applied as the outcome, mediator, and independent variables, respectively. The Cox model was fitted, including possible confounders, for causal mediation analysis. A total effect (TE), an average causal mediation effect (ACME), an average direct effect (ADE), and a proportion mediated (PM) effect were calculated.

Results: During the 129,936 person-years at risk, 31,899 individuals with a mean age of 91.79 years were included. The TE and ADE of severe tooth loss on mortality were 0.12 (95% CI: 0.08, 0.15) and 0.09 (95% CI: 0.05, 0.13); the ACME of frailty was 0.03 (95% CI: 0.02, 0.03) with 21.56% of the TE being mediated.

Discussion: This study illustrated that tooth loss is associated with mortality, and frailty appeared to mediate the relationship. It is recommended that oral health indicators and frailty status be incorporated into routine geriatric assessments to promote optimal oral health and non-frailty status.

KEYWORDS

cohort studies, inflammation, nutrition, oral medicine, public health

Introduction

Tooth loss is identified as the primary indicator of poor oral health, which is identified as the primary indicator of healthy aging (1). Over the past decade, considerable research efforts have been devoted to the finding that tooth loss is associated with an increased risk of mortality (2–5). However, the mediators of the association between tooth loss and mortality remain poorly reported, especially in the oldest old individuals.

Current studies suggest that malnutrition and inflammation are thought to be the main paths between tooth loss and increased mortality risk (6–11). However, the majority of prior research on the aforementioned mechanisms remains speculative, with only a limited

number of studies having undergone rigorous validation. In our current review, we have identified a single study within the Japanese cohort ($N = 891$) that employs mediation analysis to examine the relationship between nutritional status, tooth loss, and mortality. Interestingly, this study reveals a significant association between nutritional status and both tooth loss and mortality, while systemic inflammation does not exhibit such a correlation (12). Additionally, another study highlights weight loss as a clinically significant indicator of malnutrition. Through the utilization of follow-up mail self-reported questionnaires, it was determined that weight loss serves as a mediator in the link between tooth loss and mortality among older adults (13). However, the proportion of the above mediating effects (13.10%) that can be explained warrants further exploration of other mediating factors. In addition, no further subgroup analyses were performed in the previous studies. On the whole, limited data representations of older populations and appropriate mediators may be responsible for the lack of research.

Frailty is considered a major public health problem because of its high prevalence in the older adults population (14, 15). It was reported to be a more important predictor of mortality than biological age (16). There were quite a few studies that also reported that tooth loss could lead to frailty (17–19). Moreover, in the association of tooth loss-frailty and frailty–mortality, there were significant associations with both malnutrition and inflammation (20–23). As described, we put forward the hypothesis that tooth loss could be associated with mortality mediated by frailty.

Therefore, in this study, a large prospective cohort study in China examined the relationship between tooth loss and mortality and emphatically examined how frailty mediates the relationship between tooth loss and mortality among the oldest old individuals.

Method

Study design and participants

The Chinese Longitudinal Healthy Longevity Survey (CLHLS) was used, which is the most comprehensive survey of the oldest old individuals in China. This research aimed to gain a better understanding of the healthy longevity of human societies and to determine which biological, behavioral, social, and traditional environmental risk factors play an important role. It began in 1998 with a random selection of half of the cities and counties in 23 provinces of China, followed by follow-ups in 2000, 2002, 2005, 2008, 2011, 2014, and 2018. Detailed information about the CLHLS can be found elsewhere (24, 25). The baseline examinations were conducted using a standardized and objective method, administered by research staff who had undergone rigorous training and assessment. The field investigation team was composed of three investigators, including a leader (responsible for the coordination and organization of the team and the quality control of the investigation), an interviewer (responsible for interviews and questionnaires), and a physician (responsible for physical examination and collection of blood and urine samples). The team members collaborated closely with each other, ensuring a cohesive approach. In this study, a total of 44,612 older adults were included at baseline. We excluded 5,823 older adults aged 74 and younger, 6,672 older adults were lost to follow-up at the first follow-up survey, 134 older adults had incorrect death time, and 84 older adults had missing teeth data (Figure 1). A more detailed design of the CLHLS is described in Appendix 1.

Outcome variable

After the follow-up survey, the main outcome was mortality from all causes. The survival status of the older adults was determined by family members or relatives, determining whether or not the older adults completed the survey, died, were lost to follow-up, or were missing from the study. Lost follow-up was ascertained when older adults were not found when contacted. Censored older adults are those who survived but were lost to follow-up.

Explanatory variables

The number of remaining teeth at baseline was mainly used to assess tooth loss status. To determine the status of tooth loss, the following question was asked: "Can you tell me how many natural teeth you still have?" Based on the remaining number of natural teeth, we divided them into four categories: 0, 1–9, 10–19, and 20+.

Mediators

Frailty was constructed using a standard method. The component of frailty was comprised of deficits associated with health status if the following criteria were met: Multi-system and physiological deficits were involved. In accordance with evidence-based research (14, 16), an older adult's frailty was calculated by dividing their number of deficits by the number of deficits they have overall. There were 30 indicators of health deficits that included eight major sets of components following the established research methodology: chronic disease conditions (self-reports from a list of 11 diseases), cognitive functioning, activity of daily living disability (needing help in performing the 6 basic daily activities), functional limitations (5 objective examinations of physical function), self-rated health, visual and auditory functions, psychological distress, and others (e.g., rhythm of the heart, interviewer-rated health, number of serious illnesses in the past 2 years). Appendix Table 1 provides details of all items. The definitions of some indicators are explained in Appendix 2. Frailty items are similar to those of studies conducted in China (14, 16), Canada (26), and the United States (27).

In each deficit, the 0–1 interval was dichotomized. The healthiest state is 0 (absence of a deficit), whereas the unhealthiest state is 1 (maximal deficit expression). Finally, the total score of all questions is divided by the total value of 30 points. The resulting value is the frailty index of the respondent, which ranges from 0 to 1. The higher the score, the higher the frailty.

Covariates

As covariates, the possible confounders were evaluated based on clinical knowledge and previous studies (3, 4). The factors included

Abbreviations: CLHLS, Chinese Longitudinal Healthy Longevity Survey; ADL, activities of daily living scale; MMSE, Minimum Mental State Examination; TE, total effect; ACME, average causal mediation effect; ADE, average direct effect; PM, proportion mediated; CI, confidence interval.

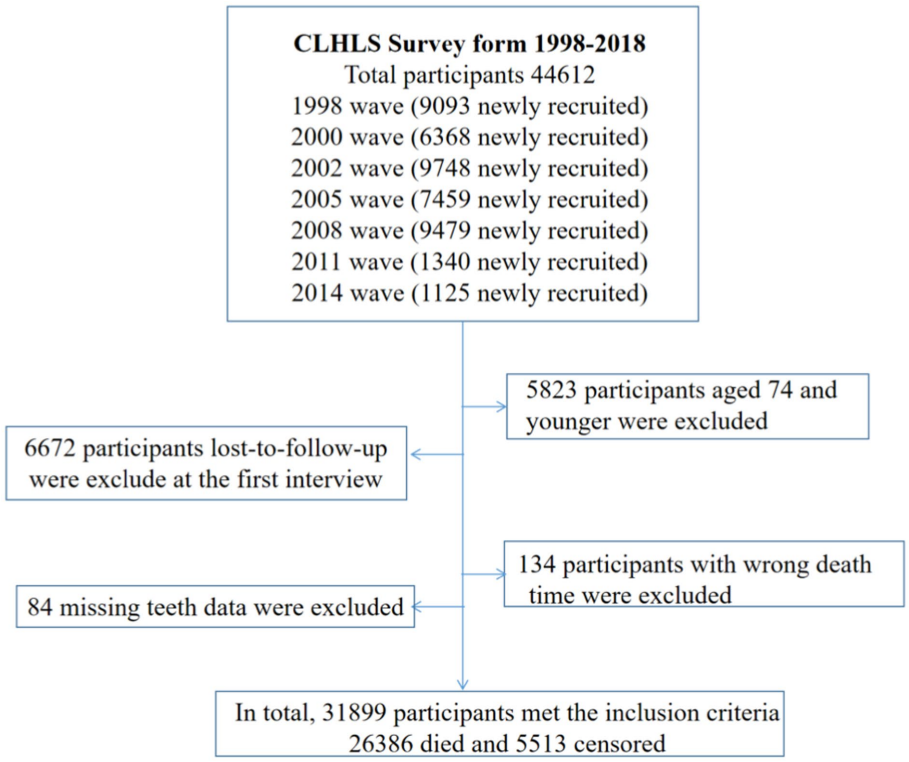

FIGURE 1
Cohort selection criteria, Chinese Longitudinal Healthy Longevity Study (CLHLS), surveyed from 1998 to 2018.

sex, age, education, marital status, smoking status, drinking status, dietary diversity, and leisure activities such as reading, watching TV, listening to the radio, doing housework, keeping pets, and growing flowers. Education background was categorized as "literate" if a participant had received >1 year of any formal education and "illiterate" if a participant had not received formal education. Dietary diversity was assessed by nine major food groups (meat, fish and seafood, eggs, beans, fruits, vegetables, tea, garlic, and sugar or candy), which were recorded as "often or almost every day" or "occasionally" or "rarely or never." One point of dietary diversity was defined as often or almost every day consuming any food group without considering a minimum intake; the maximum possible dietary diversity was 9 points (25). Leisure activities were divided into three categories (never, sometimes, and often). More details are described in Appendix 2.

Statistical analysis

Among the covariates, less than 1.09% of values were missing, and mean value imputation was applied. Age variables were summarized using interquartile ranges, and categorical variables were summarized using frequency and percentage. For categorical variables, the Cochran–Mantel–Haenszel test was used, and for continuous variables, the Kruskal–Wallis test was used.

The causal mediation analysis was conducted based on the framework for potential outcomes to investigate the mediating effects of frailty on tooth loss and mortality risk. This diagram in Figure 2 illustrates the hypothesized causal chain. In this study, the independent variable was proposed as X (tooth loss), the dependent variable was proposed as Y (subsequent mortality), and the mediator was proposed as M (frailty). A total effect (TE), an average causal mediation effect (ACME), an average direct effect (ADE), and a proportion mediated (PM) effect were estimated. The first step is to fit a mediator model in which tooth loss is modeled as a function of frailty comorbid with covariates (sex, age, education, marital status, smoking status, drinking status, dietary diversity, and leisure activities including reading, watching TV, listening to the radio, doing housework, keeping pets, and growing flowers). The next step is to model the survival variables, which are the outcome variables, including tooth loss, frailty, and covariates. As in the mediator model, the outcome model includes an explanation for tooth loss and mediation for frailty. We use the COX model for the mediator and outcome models, respectively (28).

The potential outcomes framework was to define these quantities. Let $M_i(t)$ denote the potential value of a mediator of interest for unit i under the treatment status $T_i = t$. Let $Y_i(t, m)$ denote the potential outcome that would result if the treatment and mediating variables equal t and m, respectively. Consider a standard experimental design where only the treatment variable is randomized. We observe only one of the potential outcomes, and the observed outcome, Y_i, equals $Y_i(T_i, M_i(T_i))$ where $M_i(T_i)$ represents the observed value of the mediator M_i. With this notation, the total unit treatment effect can be written as,

$$T_i \equiv Y_i\left(1, M_i(1)\right) - Y_i\left(0, M_i(0)\right) \quad (1)$$

We can decompose this total effect into two components (29). First, the causal mediation effects are represented (30).

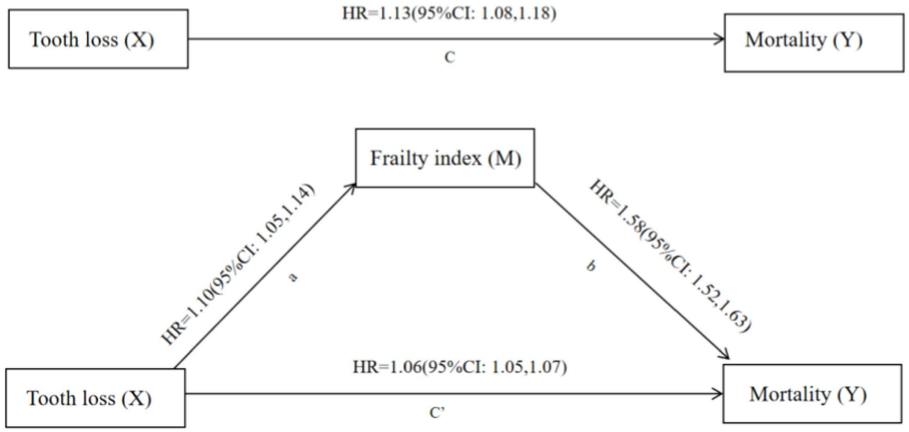

FIGURE 2
Frailty index mediates the relationship between tooth loss and mortality. X, independent variable (cause); Y, dependent variable (outcome); M, mediator; Path a, the relationship between X and M; Path b, the relationship between M and Y, with X included in the model; Path c, the relationship between X and Y; Path c', the relationship between X and Y, with M included in the model; HR, odds ratio; all models were adjusted for sex, age, education, marital status, smoking status, drinking status, dietary diversity, and leisure activities including doing housework, reading, watching TV, listening to the radio, keeping pets, and growing flowers.

$$\delta_i(t) = Y_i\left(t, M_i(1)\right) - Y_i\left(t, M_i(0)\right) \quad (2)$$

for each treatment status, $t = 0, 1$. All other causal mechanisms can be represented by the direct effects of the treatment as follows (28),

$$\zeta i(t) \equiv Y_i\left(1, M_i(\mathrm{t})\right) - Y_i\left(0, Mi(\mathrm{t})\right) \quad (3)$$

for each unit i and each treatment status, $t = 0, 1$. Together, we see that they sum up to the total effect,

$$T_i = \delta_i(t) + \zeta_i(1-t) \quad (4)$$

for $t = 0, 1$. The average causal mediation effects (ACMEs) $\bar{\delta}(t)$ and the average direct effects (ADEs) $\bar{\zeta}(t)$ represent the population averages of these causal mediation and direct effects (31).

To check the robustness of the primary results, we excluded missing data for sensitivity analysis. In addition, this study has been adjusted to exclude mortality in the first 0.5 and 1 years due to the possibility that the increase in frailty before mortality in the last year of life could influence the results.

All data were analyzed using R 4.2.2 with the packages "mediation" and "survival." Statistical significance was determined by an alpha value of 0.05 (two-sided).

Ethics approval

The Protection of Human Subjects for the CLHLS was approved by the biomedical ethics committee of Peking University (IRB00001052-13074). Informed and written consent were obtained from all participants and/or their relatives. In addition, a STROBE statement was followed to assess our study in Appendix 3.

Results

During the 129,936 person-years at risk, we included 31,899 oldest old individuals with a mean age of 91.79 years old. The baseline characteristics of the oldest old individuals are presented in Table 1. When more teeth were missing, age and frailty scores increased, ranging from 84 to 95 years old and 0.09 to 0.14 points, respectively. When more teeth were missing, some covariates accounted for an increasing proportion: the proportion of deaths increased from 71.66 to 85.20%; the proportion of illiteracy increased from 53.58 to 75.50%; and the proportion of the lowest dietary diversity score increased from 20.71 to 26.72%. When more teeth were missing, some covariates accounted for a decreasing proportion: the proportion of exercising regularly decreased from 35.65 to 21.75%; the proportion of doing housework decreased from 40.77 to 22.33%; the proportion of playing cards decreased from 7.17 to 3.03%; and the proportion of watching TV or listening to the radio decreased from 46.28 to 27.87%.

Figure 2 shows that tooth loss and mortality were mediated based on the causal steps method. For path a, tooth loss was associated with a frailty hazard ratio (HR) of 1.10 (95% confidence interval (CI): 1.05, 1.14). Based on path b, mortality was associated with frailty of 1.58 (95%CI: 1.52, 1.63) after adjusting for all covariates and tooth loss. Based on path c, there was an association between tooth loss and mortality of 1.13 (95%CI: 1.08, 1.18). Adding frailty to the models (path c') decreased the HR of tooth loss on mortality by 1.06 (95%CI: 1.05, 1.07), suggesting that frailty may mediate the relationship. Sensitivity analysis showed that the results remained stable in Appendix Figures 1–3.

Further analysis was conducted based on the above results to determine if tooth loss and death are mediated by frailty. In Figure 3, the TE and ADE of severe tooth loss on mortality were 0.12 (95%CI: 0.08, 0.15) and 0.09 (95 %CI: 0.05, 0.13); the ACME of frailty was 0.03 (95 %CI: 0.02, 0.03) with 21.56% ($p < 0.01$) of the total effect being mediated. In the age subgroup, as the age group increased, the ACME of frailty was 0.02 (95 %CI: 0.01, 0.03) with 33.64% ($p = 0.28$) of the TE being mediated, 0.03 (95 %CI: 0.02, 0.05) with 30.63% ($p < 0.01$) of

TABLE 1 Descriptive characteristics of the participants at baseline.

Variables	Total (*n* = 31,899)	>20 teeth (*n* = 3,027)	10–19 teeth (*n* = 4,036)	1–9 teeth (*n* = 11,563)	Anodontia (*n* = 13,273)	*p*
Age, Median (Q1, Q3)	92 (85, 100)	84 (80, 91)	87 (81, 93)	92 (86, 100)	95 (89, 101)	<0.01
Sex, *n* (%)						<0.01
Male	19,432 (60.92)	1,315 (43.44)	2,038 (50.50)	6,913 (59.79)	9,166 (69.06)	
Female	12,467 (39.08)	1,712 (56.56)	1,998 (49.50)	4,650 (40.21)	4,107 (30.94)	
Survival state, *n* (%)						<0.01
Survival	5,513 (17.28)	858 (28.34)	884 (21.90)	1,807 (15.63)	1,964 (14.80)	
Death	26,386 (82.72)	2,169 (71.66)	3,152 (78.10)	9,756 (84.37)	11,309 (85.20)	
Frailty index, Median (Q1, Q3)	0.12 (0.07, 0.19)	0.09 (0.05, 0.15)	0.10 (0.06, 0.16)	0.12 (0.07, 0.18)	0.14 (0.09, 0.22)	<0.01
Education, *n* (%)						<0.01
Non-illiteracy	9,581 (30.04)	1,405 (46.42)	1,571 (38.92)	3,353 (29.00)	3,252 (24.50)	
Illiteracy	22,318 (69.96)	1,622 (53.58)	2,465 (61.08)	8,210 (71.00)	10,021 (75.50)	
Marital status, *n* (%)						<0.01
Yes	26,463 (82.96)	2,480 (81.93)	3,206 (79.44)	9,502 (82.18)	11,275 (84.95)	
No	5,436 (17.04)	547 (18.07)	830 (20.56)	2,061 (17.82)	1,998 (15.05)	
Dietary diversity, *n* (%)						<0.01
Score = 6	2,673 (8.38)	414 (13.68)	356 (8.82)	815 (7.05)	1,088 (8.20)	
Score = 5	2,740 (8.59)	327 (10.80)	393 (9.74)	928 (8.03)	1,092 (8.23)	
Score = 4	4,321 (13.55)	453 (14.97)	551 (13.65)	1,522 (13.16)	1,795 (13.52)	
Score = 3	6,299 (19.75)	607 (20.05)	782 (19.38)	2,281 (19.73)	2,629 (19.81)	
Score = 2	7,381 (23.14)	599 (19.79)	938 (23.24)	2,722 (23.54)	3,122 (23.52)	
Score = 1	8,485 (26.60)	627 (20.71)	1,016 (25.17)	3,295 (28.50)	3,547 (26.72)	
Smoke, *n* (%)						<0.01
No	22,490 (70.50)	1,904 (62.90)	2,682 (66.45)	8,142 (70.41)	9,762 (73.55)	
Yes	9,409 (29.50)	1,123 (37.10)	1,354 (33.55)	3,421 (29.59)	3,511 (26.45)	
Drink, *n* (%)						<0.01
No	22,856 (71.65)	1,946 (64.29)	2,808 (69.57)	8,143 (70.42)	9,959 (75.03)	
Yes	9,043 (28.35)	1,081 (35.71)	1,228 (30.43)	3,420 (29.58)	3,314 (24.97)	
Exercise regularly, *n* (%)						<0.01
0	23,956 (75.10)	1,948 (64.35)	2,803 (69.45)	8,819 (76.27)	10,386 (78.25)	
1	7,943 (24.90)	1,079 (35.65)	1,233 (30.55)	2,744 (23.73)	2,887 (21.75)	
Garden work, *n* (%)						<0.01
Often	1,641 (5.14)	311 (10.27)	275 (6.81)	501 (4.33)	554 (4.17)	
Sometimes	1,391 (4.36)	207 (6.84)	262 (6.49)	484 (4.19)	438 (3.30)	
Never	28,867 (90.49)	2,509 (82.89)	3,499 (86.69)	10,578 (91.48)	12,281 (92.53)	
Housework, *n* (%)						<0.01
Often	9,040 (28.34)	1,232 (40.70)	1,540 (38.16)	3,304 (28.57)	2,964 (22.33)	
Sometimes	4,927 (15.45)	550 (18.17)	717 (17.77)	1,890 (16.35)	1,770 (13.34)	
Never	17,932 (56.21)	1,245 (41.13)	1,779 (44.08)	6,369 (55.08)	8,539 (64.33)	
Play card, *n* (%)						<0.01
Often	9,040 (28.34)	1,232 (40.70)	1,540 (38.16)	3,304 (28.57)	2,964 (22.33)	
Sometimes	4,927 (15.45)	550 (18.17)	717 (17.77)	1,890 (16.35)	1,770 (13.34)	
Never	17,932 (56.21)	1,245 (41.13)	1,779 (44.08)	6,369 (55.08)	8,539 (64.33)	
Watch TV or listen to the radio, *n* (%)						<0.01
Often	9,837 (30.84)	1,401 (46.28)	1,547 (38.33)	3,190 (27.59)	3,699 (27.87)	
Sometimes	7,790 (24.42)	759 (25.07)	1,062 (26.31)	3,004 (25.98)	2,965 (22.34)	
Never	14,272 (44.74)	867 (28.64)	1,427 (35.36)	5,369 (46.43)	6,609 (49.79)	

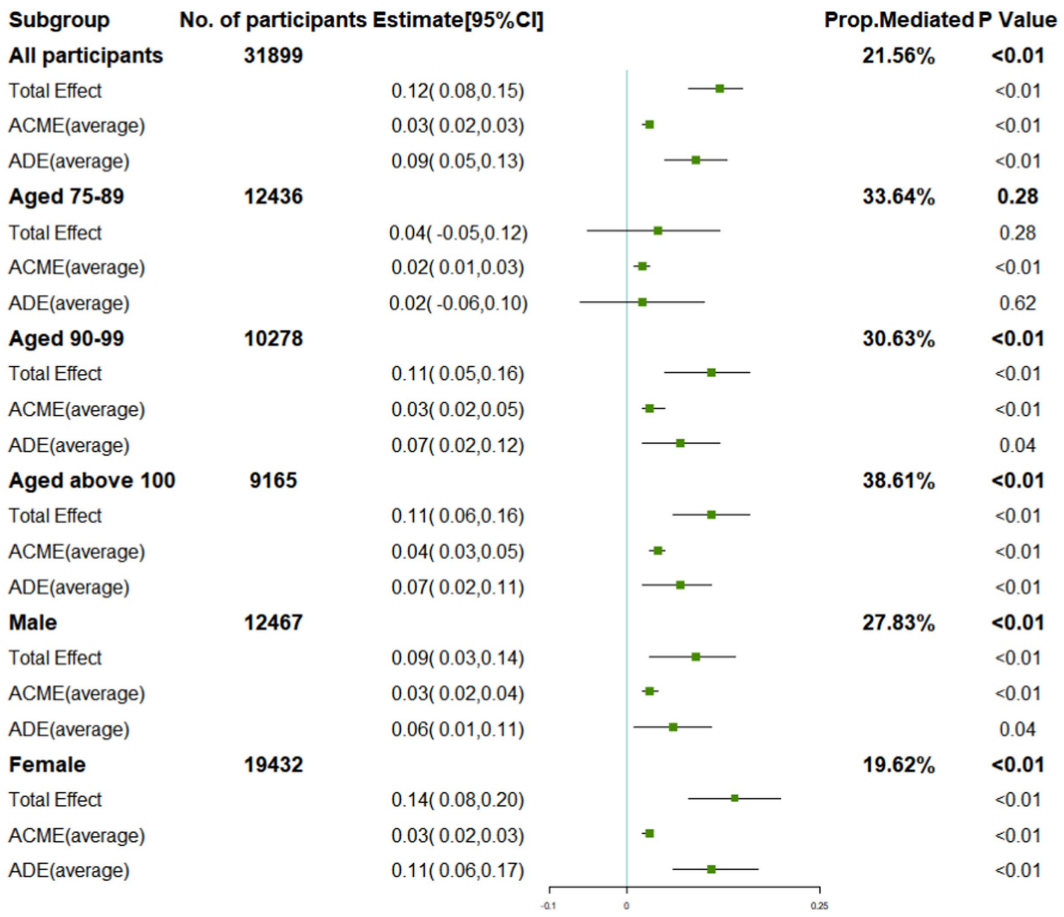

FIGURE 3
Direct and indirect effects of tooth loss and mediators on mortality and subgroup analysis.

the TE being mediated, and 0.04 (95 %CI: 0.03, 0.05) with 38.61% ($p < 0.01$) of the TE being mediated, respectively. In the sex subgroup, the ACME of frailty was 0.03 (95 %CI: 0.02, 0.04) with 27.38% ($p < 0.01$) of the TE being mediated in the male and 0.03 (95 %CI: 0.02, 0.03) with 19.62% ($p < 0.01$) of the TE being mediated in the female.

Discussion

A primary finding of this prospective cohort with a mean age of 91.79 years old is that tooth loss is mediated by frailty and represents 21.56% of the TE. In the subgroup analysis, frailty played a more important role in mediating the association between tooth loss and mortality in males (27.83%) than in females (19.62%), and the mediation proportion increased with age from 30.63 to 38.61%.

The present study adds to the limited amount of research exploring frailty as a mediator of tooth loss and mortality among the oldest old individuals. Until now, the mediators of tooth loss and mortality have been poorly understood. Most studies on malnutrition and inflammation mechanisms are still hypotheses. In the Japanese Tsurugaya project, mortality and tooth loss were mediated by nutritional status, while systemic inflammation was not (12). However, the large confidence intervals suggested inadequate power or a small sample size. Another Japan Gerontological Evaluation Study suggested that mortality increases with tooth loss that is mediated by weight loss (13). However, this study was followed up by self-reported questionnaires, and the proportion of the above mediating effects (13.10%) that can be explained warrants further exploration of other mediating factors. In addition, no further subgroup analyses were performed in the previous studies.

In this study, our work explored frailty as a mediator, which could reflect both inflammation and malnutrition (32, 33). Frailty has been implicated as a mediator in the association between tooth loss and high mortality in the following possible ways: Tooth loss might trigger higher levels of inflammation (34), which can lead to frailty and increase mortality risk. Alternatively, tooth loss can cause a change in food selection and nutrient intake that leads to malnutrition as well as frailty and increased mortality risk (35).

In the subgroup analysis, men were more affected by frailty than women when it came to the relationship between tooth loss and mortality. In general, the health-survival paradox describes how men live shorter lives but have fewer disabilities than women (36). Frailty may be more prevalent in women due to higher incidence, longer duration (i.e., low recovery), and lower severity of illness (37). Basically, a sudden death in men due to frailty is more likely, whereas women experience gradual degeneration over time. It may be to be expected that men are associated with a higher proportion of mediating explanations according to frailty between tooth loss and mortality. Regarding the age group, it is common for participants to become frailer as they age. In most cases, frailty will worsen rather than improve over time, as it is a dynamic state (15). That may be why the proportion of mediating explanations increases with age.

Overall, our results provide further evidence for the mechanisms underlying subgroup differences in the degree to which frailty mediates tooth loss and mortality.

From a public health and clinical standpoint, it is imperative to prioritize the preservation of non-frailty status in the oldest old population with tooth loss in order to mitigate subsequent mortality. Given the increasing prevalence of frailty and its association with tooth loss and mortality, the implications of frailty on the wellbeing of aging individuals and the strained healthcare system are significant. Considering the extent of tooth loss and frailty in patients can assist clinicians in delivering treatment that is more tailored to the individual's needs. In turn, delaying tooth loss and frailty through primary, secondary, and tertiary prevention could lead to better outcomes. Even though we found that the relationship between tooth loss and mortality appears to be mediated by frailty, a more thorough evaluation of frailty assessment and targeted treatment is needed to determine whether they will benefit patients and healthcare systems.

In our study, we took advantage of a prospective design and included a population of the oldest old individuals as well as a wide range of covariates for a comprehensive analysis of the associations. There are, however, several limitations to consider. First and foremost, longitudinal studies face the long-term problem of loss of follow-up. The attrition rates in cohort studies of older adults individuals are inevitable. The second issue is the reporting bias in self-reported oral health data, despite several studies showing its reliability and validity (38, 39). Third, this study might benefit from trajectories of tooth loss rather than scores based on the baseline number of teeth. Further research and evaluation are needed in future. Finally, residual confounding may have impacted our findings, even after accounting for many possible covariates. Nevertheless, we hope that this study will facilitate a better understanding of tooth loss, frailty, and mortality.

Conclusion and implications

In this study, tooth loss was associated with mortality, and frailty mediated the association. A key recommendation was the inclusion of oral health indicators and frailty status in routine geriatric assessments in order to maintain good oral health and non-frailty status in older adults. For future longitudinal studies to explore the association between tooth loss and mortality, frailty would be a better measure because it reflects a comprehensive geriatric status and may be more responsive to changes in nutrition and inflammation index.

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 Biomedical Ethics Committee of Peking University (IRB00001052-13074). 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

MW: Conceptualization, Data curation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. XD: Conceptualization, Formal analysis, Funding acquisition, Supervision, Writing – review & editing. HC: Formal analysis, Methodology, Supervision, Writing – review & editing. YD: Formal analysis, Investigation, Methodology, Project administration, Writing – review & editing. CL: Formal analysis, Methodology, Writing – review & editing. JG: Data curation, Methodology, Writing – review & editing. XT: Data curation, Methodology, Writing – review & editing. XL: Data curation, Methodology, Writing – review & editing. YL: Data curation, Methodology, Writing – review & editing. JD: Conceptualization, Funding acquisition, Methodology, Supervision, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. This study was supported by the fund of the "San-ming" Project of Medicine in Shenzhen (NO.SZSM201812088), the Scientific Research Foundation of Shenzhen Health Economics Association (202304), and the construction and verification of a risk assessment model for venous thromboembolism (JCYJ20190809111017163).

Acknowledgments

The authors are grateful to all participants and their families. The authors acknowledge all staff for their great contributions to the success of the CLHLS and the CLHLS project team for providing the shared database (https://opendata.pku.edu.cn/dataverse/CHADS).

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.2023.1285226/full#supplementary-material

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frontiers | Frontiers in Public Health

TYPE Systematic Review
PUBLISHED 05 February 2024
DOI 10.3389/fpubh.2024.1310383

OPEN ACCESS

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RECEIVED 09 October 2023
ACCEPTED 15 January 2024
PUBLISHED 05 February 2024

CITATION
Qian S, Zhang S, Lu M, Chen S, Liu L, Liu S, Jiang F and Zhang J (2024) The accuracy of screening tools for sarcopenia in older Chinese adults: a systematic review and meta-analysis.
Front. Public Health 12:1310383.
doi: 10.3389/fpubh.2024.1310383

The accuracy of screening tools for sarcopenia in older Chinese adults: a systematic review and meta-analysis

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Objective: This review aimed to analyze and compare the accuracy of eight screening tools for sarcopenia in older Chinese adults according to different diagnostic criteria.

Methods: This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The PubMed, Embase, Web of Science, China National Knowledge Infrastructure (CNKI), and Wanfang databases were searched between the publication of the first expert consensus on sarcopenia in 2010 and April 2023 using relevant MeSH terms. We evaluated the risk bias of the included studies using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool. The pooled result of sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR), and plot the summary receiver operating characteristic curve (SROC) were calculated by using a bivariate random-effects model. The accuracies of sensitivity and specificity of the screening tools were compared using the Z-test.

Results: A total of 30 studies (23,193 participants) were included, except for calf circumference (CC), Ishii, and Finger-ring Test; Screening tools for sarcopenia in older Chinese adults have consistently shown low to moderate sensitivity and moderate to high specificity. Regional and sex differences affect the accuracy of the screening tools. In terms of sensitivity and specificity, the CC, Ishii, and Finger-ring Test were superior to the other screening tools.

Conclusion: The Asian Working Group on Sarcopenia (AWGS) 2019 criteria are more appropriate for the diagnosis of sarcopenia in older Chinese adults. According to the AWGS 2019, CC and Ishii are recommended for sarcopenia screening in older Chinese adults.

KEYWORDS

sarcopenia, screening tool, older Chinese adults, accuracy, systematic review and meta-analysis

1 Introduction

Sarcopenia is a disease which seriously harms the physical health of older adults (1), resulting in reduced activity capacity, increased risk of falls, aggravated disability, and reduced ability to perform activities of daily living. Sarcopenia is also associated with cognitive decline, hospitalization, and death (2–6). Sarcopenia progression is a dynamic process that is not easily

detected in the early stages and may only be recognized when it is severe enough to cause loss of physical function, falls, and autonomy (7). The early identification of risk factors for sarcopenia and exercise interventions have been shown to be highly effective in reducing the incidence of associated adverse outcomes (e.g., falls, decreased somatic function) (8, 9), and aggressive management could reduce the prevalence of sarcopenia by 10%, which is expected to save at least $1.1 billion per year (10). Moreover, the selection of convenient and accurate sarcopenia screening tools can effectively simplify the screening process, facilitate the early identification of sarcopenia by medical personnel and researchers, and reduce the risk of its occurrence, which is of great importance for improving the quality of life of older adults.

Various screening tools for sarcopenia have been developed, including the SARC-F questionnaire (11), SARC-F combined calf circumference (SARC-CalF) questionnaire (12), Ishii score (13), Mini Sarcopenia Risk Assessment (MSRA-7/MSRA-5) (14), calf circumference (CC) (15), Finger-ring Test/ Yubi-Wakka (16), and middle upper arm circumference (MUAC) (17). The European Working Group on Sarcopenia in Older People (EWGSOP), Asian Working Group on Sarcopenia (AWGS), International Working Group on Sarcopenia (IWGS), and Foundation for the National Institutes of Health (FNIH) have published guidelines for the diagnosis and treatment of sarcopenia (15, 18–22). IWGS recommends the screening of sarcopenia using the SARC-F (21). SARC-F and Ishii were included in EWGSOP 2 of case finding (19). The AWGS 2019 recommends screening for sarcopenia using SARC-F and SARC-CalF (20). Different guidelines recommend different screening tools. If the accuracy of different screening tools can be analyzed and compared under the same diagnostic criteria, it may provide new ideas for researchers to perform sarcopenia screening in different areas, thus promoting the screening of sarcopenia in older adults.

In a study by Yang et al. (23), the sensitivity of SARC-F was highest when using the diagnostic criteria of the FNIH and lowest when using the diagnostic criteria of the IWGS. The prevalence of sarcopenia depends on the diagnostic criteria used (24), and the accuracy of the screening tools varies according to these criteria. The accuracy of the screening tools using different diagnostic criteria requires further investigation.

Several tools have been widely used for sarcopenia screening; for example, the SARC-F is easy to implement and has been validated in different populations (12, 25). However, different subject characteristics of subjects may affect the accuracy of screening tools, and several factors associated with the prevalence of sarcopenia have been reported. Yu et al. found that age, sex, and disease were related to the occurrence of sarcopenia in the Chinese population, and that differences in population, race, and living environment affected the prevalence of sarcopenia (26). A meta-analysis based on the accuracy of SARC-F screening for sarcopenia sub-grouped by population and region, showed that different populations and regions resulted in differences in the accuracy of the SARC-F screening for sarcopenia (27). Whether these risk factors affect the accuracy of the screening tools requires further investigation.

China has a growing aging population (28) and large-scale diagnosis of sarcopenia is challenging. Hence, and it is important to use a convenient tool to screen older adults for sarcopenia. China has a growing aging population and large-scale diagnosis of sarcopenia is challenging. Hence, and it is important to use a convenient tool to screen older adults for sarcopenia, our systematic review has three objectives. First, evaluating the accuracy of eight screening tools for screening sarcopenia among older Chinese adults. Second, exploring the sources of heterogeneity which may affect the accuracy of screening tools. Third, finding the screening tools and diagnostic criteria suitable for older Chinese adults, in order to provide a reference for relevant practitioners and future research.

2 Materials and methods

Our systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, the PRISMA checklist is available from the Supplementary material. The PICOS strategy was utilized for the inclusion criteria.

2.1 Literature search

The first expert consensus on sarcopenia was published in 2010 (18), until 2016 when sarcopenia was officially classified as a disease by The World Health Organization (WHO) (29), and the latest expert consensus on sarcopenia was updated in 2019 (19). Sarcopenia-related studies have been increasing and maturing after 2010, and for the literature search to be as comprehensive as possible, the PubMed, Embase, Web of Science, China National Knowledge Infrastructure (CNKI), and Wanfang databases were searched between January 2010 and April 2023. To avoid missing searches, we searched for specific screening tools in addition to the "screening tool." The search strategy was "screening tool" or "SARC-F" or "SARC-CalF" or "Mini Sarcopenia Risk Assessment" or "MSRA" or "Finger-ring Test" or "Yubi-wakka" or "Ishii" or "CC" or "calf circumference" or "MUAC" and "sarcopenia" or "muscle mass." Two authors independently conducted a literature search. If the two authors' opinions differed, a third reviewer was consulted.

2.2 Article selection

WHO has made age boundaries for the older adults, and as China is the largest developing country in the world, the starting age standard for the older adults is 60 years old. Based on the above, the inclusion criteria developed based on the PICOS strategy are as follows: P: subjects were older Chinese adults aged ≥60 years; I: study conducted screening for sarcopenia; C: diagnostic criteria for sarcopenia were derived from EWGSOP or AWGS or FNIH or IWGS guidelines, the detailed criteria are listed in (Table 1); O: study reports the accuracy of sarcopenia screening tool, including true positive (TP), false positive (FP), false negative (FN), and true negative (TN); S: diagnostic test.

Studies were excluded based on the following criteria: (1) meeting minutes, letters, comments, and reviews; (2) insufficient data and inability to contact the original authors; (3) subjects with major medical conditions such as diabetes, dialysis, cancer, stroke, psychiatric disorders or bone fractures; and (4) language other than English or Chinese.

Standardizing the inclusion and exclusion criteria before literature search can minimize the impact of heterogeneity on the accuracy of

10.3389/fpubh.2024.1310383

TABLE 1 Summary of operational diagnostic criteria for sarcopenia by sex.

	Diagnosis criteria			Diagnose
	1. Low muscle mass	2. Low HS (kg)	3. Low GS (m/s)	
AWGS 2014①	Male:≤7.0 kg/m2	Male:<26	<0.8	1 + 2† or 1 + 3†
	Female:≤5.7 kg/m2	Female:<18		
AWGS 2019②	Male:<7.0 kg/m2	Male:<28	<1.0	1 + 2† or 1 + 3†
	Female:<5.7 kg/m2	Female:<18		
EWGSOP 1③	Male:≤8.87 kg/m2	Male:<30	<0.8	1 + 2† or 1 + 3†
	Female:≤6.42 kg/m2	Female:<20		
EWGSOP 2④	Male:<7.0 kg/m2	Male:<27	<0.8	1 + 2† or 1 + 2 + 3‡
	Female:<5.5 kg/m2	Female:<16		
FNIH⑤	ASM/BMI Male: 0.789	Male:<26	<0.8	1 + 2 + 3†
	ASM/BMI Female:0.512	Female:<16		
IWGS⑥	Male:≤7.23 kg/m2	-	<1.0	1 + 3†
	Female:≤5.67 kg/m2			

①, Asian Working Group for Sarcopenia 2014; ②, Asian Working Group for Sarcopenia 2019; ③, European Working Group on Sarcopenia in Older People 2010; ④, European Working Group on Sarcopenia in Older People 2019; ⑤, International Working Group on Sarcopenia; ⑥, Foundation for the National Institutes of Health; HS, hand grip strength; GS, gait speed.
†, diagnosed with sarcopenia; ‡, diagnosed with severe sarcopenia.

study results. To avoid omissions, two reviewers with systematic training independently selected the articles. If the two reviewers disagreed, a third reviewer was consulted.

2.3 Data extraction

The following data were extracted independently by two authors: authors, year, region, population, sample size, age, percentage of females, cutoff for screening tools, diagnostic criteria for sarcopenia, prevalence, and TP, FP, TN, and FN. If the information was insufficient, the original authors were contacted via email.

2.4 Quality assessment

The quality of a meta-analysis conclusions depends not only on rigorous operational procedures but also on the control of bias by the included studies. We used the Quality Assessment for Diagnostic Accuracy Studies-2 (QUADAS-2) (30) to assess the risk of bias in four dimensions: participant selection, index test, reference standards, and flow and timing, which is available.[1] Based on responses to the relevant questions in each part, the risk level of bias could be assessed as "low," "high" or "unclear." Two authors independently assessed the quality of included studies. The results were presented graphically.

2.5 Statistical analysis

The studies were grouped according to the different sarcopenia diagnostic criteria used in the screening tool. The detailed criteria are listed in Table 1. The pooled result of sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR), 95% confidence interval (CI), and plot the summary receiver operating characteristic curve (SROC) were calculated by using a bivariate random-effects model (31). High sensitivity indicated a low missed diagnosis rate, whereas high specificity indicated a low misdiagnosis rate (32, 33). The LR is the probability ratio of patients with and without disease, which is not affected by the prevalence rate and fully reflects the value of diagnostic tests (34). The DOR reflects the degree of correlation between diagnostic test results and diseases (35). The closer the AUC value is to 1, the better the test performance, and the higher the DOR value, the higher the AUC (36). Cochran's Q test was used to assess the inter-study heterogeneity. The degree of heterogeneity was assessed using I^2, with I^2 values of 25, 50, and 75%, indicating low, moderate, and high heterogeneity, respectively (37). Z-test (38) was performed to compare the pooled sensitivity or specificity of each screening tool, in which $p \leq 0.05$ and $p \leq 0.01$ indicated differences and significant differences, respectively.

Bivariate random-effects models were used to correct for differences in index test thresholds (cutoff values) and between-test variations in test accuracy (heterogeneity) (39). Stata 17.0 was used for meta-analysis when there were more than four articles defining the diagnostic criteria using the guidelines, and Meta-DiSc1.4 was used for accuracy consolidation when there were fewer than four articles. Meta-regression and subgroup analyses were used to explore and explain the heterogeneity between studies based on region, population, and sex. Deeks' funnel plot was used to evaluate publication bias, with $p < 0.05$, indicating publication bias (40).

Statistical analyses were done using Stata 17.0 (StataCorp, College Station, TX, United States) and Meta-DiSc 1.4 (Universidad Complutense, Madrid, Spain) with the "metandi" and "midas" modules.

1 https://www.bris.ac.uk/quadas

3 Results

3.1 Description and methodological quality of the included studies

3.1.1 Literature search process

A total of 4,416 records were extracted from the literature search and 1,234 duplicate records were deleted before formal screening. 52 records remained after excluding those that did not meet the criteria, of which 30 studies (23,193 subjects) met the eligibility criteria and were included in the meta-analysis (Figure 1).

3.1.2 Characteristics of the included studies

We created a data extraction table based on study characteristics (Table 2). The mean age of the patients was 72.31 ± 4.06 years, and 54.15% of the subjects were female. The prevalence of sarcopenia was 11.22, 22.94, 10.63, 15.21, 21.9, and 19.62% among older Chinese adults according to the diagnostic criteria of AWGS 2014, AWGS 2019, EWGSOP 1, EWGSOP 2, IWGS, and FNIH diagnostic criteria, respectively.

3.1.3 Quality assessment

The results of the risk–bias analysis of the included studies are shown in Figure 2. Of the included studies, 17 studies did not indicated whether the sample of patients included was continuous or not (41–52), only the timeline included in the patient sample was explained and were evaluated as unclear, five studies were not described and were evaluated as no (23, 53–57). Thirty studies did not describe whether the experiment was blinded or not and were evaluated as unclear (23, 41–43). Fourteen studies choose the test threshold and were evaluated as no (41, 43, 45, 50, 51, 53, 55, 58–60, 64, 66–68). It was difficult to determine whether the reference standard results were interpreted without knowledge of the results of the index test in 30 studies (41, 43, 45, 50, 51, 53, 55, 58–60, 64, 66–68). The number of patients enrolled was differs from the number of patients included in the 2 × 2 table of results in 1 study (45). Although patient selection, reference standard, flow and timing had a low to unclear risk of bias. The applicability concerns were low.

3.2 Pooled results for screening tool accuracy

Table 3 shows the pooled sensitivity, specificity, PLR, NLR, DOR, and AUC of the seven screening tools according to diagnostic criteria. Figure 3 shows the sensitivity and specificity of the coupled forest plots

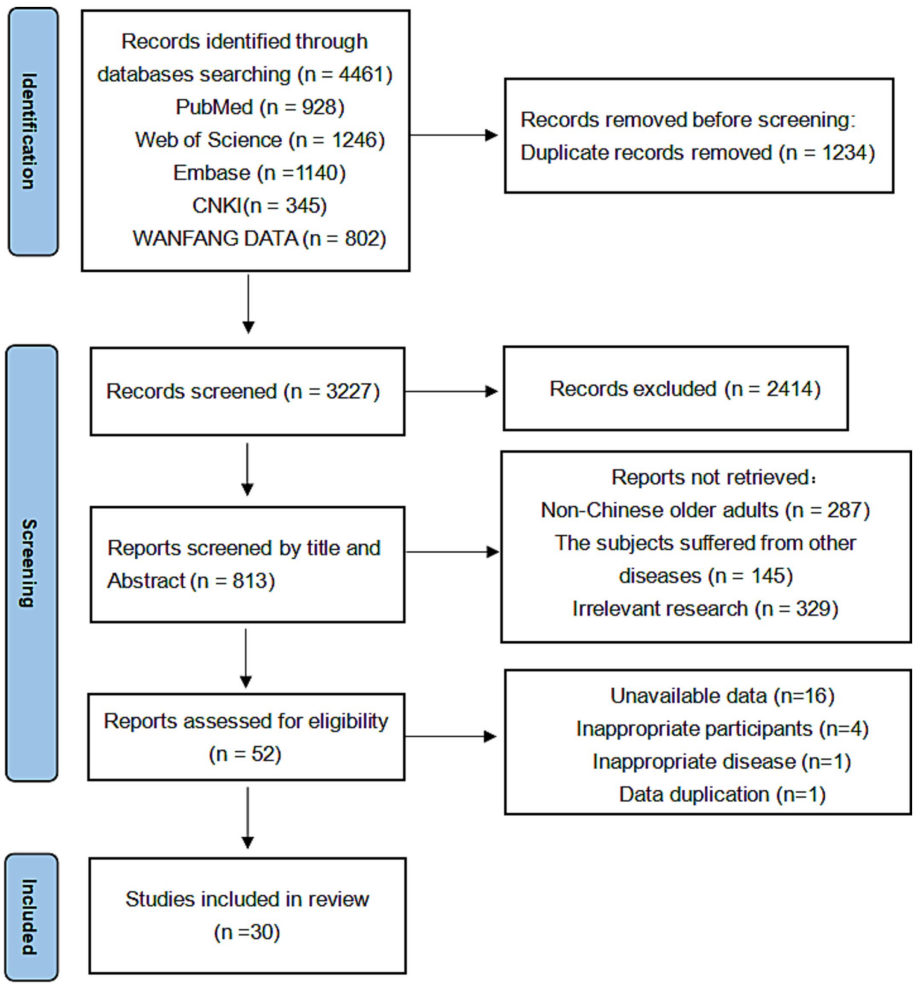

FIGURE 1
PRISMA flow chart.

TABLE 2 Characteristics of the included studies.

First Author, Year	region	Population	Sample size	Age, y	Female, %	screening tool	Cutoff	Diagnostic criteria	Prevalence, %	TP	FP	FN	TN
Yang, 2018 (23)	Cheng du	Ccommunity	384	71.5	58.33	SARC-F	4	①	15.9	18	6	43	317
								③	11.7	9	15	36	324
								⑤	25.0	19	5	77	283
								⑥	15.4	18	6	41	319
						SARC-CalF	11	①	15.9	37	17	24	306
								③	11.7	22	32	23	307
								⑤	25.0	41	13	55	275
								⑥	15.4	33	21	26	304
Lu, 2021 (41)	Yi bin	Ccommunity	588	68.8	46.77	SARC-F	4	①	10.71	49	14	14	511
Lin, 2020 (42)	Cheng du	Ccommunity	825	68.8	50.5	SARC-F	4	①	10.3	1	7	84	733
Pei Pei, 2020 (43)	Bei jing	Ccommunity	527	72.5	0	SARC-F	4	①	17.08	26	8	64	429
								④	17.46	26	8	66	427
Li, 2020 (44)	Cheng du	Ccommunity	1009	68.1	45.89	SARC-F	4	①	8.6	20	110	67	812
						SARC-CalF	11	①		36	130	51	792
Woo, 2014 (45)	Hong Kong	Ccommunity	4000	73.9	49.99	SARC-F	4	①	7.33	19	131	274	3573
							4	③	9.28	25	125	336	3511
							4	⑤	20.17	47	103	759	3088
Lin, 2021 (46)	Zi gong	Nursing home	199	NR	51.3	SARC-F	4	②	48.74	39	17	58	85
						SARC-CalF	11	②		69	40	28	62
						CC	M 34cm	②		42	17	16	22
							F 33cm	②		31	32	8	31
						Ishii	M 105	②		55	17	3	22
							F 120	②		32	9	7	54
Lin, 2023 (47)	Tai wan	Ccommunity	209	77.7	69.38	SARC-F	4	②	40.7	46	37	39	87
						SARC-CalF	11	②		65	33	20	91
						CC		②		73	39	12	85
Yang, 2018 (48)	Cheng du	Ccommunity	384	71.5	58.33	MSRA-7	30	①	15.9	53	195	8	128
						MSRA-5	45	①		55	95	6	228
Guanghui, 2020 (49)	Shang hai	Ccommunity	515	70.2	66.2	SARC-F	3	①	17.9	37	19	55	404

(Continued)

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TABLE 2 (Continued)

First Author, Year	region	Population	Sample size	Age, y	Female, %	screening tool	Cutoff	Diagnostic criteria	Prevalence, %	TP	FP	FN	TN
Li, 2019 (50)	He fei	Hospital	138	71.7	50	SARC-F	4	①	25.36	15	8	20	95
						Ishii	M 105	①		14	16	2	37
							F 120	①		15	16	4	34
Yang, 2018 (51)	Cheng du	Nursing home	277	81.6	70.03	SARC-F	4	①	34.3	19	3	76	179
								③	32.5	16	6	74	181
								⑤	38.3	18	4	88	167
								⑥	31.4	19	3	68	187
						SARC-CalF	11	①	34.3	56	26	39	156
								③	32.5	53	27	37	160
								⑤	38.3	59	23	47	148
								⑥	31.4	56	26	31	164
						MSRA-7	30	①	34.3	54	31	41	151
								③	32.5	48	37	42	150
								⑤	38.3	58	27	48	144
								⑥	31.4	50	35	37	155
						MSRA-5	45	①	34.3	51	29	44	153
								③	32.5	46	32	44	155
								⑤	38.3	52	28	54	143
								⑥	31.4	49	31	38	159
Zhou, 2022 (52)	Lu zhou	Ccommunity	439	70.51	50.4	SARC-F	4	②	26.43	13	13	93	282
						SARC-CalF	11	②		50	25	56	270
						SARC-F	4	④	12.5	10	16	40	335
						SARC-CalF	11	④		28	47	22	304
Yihan, 2021 (53)	Chang sha	Ccommunity	202	70.9	47.52	CC		②	22.8	41	34	5	122
Chen, 2022 (54)	Tai wan	Ccommunity	177	78.7	47.46	SARC-F	4	②	51.98	10	7	82	78
						SARC-CalF	11	②		35	17	57	68
						MSRA-5	45	②		56	39	36	46
						CC		②		74	24	18	61

(Continued)

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TABLE 2 (Continued)

First Author, Year	region	Population	Sample size	Age, y	Female, %	screening tool	Cutoff	Diagnostic criteria	Prevalence, %	TP	FP	FN	TN
Pengtian, 2021 (55)	Shijiazhuang	Ccommunity	303	78.35	63.04	Finger-ring Test		②	26.4	56	32	24	191
Xiaoyan, 2021 (56)	Lu liang	Ccommunity	1455	70.97	52.1	SARC-F	4	②	18.69	58	163	214	1020
						SARC-CalF	11	②		181	86	91	1097
Zhu, 2022 (57)	Zi gong	Nursing home	199	75.17	51.26	SARC-F	2	②	33.7	57	59	10	73
						SARC-CalF	12	②		46	37	11	95
						Ishii	M 130	②		34	13	6	44
							F 130	②		26	9	1	66
Pengtian, 2020 (58)	Shijiazhuang	Ccommunity	303	68	63.1	SARC-F	4	②	24.42	51	47	23	182
						Finger-ring Test		②		56	32	18	197
						MSRA-5	45	②		46	43	28	186
Youping, 2021 (59)	Yi bin	Ccommunity	503	68.4	46.72	SARC-F	4	②	12.3	46	7	16	434
Qian, 2022 (60)	Zheng zhou	Ccommunity	320	72.87	65	Finger-ring Test		②	20.63	45	45	21	209
						CC		②		48	51	18	203
Hu, 2021 (61)	Si chuan, Yun nan, Gui zhou, Xin jiang	Ccommunity	4509	63.5	64.18	MUAC	M 28.6cm	②	24.97	420	327	58	810
							F 27.5cm	②		497	498	151	1748
Mengli, 2021 (62)	Su zhou	Ccommunity	831	72.67	55.96	MUAC	M 26cm	②	13.6	30	48	5	283
							F 26cm	②		49	89	29	298
						CC	M 33cm	②		28	34	7	297
							F 33cm	②		66	120	12	267
Mengli, 2021 (63)	Su zhou	Ccommunity	1537	73.79	55.11	CC	M 33.7cm	②	12.27	38	80	5	360
							F 33cm	②		76	153	13	351
						MUAC	M 25.9cm	②		37	71	6	369
							F 26.5cm	②		63	160	26	344
Min, 2018 (64)	He fei	Ccommunity	122	71.8	57.38	Ishii	M 105	①	30.33	14	10	2	26
							F 120	①		17	14	4	35

(Continued)

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TABLE 2 (Continued)

First Author, Year	region	Population	Sample size	Age, y	Female, %	screening tool	Cutoff	Diagnostic criteria	Prevalence, %	TP	FP	FN	TN
Ping, 2019 (65)	Cheng du	Ccommunity	477	70.6	44.86	SARC-F	4	①	17	49	4	32	392
Mo, 2020 (66)	Chang sha	Ccommunity	1050	70.3	66.95	SARC-F	4	②	25.05	47	50	216	737
						SARC-CalF	11	②		125	63	138	724
						CC	M 34cm	②		61	59	23	204
							F 33cm	②		153	122	26	402
Chen, 2021 (67)	Si chuan	Ccommunity	941	NR	50.9	Ishii	M 95	②	18.38	65	69	27	301
							F 102	②		61	80	20	318
							M 105	②		60	54	32	316
							F 120	②		38	27	43	371
Jiaoling, 2023 (68)	Chang sha	Nursing home	386	80.3	56.74	Ishii	M 137	②	49.7	79	25	12	51
							F 161	②		79	32	22	86
							M 105	②		91	58	0	18
							F 120	②		100	90	1	28
Yang, 2018 (69)	Cheng du	Ccommunity	384	71.5	58.33	c-MSRA-7	30	①	15.89	53	195	8	128
								③	11.72	24	108	21	231
								⑤	25	52	80	44	208
								⑥	15.36	24	108	35	217
						c-MSRA-5	45	①	15.89	55	95	6	228
								③	11.72	32	118	13	221
								⑤	25	68	82	28	206
								⑥	15.36	53	97	6	228

①, AWGS 2014; ②, AWGS 2019; ③, EWGSOP 1; ④, EWGSOP 2; ⑤, IWGS; ⑥, FNIH; TP, true positives; FP, false positives; TN, true negative; FN, false negatives; MUAC, middle upper arm circumference; CC, calf circumference; T, total; M, male; F, female; NR, not report; c, Chinese version.

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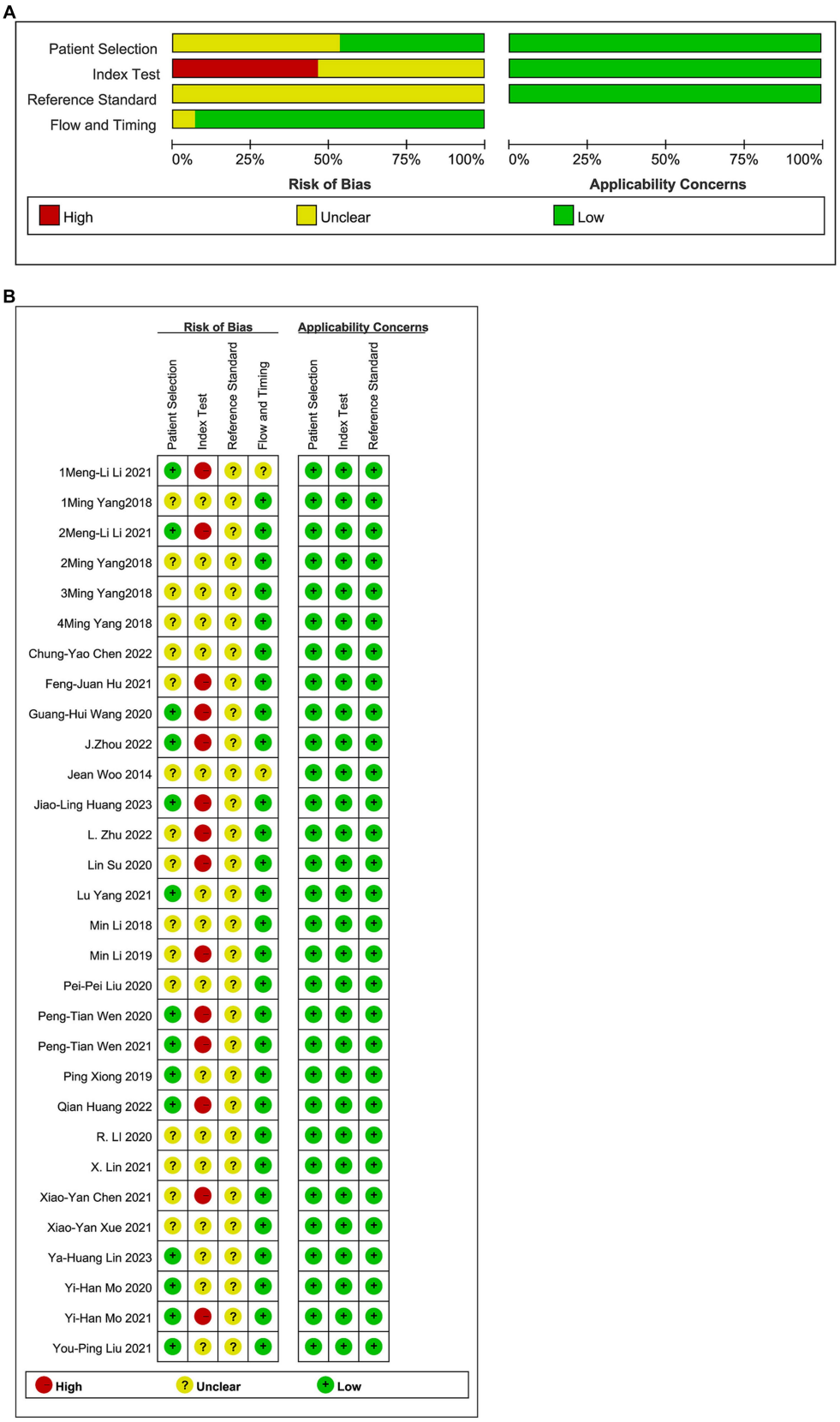

FIGURE 2
Results of the risk bias **(A)** The risk composition ratio; **(B)** The risk of each study.

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TABLE 3 Pooled results of the meta-analysis grouped by diagnostic criteria.

Diagnostic criteria	Screening tools	Sensitivity (95% CI)	I^2	Specificity (95% CI)	I^2	PLR (95% CI)	NLR (95% CI)	DOR (95% CI)	AUC
AWGS 2014①	SARC-F†	0.27(0.13–0.47)	96.20%	0.97(0.95–0.98)	98.13%	9.66(4.49–20.76)	0.75(0.59–0.95)	12.85(4.93–33.53)	0.93(0.90–0.95)
	SARC-CalF‡	0.53(0.47–0.59)	73.40%	0.88(0.86–0.90)	90.80%	5.06(2.43–10.57)	0.52(0.38–0.72)	9.81(3.53–27.27)	0.634
	MSRA-7‡	0.60(0.52–0.68)	16.10%	0.76(0.72–0.79)	88.40%	2.71(1.86–3.96)	0.51(0.42–0.62)	5.57(3.71–8.33)	——
	MSRA-5‡	0.68(0.60–0.75)	96.00%	0.75(0.71–0.79)	91.60%	3.12(2.64–3.70)	0.29(0.06–1.46)	11.10(3.10–39.74)	——
	Ishii‡	0.85(0.74–0.92)	0.00%	0.71(0.64–0.78)	0.00%	2.93(2.29–3.75)	0.22(0.12–0.38)	13.70(6.69–28.06)	——
AWGS 2019②	SARC-F†	0.34(0.19–0.53)	96.42%	0.90(0.83–0.95)	96.27%	3.53(1.65–7.51)	0.73(0.56–0.96)	4.82(1.81–12.88)	0.78(0.74–0.81)
	SARC-CalF†	0.59(0.57–0.70)	91.78%	0.85(0.75–0.92)	96.48%	3.91(2.38–6.40)	0.49(0.38–0.63)	8.03(4.38–14.70)	0.78(0.74–0.81)
	MSRA-5‡	0.61(0.54–0.69)	0.00%	0.74(0.69–0.79)	95.50%	2.09(0.85–5.12)	0.58(0.37–0.89)	3.62(0.96–13.67)	——
	CC‡	0.81(0.77–0.84)	26.50%	0.73(0.71–0.76)	89.40%	2.56(1.71–3.83)	0.29(0.20–0.42)	8.97(4.32–18.60)	0.8789
	Finger-ring Test‡	0.71(0.65–0.77)	0.00%	0.85(0.82–0.87)	0.00%	4.61(3.57–5.66)	0.34(0.28–0.42)	13.67(9.48–19.71)	0.9041
	Ishii‡	0.81(0.78–0.85)	98.50%	0.76(0.73–0.79)	99.40%	2.89(0.81–10.32)	0.15(0.04–0.61)	19.02(7.96–45.43)	0.876
EWGSOP 1③	SARC-F‡	0.10(0.08–0.13)	84.90%	0.96(0.96–0.97)	0.00%	3.39(1.71–6.72)	0.89(0.80–1.00)	3.82(1.72–8.47)	0.9782
	SARC-CalF‡	0.57(0.49–0.64)	28.00%	0.88(0.85–0.91)	77.50%	4.30(3.19–5.80)	0.51(0.43–0.60)	8.27(5.56–12.31)	——
	MSRA-7‡	0.53(0.45–0.62)	0.00%	0.72(0.68–0.76)	89.00%	2.11(1.31–3.40)	0.62(0.51–0.74)	3.43(1.84–6.41)	——
	MSRA-5‡	0.58(0.49–0.66)	80.20%	0.71(0.67–0.75)	94.90%	2.41(1.61–3.60)	0.55(0.42–0.71)	4.88(3.16–7.52)	——
EWGSOP 2④	SARC-F‡	0.25(0.18–0.33)	16.60%	0.97(0.95–0.98)	79.40%	8.18(2.35–28.41)	0.78(0.68–0.89)	10.53(2.68–41.32)	——
FNIH⑤	SARC-F‡	0.25(0.19–0.33)	27.60%	0.98(0.97–0.99)	0.00%	15.52(7.64–31.51)	0.76(0.68–0.85)	20.88(9.66–45.13)	——
	SARC-CalF‡	0.65(0.57–0.73)	75.90%	0.91(0.88–0.93)	86.20%	6.65(4.12–10.72)	0.39(0.26–0.58)	17.55(10.98–28.06)	——
	MSRA-7‡	0.51(0.42–0.59)	74.90%	0.72(0.68–0.76)	92.70%	1.95(0.78–4.89)	0.68(0.40–1.16)	2.87(0.68–12.12)	——
	MSRA-5‡	0.70(0.62–0.77)	95.20%	0.75(0.71–0.79)	91.90%	3.09(2.62–3.66)	0.29(0.07–1.25)	11.17(3.57–34.88)	——
IWGS⑥	SARC-F‡	0.08(0.07–0.10)	92.80%	0.97(0.96–0.97)	24.00%	4.98(1.34–18.56)	0.88(0.77–1.01)	5.67(1.35–23.84)	0.9995
	SARC-CalF‡	0.50(0.42–0.57)	70.50%	0.92(0.89–0.94)	91.20%	6.10(2.71–13.71)	0.56(0.48–0.66)	11.00(5.72–21.15)	——
	MSRA-7‡	0.54(0.47–0.61)	0.00%	0.77(0.73–0.80)	88.90%	2.55(1.44–4.53)	0.58(0.49–0.68)	4.38(2.12–9.05)	——
	MSRA-5‡	0.59(0.52–0.66)	90.00%	0.76(0.72–0.80)	88.90%	2.60(2.15–3.16)	0.51(0.34–0.77)	5.53(3.80–8.05)	——

①, Asian Working Group for Sarcopenia 2014; ②, Asian Working Group for Sarcopenia 2019; ③, European Working Group on Sarcopenia in Older People 2010; ④, European Working Group on Sarcopenia in Older People 2019; ⑤, International Working Group on Sarcopenia; ⑥, Foundation for the National Institutes of Health.

†, Use Stata 17.0 to merge accuracy; ‡, Use Meta-DiSc 1.4 to merge accuracy.

and SROC curves for SARC-F based on AWGS 2014 and AWGS 2019, and SARC-CalF based on AWGS 2019, respectively. The study for the MUAC was insufficient and not pooled for the accuracy. Meta-regression was used to account for sources of heterogeneity, and a subgroup analysis of the sources of heterogeneity was performed when the number of references met the criteria for the meta-analysis.

3.2.1 Comparative results of the accuracy of the same screening tool based on different diagnostic criteria

Figures 4A,B showed the comparative results of the accuracy of the same screening tool based on different diagnostic criteria in 29 studies. Based on different diagnostic criteria, the sensitivity and specificity of SARC-F, SARC-CalF, and MSRA-5 were statistically different but remained at the same level. Overall, the SARC-F showed low sensitivity and high specificity, SARC-CalF showed moderate sensitivity and high specificity, MSRA-7 and MSRA-5 showed moderate sensitivity and specificity, Ishii showed high sensitivity and moderate specificity, CC showed high sensitivity and moderate specificity, and the Finger-ring Test showed moderate sensitivity and high specificity.

3.2.2 Comparative results of the accuracy of different screening tools based on the same diagnostic criteria

Figures 4C,D show the comparative accuracy results of the different screening tools based on the same diagnostic criteria in 29 studies. In Chinese older adults, when AWGS 2014 as a diagnostic criterion for sarcopenia, Ishii had relatively high sensitivity (85%) but relatively low specificity (71%), SARC-F had relatively high specificity (97%) but relatively low sensitivity (27%). When AWGS 2019 as a diagnostic criterion for sarcopenia, CC and Ishii had relatively high sensitivity (81, 81%) but relatively low specificity (73, 76%); SARC-F had relatively high specificity (90%) but relatively low sensitivity (34%). When EWGSOP 1 as a diagnostic criterion for sarcopenia, MSRA-5 had relatively high sensitivity (58%), but relatively low specificity (71%), and SARC-F had relatively high specificity (96%), but relatively low sensitivity (10%). When FNIH as a diagnostic criterion for sarcopenia, MSRA-5 had relatively high sensitivity (70%), but relatively low specificity (75%), and SARC-F had relatively high specificity (98%), but relatively low sensitivity (25%); When IWGS was used as a diagnostic criterion for sarcopenia, MSRA-5 had relatively high sensitivity (59%), but relatively low specificity (76%), and SARC-F had relatively high specificity (97%), but relatively low sensitivity (8%).

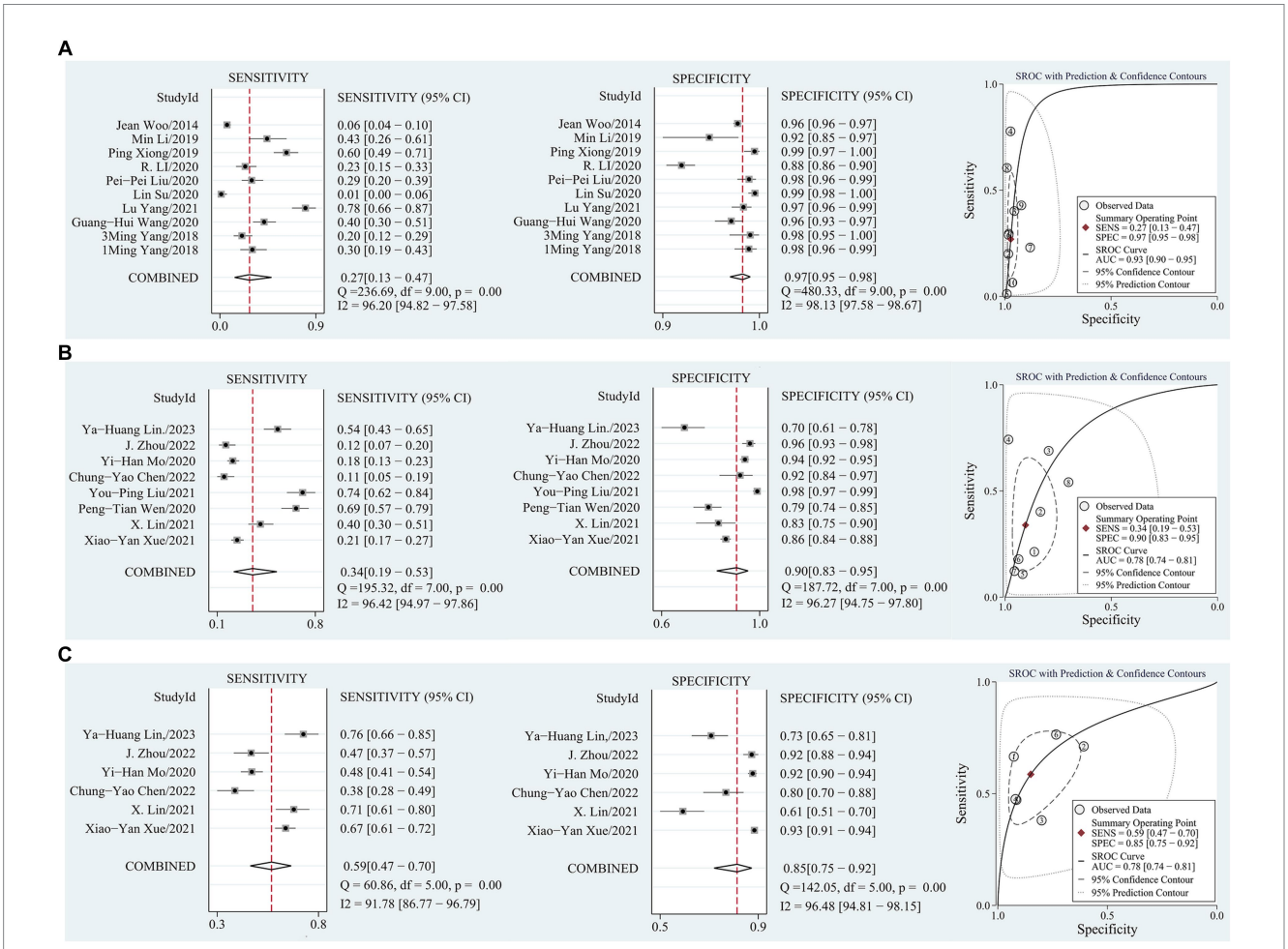

FIGURE 3
(A) Sensitivity and specificity coupled forest plot, SROC curve of SARC-F based on AWGS 2014; **(B)** Sensitivity and specificity coupled forest plot, SROC curve of SARC-F based on AWGS 2019; **(C)** Sensitivity and specificity coupled forest plot, SROC curve of SARC-CalF based on AWGS 2019.

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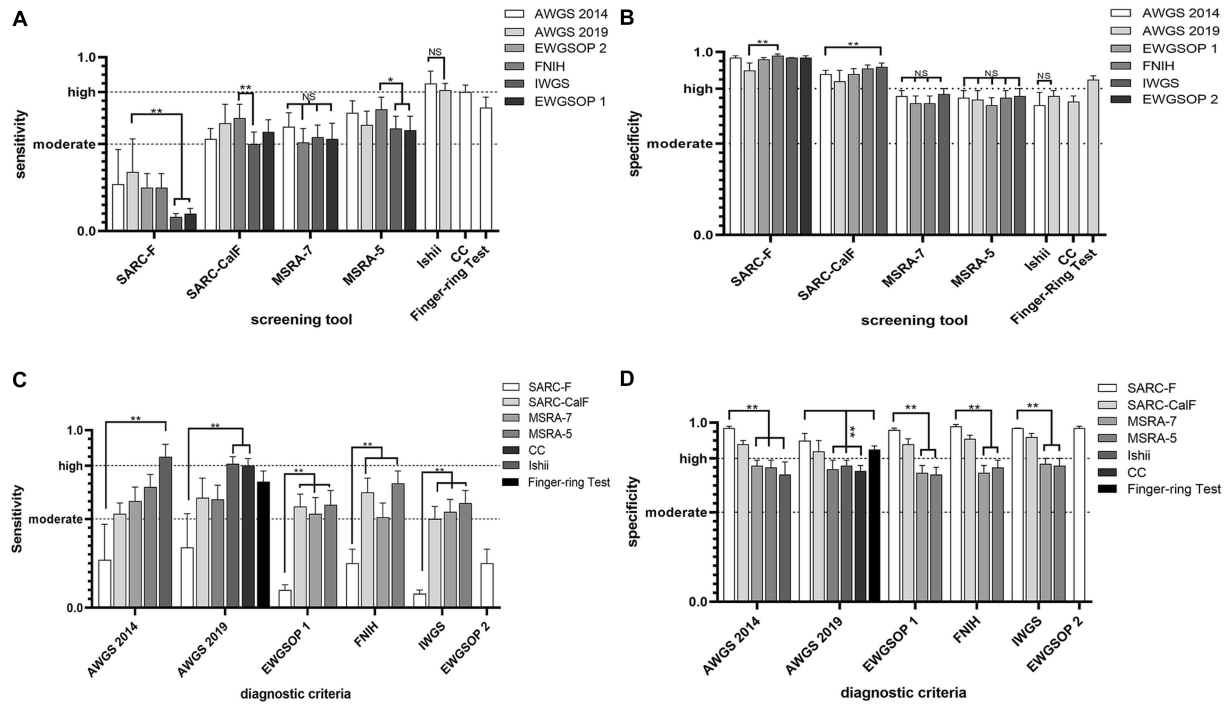

FIGURE 4
(A) Comparative results of sensitivity (highest and lowest), based on different diagnostic criteria; **(B)** Comparative results of specificity (highest and lowest), based on different diagnostic criteria. **(C)** Comparative results of sensitivity (highest and lowest), based on the same criteria. **(D)** Comparative results of specificity (highest and lowest), based on the same criteria.

3.2.3 Exploring heterogeneity in the accuracy of different screening tools combined results based on different diagnostic criteria

Using AWGS 2014 as the diagnostic criterion, I^2 showed high heterogeneity for pooled sensitivity of SARC-F and MSRA-5 ($I^2 = 96.2$ and 96.0%, respectively) and specificity ($I^2 = 88.4$–98.13%) for all screening tools with the exception of Ishii. Using AWGS 2019 as the diagnostic criterion, I^2 showed high heterogeneity for pooled sensitivity of SARC-F, SARC-CalF and Ishii ($I^2 = 91.78$–98.5%) and specificity ($I^2 = 89.4$–99.4%) for all screening tools with the exception of Finger-ring Test. Using EWGSOP 1 as the diagnostic criterion, I^2 showed high heterogeneity for pooled sensitivity of SARC-F and MSRA-5 ($I^2 = 84.9$ and 80.2%, respectively) and specificity of MSRA-7 and MSRA-5 ($I^2 = 89.0$ and 94.9%, respectively). Using FNIH as the diagnostic criterion, I^2 showed high heterogeneity for pooled sensitivity of MSRA-5 ($I^2 = 95.2\%$) and specificity of SARC-CalF, MSRA-7 and MSRA-5 ($I^2 = 86.2$–92.7%). Using IWGS as the diagnostic criterion, I^2 showed high heterogeneity for pooled sensitivity of SARC-F and MSRA-5 ($I^2 = 92.8$ and 90.0%, respectively) and specificity of SARC-CalF, MSRA-7 and MSRA-5 ($I^2 = 88.9$–91.2%).

Owing to the insufficient number of included references, we only performed a meta-regression of the screening tools using AWGS 2014 and AWGS 2019 as diagnostic criteria to explain the sources of heterogeneity. When the number of references met the criteria for meta-analysis, subgroup analysis was performed on the sources of heterogeneity.

Among the various potential covariates, SARC-F used the diagnostic criteria of AWGS 2014 (n = 10), meta-regression showed a statistically significant difference in specificity for the region (eastern vs. western), with a specificity of 0.98 (95% CI, 0.96–0.99) vs. 0.96 (95% CI, 0.93–0.99), ($p = 0.03$). CC used the diagnostic criteria of AWGS 2019 ($n = 6$), meta-regression showed that sex (female vs. male) was a significant factor associated with study heterogeneity, with a statistically significant difference in sensitivity of 0.75 (95% CI, 0.69–0.81) vs. 0.85 (95% CI, 0.81–0.88), ($p = 0.00$).

Because the cutoff values for CC and Ishii screening for sarcopenia were sex-differentiated, they were analyzed in the sex subgroups (Table 4).

3.3 Publication bias

Given the number of included references, Deeks' funnel plot asymmetry test was applied separately to references based on AWGS 2014 ($n = 10$) (23, 41–45, 49–51, 65) to estimate publication bias. Deeks' funnel plot (Figure 5) did not reveal any evidence of publication bias ($p = 0.06$).

4 Discussion

4.1 Prevalence of sarcopenia in China

Using different diagnostic criteria, the prevalence of sarcopenia in older Chinese adults in this study ranged from 10.63 to 22.94%, similar to the results of a previous study on the prevalence of sarcopenia in older Chinese adults (70, 71). The prevalence of using the AWGS 2019 diagnostic criteria (22.94%) was much higher than

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TABLE 4 The pooled results of the CC and Ishii meta-analysis grouped by definition and sex.

Diagnostic criteria	Screening tools	Sex	Sensitivity (95% CI)	I^2	Specificity (95% CI)	I^2	PLR (95% CI)	NLR (95% CI)	DOR (95% CI)	AUC
②	CC†	Male	0.75(0.68–0.80)	0.00%	0.74(0.64–0.81)	67.36%	2.58(2.01–4.06)	0.34(0.26–0.46)	8.34(4.57–15.20)	0.79(0.75–0.82)
		Female	0.85(0.81–0.88)	0.00%	0.67(0.61–0.73)	83.04%	2.60(2.11–3.20)	0.23(0.17–0.30)	11.45(7.39–17.74)	0.86(0.83–0.89)
①	Ishii‡	Male	0.88(0.71–0.96)	0.00%	0.71(0.60–0.80)	0.00%	2.99(2.11–4.25)	0.18(0.07–0.44)	17.13(5.44–53.91)	——
		Female	0.80(0.64–0.91)	0.00%	0.70(0.60–0.79)	0.00%	2.64(1.88–3.69)	0.29(0.15–0.54)	9.20(3.79–22.32)	——
②	Ishii‡	Male	0.85(0.80–0.90)	96.50%	0.73(0.69–0.77)	98.30%	2.32(0.92–5.84)	0.14(0.03–0.66)	14.41(7.14–29.12)	0.8579
		Female	0.77(0.71–0.82)	97.50%	0.78(0.75–0.82)	99.10%	3.68(0.68–19.98)	0.23(0.07–0.78)	16.36(8.89–30.09)	0.8852

①, Asian Working Group for Sarcopenia 2014; ②, Asian Working Group for Sarcopenia 2019; PLR, positive likelihood ratio; NLR, negative likelihood ratio; DOR, diagnostic odds ratio; AUC, area under the curve.
†, Use Stata 17.0 to merge accuracy; ‡, Use Meta-DiSc 1.4 to merge accuracy.

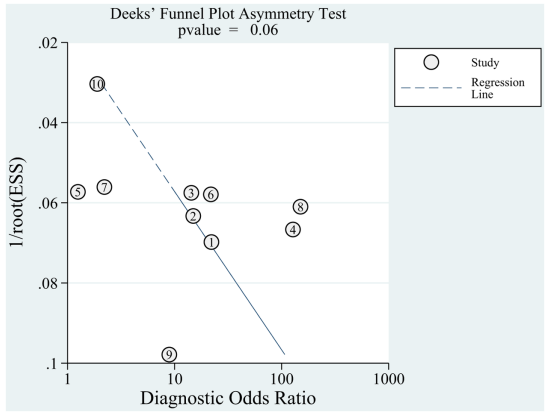

FIGURE 5
Funnel plot with superimposed regression line.

that of the AWGS 2014 diagnostic criteria (11.22%) because the AWGS 2019 diagnostic criteria increased the cutoff points for gait speed and male grip strength. In a global meta-analysis of the prevalence of sarcopenia that included 151 studies (72), the prevalence of diagnostic criteria using EWGSOP 1 was 22%, which was significantly different from the prevalence using EWGSOP 1 in this study (10.63%) and partially influenced by the small number of relevant references included in this study. Furthermore, differences in the prevalence of sarcopenia may be influenced by the population (the study and reference populations), and different methods of assessment and race may play a role when the reference and study populations are mismatched (73, 74).

4.2 Heterogeneity

The screening tools for sarcopenia included in this study, except for the CC, Ishii, and Finger-ring Test, generally showed low to moderate sensitivity and moderate to high specificity, and the screening tools have poor sensitivity for screening sarcopenia in older Chinese adults. The pooled results for accuracy of some screening tools showed high heterogeneity, and exploration of heterogeneity using meta-regression showed that regional and sex differences affected the accuracy of the screening tools. A meta-analysis based on global validation of the accuracy of SARC-F screening for sarcopenia showed that the accuracy of SARC-F for screening for sarcopenia in Asian and non-Asian countries differed (75). Expert consensus on the diagnosis and treatment of sarcopenia in older Chinese adults suggests that western China is at a higher altitude than eastern China and that lifestyle and environment are the main factors affecting the prevalence of sarcopenia (76). In addition, the prevalence was slightly higher in males than in females. This shows that the same screening tool cannot be applied simultaneously in the eastern and western regions of China and that the screening tool should establish corresponding cutoff values for males and females.

4.3 The accuracy of screening tools

In older Chinese adults, the accuracy of the same screening tool under different diagnostic criteria varies but remains at the same level. Based on different diagnostic criteria, SARC-F shows high specificity, but its low sensitivity is a major weakness as a screening tool for sarcopenia; that is, SARC-F has a low rate of misdiagnosis when screening for sarcopenia, but a high rate of misdiagnosis (32, 33). Barbosa-Silva et al. believed that low sensitivity was due to the omission of low muscle mass in the questionnaire, in which CC was added to the SARC-F questionnaire to increase sensitivity (12). The sensitivity of the SARC-CalF test was higher than that of the SARC-F test. However, an increase in sensitivity led to a decrease in specificity. This is similar to the results of a Korean study based on 2,123 community-dwelling older adults (mean age, 75.9 ± 3.9 years) (77). However, the sensitivity of the SARC-CalF test is less than perfect. MSRA-5, which is based on MSRA-7 with removed food intake questions,

increases the proportion of weight and physical activity level scores; compared to MSRA-7, MSRA-5 improves sensitivity while maintaining the same specificity, indicating that weight loss and low physical activity levels are predictors of sarcopenia in older Chinese adults. This conjecture was confirmed by Van Kan et al. (78, 79). Compared to other screening tools, CC, Ishii, and Finger-ring Test performed better in screening for sarcopenia in older Chinese adults. However, they are not perfect screening tools for sarcopenia because missing sarcopenia may make these high-risk individuals prone to adverse health outcomes (80, 81), A high sensitivity of SARC-CalF, high sensitivity and moderate specificity of CC and Ishii, and moderate sensitivity and high specificity of the Finger-ring Test indicate that CC may be a simple but valuable screening tool for sarcopenia or a valid indicator of a high correlation with muscle mass, and may improve screening accuracy when combined with other relevant parameters as a screening tool. The findings from the present study are consistent with those from earlier studies (82–84).

4.4 Diagnostic criteria of sarcopenia for the older adults in China

AWGS 2019 considers ethnic differences in different populations and is more applicable to the diagnosis of sarcopenia in Asians than other diagnostic criteria. AWGS 2019 also introduces the concept of "probable sarcopenia" to facilitate timely interventions (20). Aging is an important risk factor associated with decreased muscle function (85, 86), and with timely intervention it is possible to improve physical function and slow the decreases in muscle quantity and quality (8, 9, 87). Therefore, it is not too late for older adults to undergo screening for sarcopenia or interventions. Although the AWGS 2019 consensus recommends the use of SARC-F and SARC-CalF for sarcopenia screening, the low sensitivity of the screening tool leads to a higher risk of missed diagnoses. We believe that CC and Ishii have better sarcopenia screening performance and that SARC-F and SARC-CalF should be used with caution in screening for sarcopenia.

4.5 Areas for further research

As the accuracy of screening tools is affected by regional differences, it is necessary to improve or develop screening tools for sarcopenia in different regions of China. The pooled results of the accuracy of the screening tool for sarcopenia showed that there is room for improvement in the sensitivity of the screening tool. CC was strongly correlated with muscle mass and its inclusion should be considered in the future to improve the accuracy of the screening tools. Further experimental studies are required to validate this screening tool for sarcopenia in Chinese older adults.

5 Strengths and limitations

This study compared the accuracy of sarcopenia screening tools based on different diagnostic criteria in older Chinese adults. We included several studies with an "unclear" to "high" risk of bias in the experiments to be evaluated, and the selection of the cutoff value to optimize sensitivity and specificity may lead to increased screening accuracy which may have an impact on the accuracy of the study results. The cutoff values of MUAC have not been standardized, and the number of references is insufficient for meta-analysis; this study only reported the accuracy range of MUAC screening for sarcopenia in Chinese older adults using different cutoff values. Due to the small number of relevant references, meta-regression could not be performed to explain the existence of partial heterogeneity, which may have affected the objectivity of the pooled results. However, further research is required to confirm the accuracy of these screening tools.

6 Conclusion

Comparisons of the accuracy of the same screening tools with different diagnostic criteria showed that the AWGS 2019 diagnostic criteria were more appropriate for the diagnosis of sarcopenia in older Chinese adults. Although there are screening tools that showed higher DOR and AUC using the diagnostic criteria of AWGS 2019, CC and Ishii have relatively high sensitivity. Considering the importance of high sensitivity in sarcopenia screening, CC and Ishii score are recommended for sarcopenia screening in older Chinese adults.

Data availability statement

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

Author contributions

SQ: Writing – review & editing, Conceptualization, Formal analysis, Methodology, Validation, Writing – original draft. SZ: Formal analysis, Methodology, Validation, Writing – original draft, Writing – review & editing. ML: Formal analysis, Validation, Writing – original draft, Writing – review & editing. SC: Data curation, Visualization, Writing – review & editing. LL: Data curation, Visualization, Writing – review & editing. SL: Data curation, Visualization, Writing – review & editing. FJ: Conceptualization, Methodology, Supervision, Writing – review & editing. JZ: Conceptualization, Methodology, Supervision, Writing – review & editing.

Funding

The authors(s) declare financial support was received for the research, authorship, and/or publication of this article. This work was supported by the Project of Hunan Provincial Sports Bureau (2023KT0128), and Social Science Fund Project of Hunan Provincial (23YBA153).

Conflict of interest

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

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1310383/full#supplementary-material

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10.3389/fpubh.2024.1310383

Glossary

AWGS	Asian Working Group on Sarcopenia
EWGSOP	European Working Group on Sarcopenia in Older People
IWGS	International Working Group on Sarcopenia
FNIH	Foundation for the National Institutes of Health
SARC-CalF	SARC-F combined calf circumference
MSRA	Mini Sarcopenia Risk Assessment
CC	Calf Circumference
MUAC	middle upper arm circumference
PLR	positive likelihood ratio
NLR	negative likelihood ratio
DOR	diagnostic odds ratio
AUC	area under the curve
TP	true positives
FP	false positives
TN	true negative
FN	false negatives
M	male
F	female
T	total

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 08 February 2024
DOI 10.3389/fpubh.2024.1330221

OPEN ACCESS

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RECEIVED 30 October 2023
ACCEPTED 29 January 2024
PUBLISHED 08 February 2024

CITATION
Atabieke F, Li X-J, Aierken A, Li J, Zhang Y, Aizezi Y, Gao H-L and Zhang Z-Q (2024) Association between frailty and hepatic fibrosis in NAFLD among middle-aged and older adults: results from NHANES 2017–2020.
Front. Public Health 12:1330221.
doi: 10.3389/fpubh.2024.1330221

Association between frailty and hepatic fibrosis in NAFLD among middle-aged and older adults: results from NHANES 2017–2020

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Background: Although previous studies found that frailty is prevalent in NAFLD patients with advanced liver fibrosis and cirrhosis, studies examining the relationship are spare.

Aim: Our study aspires to investigate the potential correlation between the Frailty Index (FI) and hepatic fibrosis among middle-aged and older adults with NAFLD.

Methods: Data from the 2017–2020.03 National Health and Nutrition Examination Survey (NHANES) were utilized for this study, with a final of 2,383 participants aged 50years and older included. The quantification of frailty was executed employing a 49-item frailty index. The recognition of hepatic steatosis and fibrosis was accomplished through the utilization of the controlling attenuation parameter (CAP) and transient elastography (TE). The relationship between the FI and hepatic fibrosis were investigated employing univariable and multivariable-adjusted logistic regression analyses. A subgroup analysis was conducted, dividing the subjects based on gender, Body Mass Index (BMI), and the presence of hyperlipidemia.

Results: The findings demonstrated a positive correlation between the FI and significant hepatic fibrosis in NAFLD, even after using multivariate logistic regression models adjusting for potential confounding factors (OR = 1.022, 95% CI, 1.004–1.041) and in tertiles (Q3vs Q1: OR = 2.004, 95% CI, 1.162–3.455). In the subgroup analysis, the correlation was more statistically significant in male (OR = 1.046, 95% CI, 1.022–1.071), under/normal weight (OR = 1.077, 95% CI, 1.009–1.150), overweight (OR = 1.040, 95% CI, 1.010–1.071), and subjects without hyperlipidemia (OR = 1.054, 95% CI, 1.012–1.097). The area under the Receiver Operating Characteristic (ROC) curve for the FI in assessing the existence of substantial fibrosis in NAFLD was 0.612 (95% CI, 0.596–0.628).

Conclusion: This study demonstrated a positive correlation between significant hepatic fibrosis and frailty, particularly among males aged 50 years and older, who were non-obese and did not have hyperlipidemia with NAFLD. Additional studies are required to further validate these findings.

KEYWORDS

frailty, hepatic fibrosis, non-alcoholic fatty liver disease, national health and nutrition examination survey, controlled attenuation parameter

Introduction

Non-alcoholic fatty liver disease (NAFLD) is generally acknowledged as the liver representation of metabolic syndrome (1), affecting a spectrum of hepatic conditions in individuals who consume little to no alcohol. The defining characteristic of NAFLD is the accumulation of excessive fat within liver cells. Recent research suggests that the emergence of NAFLD is associated with the accumulation of lipids, endoplasmic reticulum stress, oxidative stress, lipotoxicity within the liver (2). If left untreated, the condition can potentially lead to hepatic fibrosis, cirrhosis and ultimately, hepatocellular carcinoma (3). Consequently, preventing the advancement of fibrosis can serve as a crucial measure to reduce liver-related mortality. Non-invasive assessment methods are increasingly being recognized as alternatives besides of liver biopsy (4). Transient elastography (TE), delivering accurate staging of liver fibrosis in NAFLD using non-invasive methods, is a promising technique, particularly for advanced fibrosis and cirrhosis. Controlled attenuation parameter (CAP) method is routinely used to determine steatosis severity and also being studied for the grading of hepatic steatosis (5, 6).

Frailty, which was marked by age-related reduced functional reserves through multiple organ systems, is a prevalent and significant geriatric syndrome and can result in heightened susceptibility to negative health outcomes (7). Understanding the risks of frailty and associated adverse health outcomes can help to better treat this most vulnerable group of patients. Although there is no gold standard for detecting frailty, a variety of screening tools for frailty have been developed and used in risk assessment and epidemiologic studies (8). The frailty index (FI) is calculated based on the presence or absence of multiple health-related deficits or impairments (9), such as chronic diseases, disabilities, cognitive decline, or other age-related conditions. The FI provides a numerical score or index that represents the overall frailty status of an individual, with higher scores indicating greater frailty. A total of 49 health indicators were incorporated to create the FI as a ratio of accumulated health deficits.

In the previous studies, researchers found that frailty is prevalent in NAFLD patients with advanced liver fibrosis and cirrhosis (10). In this study, we analyzed the relevance of the FI and hepatic fibrosis among middle-aged and older adults in US with NAFLD using the 2017–2020.03 National Health and Nutrition Examination Survey (NHANES) data.

Methods

Study design and participants

The NHANES is a nationally representative database, which delivers comprehensive data regarding nutrition and health for the common U.S. population (11). The technique and data acquisition process of NHANES have been thoroughly detailed in prior publications, and can be accessed on the official NHANES website[1] (12). 2017–2020.03 NHANES survey cycles were selected due to the availability of specific data on assessment of hepatic fibrosis is not available in the former waves. TE, which is capable of executing with remarkable diagnostic precision, regardless of the underlying liver condition, for the identification of cirrhosis, was used to assess hepatic fibrosis in our study (13). In a study executed by Karlas et al. (6), a CAP score of ≥248 dB/m was recognized as an indicator of NAFLD, and individuals without NAFLD were not included. Based on the latest guidelines of the European Association (14), a median liver stiffness of ≥8.2 kPa was used to judge significant hepatic fibrosis (≥F2). Individuals were deemed ineligible if they could not lie on the examination table, were pregnant or uncertain about their pregnancy status during the testing period.

Weighted 2017–2020.03 cycles were calculated and utilized throughout the analysis due to the Covid-19 pandemic. We included individuals aged 50 years and older who had no other potential causes of chronic liver disease such as hepatitis B, hepatitis C, liver cancer, autoimmune hepatitis, or serious alcoholism. In the NHANES cycles from 2017 to 2020.03, 24,814 individuals participated in the study, with 8,056 of them being 50 years old or older. While excluding subjects without data on assessment of hepatic fibrosis or the FI, as well as any other covariates such as age, gender, race/ethnicity, educational level, body mass index (BMI), smoking status and alcohol behavior, 2,383 remaining sample was used for analysis. Details are shown in Figure 1.

Detection methods

The primary object of TE is offering a reliable detection method for 2 significant hepatic diseases: hepatic fibrosis, hepatic steatosis. The elastography measurements were conducted in the Mobile Examination Center (MEC) of the NHANES, using the FibroScan® model 502 V2 Touch equipped with a medium (M) or extra large (XL) wand. Simultaneously, the ultrasound attenuation associated with hepatic steatosis was also assessed, and the index of hepatic steatosis was recorded from CAP. A meta-analysis included 19 biopsy control studies in more than 2,700 patients suggested that the best critical value for liver steatosis grade was 248 dB/m (95% CI 237–261) (6). Others have evaluated elastography for its accuracy in assessing hepatic steatosis and fibrosis (15).

Frailty index

The FI is an integrative assessment tool designed to appraise the degree of vulnerability to adverse outcomes typically in the context of aging and health, which counts 49 deficits in health that covered multiple systems constructed by Hakeem FF (16). The FI computation encompassed the incorporation of symptoms, signs, disabilities and diseases in this study (17). These deficits encompassed limited activity, cognitive impairments and physical performance deficits (such as weakened grip strength, difficulty walking), co-existing medical conditions, self-assessed health status, and mood/depression issues (18). Depending on the severity of the deficit, a value between 0 and 1 was assigned. The FI value represents the ratio of deficits acquired by the participant to the sum of potential deficits. Consider a scenario where 40 potential deficits are evaluated, if an individual exhibits 10 of these deficits, his frailty index would be calculated as 10/40 = 0.25

1 http://www.cdc.gov/nchs/nhanes.htm

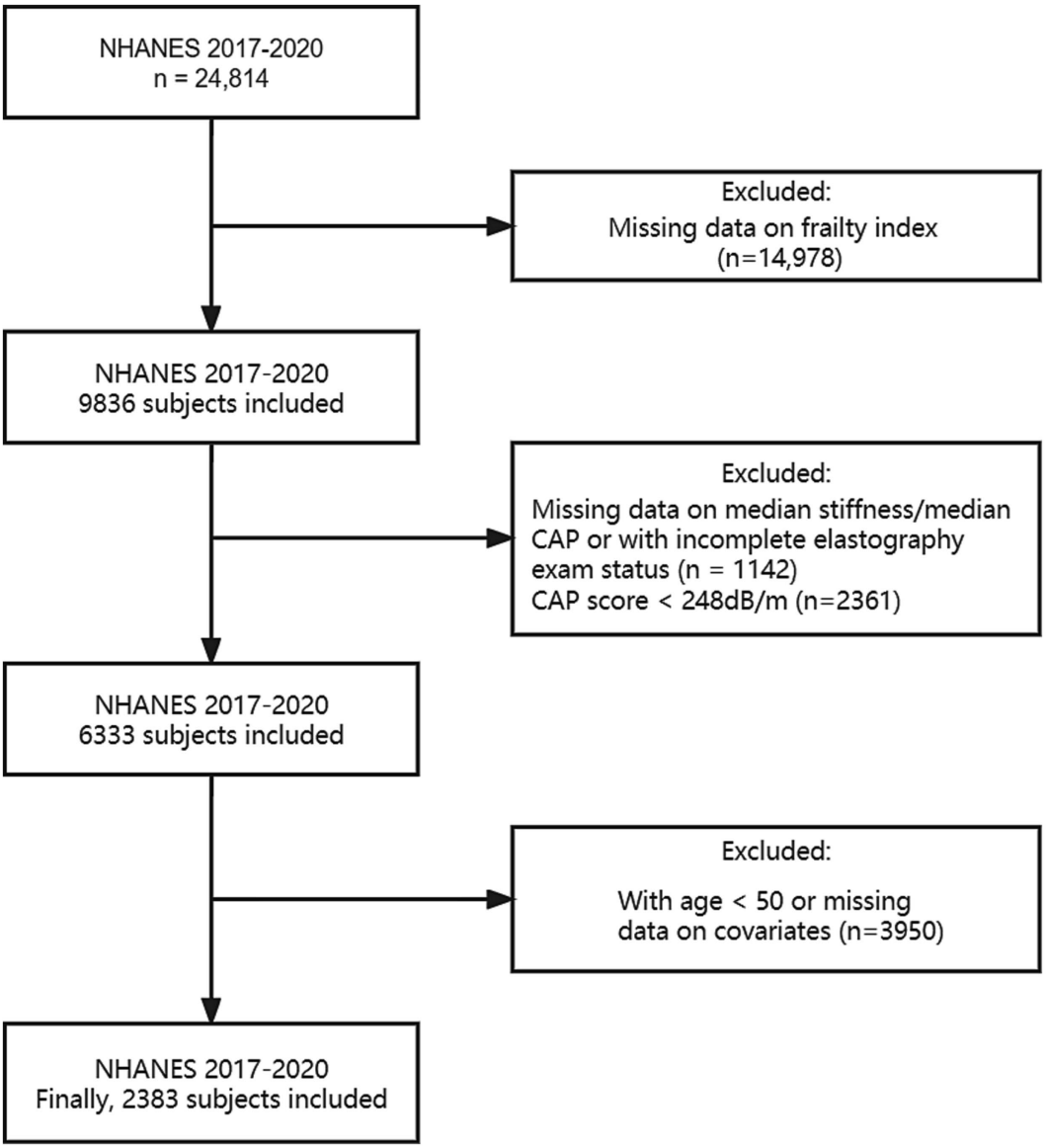

FIGURE 1
Flow chart for inclusion and exclusion.

(18). It's important to note that the probability of an individual being categorized as frail escalates in direct proportion to the number of deficits they manifest. The variables of the FI with their corresponding values are shown in Supplementary Table S1.

Covariate

Several factors were scrutinized as potential confounders, and were duly incorporated as adjustments within the analytical framework. Demographic data included age, sex, race/ethnicity and education level. Race/ethnicity categories were "non-Hispanic white," "non-Hispanic black," "Mexican American," "other races." Educational level included "<high school" and "≥high school." BMI, smoking status and alcohol behavior were evaluated as health conditions and lifestyle habits.

The smoking status classification divides the population into three segments based on whether or not they have smoked 100 cigarettes: never, former, and current smokers. Former and current smokers were differentiated according to whether or not they currently smoked (19). The alcohol behavior was divided into three separate categories, each representing unique patterns of alcohol consumption. Individuals who claimed to have consumed fewer than 12 alcoholic beverages throughout their lifetime were never-drinkers. Moderate drinkers were defined as 2 or more alcoholic beverage consumption in women or 3 or more in men per day. 3 or more alcoholic beverage consumption daily in women, or 4 or more drinks per day in men, combining a minimum of 5 binge drinking episodes per month were defined as heavy drinkers (20). Participants needed to be excluded if they were heavy drinkers. BMI was calculated by dividing the individual's measured weight in kilograms (kg) by the square of their measured height in meters (m^2), participants were divided into three

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categories and their corresponding values were: under/normal weight (<25 kg/m^2), overweight (25–29.9 kg/m^2) or obese (>30 kg/m^2). Hyperlipidemia (yes or no), globulin level (g/dL) and median CAP (dB/m) were also inserted in the adjustments. Hyperlipidemia was defined as triglycerides ≥150 mg/dL, total cholesterol ≥200 mg/dL, low-density lipoprotein (LDL) ≥130 mg/dL or high-density lipoprotein (HDL) ≤50 mg/dL in females and ≤40 mg/dL in males according to the National Cholesterol Education Program (21). All covariates are presented in Table 1.

Statistical analysis

Participants involved in this study were summarized and compared by groups with or without significant hepatic fibrosis. Continuous variables are expressed as mean ± SD, and categorical variables are presented as numbers (percentage). The Wilcoxon rank-sum test was used to test continuous data and linear regression analysis (coefficients and 95% confidence intervals) was performed to see the association between hepatic fibrosis with globulin level, median CAP and the FI. Chi-square test was used to calculate the difference in categorical variables presented as numbers (percentage) by group. The independent correlation between the frailty index and significance of hepatic fibrosis was calculated using multivariate logistic regression models by calculating odds ratios (ORs) and corresponding 95% confidence intervals (CIs). In order to minimize the risk of excessive adjustment for confounding variables that may mediate the relationships between the FI and significant hepatic fibrosis, we constructed three models. No variable was adjusted in model 0. Age, sex and race were adjusted in model 1. In model 2, age,

TABLE 1 Characteristics of participants with NAFLD by significant hepatic fibrosis status in the 2017–2020 NHANES.

		Significant fibrosis		
Characteristic	Overall, (*n* = 2,383)[a]	No, (*n* = 2001)[a]	Yes, (*n* = 382)[a]	*p* value[b]
Age (years)	62.88 ± 8.63	62.92 ± 8.53	62.63 ± 9.22	0.5
Gender, *n* (%)				0.7
Male	49.57	49.80	48.22	
Female	50.43	50.20	51.78	
Race/ethnicity, *n* (%)				0.011
Non-Hispanic White	71.60	72.78	64.37	
Non-Hispanic Black	7.83	7.40	10.47	
Mexican American	5.38	4.91	8.29	
Other	15.19	14.92	16.87	
Education level, *n* (%)				0.6
High school or above	90.75	90.91	89.75	
Less than high school	9.25	9.09	10.25	
BMI group, *n* (%)				<0.001
Under/normal weight	11.76	13.05	3.92	
Overweight	31.96	34.99	13.44	
Obese	56.27	51.96	82.65	
Smoking status, *n* (%)				0.10
Former	30.00	29.09	35.59	
Never	62.50	63.00	59.43	
Now	7.50	7.91	4.98	
Alcohol behavior, *n* (%)				0.086
Mild	65.88	66.02	65.03	
Moderate	22.37	23.06	18.12	
Never	11.75	10.92	16.85	
Hyperlipidemia, *n* (%)				0.7
No	15.73	15.93	14.51	
Yes	84.27	84.07	85.49	
Globulin (g/dL)	2.97 ± 0.40	2.95 ± 0.38	3.12 ± 0.47	0.001
Median CAP (dB/m)	307.31 ± 40.87	303.46 ± 39.17	330.89 ± 43.16	<0.001
FI	17.75 ± 9.85	17.29 ± 9.83	20.60 ± 9.48	<0.001

[a]Mean ± SD for continuous; *n* (%) for categorical.
[b]Wilcoxon rank-sum test for complex survey samples; chi-squared test with Rao & Scott's second-order correction.

sex, race, educational level, smoking status, alcohol behavior were adjusted. In model 3, BMI, hyperlipidemia, and globulin level was further adjusted. The FI (as continuous variable) was further divided into tertiles, and the lowest tertile serves as the reference group. Additionally, subgroup analyses were conducted, stratifying the subjects by gender, BMI, and hyperlipidemia. A value of $p < 0.05$ (two-sided) indicates statistical significance. We multiplied the frailty index by 100 to yield integer values. All analyses were performed using R (version 4.3.1).

Results

Study participants and baseline characteristics

Our study ultimately included 2,383 participants, of which 382 participants with significant fibrosis in NAFLD. 61.69% used medium (M) wand ($n = 1,470$), while 38.31% used extra large (XL) wand ($n = 913$), 16.03% subjects with NAFLD have significant fibrosis, and the characteristics of the participants are presented in Table 1. The average age of the population was 62.88 ± 8.63, and 50.43% were female. Statistically significant differences were observed in race, BMI, globulin levels, median CAP and FI between the two groups with or without significant fibrosis ($p < 0.05$). Specifically, the group with significant fibrosis had a higher proportion of females, obese, former smokers, never had alcohol behavior, higher globulin levels and higher FI as delineated in Table 1 and Figure 2.

Associations between the FI and significant fibrosis

A linear regression analysis was undertaken to explore the association between hepatic fibrosis and the variables in question among middle-aged and older adults, details are shown in Table 2. In the context of multivariate analysis, demographic attributes such as gender ($p = 0.194$) and educational level ($p = 0.599$) did not exhibit a significant correlation with the presence of hepatic fibrosis. However, age and races were discernibly linked with the status of hepatic fibrosis. Smoking status and BMI were associated with fibrosis ($p < 0.001$), while alcohol behavior was not ($p = 0.135$). There was a notable statistical correlation observed between the FI and hepatic fibrosis.

Three multivariable logistic regression analysis were constructed to examine the association between the FI and significance of hepatic fibrosis. In model 3, when considering the FI as a continuous variable, a one standard deviation increase in the FI was associated with an adjusted odds ratio (OR) of 1.022 (95% CI, 1.004–1.041) for significant fibrosis. Participants in the higher two tertiles of the FI displayed a significantly elevated risk of significant fibrosis when compared to those in the lowest tertile (Q1). Moreover, a positive correlation was observed between the FI and the presence of significant fibrosis in both the second (Q2) and third (Q3) tertiles. Additionally, this correlation remained significant even after controlling for potential confounding factors in model 2 (Q3 vs. Q1: OR = 2.874, 95% CI, 1.698–4.866) and model 3 (Q3vs Q1: OR = 2.004, 95% CI, 1.162–3.455). Details are presented in Table 3.

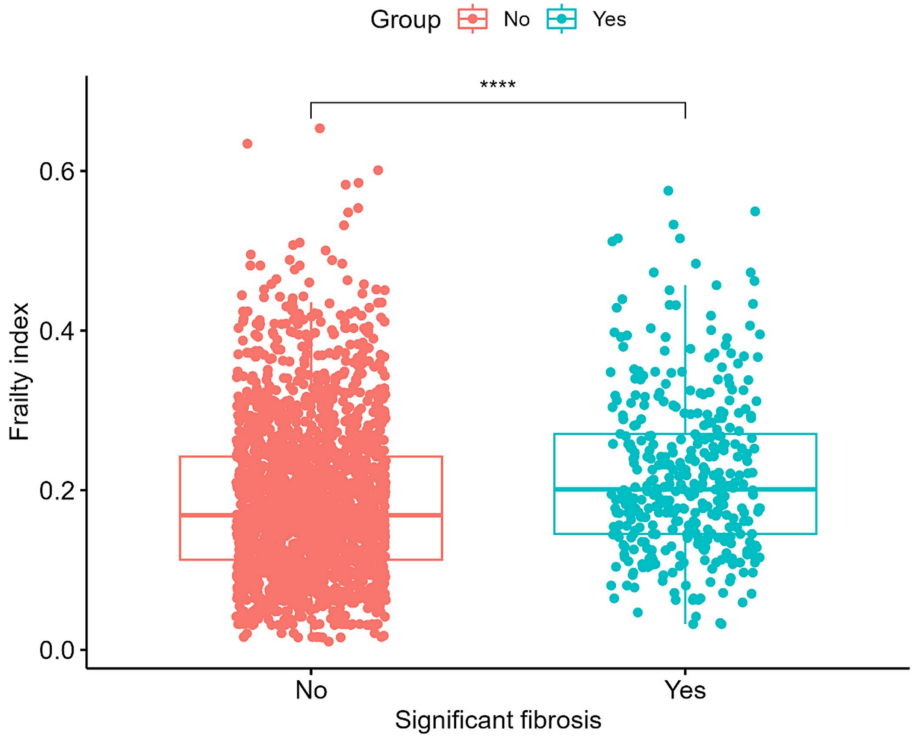

FIGURE 2
Levels of the frailty index in patients with and without significant hepatic fibrosis. ****$p < 0.0001$.

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TABLE 2 Risk factors for significant hepatic fibrosis.

Variable	β	Standard error	95% CI	*p* value
Age	−0.025	0.011	(−0.049 to-0.002)	0.038
Sex	0.257	0.198	(−0.151 to 0.665)	0.206
Races	1.278	0.391	(0.474 to 2.083)	0.003
Education	−0.235	0.466	(−1.155 to 0.685)	0.603
Smoke	−1.232	0.246	(−1.738 to-0.726)	0.001
Alcohol	−0.415	0.291	(−1.015 to 0.185)	0.167
BMI	1.551	0.338	(0.856 to 2.247)	0.001
Hyperlipidemia	0.142	0.282	(−0.439 to 0.723)	0.62
Globulin	0.975	0.341	(0.272 to 1.678)	0.008
FI	0.564	0.139	(0.278 to 0.850)	0.001

BMI, body mass index; FI, frailty index.

TABLE 3 Association between the frailty index and significant hepatic fibrosis in NAFLD.

Variable	Event/total	OR (95% CI)			
		Model 0[a]	Model 1[b]	Model 2[c]	Model 3[d]
FI	382/2383	1.032 (1.018, 1.046)***	1.033 (1.017, 1.050)***	1.036 (1.019, 1.053)***	1.022 (1.004, 1.041)*
FI (tertiles)					
Q1	79/792	Ref.	Ref.	Ref.	Ref.
Q2	140/798	2.745 (1.659, 4.540)**	2.852 (1.690, 4.815)**	2.859 (1.699, 4.812)**	2.386 (1.425, 3.994)**
Q3	163/793	2.688 (1.694, 4.268)**	2.792 (1.684, 4.627)**	2.874 (1.698, 4.866)**	2.004 (1.162, 3.455)*

[a]Model 0 no variable was adjusted.
[b]Model 1 adjusted for Age, Sex, and Races.
[c]Model 2 adjusted for Age, Sex, Races, Education, Smoke, and Alcohol.
[d]Model 3 adjusted for Age, Sex, Races, Education, Smoke, Alcohol, BMI, Hyperlipidemia, and Globulin.
*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

TABLE 4 Association between the frailty index and significant hepatic fibrosis in NAFLD by gender, BMI and hyperlipidemia.

Variable	OR (95% CI)		
	Model 1[a]	Model 2[b]	Model 3[c]
Stratified by gender[d]			
Male	1.057 (1.031, 1.082)***	1.058 (1.031, 1.086)***	1.046 (1.022, 1.071)***
Female	1.012 (0.990, 1.033)	1.014 (0.991, 1.039)	0.996 (0.970, 1.022)
Stratified by BMI			
Under/normal weight	1.029 (0.923, 1.148)	1.072 (1.009, 1.140)*	1.077 (1.009, 1.150)*
Overweight	1.046 (1.019, 1.073)***	1.042 (1.012, 1.072)**	1.040 (1.010, 1.071)**
Obese	1.018 (1.000, 1.037)	1.019 (0.997, 1.041)	1.016 (0.995, 1.038)
Stratified by Hyperlipidemia			
Yes	1.031 (1.016, 1.047)***	1.033 (1.017, 1.050)***	1.018 (0.999, 1.038)
No	1.050 (1.004, 1.098)*	1.051 (1.007, 1.096)*	1.054 (1.012, 1.097)*

[a]Model 1 adjusted for Age, Sex, and Races.
[b]Model 2 adjusted for Age, Sex, Races, Education, Smoke, and Alcohol.
[c]Model 3 adjusted for Age, Sex, Races, Education, Smoke, Alcohol, BMI, Hyperlipidemia, and Globulin.
[d]In the subgroup analysis by gender, the model was not adjusted for the stratification variable itself.*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

Nonetheless, upon stratification by gender, BMI, and hyperlipidemia, this association was not statistically significant among female (OR = 0.996, 95% CI, 0.970–1.022), obese (OR = 1.016, 95% CI, 0.995–1.038) and participants with hyperlipidemia (OR = 1.018, 95% CI, 0.999–1.038). The association between the FI and significant fibrosis in male has a similar result of the total population (OR = 1.046, 95% CI, 1.022–1.071) shown in Table 4.

Within the subgroup analyses that were stratified according to BMI classifications, a positive correlation was identified between the FI and significant fibrosis among participants under/normal weight (OR = 1.077,

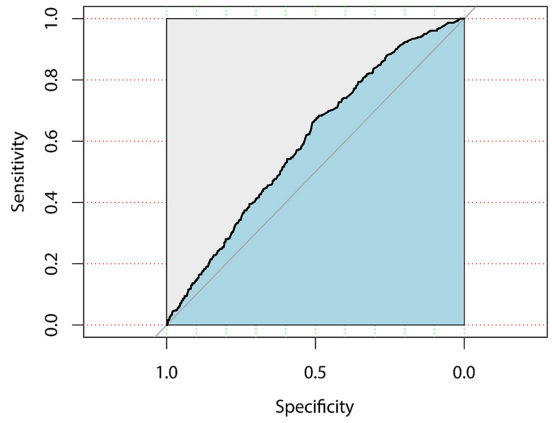

FIGURE 3
ROC curve for the frailty index in assessing the existence of significant fibrosis in NAFLD.

95% CI, 1.009–1.150) and overweight (OR = 1.040, 95% CI, 1.010–1.071) subjects in model3. Anyway, the positive association between the FI and significant fibrosis in NAFLD demonstrated variability in accordance with factors such as gender, BMI, and hyperlipidemia. The area under the Receiver Operating Characteristic (ROC) curve for the FI in assessing the existence of significant fibrosis in NAFLD was 0.612 (95% CI, 0.596–0.628), the ROC plot is presented in Figure 3.

Discussion

With the progression of population aging, there is an escalating prevalence of physiological decline and age-associated frailty among the older populace. This diminishment curtails their capacity to effectively confront ailments or traumas, consequently engendering a heightened susceptibility to adverse consequences. In recent years, the relationship between hepatic fibrosis and frailty has increasingly captured the attention of the academic community (22). Through an in-depth analysis of NHANES, our findings suggest that significant hepatic fibrosis is an important risk factor for frailty in middle-aged and older adults. The correlation was more statistically significant for non-obese males without hyperlipidemia.

Existing evidence indicate that the deterioration of health functions significantly contributes to the onset of frailty. This underscores the significance of safeguarding health conditions as a key lifeline for maintaining overall well-being and vitality. While geriatric studies have traditionally concentrated on exploring the connection between specific disorders and disease outcomes, taking into account overall frailty can offer a more holistic understanding. This is because frailty serves as a common endpoint for various health dysfunctions (23). Utilizing frailty indices, such as the FI, defined as a heightened susceptibility to physiological stress stemming from functional decline in various organ systems, can be advantageous in examining this aspect. The FI can help predict the risk of mortality, guide treatment decisions, and provide a more comprehensive understanding of the patient's health status (17). It is noteworthy that numerous studies have identified potential associations between the FI and a variety of age-related diseases, including heart failure (24), stroke (25), diabetes (26), and depression (27). The elucidated discoveries underscore the latent capability of evaluating comprehensive health condition as a means to comprehend the intricate nexus between factors of frailty and disease outcomes. Historical investigations have alluded to the fact that frailty is frequently observed in patients afflicted with NAFLD which is accompanied by advanced hepatic fibrosis or cirrhosis (28). This makes the evaluation of frailty assumes a pivotal role in managing patients with hepatic fibrosis.

Frailty and hepatic fibrosis are two interconnected conditions, and the connection between these two conditions lies in the impact of hepatic fibrosis on an individual's physical strength and resilience (29). A systematic review found that as hepatic fibrosis advances, a deterioration in patients' physical conditions is usually observed, triggering an increase in frailty (30). Factors such as fatigue, malnutrition and muscle wasting, commonly linked with advanced liver disease, are direct contributors to this increase in frailty. When NAFLD progresses to advanced stages, physiological resilience decreases and frailty ensues.

Several explanations can be offered to elucidate the potential mechanism of frailty in patients with significant fibrosis. First, in a large NAFLD cohort study performed by Koo et al. (31), sarcopenia was found to be significantly associated with significant fibrosis. At the pathophysiological echelon, alterations in the metabolic state of hepatic fibrosis engender a disequilibrium between energy requisites and intake, thereby instigating a metamorphosis in protein metabolism. This is particularly evident in the diminished circulating levels of branched-chain amino acids (bCAAs), which in turn accelerates muscular catabolism (32). The ratio of serum creatinine/serum cystatin C, as a surrogate marker for muscle mass, has been found to be significantly associated with frailty in multiple studies (33–35), consider that it is associated with falls, functional decline, disability and increased mortality in older adults.

Second, a study conducted by Leng et al. (36) revealed that pro-inflammatory markers such as IL-6 and tumor necrosis factor II were found to be elevated in individuals classified as frail. This highlights inflammation as a potential physiological source of frailty and suggests that it may serve as a biomarker for identifying high-risk patients. The intricate interplay among hepatocytes, macrophages, and hepatic stellate cells (HSCs), set within the context of the liver's inflammatory and oxidative milieu, serves as a pivotal determinant in the pathogenesis of fibrosis (37, 38). Thus, it is undeniable that liver fibrosis is intrinsically linked to frailty through inflammatory responses and elevated levels of oxidative stress (39, 40). Moreover, in a large community-based cohort study, researchers have found that cognitive function may be poorer in high-risk patients with advanced fibrosis compared to low-risk patients, particularly in terms of executive function and abstract reasoning (41). Current explanations for the relationship between liver fibrosis and low cognitive function include oxidative stress, insulin resistance, and adipokine secretion (42). At the same time, among older adults, frailty is associated with poorer processing speed, sustained attention, working memory, and global cognition (43). From there, it is considered that significant hepatic fibrosis may be associated with frailty in the older people through altered cognitive status. The compounding effects of these biological processes underscore the confluence of systemic biological deterioration that typifies the frailty syndrome. This provides a plausible explanation for more than one interaction between significant hepatic fibrosis and frailty.

The relationship between significant hepatic fibrosis and the FI can have important clinical implications. For example, the coexistence of hepatic fibrosis and a high FI can stratify patients into higher risk categories, as both conditions can synergistically lower a patient's

physiological reserve and increase the risk of adverse outcomes. This stratification can be critical in managing patient care. Also, before considering a patient for a liver transplant or other major surgeries, the FI can be a valuable tool to assess their ability to withstand surgery and recover postoperatively. Those with higher frailty may require more rigorous preoperative optimization.

Interventions aimed at reducing frailty – such as nutritional support, physical activity, and muscle training – can also play a crucial role in managing hepatic fibrosis (31). It warrants acknowledgment that the interplay between frailty and hepatic fibrosis presents complexity, given their potential to reciprocally influence each other in numerous ways, thereby posing challenges to the efficacy of management strategies.

Yet, there is still a lack of comprehensive understanding regarding the influence of hepatic fibrosis on frailty (44) and the potential underlying mechanisms need more large-sample studies. It is also possible that hepatic fibrosis is associated with frailty through hepatocellular carcinoma as an ultimate consequence of liver disease and its impact on metabolic dysregulation and nutritional status. Exploring the possible link between hepatic fibrosis and frailty cannot be accomplished with cross-sectional data. To confirm the association between fibrosis and frailty, future studies must be longitudinal in design.

The research undertook an extensive examination of the correlation between the FI and substantial hepatic fibrosis using an expansive sample study in NAFLD. It also accounted variables that could skew the data, thereby enhancing the credibility of the findings. However, there are limitations to our studies. Firstly, the use of the FI and their respective scorings for frailty appraisal may have led to inaccuracies and unclear categorization. Secondly, the individuals of this research were all aged 50 years and above, so there may be limitations to the applicability of our findings to individuals below the age of 50. Finally, the liver stiffness measurement (LSM) threshold for evaluating hepatic fibrosis has shown variations across distinct studies, thus lacking a consensus standard for detecting steatosis.

Conclusion

In summarization, an evaluation of frailty via the FI revealed a correlation with the significant hepatic fibrosis of NAFLD in middle-aged and older adults. Elevated FI exhibited a direct correlation with significant fibrosis in NAFLD patients, suggesting the FI may be a potential prospective biomarker for the assessment of hepatic fibrosis in this patient cohort. This association was particularly pronounced among male individuals, those categorized as non-obese, and subjects devoid of hyperlipidemia. Further studies, such as longitudinal studies, are needed to confirm the exact relationship between the FI and hepatic fibrosis and the underlying mechanisms.

Data availability statement

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

Ethics statement

The studies involving human data were conducted by utilizing the publicly available datasets provided by the National Health and Nutrition Examination Survey (NHANES), which is a program of studies designed to assess the health and nutritional status of adults and children in the United States and is managed by the Centers for Disease Control and Prevention (CDC). These datasets are collected by the NHANES with the appropriate consent and ethical approval from the participants, in compliance with the CDC's ethical standards as stated on their website (https://www.cdc.gov/nchs/nhanes/). Given that our study did not involve direct interaction with human subjects and relied entirely on these de-identified, publicly available datasets, further ethical approval from our institution was not necessary.

Author contributions

FA: Writing – original draft, Writing – review & editing. X-JL: Writing – review & editing. AA: Writing – review & editing. JL: Software, Writing – review & editing. YZ: Data curation, Writing – review & editing. YA: Methodology, Writing – review & editing. H-LG: Conceptualization, Writing – review & editing. Z-QZ: Conceptualization, Funding acquisition, Writing – review & editing.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. This work was supported by grants from the Tianshan Innovative Research Team of Xinjiang Uygur Autonomous Region, China (grant number 2022TSYCTD0018).

Acknowledgments

We extend our gratitude to the NHANES team for their provision of the data.

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.2024.1330221/full#supplementary-material

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frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 05 April 2024
DOI 10.3389/fpubh.2024.1361745

OPEN ACCESS

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RECEIVED 26 December 2023
ACCEPTED 21 March 2024
PUBLISHED 05 April 2024

CITATION
Zhang Y, Yu G, Bai W, Wu S, Geng X, Zhang W, Liu Y, Meng Y, Gao J, Li W and Kou C (2024) Association of depression and sleep quality with frailty: a cross-sectional study in China. *Front. Public Health* 12:1361745. doi: 10.3389/fpubh.2024.1361745

Association of depression and sleep quality with frailty: a cross-sectional study in China

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Background: With the rapid growth of global aging, frailty has become a serious public health burden, affecting the life quality of older adults. Depressive symptoms (depression hereafter) and sleep quality are associated with frailty, but the pathways in which sleep quality and depression affect frailty remain unclear.

Method: This cross-sectional study included 1866 community-dwelling older adults. Demographic characteristics and health-related data of them was collected, and we also assessed frailty, depression, and sleep quality. Descriptive statistics were carried out and ordinal logistic regression analysis was used to identify the factors correlated with frailty. Spearman correlation analysis and mediation analysis were employed to assess associations between sleep quality, depression and frailty. Two-sided $p < 0.05$ was considered as significant.

Results: The results showed that 4.1% older adults were frail and 31.0% were pre-frail. Ordinal logistic regression showed that age, consumptions of vegetables, exercise, sleep quality, depression, number of chronic diseases, chronic pain, and self-rated health were correlated with frailty. Spearman correlation analysis revealed that frailty was associated with depression and sleep quality. There was a mediation effect that sleep quality was a significant and positive predictor of frailty (total effect = 0.0545, 95% boot CI = 0.0449–0.0641), and depression was a mediator between sleep quality and frailty (mediation effect = 60.4%).

Conclusion: Depression and poor sleep quality may be early indicators of frailty in older adults. Improving the sleep quality and psychological state of older adults can improve frailty, which is beneficial for healthy aging.

KEYWORDS

frailty, depression, sleep quality, older adults, community, mediation effect

1 Introduction

Population aging is an increasing global social concern (1). The proportion of the population over 65 years old is expected to rise from 10% in 2022 to 16% by 2050 (2). Physical function varies among older adults, with some older adults being dependent and limited by disease or disability (3). Severe functional impairments can lower life quality in older adults, and occupy medical financed or community care systems (4, 5). Therefore, while prolonging

remaining years of life of older adults, more attention should be paid to extending healthy life expectancy (6).

Frailty of older adults is a new frontier in medicine, often seen as a precursor to age-related diseases (7, 8). It describes a clinical state of decompensation in the presence of stressors, as a result of the unstable homeostasis of body composition and physiological systems due to multisystem changes (9). This implies that minor stressor events could also lead to major changes in the health status of the older adults with frailty (10). Frailty is considered as a biological syndrome, and includes five physical components, which are fatigue, resistance, ambulation, illness, and loss of weight. Frailty is considered when three or more of these components are present. Pre-frailty is the classification given when one or two of the components, and robust is given to an individual who has no frailty component (10, 11). A previous study in Chinese older adults found that 27.5% were frail, and 51.3% were pre-frail (12). Besides, frailty is a dynamic process, which means that pre-frail older adults may progress to a robust or frail state, but more commonly, the transition tends to be in a worse direction (10, 13). A 10-year prospective cohort study proved that frailty was the principal cause of death (14). Additionally, a meta-analysis indicated that reducing frailty could effectively improve life quality in older adults (15). Hence, it is vital to identify the high-risk population with frailty and provide early intervention to them.

According to current research, psychological problems and sleep problems in older adults were related to frailty (16, 17). Depression is widely prevalent among older adults, and its presentation and outcomes differ from those of young people. A study reported that 40.4% of older adults with depression also had frailty, and the odds of experiencing frailty increased compared with those who did not have depression (18). Sleep disturbances and fatigue are widespread in older adults (19). As people grow older, sleep patterns tend to change gradually, which may affect their ability to fall asleep and stay asleep (20). A prospective study discovered that keeping healthy sleep patterns contributed to a lower risk of being frail and pre-frail, and sleep difficulties were associated with frailty (21). However, some studies demonstrated a potential bidirectional association between depression and sleep quality, in which sleep disturbances might exacerbate depression, and older adults with depression often experienced poor sleep quality (22–24). Furthermore, depression and sleep disturbances usually exist as comorbidities (25). Sleep disturbance is a core symptom of depression, and more than 90% of patients with depression have sleep disturbances (26).

Given the aforementioned, frailty had a major impact on older adults, but unlike certain irreversible physical disabilities, it could be prevented and reversed. Psychological and sleep problems were closely associated with frailty. Addressing the psychological and sleep issues of older adults provides a solution to dealing with frailty. However, few studies have investigated the paths in which sleep and depression affect frailty (27). Hence, the objectives of this study were to explore the mediating effect of depression and sleep quality on frailty, and analyzing the factors that increase the risk of frailty in older adults.

Abbreviations: CHSC, community health service centers; g, gram; FRAIL, Fatigue, Resistance, Ambulation, Illness and Loss of Weight Index; PHQ-9, Patient Health Questionnaire-9; PSQI, Pittsburgh Sleep Quality Index; CI, confidence intervals; OR, odds ratio.

2 Materials and methods

2.1 Data

Data were collected from 10 communities in Changchun, Jilin Province, China between July 2022 and September 2022. The participants were included if they were older adults aged 65 or older, were willing to participate, lived in the community for at least 6 months, had clear consciousness, and communicated normally. We excluded those with severe cognitive dysfunction or physical illness, and questionnaires that did not pass consistent quality control measures. All participants or their respondents provided informed consent. The study finally included 1866 participants after excluding 152 invalid questionnaires. Considering the simultaneity of the implementation of the study with the COVID-19 pandemic, both investigators and participants were with necessary precaution to avoid the risk of contagion. Moreover, at the time of the investigation, the region was not experiencing a pandemic outbreak, and the permanent residents had largely returned to their normal routines. Therefore, face-to-face interviews could be carried out normally. During face-to-face interviews with, investigators who received standardized training completed the questionnaires based on the answers provided by the older adults at community health service centers (CHSC). The gathered data was entered into digital survey forms. Before conducting formal investigations, preliminary investigations were carried out to ensure the feasibility and appropriateness of the projects. Participants completed the informed consent, and were informed that there were no unknown risks present throughout the study to promote cooperation. The filling process of the questionnaires was conducted objectively.

2.2 Basic characteristics

Sociodemographic and health-related data were obtained using a structured questionnaire: (i) age, gender, nation, education, marital status, live alone, and monthly income; (ii) smoking, drinking, vegetables, fruits, and exercise; (iii) number of chronic diseases, chronic pain, and self-rated health. Smoking and drinking were determined by cigarette consumption and drinking frequency, respectively. Based on the Dietary Guidelines for Chinese Residents (28) and recommendations of the EAT-Lancet Commission (29), consumptions of vegetables were divided into the following groups based on weight of uncooked edible portions per day: 0–200 g, 201–300 g, 301–500 g, and more than 500 g. Similarly, consumptions of fruits were categorized into the following groups by edible portion: 0–100 g, 101–200 g, 201–350 g, and more than 350 g (28, 29). Exercise was defined as physical activities, such as dancing or exercises, which could cause a faster heartbeat or mild sweating. Chronic diseases referred to diseases previously diagnosed by hospitals. Chronic pain was considered as self-perceived chronic pain with a frequency of at least 3–4 times a week, and self-rated health was classified as good, moderate, or bad.

2.3 Questionnaires

Frailty was assessed using the Fatigue, Resistance, Ambulation, Illness and Loss of Weight Index (FRAIL), which was developed in

2008 by the International Association of Nutrition and Aging (30), and modified by Morley et al. (11). Compared with other short screening tools, FRAIL had good performance in frailty (31). The scale contained 5 items: (i) fatigue: feeling tired most of the time in the past month; (ii) resistance: feeling difficult to climb 10 steps by yourself and not using aids; (iii) ambulation: unable to walk continuously for 100 meters independently; (iv) illness: more than 5 illnesses; (v) loss of weight: weight loss of unknown reason more than 5% within 1 year. Each item was answered using a dichotomous "yes" or "no" response, and 1 point was given if the answer was "yes." The total score ranged from 0 to 5, with 0 as not-frail, 1–2 points as pre-frail, and ≥3 points as frail. The Cronbach's alpha was 0.716 in this study.

The Pittsburgh Sleep Quality Index (PSQI) was used to measure sleep quality which was designed by Buysse et al. (32). The scale included a total of 24 items, with 19 self-rated questions used for scoring. The PSQI was divided into 7 component scores, including sleep latency, sleep duration, sleep disturbances, subjective sleep quality, use of sleeping medications, habitual sleep efficiency, and daytime dysfunction. The score of each component was 0–3 points, and the total score of PSQI was the sum of the above 7 component scores, resulting in a range of 0–21 points. Participants were considered as poor sleep quality when the total score of PSQI was above 5. A higher score indicates worse sleep quality. The Cronbach's alpha was 0.715 in this study.

The Patient Health Questionnaire-9 (PHQ-9), a concise and valid tool to identify the severity of depressive symptoms, was developed by Columbia University in the United States, and has been widely used for depression screening (33, 34). The scale consisted of 9 items, with each item scoring from 0 (not at all) to 3 (nearly every day). The total scores ranged from 0 to 27, which was divided into normal (0–4), mild depression (5–9), moderate depression (10–14), moderate severe depression (15–19), and severe depression (20–27). The PHQ-9 was found to have excellent internal reliability (35), with a Cronbach's alpha of 0.882 in this study.

2.4 Statistical analysis

Sociodemographic characteristics and health-related factors used in this study were all categorical variables, and descriptive statistics were utilized to summarize. Frailty was classified it into three states: robust, pre-frail, and frail, with a hierarchical relationship among them. Distributions of frailty status were compared across different groups (i.e., demographic variables) using Mann–Whitney *U* test or Kruskal–Wallis test as appropriate. A multivariate analysis was performed by ordinal logistic regression to evaluate the risk factors for frailty in older adults. The test of parallel lines was used to assess whether the proportional odds assumption was violated in the ordinal logistic regression model. Spearman correlation analysis was used to find whether there was a connection between sleep quality, depression, and frailty. Moreover, mediation analysis was carried out, and 95% confidence intervals (CI) were assessed using bootstrapping (5,000 bootstrapped samples). SPSS (Version 24.0) and R (version 4.2.2), and PROCESS Procedure for SPSS v3.5 were used. A significant level was set at 2-sided $p < 0.05$.

3 Results

3.1 Demographic characteristics

The results showed that 53.1% participants were 65–69 years old. And the participants were classified into three frailty status, non-frail (64.9%), pre-frail (31.0%), and frail (4.1%). As is shown in Table 1, differences were significant in different age groups across three frailty status groups (χ^2=9.480, $p = 0.024$). Female participants had higher ratios of pre-frailty and frailty compared to male participants ($Z = -2.723$, $p = 0.006$). Among participants with a college degree and above, the prevalence of pre-frailty was higher, with a prevalence of 40.2%, than in other participants. However, there was no significant effect of nation, marital status, live alone, and monthly income across three frailty status groups.

3.2 Social and health factors

The results showed that there were significant differences between non-frail, pre-frailty, and frailty participants in terms of their daily consumption of vegetables ($\chi^2 = 27.395$, $p < 0.001$) and fruits ($\chi^2 = 15.802$, $p = 0.001$). Prevalence of pre-frailty (29.6%) and frailty (3.6%) was lower in participants who usually exercise, compared to those who did not ($Z = -4.864$, $p < 0.001$). In addition, results indicated that depression was also a significant factor across three frailty status groups ($Z = -16.710$, $p < 0.001$). Furthermore, participants with pre-frailty and frailty tended to have poorer sleep quality ($Z = -14.868$, $p < 0.001$). The results also revealed significant differences in the number of chronic diseases ($\chi^2 = 218.491$, $p < 0.001$), chronic pain ($Z = -17.724$, $p < 0.001$), and self-rated health ($\chi^2 = 266.489$, $p < 0.001$) across different status of frailty (Table 2 and Figure 1).

3.3 Ordinal logistic regression analysis

In the ordinal logistic regression analysis, age ≥ 80 displayed a significant increase in the ordinal frailty status (OR = 1.474, 95% CI = 1.065–2.040). Daily consumption of vegetables more than 300 g had positive effects on pre-frailty and frailty. Exercise was associated with decreased risks of pre-frailty and frailty (OR = 0.562, 95% CI = 0.414–0.762). Poor sleep quality (OR = 1.795, 95% CI = 1.373–2.346), and depression (OR = 3.899, 95% CI = 2.783–5.464) were found to be associated with increased risks. Significant associations between number of chronic diseases, chronic pain, self-rated health and frailty status were also found, indicating that number of chronic diseases (≥2) (OR = 2.248, 95% CI = 1.659–3.047), participants experiencing chronic pain (OR = 3.322, 95% CI = 2.557–4.315), and a moderate (OR = 1.397, 95% CI = 1.084–1.801) or bad health state (OR = 5.795, 95% CI = 3.734–8.995) had negative effects on frailty status. However, no statistically significant differences were found in gender, education, and fruits in the ordinal frailty status. The results of test of parallel lines showed that the model followed the proportional odds assumption ($p = 0.200$) (Table 3 and Supplementary Figure S1).

TABLE 1 Distributions of frailty status across different demographic characteristics.

Variable		Overall *n* (%)	Frailty status			Z/χ^2	*p*
			Non-frail *n* (%)	Pre-frail *n* (%)	Frail *n* (%)		
Overall	–	1866 (100.0)	1,211 (64.9)	578 (31.0)	77 (4.1)	–	–
Age, years	65–69	990 (53.1)	656 (66.3)	295 (29.8)	39 (3.9)	9.480	0.024
	70–74	421 (22.6)	285 (67.7)	121 (28.7)	15 (3.6)		
	75–79	197 (10.6)	122 (61.9)	65 (33.0)	10 (5.1)		
	≥80	258 (13.8)	148 (57.4)	97 (37.6)	13 (5.0)		
Gender	Man	619 (33.2)	429 (69.3)	166 (26.8)	24 (3.9)	−2.723	0.006
	Woman	1,247 (66.8)	782 (62.7)	412 (33.0)	53 (4.3)		
Nation	Han	1779 (95.3)	1,150 (64.6)	555 (31.2)	74 (4.2)	−1.038	0.299
	Others	87 (4.7)	61 (70.1)	23 (26.4)	3 (3.4)		
Education	Primary school and below	377 (20.2)	239 (63.4)	118 (31.3)	20 (5.3)	14.098	0.003
	Junior middle school	758 (40.6)	511 (67.4)	222 (29.3)	25 (3.3)		
	Senior middle school/technical secondary school	487 (26.1)	327 (67.1)	140 (28.7)	20 (4.1)		
	College degree and above	244 (13.1)	134 (54.9)	98 (40.2)	12 (4.9)		
Marital status	Married	1,306 (70.0)	862 (66.0)	386 (29.6)	58 (4.4)	−1.298	0.194
	Not married	560 (30.0)	349 (62.3)	192 (34.3)	19 (3.4)		
Live alone	Yes	356 (19.1)	235 (66.0)	109 (30.6)	12 (3.4)	−0.580	0.562
	No	1,510 (80.9)	976 (64.6)	469 (31.1)	65 (4.3)		
Monthly income, yuan	<2000	425 (22.8)	271 (63.8)	137 (32.2)	17 (4.0)	4.017	0.134
	2000–5,000	1,261 (67.6)	835 (66.2)	373 (29.6)	53 (4.2)		
	>5,000	180 (9.6)	105 (58.3)	68 (37.8)	7 (3.9)		

3.4 Spearman correlation analysis and mediation effect

Spearman correlation analysis revealed that participants with depression had worse sleep quality ($r = 0.602$, $p < 0.001$) and higher frailty ($r = 0.492$, $p < 0.001$). In addition, there was a correlation between poor sleep quality and frailty ($r = 0.403$, $p < 0.001$), presented in Table 4. In this study, age, vegetables, exercise, number of chronic diseases, chronic pain, and self-rated health were associated with frailty through ordinal logistic regression, which we deemed as covariates. And according to previous research (36), we also included gender as a covariate. After controlling for covariates, results of mediation analysis revealed that poor sleep quality was a significant positive predictor of frailty (total effect = 0.0545, 95% boot CI = 0.0449–0.0641). The indirect effect of poor sleep quality on frailty mediated by depression was found (indirect effect = 0.0329, 95% boot CI = 0.0246–0.0416), and the indirect effect accounted for 60.4% of the total effect of poor sleep quality on frailty. Considering the bidirectional effect of depression and sleep quality, the study also selected sleep quality as a mediator variable. The direct effect of depression on frailty was 0.0721 (95% boot CI = 0.0614–0.0829), which accounted for 87.3% of the total effect of depression on frailty (total effect = 0.0826, 95% boot CI = 0.0731–0.0922) (Supplementary Table S1 and Figure 2).

4 Discussion

The study found that depression mediated the effect of sleep quality on frailty, and sleep quality also mediated the effect of depression on frailty. The latter had a weaker effect than the former. The results indicated that roughly 35% of community-dwelling older adults were either frail or pre-frail. Demographic characteristics and health-related factors were associated with pre-frailty and frailty in older adults.

Results showed that 4.1% of participants in Chinese community-dwelling older adults were frail, and 31.0% were pre-frail, which was similar to Li's study (37), but lower than the findings reported in other previous studies (38–40). Differences in the tools used for assessing frailty may explain this variation (31). The prevalence of frailty in older adults also differed across various regions and cultures (36, 41). Moreover, the analyzed participants may differ in age and other factors from previous studies. In this study, age, vegetables, exercise, sleep quality, depression, number of chronic diseases, chronic pain, and self-rated health had associations with frailty, which had also been supported by previous studies (42, 43). Although, some studies had suggested a connection between gender and frailty (44, 45), this study did not support this finding. In addition, after adjusting for covariates, education level was no longer significantly associated with frailty in older adults. The effect of education level as a social factor on frailty varies among individuals. Contrary to some previous studies, daily consumption of fruits did not have significant associations with frailty in this study (44,

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TABLE 2 Distributions of frailty status across different social and health factors.

Variable		Overall *n* (%)	Frailty status			Z/χ^2	*p*
			Non-frail *n* (%)	Pre-frail *n* (%)	Frail *n* (%)		
Smoking	Yes	352 (18.9)	236 (67.0)	97 (27.6)	19 (5.4)	−0.697	0.486
	No	1,514 (81.1)	975 (64.4)	481 (31.8)	58 (3.8)		
Drinking	Yes	268 (14.4)	171 (63.8)	89 (33.2)	8 (3.0)	−0.237	0.812
	No	1,598 (85.6)	1,040 (65.1)	489 (30.6)	69 (4.3)		
Vegetables, gram	0–200	87 (4.7)	37 (42.5)	39 (44.8)	11 (12.6)	27.395	<0.001
	201–300	440 (23.6)	275 (62.5)	141 (32.0)	24 (5.5)		
	301–500	651 (34.9)	437 (67.1)	192 (29.5)	22 (3.4)		
	≥501	688 (36.9)	462 (67.2)	206 (29.9)	20 (2.9)		
Fruits, gram	0–100	411 (22.0)	236 (57.4)	151 (36.7)	24 (5.8)	15.802	0.001
	101–200	541 (29.0)	374 (69.1)	150 (27.7)	17 (3.1)		
	201–350	543 (29.1)	355 (65.4)	161 (29.7)	27 (5.0)		
	≥351	371 (19.9)	246 (66.3)	116 (31.3)	9 (2.4)		
Exercise	Yes	1,629 (87.3)	1,089 (66.9)	482 (29.6)	58 (3.6)	−4.864	<0.001
	No	237 (12.7)	122 (51.5)	96 (40.5)	19 (8.0)		
Sleep quality	High	1,400 (75.0)	1,036 (74.0)	340 (24.3)	24 (1.7)	−14.868	<0.001
	Poor	466 (25.0)	175 (37.6)	238 (51.1)	53 (11.4)		
Depression	Yes	255 (13.7)	56 (22.0)	147 (57.6)	52 (20.4)	−16.710	<0.001
	No	1,611 (86.3)	1,155 (71.7)	431 (26.8)	25 (1.6)		
Number of chronic diseases	0	576 (30.9)	473 (82.1)	100 (17.4)	3 (0.5)	218.491	<0.001
	1	455 (24.4)	340 (74.7)	113 (24.8)	2 (0.4)		
	≥2	835 (44.7)	398 (47.7)	365 (43.7)	72 (8.6)		
Chronic pain	Yes	452 (24.2)	145 (32.1)	243 (53.8)	64 (14.2)	−17.724	<0.001
	No	1,414 (75.8)	1,066 (75.4)	335 (23.7)	13 (0.9)		
Self-rated health	Good	1,091 (58.5)	838 (76.8)	246 (22.5)	7 (0.6)	266.489	<0.001
	Moderate	645 (34.6)	350 (54.3)	261 (40.5)	34 (5.3)		
	Bad	130 (7.0)	23 (17.7)	71 (54.6)	36 (27.7)		

46). Several studies have shown that poor nutrition has been identified as a risk factor for frailty (47, 48). However, nutrition may not be entirely equivalent to the consumption of fruits and vegetables, and older adults may consume dairy products and nutraceuticals in addition to meals to supplement their nutritional needs. Additionally, dietary intervention is usually combined with exercise training, and there is insufficient evidence to suggest that diet alone can prevent or cure frailty (48).

Consistent with previous studies, the prevalence of pre-frailty was higher than that of frailty (12, 37). Similar to frailty, pre-frailty is also associated with an increased risk of psychological distress, diabetes, multiple sclerosis, stroke, myocardial infarction, and other chronic diseases, and mortality (49, 50). According to the findings, 31.0% of older adults aged ≥65 in the community had pre-frailty. Given the dynamics of frailty, it is important to pay attention to the pre-frailty, as it has the potential to advance to a worse state of frailty at any given moment (51, 52). Some studies suggested that frailty should be seen as a continuous procession, with the occurrence of frailty being associated with an increased risk of adverse outcomes, and there was a dose–response association between frailty and adverse outcomes (51, 52). Lifestyle or behavioral interventions, a balanced diet, regular exercise, and increased social engagement can aid in the prevention of frailty (53, 54). It is, therefore, advisable for a rapid screening test for frailty to be included in routine community screening programs, which contributes to timely management of continuous and dynamic frailty process in older adults, and provides appropriate intervention measures. This work has the potential to alleviate the economic and psychological strain of frailty on individuals, families, and caregivers, as well as reduce the burden on the national healthcare system.

Older adults residing in communities with poorer sleep quality were at greater risk of frailty. The prevalence of frailty in older adults with poor sleep quality was 1.795 times higher than those with good sleep quality, consistent with prior research (17). Older adults with sleep disorders may experience adverse outcomes such as decreased grip strength, fatigue, and slow walking speed, which are typical symptoms of frailty (55–57). Studies have shown that a correlation between prolonged or decreased sleeping hours and frailty (17, 58). In addition to sleep duration, the components of sleep quality in PSQI, such as sleep latency, sleep disturbance, poor subjective sleep quality, sleep efficiency, and daytime dysfunction components have also been proven to be associated with frailty (59). Thus, it is important for older

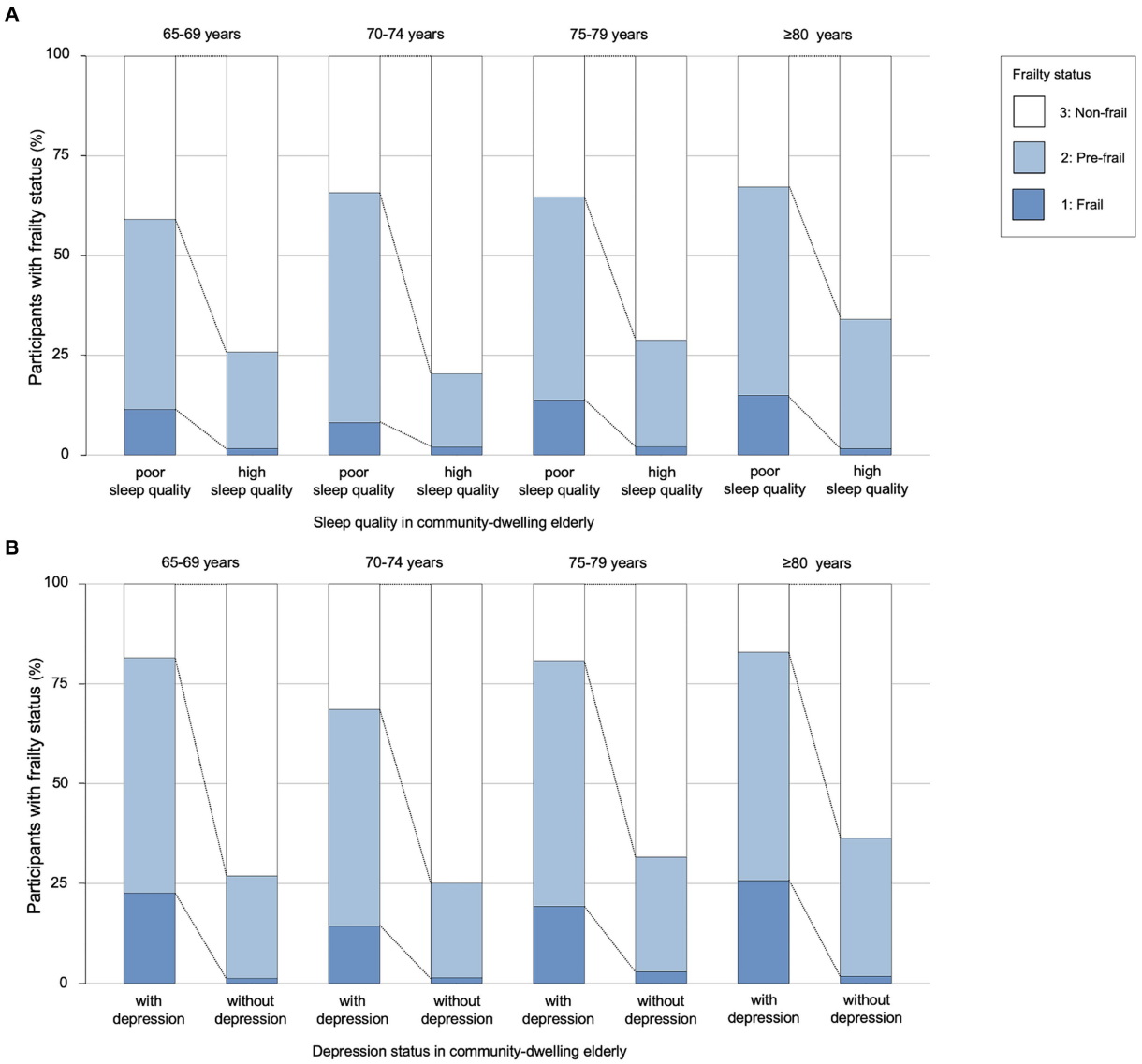

FIGURE 1
The association between sleep quality, depression and frailty in four age groups. **(A)** Sleep quality in community-dwelling older adults. **(B)** Depression status in community-dwelling older adults. The older adults were divided into four age groups. Each group was divided by sleep quality in **(A)** and by depression status in **(B)**. There were significant differences in the prevalence of frailty between the sleep quality groups and the depression status groups of older adults.

adults experiencing a decline in sleep quality to be alert to the possibility of developing or worsening frailty.

Depression in older adults is also associated with frailty. Given the results of this study, 13.7% of older adults experienced depression. Older adults with depression in the community were 3.8 times more likely to suffer from frailty than those without depression, which was consistent with a previous prospective cohort study (16). Studies have demonstrated that older adults with depression and frailty are more likely to develop suicidal ideation, which poses a serious threat to their safety (60). Common symptoms of depression include low mood, cognitive decline, worsening physical illness, decreased positive affect or pleasure in response to social contacts and routine activities, and social isolation or withdrawal (61). Such symptoms often lead to a decrease in social activity in older adults with depression and may trigger sarcopenia, thus increasing the likelihood of frailty in this population (62, 63). Furthermore, chronic pain was identified to be correlated with of frailty. Previous studies have shown that depression may play a mediating role, and that non-frail older adults with chronic pain are more likely to experience physical frailty after a follow-up period (64). Chronic pain in older adults should be effectively intervened, because it may alleviate their depression and improve their frailty. Additionally, exercise has been shown to effectively treat depression and is associated with frailty (65, 66). However, it should be noted that exercise may pose a risk to some older adults with chronic diseases. This study indicated that frail older adults had a higher risk of multiple chronic diseases than robust older adults. Furthermore, previous research suggested that older adults with multiple chronic diseases had an increased risk of depression (67).

We proposed that depression and poor sleep quality were potential early indicators of frailty. Building on the known findings that both

10.3389/fpubh.2024.1361745

TABLE 3 Model of factors associated frailty.

Variable	β	*SE*	Waldχ^2	*p*	OR (95%CI)
Age, years					
65–69	–	–	–	–	1.000
70–74	−0.366	0.147	6.228	0.013	0.694 (0.520–0.924)
75–79	0.076	0.183	0.172	0.678	1.079 (0.754–1.543)
≥80	0.388	0.166	5.462	0.019	1.474 (1.065–2.040)
Gender					
Man	–	–	–	–	1.000
Woman	−0.021	0.123	0.029	0.865	0.979 (0.770–1.246)
Education					
Primary school and below	–	–	–	–	1.000
Junior middle school	−0.074	0.156	0.228	0.633	0.928 (0.684–1.259)
Senior middle school/ technical secondary school	−0.203	0.171	1.411	0.235	0.816 (0.584–1.141)
College degree and above	0.044	0.194	0.052	0.819	1.045 (0.715–1.529)
Vegetables, gram					
0–200	–	–	–	–	1.000
201–300	−0.501	0.264	3.608	0.058	0.606 (0.361–1.016)
301–500	−0.581	0.261	4.962	0.026	0.559 (0.335–0.933)
≥501	−0.694	0.264	6.915	0.009	0.499 (0.298–0.838)
Fruits, gram					
0–100	–	–	–	–	1.000
101–200	−0.230	0.160	2.082	0.149	0.794 (0.581–1.086)
201–350	0.074	0.159	0.214	0.644	1.076 (0.788–1.471)
≥351	0.149	0.182	0.674	0.412	1.161 (0.813–1.657)
Exercise					
No	–	–	–	–	1.000
Yes	−0.576	0.156	13.718	<0.001	0.562 (0.414–0.762)
Sleep quality					
High	–	–	–	–	1.000
Poor	0.585	0.137	18.288	<0.001	1.795 (1.373–2.346)
Depression					
No	–	–	–	–	1.000
Yes	1.361	0.172	62.490	<0.001	3.899 (2.783–5.464)
Number of chronic diseases					
0	–	–	–	–	1.000
1	0.178	0.167	1.133	0.287	1.194 (0.861–1.657)
≥2	0.810	0.155	27.299	<0.001	2.248 (1.659–3.047)
Chronic pain					
No	–	–	–	–	1.000
Yes	1.201	0.134	80.919	<0.001	3.322 (2.557–4.315)
Self-rated health					
Good	–	–	–	–	1.000
Moderate	0.335	0.129	6.692	0.010	1.397 (1.084–1.801)
Bad	1.757	0.224	61.370	<0.001	5.795 (3.734–8.995)

OR, odds ratio; CI, confidence intervals.

sleep quality and depression were independently associated with frailty, we also considered the bidirectional association between depression and sleep quality. The existence of this bidirectional association may be explained by shared risk factors and pathophysiological mechanisms. Inflammation and hypothalamic–pituitary–adrenal axis (HPA) dysregulation have been proven as causative mechanisms of depression among older adults, and are closely associated with sleep disorders (16, 68, 69). Neuroendocrine dysregulation is associated with abnormal levels of insulin-like growth factor 1, testosterone, and cortisol, which is also a frequent underlying mechanism of frailty (70). Meanwhile, there is a positive association between frailty and levels of inflammatory cytokines, which are associated with depression and sleep quality, including interleukin 6 (IL-6) (71).

The mediation analysis revealed that depression had a mediating effect on the relationship between sleep quality and frailty, indicating that sleep quality impacted frailty not only directly, but also indirectly through depression. This finding was consistent with previous studies in Chinese community-dwelling older adults (27). Depression was found to play an important mediating role between sleep quality and frailty, with a mediation proportion of up to 60.4%. Sleep quality also mediated the association between depression and frailty in this study, with a mediation effect of 12.7%. Therefore, providing comprehensive care to prevent and improve frailty in older adults should not only focus on the physical aspects, but also on the psychological and lifestyle perspectives. Moreover, it is vital to take appropriate preventive measures for biological, psychological, and social factors that lead to frailty in order to enhance social functioning and life quality among the older adults (8). Healthy aging necessitates a collaborative effort from healthcare system, in addition to self-care of older adults and support from their families. We recommend early screening and intervention to identify potential frailty targets in order to promote healthy lifestyles and positive attitudes among older adults. This can help delay the onset of frailty or reverse its development in the older adults who have already experienced it. Ultimately, this research will lead to increased wellbeing among the older adults with frailty.

TABLE 4 Spearman correlation coefficients between depression, sleep quality and frailty.

Variable	Depression	Sleep quality	Frailty
Depression	1		
Sleep quality	0.602***	1	
Frailty	0.492***	0.403***	1

***$p < 0.001$.

However, there are some limitations to this study. First, depression was assessed using a self-rating scale PHQ-9, and items of other scales were also mostly reported by the respondents. Although the use of self-report measure is common in epidemiological studies, it does increase the risk of reporting bias (72). Additionally, the screening scales we used for depressive symptoms and sleep disturbances cannot replace the diagnoses made by an experienced clinician. Diagnosing diseases requires a hospital visit or the utilization of specialized tools. Second, the PSQI is incapable of distinguishing between temporary and persistent sleep disturbances (73), necessitating the regular reassessment of sleep quality in older adults to grasp the changes and provide timely intervention measures. Third, frailty is a multidimensional indicator, including physical factors, psychological factors, and social factors (74). However, this study focused on physical frailty, lacking of the measurement of other dimensions. Fourth, it should be noted that causal associations

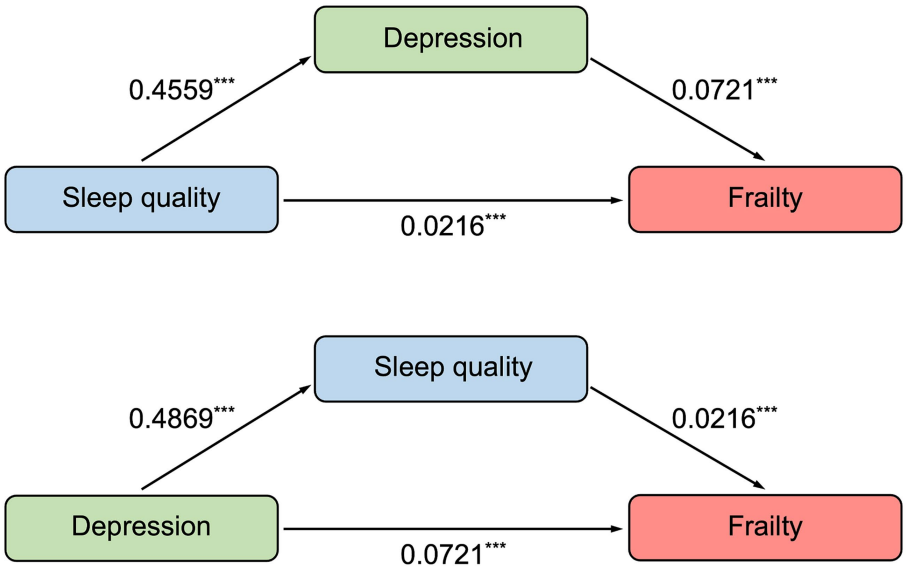

FIGURE 2
The mediation model of sleep quality and depression to frailty. ***$p < 0.001$. Results of mediation analysis showed that there was a mediation effect that sleep quality was a significant and positive predictor of frailty (direct effect = 0.0216), with depression being a mediator between sleep quality and frailty. And considering the bidirectional effect of depression and sleep quality, we also examined the mediation effect between depression and frailty (direct effect = 0.0721), with sleep quality as a mediator.

cannot be inferred from the cross-sectional data used in this study (75). This study considered a bidirectional association between depression and sleep quality, but it cannot be ruled out that there may also be a bidirectional association between depression and frailty, as well as between sleep and frailty. The findings indicated that enhancing the psychological state and sleep quality of older adults might be a feasible strategy for improving frailty. Further studies are required to verify if there are any other associations between depression, sleep quality and frailty. In addition, the proportion of female participants in this study outweighed that of male ones, with females accounting for 65%. Nevertheless, the findings did not find any statistically significant differences in frailty among community older adults based on gender, and we also included it as a covariate for adjustment conducting mediation analysis. Last, this study mainly focused on the older adults who lived in the community, and, therefore, it would be inappropriate to extrapolate the findings to all older adults. In the actual process of the survey, some older adults with severe frailty might not be able to participate since it was not easy for them to get out of the house. Consequently, the obtained prevalence rate of frailty in the older adults may be lower than the actual prevalence rate.

5 Conclusion

In conclusion, the prevalence of frailty and pre frailty was as high as 35.1%. Age, consumptions of vegetables, exercise, sleep quality, depression, number of chronic diseases, chronic pain, and self-rated health were correlated with frailty. And this study revealed the bidirectional effect of depression and sleep quality, as well as the pathways contributing to frailty. Therefore, it is important to pay attention to frailty, depression, and sleep status of older adults. Timely intervention should be provided to those who suffered from frailty and pre frailty to improve their quality of life and reduce the burden on the medical system.

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 ethics committee of School of Public Health, Fudan University (IRB00002408 and FWA00002399), and all participants or their respondents provided informed consent. 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

YZ: Conceptualization, Formal analysis, Methodology, Writing – original draft. GY: Formal analysis, Investigation, Writing – original draft. WB: Writing – review & editing. SW: Data curation, Investigation, Writing – original draft. XG: Data curation, Investigation, Writing – original draft. WZ: Data curation, Investigation, Writing – original draft. YL: Data curation, Investigation, Writing – original draft. YM: Data curation, Investigation, Writing – original draft. JG: Funding acquisition, Project administration, Writing – review & editing. WL: Funding acquisition, Project administration, Writing – review & editing. CK: Conceptualization, Methodology, Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research, authorship, and/or publication of this article. This work was supported by grants from the National Key R&D Program of China (nos. 2018YFC2002000 and 2018YFC2002001), and the Humanities and Social Sciences Research Project of the Education Department of Jilin Province (JJKH20231249SK).

Acknowledgments

We want to acknowledge Fudan University for authorization to use the data, and we would like to thank all the investigators for their contributions in the process of collecting data.

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.2024.1361745/full#supplementary-material

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frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 25 April 2024
DOI 10.3389/fpubh.2024.1347219

OPEN ACCESS

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RECEIVED 30 November 2023
ACCEPTED 29 March 2024
PUBLISHED 25 April 2024

CITATION
Xu R, Chen Y, Yao Z, Wu W, Cui J, Wang R, Diao Y, Jin C, Hong Z and Li X (2024) Application of machine learning algorithms to identify people with low bone density. *Front. Public Health* 12:1347219. doi: 10.3389/fpubh.2024.1347219

Application of machine learning algorithms to identify people with low bone density

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Background: Osteoporosis is becoming more common worldwide, imposing a substantial burden on individuals and society. The onset of osteoporosis is subtle, early detection is challenging, and population-wide screening is infeasible. Thus, there is a need to develop a method to identify those at high risk for osteoporosis.

Objective: This study aimed to develop a machine learning algorithm to effectively identify people with low bone density, using readily available demographic and blood biochemical data.

Methods: Using NHANES 2017–2020 data, participants over 50 years old with complete femoral neck BMD data were selected. This cohort was randomly divided into training (70%) and test (30%) sets. Lasso regression selected variables for inclusion in six machine learning models built on the training data: logistic regression (LR), support vector machine (SVM), gradient boosting machine (GBM), naive Bayes (NB), artificial neural network (ANN) and random forest (RF). NHANES data from the 2013–2014 cycle was used as an external validation set input into the models to verify their generalizability. Model discrimination was assessed via AUC, accuracy, sensitivity, specificity, precision and F1 score. Calibration curves evaluated goodness-of-fit. Decision curves determined clinical utility. The SHAP framework analyzed variable importance.

Results: A total of 3,545 participants were included in the internal validation set of this study, of whom 1870 had normal bone density and 1,675 had low bone density Lasso regression selected 19 variables. In the test set, AUC was 0.785 (LR), 0.780 (SVM), 0.775 (GBM), 0.729 (NB), 0.771 (ANN), and 0.768 (RF). The LR model has the best discrimination and a better calibration curve fit, the best clinical net benefit for the decision curve, and it also reflects good predictive power in the external validation dataset The top variables in the LR model were: age, BMI, gender, creatine phosphokinase, total cholesterol and alkaline phosphatase.

Conclusion: The machine learning model demonstrated effective classification of low BMD using blood biomarkers. This could aid clinical decision making for osteoporosis prevention and management.

KEYWORDS

low bone density, osteoporosis, machine learning, blood biochemical indicators, National Health and Nutrition Examination Survey

1 Introduction

Osteoporosis, the most prevalent metabolic bone disorder, is characterized by low bone mass, microarchitectural deterioration, fragility, and increased fracture risk (1–3). The growing older adult/adults population has contributed to rising osteoporosis prevalence globally - currently estimated at 19.7% (4–6). Fractures in six EU nations may increase from 2.7 million in 2017 to 3.3 million by 2030, with costs rising by 27% to $37.5 billion (7). Thus osteoporosis imposes substantial socioeconomic burdens worldwide. However, its subtle onset often delays diagnosis until fractures occur (8). Effective screening and early interventions are critical for prevention. In other words, it is important to screen for osteopenia and osteoporosis in the general population, in order to enable timely interventions to prevent fragility fractures. Dual-energy X-ray absorptiometry remains the gold standard for measuring BMD (9). However, the need for skilled technicians and radiation exposure limit its widespread use (10, 11). Since some blood biomarkers have shown modest correlations with osteoporosis and are easily obtained, this study aimed to develop biomarker-based models to identify those with low BMD (12–14). Machine learning, an important artificial intelligence tool, discovers patterns in big datasets via complex algorithms (15). Advancements in healthcare big data have expanded ML applications (16). The purpose of this study is to utilize the data from the National Health and Nutrition Examination Survey (NHANES) database to build models and test them using six machine learning algorithms, namely, logistic regression (LR), support vector machine (SVM), gradient boosting machine (GBM), naive Bayesian (NB), artificial neural network (ANN), and random forest (RF), which were modeled and tested to compare the accuracy of several methods in predicting low bone density in the test set, and to explore the application value of machine learning algorithms in low bone density prediction and auxiliary diagnosis.

2 Materials and methods

2.1 Dataset source

The National Health and Nutrition Examination Survey (NHANES) database was selected for this study. The NHANES is a program designed by the National Center for Health Statistics (NCHS) to assess the health and nutritional status of the U.S. population by surveying a national sample of 5,000 citizens annually since 1999. NHANES protocols were approved by the NCHS Research Ethics Review Board with written informed consent obtained from all participants (17).

2.2 Participants

In this study, NHANES data for the cycle 2017–2020 was selected as the internal validation set, and NHANES data for the cycle 2013–2014 was used as the external validation set, excluding participants younger than 50 years of age and participants with missing or invalid Femoral neck BMD data in Dual-Energy X-ray Absorptiometry – Femur.

2.3 Variable selection and definition

Based on previous literature (18, 19) and the purpose of the study, the following four components of variables were included: (a) Demographic information: age, gender, race and education, marital status, poverty index. (b) Examination data: Dual-Energy X-ray Absorptiometry - Femur (Femoral neck BMD), body mass index (BMI). (c) Laboratory data: Standard Biochemical Profile, Plasma Fasting Glucose, HDL, LDL & Triglycerides, Total Cholesterol, Complete Blood Count, Glycohemoglobin. (d) Questionnaire information: Osteoporosis, Alcohol Use, Blood Pressure &Cholesterol, Diabetes, Smoking-Cigarette Use. Alcohol use was defined as having ever had 4/5 drinks or more per day; smoking was defined as having smoked at least 100 cigarettes in one's lifetime; having ever been told that one has high blood pressure or is on prescription medication for high blood pressure was defined as high blood pressure; having ever been told that one has diabetes or is on insulin or glucose-lowering medication was defined as diabetes; and history of personal osteoporosis or fracture is defined as having at least one of the following: ever had a hip, wrist, spine or other fracture; been told by a doctor that you have osteoporosis. Parental history of osteoporosis or fracture was defined as having at least one of the following: self-reported fracture of a parent; parent had been told that he or she had osteoporosis.

2.4 Evaluation of low bone density

Bone mineral density (BMD) measurements in the NHANES database were primarily determined using dual-energy X-ray absorptiometry (DXA). In 2017–18, the femur scans were acquired on Hologic Discovery model A densitometers (Hologic, Inc., Bedford, Massachusetts), using software version Apex 3.2. Bedford, Massachusetts, using software version Apex 3.2. In 2019-March 2020, the femur scans were acquired on Hologic Horizon model A densitometers (Hologic, Inc., Bedford, Massachusetts), using software version Apex version 5.6.0.5. The 2013–2014 femur scans were acquired on Hologic QDR-4500A fan-beam densitometers (Hologic, Inc., Bedford, Massachusetts) using software version Apex 3.2. All scans were analyzed with Hologic APEX version 4.0 software. In this study, the BMD of the femoral neck was chosen as a criterion because it has been proposed as a reference skeletal site for defining osteoporosis in several epidemiologic studies (11). The diagnosis of primary osteoporosis and osteopenia is mainly based on the T-value obtained after the calculation of BMD measurements (20). T-value = bone mineral density of the study population – mean value of bone mineral density of the reference group (age group of peak bone mineral density)/standard deviation of that reference age group (World Health Organization recommendations use bone mineral density data of non-Hispanic white women aged 20–29 years from NHANES III as the reference group).

T-value ≥ -1: healthy $\quad -2.5 < T$-value < -1: osteopenia

T-value ≤ -2.5: osteoporosis

Both conditions, osteopenia and osteoporosis, are considered to be low bone mineral density (21), and are therefore defined as low bone mineral density when either of the following is met: (1) femoral neck T-score < -1 (2) patient said "yes" to the question: Has a doctor

ever told you that you had osteoporosis, sometimes called thin or brittle bones?

2.5 Statistical analysis

2.5.1 Data cleaning

Participants aged ≥50 years with complete femoral neck BMD data were included. Due to substantial missingness and outliers, data preprocessing was performed. We assigned "NA" to the data with "7, 9, 77, 99," deleted the variables with more than 30% missing values (22, 23), and used the MI package in the R software to perform multiple interpolation for the variables with less than 30% missing values. Summary statistics were calculated following imputation. Normally or near-normally distributed continuous variables were presented as mean ± standard deviation and compared between groups by independent t-tests. Non-normally distributed continuous data were expressed as median (interquartile range) and compared using non-parametric tests. Categorical variables were presented as *n* (%) and compared via chi-squared tests.

2.5.2 Feature selection

In this study, Lasso (Least Absolute Shrinkage and Selection Operator) feature selection was performed using the 'glmnet' package in the R software. By adding an L1 regularization term to the least squares function, LASSO forces some coefficients to zero, effectively removing those variables from the model. An important tuning parameter in LASSO is λ (λ ≥ 0), controlling the degree of coefficient shrinkage. When λ = 0, LASSO is equivalent to ordinary linear regression. This study performs 10-fold cross-validation through the 'cv.glmnet' function, that is, the data are randomly divided into 10 groups, nine of which are used as the training set and one as the test set, and one extreme value of λ is generally selected for the training set, and then the parameters obtained from the training set are used for the prediction of the remaining set of data, and this process is repeated for 10 times, and the optimal value of λ is finally determined by the mean-square error obtained from the calculation of the results of the 10 predictions. Under this function, there are usually two choices for the optimal λ value, one is λ.min, the value of λ that minimizes the cross-validation error; the other is λ.1se, which keeps the cross-validation error within one standard error. The choice of the optimal λ varies from study to study depending on the specifics of the study and the purpose of the study. In addition, Lasso performs well in coping with the problem of the existence of multiple covariates among variables, and the independent variables in this study are mainly common blood biochemical indexes in clinics, and there is often the effect of multiple covariates among these variables, while Lasso regression can effectively deal with the problem of covariates by forcing some of the coefficients to be contracted to zero, which improves the stability and interpretability of the models (24).

2.5.3 Modeling and evaluation

In machine learning, there are four main methods: supervised learning, unsupervised learning, semi-supervised learning and reinforcement learning. The goal of this study is to categorize the population with normal bone density and the population with low bone density. Since this is a classification problem, the use of supervised learning algorithms is most appropriate (25). Therefore, six commonly used supervised learning algorithms, logistic regression (LR), support vector machine (SVM), gradient boosting machine (GBM), naive Bayes (NB), artificial neural network (ANN), and random forest (RF), were used to construct the model in this study. The internal validation dataset was randomly divided into training set and test set according to the ratio of 7:3. During the model training process, 10-fold cross-validation was used to select and adjust the model parameters. Then, 30% of the test dataset was input into the trained model for prediction. Additionally, NHANES data from 2013 to 2014 was entered into the model for external validation. The model performance was evaluated in terms of model differentiation ability, calibration ability and clinical application value. The area under the receiver operating characteristic curve (ROC) (AUC), accuracy, sensitivity, specificity, precision and F1 score were utilized to assess the discriminative ability of the model. Calibration ability of the model was assessed using calibration curves. The clinical applicability of the models was assessed by decision curve (DCA), and the confusion matrices of several models were visualized to provide a more intuitive understanding of the classification ability of the models.

2.5.4 Evaluation of the importance of variables

SHAP (SHapley Additive exPlanation) is a post-hoc explanation framework for machine learning models based on game theory (26). It quantifies the importance of each feature in the model by calculating the contribution value, known as the Shapley value, for each feature towards the predicted outcome. This study utilizes the SHAP method to enhance the interpretability and transparency of the model. The data analysis process was conducted using R 4.3.1 and Python 3.11.3, and a significance level of $p < 0.05$ was considered statistically significant.

3 Results

3.1 Baseline characteristics

Based on the inclusion and exclusion criteria, a total of 3,545 study participants who were ≥50 years of age and had complete femoral neck BMD data were included in the internal validation set of this study (Figure 1). The baseline information of the study subjects is shown in Table 1, of which 1870 were in the normal BMD group and 1,675 in the low BMD group, and a total of 60 initial variables were included after deletion of variables with more than 30% of missing values (Fasting Glucose, LDL-Cholesterol, and Triglyceride); among the demographic factors, lifestyle factors and past medical history, it can be seen that compared to the normal BMD group, the low BMD group was more likely to be older, female, non-Hispanic white or other race, widowed/divorced/separated, no history of smoking and alcohol consumption, lower BMI, no diabetes, and have a personal and parental history of osteoporosis and fracture; among the blood biochemical indexes, the mean values of direct HDL-Cholesterol, Total Cholesterol, Segmented neutrophils percent, Mean cell volume, Mean cell hemoglobin, Alkaline Phosphatase (ALP) were greater in the low bone density group than in the normal bone density group, while the mean values of Red blood cell count, Hemoglobin, Hematocrit, Glycohemoglobin, Alanine Aminotransferase (ALT), Creatine Phosphokinase (CPK), Creatinine, Globulin, Glucose, Gamma Glutamyl Transferase (GGT), Total Protein, Uric acid were

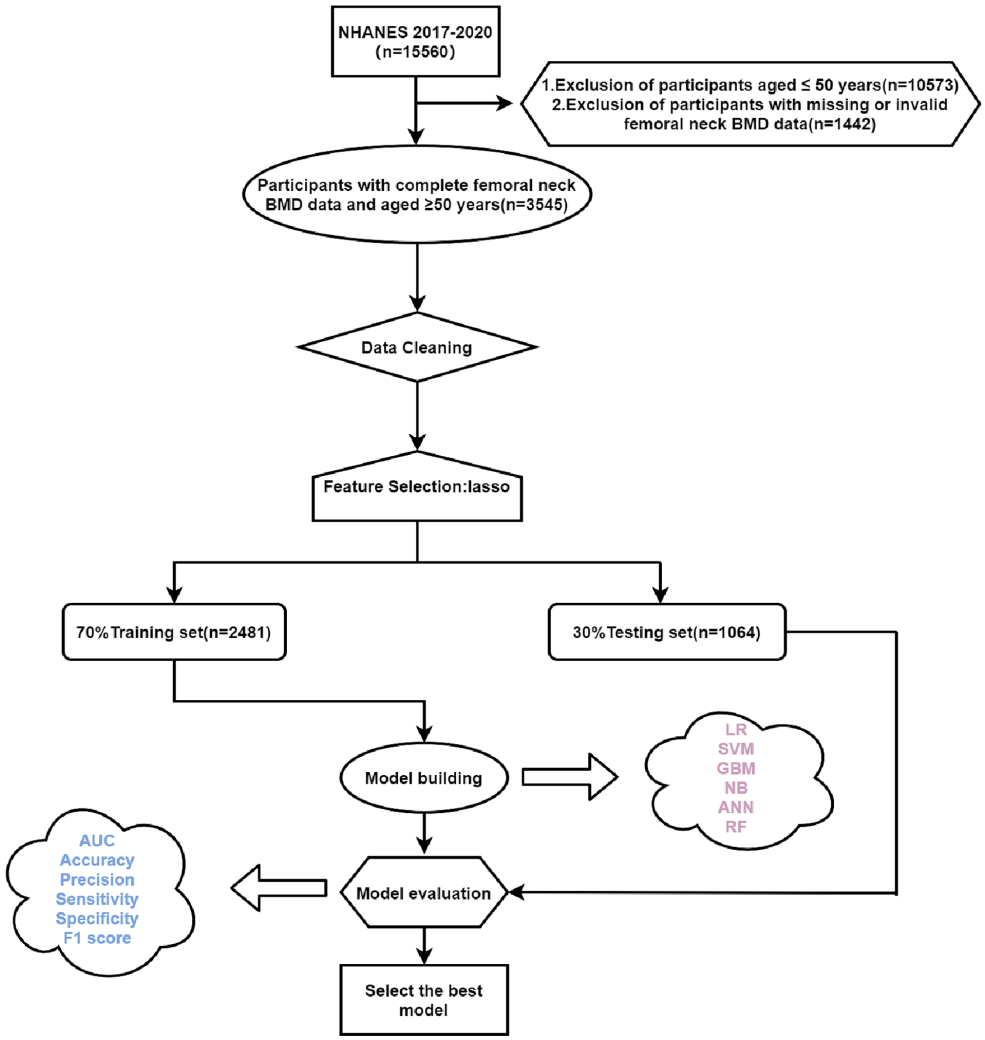

FIGURE 1
Flow chart of this study. LR, logistic regression; SVM, support vector machine; GBM, gradient boosting machine; NB, naive Bayesian; ANN, artificial neural network; RF, random forest; Lasso, Least Absolute Shrinkage and Selection Operator.

smaller than those of the normal BMD group ($p < 0.001$). The external validation set screened 3,127 study participants, of whom 1,796 were in the normal BMD group and 1,331 in the reduced BMD group, and the baseline information table is shown in Supplementary Table S1.

3.2 Feature selection

Variable selection was performed by Lasso (Least Absolute Shrinkage and Selection Operator), as shown in Figure 2, and 10-fold cross-validation was used to select λ. Due to the large number of characteristic variables in this study, if λ.min is used as the optimal λ value, there will be 41 variables included in the final model, which makes the model too complex and may have the risk of overfitting. On the other hand, when λ.1se is chosen as the optimal λ value, 19 variables will be included in the model, which is more concise and has a good prediction performance. Therefore, λ.1se is finally chosen as the optimal λ value in this study. The 19 variables included in the machine learning model were Age, Gender, Ratio of family income to poverty, BMI, Diabetes, and History of personal osteoporosis and fracture, Parental history of osteoporosis and fracture, Total Cholesterol, Monocyte percent, Segmented neutrophils percent, Mean cell volume, Red cell distribution width, Glycohemoglobin, Alkaline Phosphatase (ALP), Creatine Phosphokinase (CPK), Globulin, Osmolality, Total Protein, Uric acid.

3.3 Evaluation of model performance

Six machine learning models were constructed in this study, Figure 3 shows the ROC curves for the training and test sets of the model in the internal validation set, in the test set, LR (AUC = 0.785) has the highest AUC value and the best model discrimination, followed by SVM (AUC = 0.78), GBM (AUC = 0.775), ANN (AUC = 0.771), RF (AUC = 0.761), and NB (AUC = 0.729); LR also had higher accuracy (0.733), specificity (0.829), and precision (0.766) than the remaining five models; RF had the highest sensitivity (0.684); and GBM had a higher F1 score (0.693) than the other models (Table 2).

10.3389/fpubh.2024.1347219

TABLE 1 Comparison of general characteristics of the group with normal bone mineral density and the group with low bone mineral density.

	Normal bone density *N* = 1870	Low bone density *N* = 1,675	*P*
Age(year)	62.5 (8.49)	66.6 (9.09)	<0.001
Gender (*n*, %)			<0.001
Male	1,234 (66.0%)	642 (38.3%)	
Female	636 (34.0%)	1,033 (61.7%)	
Race (*n*, %)			<0.001
Mexican American	192 (10.3%)	141 (8.42%)	
Other Hispanic	214 (11.4%)	173 (10.3%)	
Non-Hispanic White	599 (32.0%)	773 (46.1%)	
Non-Hispanic Black	630 (33.7%)	280 (16.7%)	
Other Race	235 (12.6%)	308 (18.4%)	
Education level (*n*, %)			0.641
Less than 9th grade	172 (9.20%)	156 (9.31%)	
9–11th grade	190 (10.2%)	173 (10.3%)	
High school graduate/GED or equivalent	473 (25.3%)	426 (25.4%)	
Some college or AA degree	590 (31.6%)	492 (29.4%)	
College graduate or above	445 (23.8%)	428 (25.6%)	
Marital status (*n*, %)			<0.001
Married/Living with Partner	1,182 (63.2%)	939 (56.1%)	
Widowed/Divorced/Separated	519 (27.8%)	616 (36.8%)	
Never married	169 (9.04%)	120 (7.16%)	
Ratio of family income to poverty (*n*, %)			0.011
≤1	298 (15.9%)	313 (18.7%)	
1 ~ 3	791 (42.3%)	738 (44.1%)	
>3	781 (41.8%)	624 (37.3%)	
Smoke (*n*, %)			<0.001
Yes	927 (49.6%)	723 (43.2%)	
No	943 (50.4%)	952 (56.8%)	
Drinking alcohol (*n*, %)			<0.001
Yes	368 (19.7%)	240 (14.3%)	
No	1,502 (80.3%)	1,435 (85.7%)	
BMI (*n*, %)			<0.001
<25	303 (16.2%)	580 (34.6%)	
25 ~ 30	680 (36.4%)	647 (38.6%)	
≥30	887 (47.4%)	448 (26.7%)	
Diabetes (*n*, %)			<0.001
Yes	489 (26.1%)	310 (18.5%)	
No	1,381 (73.9%)	1,365 (81.5%)	
Hypertension (*n*, %)			0.319
Yes	1,017 (54.4%)	882 (52.7%)	
No	853 (45.6%)	793 (47.3%)	
History of personal osteoporosis and fracture (*n*, %)			<0.001
Yes	560 (29.9%)	612 (36.5%)	
No	1,310 (70.1%)	1,063 (63.5%)	

(Continued)

TABLE 1 (Continued)

	Normal bone density *N* = 1870	Low bone density *N* = 1,675	*P*
Parental history of osteoporosis and fracture (*n*, %)			<0.001
Yes	315 (16.8%)	410 (24.5%)	
No	1,555 (83.2%)	1,265 (75.5%)	
Direct HDL-Cholesterol (mmol/L)	1.36 (0.40)	1.50 (0.45)	<0.001
Total Cholesterol (mmol/L)	4.84 (1.13)	5.01 (1.14)	<0.001
White blood cell count (1000 cells/uL)	7.21 (9.31)	6.91 (2.20)	0.181
Lymphocyte percent (%)	30.9 (9.27)	30.0 (9.10)	0.003
Monocyte percent (%)	8.60 (2.59)	8.37 (2.12)	0.003
Segmented neutrophils percent (%)	56.8 (9.92)	58.1 (9.62)	<0.001
Eosinophils percent (%)	2.96 (2.22)	2.84 (2.04)	0.079
Basophils percent (%)	0.83 (0.34)	0.84 (0.35)	0.464
Lymphocyte number (1,000 cells/uL)	2.35 (8.55)	2.12 (3.41)	0.303
Monocyte number (1,000 cells/uL)	0.59 (0.25)	0.56 (0.20)	0.001
Segmented neutrophils num (1,000 cell/uL)	4.08 (1.74)	4.08 (1.63)	0.948
Eosinophils number (1,000 cells/uL)	0.21 (0.18)	0.19 (0.16)	0.013
Basophils number (1,000 cells/uL)	0.05 (0.05)	0.05 (0.05)	0.696
Red blood cell count (million cells/uL)	4.76 (0.50)	4.59 (0.49)	<0.001
Hemoglobin (g/dL)	14.2 (1.53)	13.9 (1.41)	<0.001
Hematocrit (%)	42.2 (4.16)	41.3 (3.92)	<0.001
Mean cell volume (fL)	89.0 (6.06)	90.1 (5.51)	<0.001
Mean cell hemoglobin concentration (g/dL)	33.6 (0.95)	33.5 (0.85)	0.229
Mean cell hemoglobin (pg)	29.9 (2.47)	30.2 (2.18)	<0.001
Red cell distribution width (%)	14.0 (1.26)	13.9 (1.27)	0.003
Platelet count (1,000 cells/uL)	230 (61.4)	236 (65.5)	0.006
Mean platelet volume (fL)	8.32 (0.93)	8.24 (0.91)	0.012
Nucleated red blood cells	0.09 (0.09)	0.08 (0.08)	0.036
Glycohemoglobin (%)	6.22 (1.26)	6.00 (1.13)	<0.001
Alanine aminotransferase (ALT) (U/L)	22.9 (16.3)	20.4 (20.8)	<0.001
Albumin, refrigerated serum (g/L)	40.5 (3.22)	40.3 (3.27)	0.321
Alkaline phosphatase (ALP) (IU/L)	79.6 (26.1)	83.8 (27.3)	<0.001
Aspartate aminotransferase (AST) (U/L)	22.5 (12.9)	22.0 (15.7)	0.346
Bicarbonate (mmol/L)	25.6 (2.47)	25.8 (2.52)	0.028
Blood urea nitrogen (mmol/L)	5.91 (2.26)	5.94 (2.27)	0.741
Chloride (mmol/L)	101 (3.06)	101 (3.21)	0.045
Creatine phosphokinase (CPK) (IU/L)	175 (232)	117 (116)	<0.001
Creatinine, refrigerated serum (umol/L)	85.5 (43.4)	79.3 (41.4)	<0.001
Globulin (g/L)	31.0 (4.43)	30.4 (4.58)	<0.001
Glucose, refrigerated serum (mmol/L)	6.13 (2.51)	5.84 (2.15)	<0.001
Gamma glutamyl transferase (GGT) (IU/L)	37.5 (46.9)	30.5 (40.4)	<0.001
Iron, refrigerated serum (umol/L)	15.9 (6.12)	16.1 (6.16)	0.384
Lactate dehydrogenase (LDH) (IU/L)	163 (36.3)	167 (36.1)	0.009
Osmolality (mmol/Kg)	283 (5.42)	282 (6.08)	0.069
Phosphorus (mmol/L)	1.14 (0.18)	1.15 (0.16)	0.011
Potassium (mmol/L)	4.12 (0.40)	4.13 (0.39)	0.660

(Continued)

TABLE 1 (Continued)

	Normal bone density *N* = 1870	Low bone density *N* = 1,675	*P*
Sodium (mmol/L)	141 (2.63)	141 (2.98)	0.597
Total bilirubin (umol/L)	8.44 (5.00)	7.99 (4.93)	0.007
Total calcium (mmol/L)	2.32 (0.09)	2.33 (0.10)	0.017
Total protein (g/L)	71.5 (4.37)	70.8 (4.65)	<0.001
Uric acid (umol/L)	344 (88.6)	312 (85.7)	<0.001

BMI, body mass index.

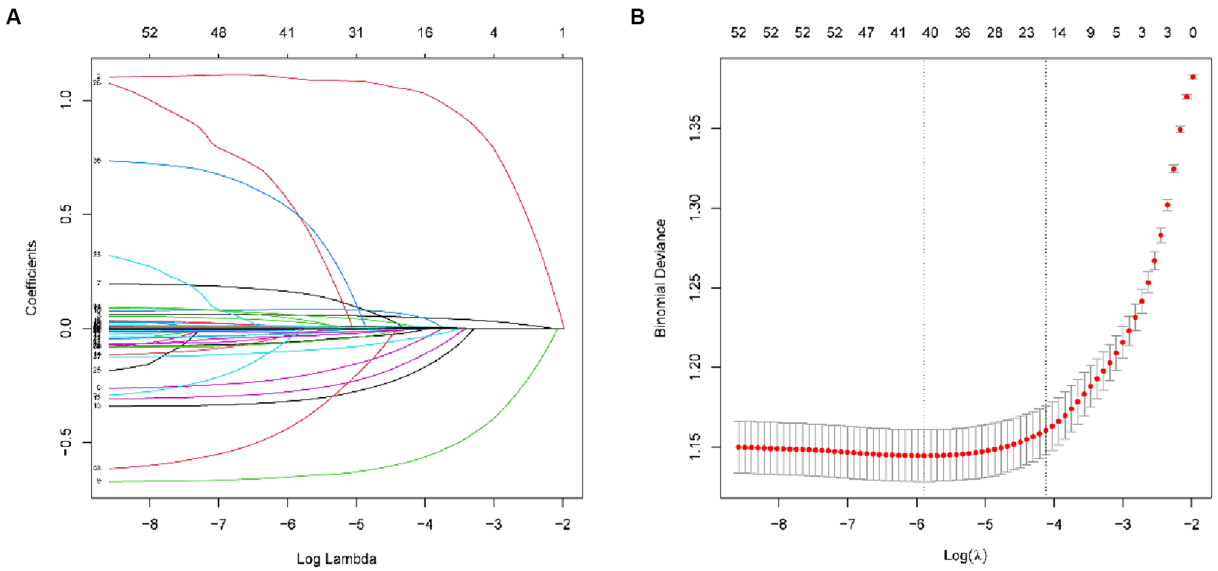

FIGURE 2
(A) Lasso coefficient path plots for 59 variables. **(B)** Cross-validation curves (10-fold cross validation). The left dashed line represents lambda.min and the right dashed line represents lambda.1se.

Figure 4 shows the confusion matrix for the model test set, from which it can also be seen that LR has the strongest ability to discriminate between people with normal bone density and those with low bone density among the six models. The calibration curves of the six model training and validation sets are shown in Figure 5, and in the test set, the calibration curve of RF fits the ideal curve to the highest degree, and the calibration curves of the rest of the models fit the ideal curve reasonably well except for NB, which has a worse fit, suggesting a better match between the predicted probabilities of the models and the actual observed incidence rates. The results of Decision Curve Analysis (DCA) on the training and test sets of the models are shown in Figure 6, which shows that when the predictive probability threshold is certain, LR has the largest net gain compared to the other five models, indicating that LR has better clinical utility. In the external validation of the model, the AUC value (0.78), accuracy (0.718), specificity (0.752), and precision (0.667) of LR were higher than those of the other models, and good robustness and extrapolation ability could also be seen from the confusion matrix, ROC curve, calibration curve, and decision curve of the model (Supplementary Figures S3, S4 and Supplementary Table S3). Therefore, from the comprehensive evaluation of model differentiation, calibration, and clinical gain, LR is the optimal model for predicting low BMD population.

3.4 Evaluation of the importance of variables

We interpreted the importance of predictor variables based on the SHAP algorithm for the LR model with the best predictive performance (Figure 7). The extent to which a variable contributes to the model is reflected by the SHAP value. A higher SHAP value of a variable means a higher degree of its contribution to the model (26). As shown in Figure 7A, the top-down ordering of the variables means that their contribution to low BMD is in ascending order, with the line with a SHAP value of 0 as the vertical axis, the variables with red color on the right side of the line represent the positive contribution of the variable to the predicted outcome, while the variables with blue color on the right side of the line have a negative contribution. Therefore, the top six variables in terms of importance for predicting low bone

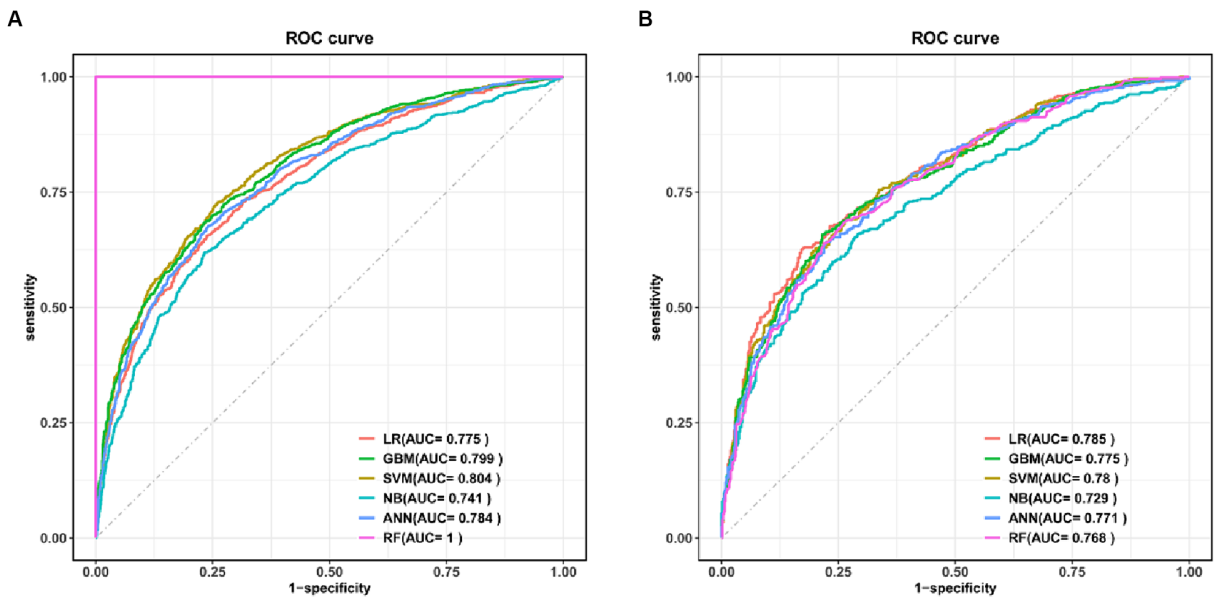

FIGURE 3
ROC curves for the six models in the training set **(A)** and test set **(B)**. LR, logistic regression; SVM, support vector machine; GBM, gradient boosting machine; NB, naive Bayesian; ANN, artificial neural network; RF, random forest.

TABLE 2 Comparison of the predictive power of several models in the test set.

Model	AUC	Accuracy	Sensitivity	Specificity	Precision	F1
LR	0.785	0.733	0.626	0.829	0.766	0.689
SVM	0.78	0.718	0.628	0.799	0.737	0.678
GBM	0.775	0.725	0.658	0.784	0.732	0.693
NB	0.729	0.685	0.66	0.708	0.669	0.665
ANN	0.771	0.712	0.642	0.775	0.719	0.679
RF	0.768	0.712	0.684	0.738	0.701	0.692

mass in the population were: age > BMI > gender > creatine phosphokinase > total cholesterol > alkaline phosphatase, in which age, total cholesterol, and alkaline phosphatase were positively correlated with the occurrence of low bone mineral density, i.e., the older the age, the higher the indexes of total cholesterol and alkaline phosphatase, and the higher the probability of developing low bone mineral density. BMI, gender, and creatine phosphokinase were negatively correlated with the occurrence of low BMD, i.e., the lower the BMI, the female, and the lower the creatine phosphokinase index, the higher the probability of low BMD. Given that age was the variable with the highest variable importance in the model of this study, we explored the effect of age on the occurrence of low BMD as well as other blood biochemical indices. Comparison of the study subjects divided into groups with a cutoff of 5 years of age revealed that most of the blood biochemical indices were significantly associated with age (Supplementary Table S2). Their associations were further explored by applying restricted cubic spline (RCS), and age was found to be linearly related to the occurrence of low BMD, with the older the age, the higher the risk of low BMD (Supplementary Figure S1). Among the blood biochemical indices, except for Alkaline Phosphatase (ALP), Mean cell volume, Segmented neutrophils percent, and Total Cholesterol, all of them showed a linear trend with age (Supplementary Figure S2).

4 Discussion

With the aging of the population worldwide in recent years, the incidence of osteoporosis in older adult/adults men and women remains high, and fractures caused by osteoporosis can lead to disability, prolonged bed rest, impaired function, and even death, bringing serious economic and physical and psychological burdens to the affected families as well as to individuals (27). Some studies have shown that early diagnosis and intervention for patients with osteopenia and osteoporosis can effectively reduce their fracture incidence (28), so we developed several machine learning algorithms to identify abnormal bone density in the population with osteopenia and osteoporosis. In medical research, the collection of clinical data is difficult and the collected data are heterogeneous and non-standardized, while public databases such as SEER, MIMIC, and NHANES have the advantages of large amount of data and richness of the information contained in them, and thus they are widely favored

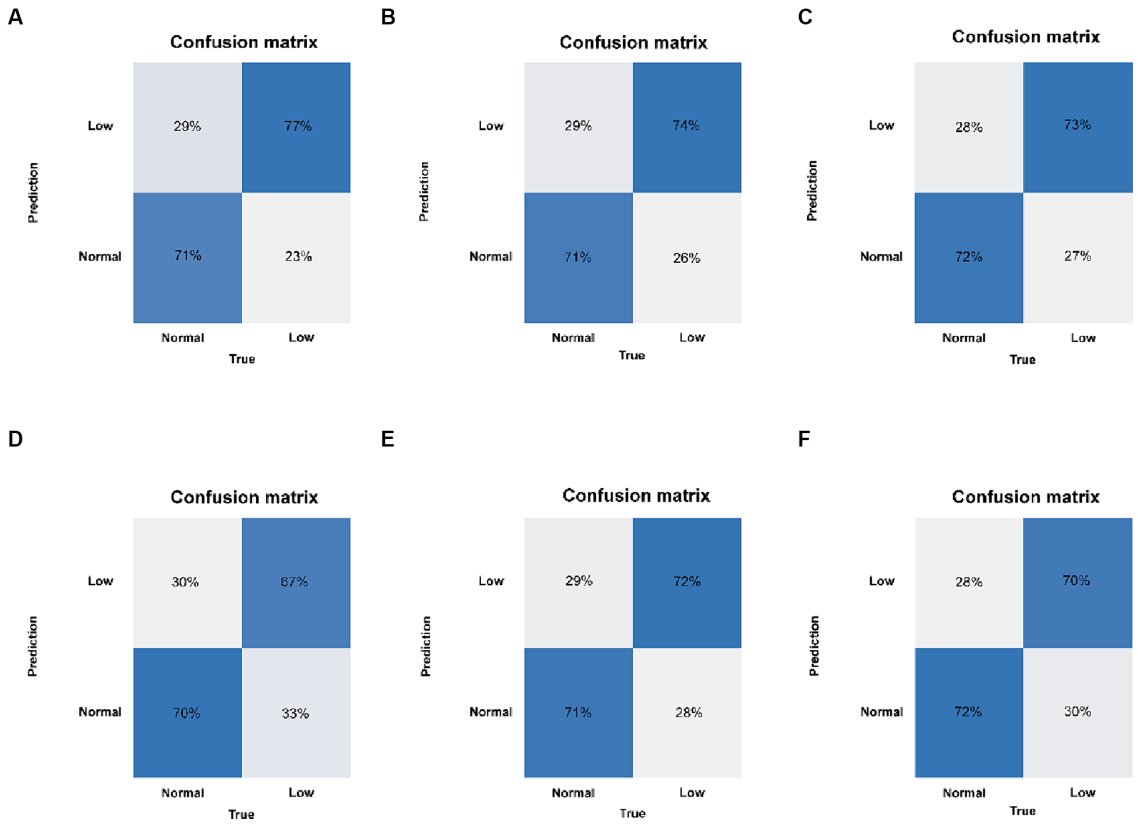

FIGURE 4
Confusion matrix of the six models in the test set. **(A)** LR, logistic regression. **(B)** SVM, support vector machine. **(C)** GBM, gradient boosting machine. **(D)** NB, naive Bayesian. **(E)** ANN, artificial neural network. **(F)** RF, random forest.

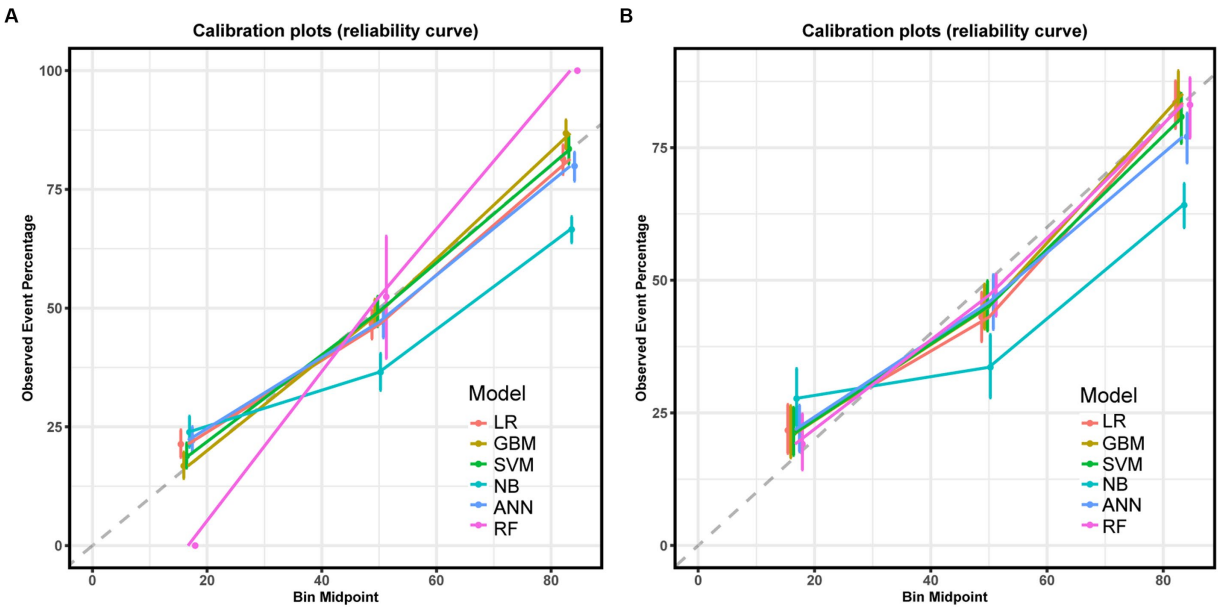

FIGURE 5
Calibration curve for the six models in the training set **(A)** and test set **(B)**.

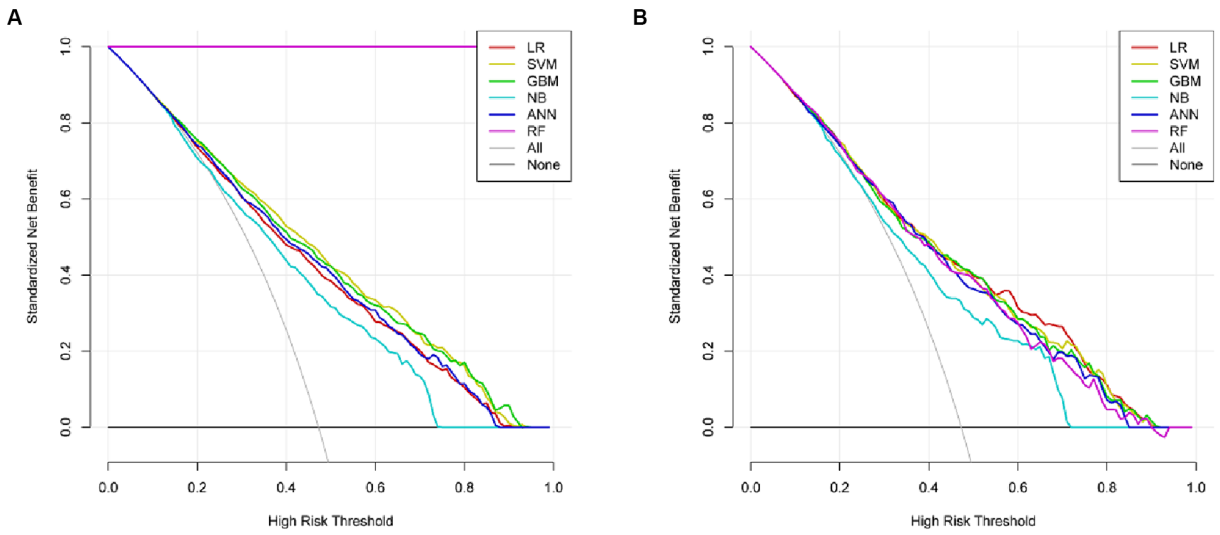

FIGURE 6
Decision curves for the six models in the training set **(A)** and test set **(B)**.

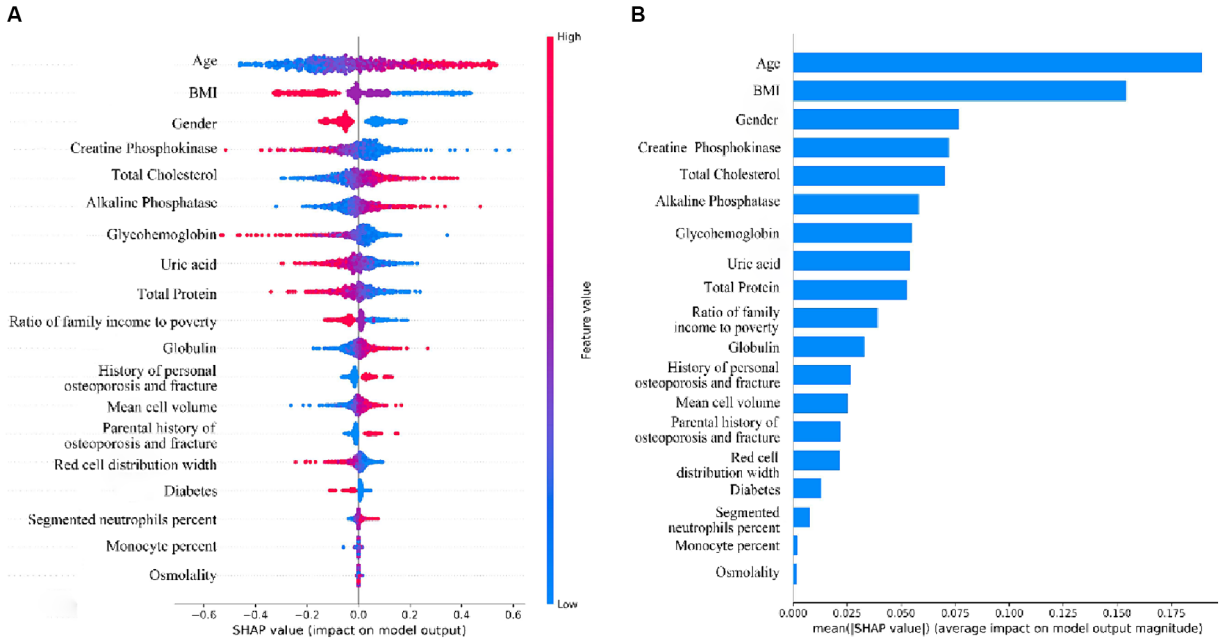

FIGURE 7
(A) Beeswarm plots of the LR Model. Generate SHAP values for each variable and reveal its relationship with low bone density. **(B)** Importance ranking plot of variables for LR model.

by researchers (29). Many previous studies (30–32) have applied machine learning algorithms to mine public databases and achieved good prediction results. Our study included 3,545 participants with complete femoral neck BMD measurements from 2017 to 2020 from the National Household Nutrition and Exercise Survey (NHANES) database, which were divided into a training set and a test set according to the ratio of 7:3, with 2,841 participants in the training set and 1,064 participants in the test set, and the data from the training set were analyzed by using demographic factors, blood biochemical indices, and questionnaire information, which are clinically readily available variables, six common supervised machine learning models were built using the training set data and the model performance was tested with the test set data, and the model with the best predictive performance, LR, was finally selected based on the ROC curves, calibration curves, decision curves, confusion matrices, as well as model performance evaluation indexes, such as accuracy and sensitivity, etc. It is worth noting that the performances of the three models, GBM, SVM, and ANN, are also very well. Especially in the training set (Table 3), the AUC values of SVM (AUC = 0.804), GBM (AUC = 0.799), and ANN (AUC = 0.784) even exceed that of LR

TABLE 3 Comparison of the predictive ability of several models in the training set.

Model	AUC	Accuracy	Sensitivity	Specificity	Precision	F1
LR	0.775	0.712	0.657	0.761	0.711	0.683
SVM	0.804	0.734	0.728	0.739	0.714	0.721
GBM	0.799	0.728	0.687	0.765	0.724	0.705
NB	0.741	0.697	0.619	0.767	0.704	0.659
ANN	0.784	0.721	0.677	0.76	0.716	0.696
RF	1	1	1	1	1	1

(AUC = 0.775), and it can be seen from the calibration curves and the decision curves of the training set that the fit of the calibration curves of GBM and SVM is better than that of LR, and ANN is on a par with LR. The decision curve performance of GBM, SVM and ANN is also better than that of LR. The ability of two models, RF and NB, to predict the population with low bone density is relatively weak. RF has an overfitting problem in the training set, and in the test set, although the calibration curves fit the ideal curves better, the AUC value is low, and the model's differentiation is average. Several model evaluation indexes of NB are lower in the training set and the test set. The model's ROC curve, calibration curve, and decision curve are poor compared to the rest of the models, and the predictive ability is the weakest among the six models.

We analyzed the variable importance of the 19 independent variables included in the model through the SHAP framework, and found that the top three variables in terms of importance were age, BMI, and gender, and that older age, lower BMI, and female gender were risk factors for lower BMD. In previous studies, age and gender have been recognized as established risk factors for osteoporosis (33, 34), especially in women, after menopause, the level of estrogen in the body decreases, and BMD decreases, and the prevalence of osteoporosis rises dramatically, so that women over the age of 50 years are often a priority population for osteoporosis screening (35). Whereas the relationship between BMI and BMD is unclear, a two-sample Mendelian randomization study showed a positive causal association between BMI and BMD levels (36); a meta-analysis that included 108 studies showed that the risk of osteoporosis in people with low BMI was 2.76 times higher than that in people with high BMI (6), which are in keeping with the conclusions we have drawn. However, a prospective study concluded that the contribution of BMI to fragility fractures varies by gender and by skeletal site, with a more complex association between the two (37). Therefore, further exploration of the relationship between BMI and BMD is warranted.

Among the blood biochemical indices, the three variables that contribute most to low BMD are creatine phosphokinase, total cholesterol, and alkaline phosphatase, where the higher the two indices of total cholesterol and alkaline phosphatase, the higher the likelihood of lower BMD, and the opposite is true of creatine phosphokinase, where the lower the value, the higher the likelihood of lower BMD. Creatine phosphokinase (CPK), also known as creatine kinase (CK), plays an important role in cellular energy metabolism, and fewer studies have been conducted on the association between CK and BMD. A retrospective and prospective cohort study found that the group with a history of previous fracture had a higher level of CK values than the group without a history of fracture, and the group that presented with a new fracture also had a higher level than the group that did not present with a fracture, which is contrary to our opinion, but the study was only conducted on young female athletes, which has some limitations, and the number of subjects was small, so this conclusion also needs to be further confirmed (38). Alkaline phosphatase is a bone turnover marker that is widely found in bone, liver, and intestine and plays an important role in bone growth and metabolism (39). Previous studies have shown that higher ALP levels are positively associated with low BMD or osteoporosis, which is consistent with the conclusions we have drawn, probably because alkaline phosphatase activity is increased when skeletal disease is present to meet the demands of bone growth and reconstruction (40, 41). There is no clear consensus on the relationship between total cholesterol and BMD, and most studies agree with us (42–44) that there is a negative correlation between the two, however, there are also studies that take the opposite view (40), and a cross-sectional study from China found that the associations were very different in men and women, with TC positively correlated with BMD in men and In women, the association was U-shaped, with curve inflection points varying by age and BMI (45). Therefore, the association and mechanisms between TC and BMD need to be explored in further studies.

The present study also has some limitations. First, in the NHANES database, those who participated in BMD measurement by dual-energy X-ray absorptiometry were older than 50 years, and nowadays there is a trend of younger age for both osteoporosis and bone loss (46), so screening should not be limited to the middle-aged and older population. Second, our study is based on the U.S. NHANES database, which, although covering multiple races in the U.S., may have limitations when applied to other racial or national populations. Therefore, data from different countries and regions will be collected and analyzed in the future to increase the generalizability of the model. Third, although several variables such as demographic and blood biochemical indicators were included in this study, there are many factors that were not included in the study, such as lifestyle, dietary habits, genomic data, and imaging data, which are also closely related to BMD. It is hoped that more data such as these will be included in future studies to further improve the accuracy of the model and expand its scope of application. Fourth, with the rapid development of the field of artificial intelligence, new algorithms such as deep learning algorithms (47, 48) and image recognition technology (49) are constantly emerging. In addition, more and more research tends to explore diseases from the perspective of pathogenic mechanisms (50) and drug development (51), and we are looking forward to making more progress in these areas in the future.

5 Conclusion

In this study, we applied six machine learning algorithms to construct a prediction model for low bone mass based on clinically accessible metrics in the NHANES database, and used 10-fold cross-validation to internally validate the model and NHANES data from different time periods to input into the model as an external validation, applying multiple metrics to evaluate the model performance, and finally selecting the best predictive performance of the ML model, LR. The model can screen out people osteopenia and osteoporosis, and assist clinicians in making decisions to better realize the primary and secondary prevention of osteoporosis.

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 authors.

Ethics statement

The NHANES protocols and studies involving human participants were reviewed and approved by NCHS Research Ethics Review Board. The patients/participants provided their written informed consent to participate in this study.

Author contributions

RX: Conceptualization, Data curation, Methodology, Software, Writing – original draft. YC: Data curation, Software, Writing – review & editing. ZY: Methodology, Writing – review & editing. WW: Data curation, Writing – review & editing. JC: Validation, Writing – review & editing. RW: Software, Writing – review & editing. YD: Methodology, Writing – review & editing. CJ: Data curation, Writing – review & editing. ZH: Supervision, Writing – review & editing. XL: Supervision, Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research, authorship, and/or publication of this article. This study was supported by the Foundation of Liaoning Province Education Administration (No. LJKZ0849).

Conflict of interest

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

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1347219/full#supplementary-material

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frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 30 April 2024
DOI 10.3389/fpubh.2024.1382384

OPEN ACCESS

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RECEIVED 05 February 2024
ACCEPTED 12 April 2024
PUBLISHED 30 April 2024

CITATION
Li X, Li X, Sun L, Yang L, Wang C, Yuan T, Lei Y, Li J, Liu M, Zhang D, Hua Y, Liu H and Zhang L (2024) The bidirectional relationship between activities of daily living and frailty during short-and long-term follow-up period among the middle-aged and older population: findings from the Chinese nationwide cohort study.
Front. Public Health 12:1382384.
doi: 10.3389/fpubh.2024.1382384

The bidirectional relationship between activities of daily living and frailty during short-and long-term follow-up period among the middle-aged and older population: findings from the Chinese nationwide cohort study

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Objective: Frailty and activities of daily living (ADL) disability are common conditions among older population. Studies on the bidirectional relationship between frailty and ADL are limited. The current study examined the cross-sectional and longitudinal associations between frailty and ADL in middle-aged and older Chinese individuals.

Methods: The data was collected through the China Health and Retirement Longitudinal Study (CHARLS), conducted in 2011, 2013, and 2015, encompassing 17,284 individuals aged ≥45 years. We excluded individuals without follow-up data. 2,631 participants finished the baseline survey. The definition of ADL disability encompasses difficulty in engaging in either basic activities of daily living (BADL) or instrumental activities of daily living (IADL). Frailty was assessed according to the Fried criteria. Logistic regression was utilized to examine odds ratios (ORs) and 95% confidence intervals (CIs) for assessing the cross-sectional relationships between ADL with frailty at baseline. The prediction effects were explored using Cox proportional hazards analysis, testing hazard ratios (HRs) and 95%CIs.

Results: In cross-sectional analysis, BADL [OR = 6.660 (4.519–9.815)], IADL [OR = 5.950 (4.490–7.866)], and ADL [OR = 5.658 (4.278–7.483)] exhibited significant associations with frailty; frailty demonstrated significant associations with BADL [OR = 6.741 (4.574–9.933)], IADL [OR = 6.042 (4.555–8.016)] and ADL [OR = 5.735 (4.333–7.591)]. In longitudinal analysis, IADL and ADL were significantly associated with frailty in participants without baseline frailty in the short-term period [IADL: HR = 1.971 (1.150–3.379), ADL: HR = 1.920

(1.146–3.215)], IADL exhibited a significant association with frailty in the long-term period [HR = 2.056 (1.085–3.895)]. There was no significant link observed between frailty and an elevated risk of disability onset in BADL, IADL and ADL during the short-term period. When considering the long-term perspective, frailty exhibited a significant association with an elevated risk of disability onset in BADL [HR= 1.820 (1.126–2.939)] and IADL [HR = 1.724 (1.103–2.694)].

Conclusion: In middle-aged and older adults, ADL and IADL disability predicted frailty after 2-year follow-up, IADL disability predicted frailty after 4-year follow-up. Moreover, frailty did not predict BADL, IADL and ADL disability after 2-year follow-up. However, frailty predicted BADL and IADL disability after 4-year follow-up.

KEYWORDS

frailty, activities of daily living, bidirectional relationship, middle-aged and older adults, basic activities of daily living, instrumental activities of daily living

Introduction

Frailty is a geriatric syndrome with multiple dimensions, characterized by an increased vulnerability to different stressors. Frailty is associated with poor health outcomes and signifies a decline in physiological reserve and function, which becomes increasingly prevalent with advancing age (1, 2). Frailty is prevalent among middle-aged and older people. Previous studies have reported varying prevalence rates of frailty in middle-aged and older population of 3% in United Kingdom (3), 4.1% in Europe (4), 11.8% in Chilean and 3.1% in China (5). Older population has a higher prevalence of frailty. According to a comprehensive meta-analysis (included studies of cross-sectional and cohort), the prevalence of frailty among Chinese older community-dwelling population was 7–20% (2, 6–8), 11% for females and 8% for males (6). The presence of frailty is associated with elevated rates of hospitalization, dementia, disability, and early mortality (9–11), and presents significant challenges to global healthcare systems. With the aging of China's population, frailty has emerged as one pressing concern for healthcare systems, posing a significant public health burden. Relevant literature have extensively documented a large number of risk factors for frailty, such as advanced ages, unmarried, women, rural areas, living alone, lower levels of education, worse economic conditions, three or more chronic diseases, and ADL disability (2, 6, 7, 12).

According to the explanations provided in medical and rehabilitation literature, the Activities of Daily Living (ADL) refers to activities focused on self-care and personal hygiene (13). ADL are widely acknowledged as reliable indicators of functional restrictions among older individuals and are commonly categorized into basic activities of daily living (BADL) and instrumental activities of daily living (IADL) (14). BADL reflects the fundamental self-care ability that individual must consistently perform repeatedly every day to maintain their independence, while IADL refers to the more complex ability to participate in social activities and live independently (15). The adverse outcomes of ADL disability encompass hospitalization (16), mortality (17), and diminished levels of quality of life (18), among others. Several factors were associated with ADL disability, including age, chronic pain, polypharmacy, being separated/divorced, physical activity, and frailty (19–21). Most of the studies encompassed individuals aged ≥65 years, 26% of community-dwelling older people in China exhibited limitations in ADL (17), 19.02% limitations in BADL and 25.29% limitations in IADL (22). The prevalence rate of BADL disability among middle-aged and older community-dwelling adults in China was found to be 16.7%, IADL disability was 21.5% (23), and ADL disability was 19.4% (24). 2006–2018 study in United States including middle-aged and older participants showed that 25.4% presented IADL impairments, and the prevalence of impairments in IADL was highest among females and older individuals (25). A cross-sectional study of older adults residing in Brazilian communities in 2015–2016 found that the prevalence of IADL and BADL disabilities was 45.1 and 13.5%, respectively (26). A study conducted in India population aged ≥60 years revealed the prevalence of ADL and IADL were 19.89 and 45.00%, respectively (27). Other studies have described a prevalence rate of 48.5% for ADL disability among middle-aged and older individuals with chronic obstructive pulmonary disease (COPD) (28), the prevalence of IADL and BADL disability among cancer patients was reported as 54.6 and 36.7%, respectively (29).

Previous studies have researched the association of ADL and frailty. A meta-analysis performed for 31 prospective studies (9) showed a prospective association between frailty and ADL disability, with frailty leading to a significantly higher risk of BADL disability (OR: 2.05, 95% CI: 1.73–2.44) and IADL disability (OR: 2.52, 95% CI: 2.08–3.06); frailty increases the risk of losing ADL by 1.6 to 2.0 times. Another meta-analysis also showed that associations persisted among community-dwelling middle-aged and older population (30). Meta-analysis encompassed 20 studies that examined the risks of disability in IADL and ADL, it was found that frail older individuals were more prone to developing or exacerbating disability in IADL and ADL, the pooled OR and pooled HR exhibited statistically significant results (31). The cross-sectional study reported that frailty

Abbreviations: ADL, activities of daily living; BADL, basic activities of daily living; IADL, instrumental activities of daily living; CHARLS, China Health and Retirement Longitudinal Study; BMI, Body mass index; CI, Confidence interval; OR, Odds ratios; HR, hazard ratio.

group exhibited significantly worse scores for the ADL than the non-frailty group in community-dwelling older adults ($p < 0.05$) (32). Analysis of Italian population cohort, the incident risk of IADL disability was increased in frailty individuals (HR: 2.56, 95%CI: 1.58–4.16) and ADL (HR: 3.58, 95%CI: 1.97–6.52) after a four-year follow-up; pre-frailty participants displayed a higher incidence of frailty compared to those without frailty at follow-up entry (33). On the other side, a meta-analysis comprising 14 studies (encompassing cross-sectional studies and cohort studies) (6) reported that having ADL disability was a risk factor for frailty among the older Chinese population in communities. Another meta-analysis collected cross-sectional data on the frailty prevalence among rural older individuals and revealed that ADL disability was significantly associated with frailty (34).

However, the existing studies mostly focus on the prevalence and risk factors of frailty (2, 6, 7, 34), whereas the effect of ADL on the incidence of frailty in longitudinal studies has been poorly understood (1). In addition, previous research primarily examined the unidirectional associations between ADL and frailty, and were limited by cross-sectional designs or small sample sizes. Considering the shared risk factors and pathophysiological mechanisms involved, our study hypothesizes a bidirectional relationship between frailty and ADL. It is imperative to prospectively investigate the bidirectional association of frailty and ADL disability utilizing a large and representative sample, to provide new references for the development of frailty and ADL disability interventions.

In the study, we utilized a four-year (2011 to 2015) longitudinal dataset from a nationally representative sample of community-dwelling adults in China, aged middle-aged and older. We aimed to explore the bidirectional relationship of ADL and frailty over short-term (2-year, 2011–2013) and long-term (4-year, 2011–2015) periods. We hypothesized that baseline ADL disability is predictive of the following frailty occurrence. Similarly, baseline frailty is predictive of subsequent changes in ADL disability.

Method

Participants

The research is based on the China Health and Retirement Longitudinal Study (CHARLS), which collected data from a cohort of 17,284 individuals aged ≥45 years in 2011 (Wave 1). Subsequent data collection occurred in 2013 and 2015 (Waves2 and Waves3). Participants were selected for in-person interviews, computer-aided personal interview (CAPI), and structured questionnaires conducted biennially. This study utilized longitudinal data from individuals who participated in Wave1, Wave2, and Wave3. The following exclusion criteria were formulated for this study: (1) lack of components of frailty data, (2) lack of components of activities of daily living disability data, and (3) lack of sex/age/current residence/educational level/marital status/alcohol drinking/smoking status/taking activities/physical exercise/BMI/chronic diseases data. Furthermore, participants without follow-up data were excluded. A total of 2,631 participants finished the baseline assessments, with 1936 participants finished the short-term follow-up surveys (spanning from 2011 to 2013) and 1879 participants finished the long-term follow-up surveys (spanning from 2011 to 2015).

Frailty assessment

Frailty assessment was conducted based on the widely accepted criteria initially proposed by Fried et al. (35), which were subsequently refined based on the data available in CHARLS. The definition of frailty comprised five essential elements, including exhaustion, slowness, weight loss, weakness, and low physical activity. The evaluation and definition of the five components of frailty were conducted in our study as follows: (1) Slowness: Participants were asked to self-report whether they had difficulty while walking 100-meter or climbing multiple flights of stairs without taking breaks, following a methodology similar to previous studies (30). Individuals who faced difficulty in performing climbing or walking were classified as slowness, (2) Weakness: it was assessed through self-report question "having difficulty in carrying or lifting weights exceeding 10 jin, such as heavy grocery bags" (36), (3) Exhaustion: it was considered present if the individuals responded with either "Most or all of the time" or "Occasionally or a moderate amount of the time" to anyone questions of the Center for Epidemiologic Studies-Depression scale in the Chinese version (CES-D) (37): "I could not get going during last week" or "I felt everything I did was an effort during last week." The construction of this component was identical to that initially suggested by Fried et al. (35), (4) Weight loss: it was characterized as the inadvertent reduction of ≥5 kilograms within the past year (36), or a present body mass index (BMI) ≤ 18.5 kg/m^2 (38), and (5) Low physical activity: WALK was defined as walking by CHARLS, referred to recreational, sporting, exercise or leisure purposes within workplaces and residences, pedestrian travel between different locations, and other forms of walking. Low physical activity represented the absence of any physical activity or WALK ≥10 min at a time in a typical week. Although differing from the component proposed by Fried et al. (35), similar treatment variables have been previously utilized to assess low physical activity (39). In our study, frailty was defined as the existence of three or more components.

Activities of daily living

In CHARLS, the ADL scale was employed to assess the level of disability among older people. The assessment of ADL was categorized into BADL and IADL. BADL disability was described as difficulty in eating, bathing, dressing, indoor moving, toileting and continence control. IADL disability was described as difficulty in performing housework, shopping, cooking, taking medicine, and financial management. Each question is categorized into 4 possible responses: "I cannot do it," "Yes, I have difficulty and need help," "I have difficulty but still can do it" and "No, I do not have any difficulty" (40). The individuals were classified as experiencing ADL disability if they had inability or difficulty to complete any of the 11 items, BADL disability and IADL disability represented inability or difficulty to complete any of the items about BADL and IADL, respectively (28).

Body measurement

The body mass index (BMI) is calculated by dividing weight (kilograms) by the square of height (meters). BMI is easy to measure and widely recorded in research, clinical nutrition, and epidemiology.

We used the cut-off points standard of BMI for Chinese adults (41). BMI can be classified into 4 categories: BMI < 18.5 kg/m^2 for underweight, BMI 18.5-24 kg/m^2 for normal weight, BMI 24-28 kg/m^2 for overweight and BMI ≥ 28 kg/m^2 for obese (42–44).

Covariates

Age/sex (female and male)/marital status/educational level/current residence /alcohol drinking/smoking status/taking activities/physical exercise/BMI data/chronic diseases at baseline were included as covariates in our study. (1) The age groups were categorized as four groups: 45–54, 55–64, 65–74, and ≥ 75 years old, (2) Marital status was classified into married or single (including never married, divorced, separated, or widowed), (3) Educational levels range from illiterate (no formal education), below elementary school (incomplete primary education but capable of writing or reading, to graduates of home school/sishu, middle or elementary school), high school, and above vocational school (holding a two- or three-year associate/college degree, as well as a postgraduate or doctoral degree/Ph. D), (4) Current residence encompassing urban and rural, (5) Alcohol drinking encompassing more than once a month, less than once a month, and never drinker, (6) Smoking status encompassing never smoked, former-smoker and current smoker, (7) Taking activities (such as socializing with friends, providing unpaid assistance to non-cohabiting family members, neighbors or friends, participating in social/sports/other kinds of club, playing cards/chess/mahjong/participating in community club, attending the organization of community-related, engaging in charity or voluntary work, caregiving for an uncohabiting disabled or sick people without receiving compensation, attending a training or educational course, using the Internet, stocking investment) were classified into two categories: ever (at least once a month) and never, (8) Physical exercise encompassing regular physical exercises, less than regular physical exercises, and no physical exercise, and (9) Chronic diseases, including 1) hypertension, 2) high blood or sugar diabetes, 3) dyslipidemia, 4) stroke, 5) chronic lung diseases, 6) malignant tumor or cancer (excluding minor skin cancers), 7) kidney disease(except for cancer or tumor), 8) liver disease (except cancer, tumors, and fatty liver), 9) stomach or other digestive diseases (except for cancer or tumor), 10) angina, congestive heart failure, heart attack, coronary heart disease, or other heart problems, 11) nervous, emotional, or psychiatric problems, 12) asthma of self-reported (diagnosed by a doctor), 13) memory related disease, and 14) arthritis or rheumatism. By our previous criteria (45, 46), a continuous variable ranging from 0 to 14 was employed to quantify the chronic health issues in 14 common diseases. The numbers representing the chronic disease condition were categorized into 3 groups: 0, 1–2, and 3–14. These categories have been extensively employed in our prior research (39, 43–45, 47–50).

Statistical analysis

The statistical analyses were conducted using IBM SPSS version 23.0. Categorical variables were compared using the χ^2 test and presented as frequencies and percentages. Logistic regression was employed to analyze the odds ratios (ORs) and 95% confidence intervals (CIs) to examine the cross-sectional relationships of ADL disability and frailty in the individuals at baseline. The binary dependent variable of frailty (no-frailty and frailty) and ADL disability (no and yes) were subjected to analysis, with the regression models sequentially incorporating covariates, which were also used in our previous studies (50–52). Model 1 comprised activities of daily living disability and frailty, while model 2 additionally incorporated characteristics of socio-demographic (age, sex, marital status, educational level, current residence). Model 3 additionally encompassed health conditions and behaviors (alcohol drinking, smoking status, taking activities, physical exercise, chronic diseases). Lastly, model 4 incorporated BMI as an additional covariate. The Cox proportional hazards analysis was performed using hazard ratios (HRs) and 95% CIs to examine the prospective associations between baseline ADL disability in individuals without frailty at baseline, as well as the prospective associations between baseline frailty in individuals without ADL disability at baseline. The covariates were modeled through the same methods as those employed in cross-sectional analyses. The statistical significance of the results was determined based on a p-value<5%. The VIF (Variance Inflation Factor) multicollinearity diagnostic test in linear regression was conducted to detect collinearity among independent variables (53), and no collinear relationships were found between frailty and ADL (VIF < 5).

Results

Table 1 presents the baseline characteristics of individuals according to frailty status. The mean age of participants was 61.21 (SD ± 10.19), 37.74% were male; 2.62% were above vocational school, 3.88% were in high school, and 58.27% were less than elementary school; 83.88% were single; 92.02% were living in rural; 19.35% were drinking more than once a month, and 6.96% were drinking less than once a month. 48.99% were taking activities; 24.33% were current smoking, and 8.97% were former smoking; 45.12% were regular physical exercises, and 42.80% were less than regular physical exercises; 27.48% had 3–14 chronic diseases, and 51.24% had 1–2 chronic diseases; 6.16% had BADL disability, 17.71% had IADL disability, and 19.84% had ADL disability. The frequency of frailty was 11.78%. The distribution of age, age groups, sex, educational level, marital status, alcohol drinking, taking activities, physical exercise, chronic diseases, BADL, IADL, and ADL exhibited significant differences between individuals with or without frailty.

Table 2 demonstrates the baseline characteristics of individuals according to the status of BADL, IADL and ADL. A total of 2,638 BADL disability individuals 162 (6.14%) and BADL normal 2,476 (93.86%) at baseline were incorporated into the cross-sectional analysis. The distribution of age groups, educational level, smoking status, taking activities, physical exercise, and chronic diseases exhibited variations among the components of BADL. A total of 2,671 IADL disability individuals 466 (17.45%) and IADL normal 2,205 (82.55%) at baseline were incorporated into the cross-sectional analyses. The distribution of age groups, sex, educational level, current residence, alcohol drinking status, taking activities, physical exercise, chronic diseases, and BMI exhibited significant variations among the components of IADL. A total of 2,631 ADL disability individuals 522 (19.84%) and ADL normal 2,109 (80.16%) at baseline were incorporated into the cross-sectional analysis. The distribution of age

10.3389/fpubh.2024.1382384

TABLE 1 Baseline characteristics of participants according to the status of frailty in CHARLS Waves 2011 (*N*, %).

Variables	No- frailty (2321)	Frailty (310)	All participants (2631)	*t*/$\chi 2$	*p*-value
Age (years)	60.57 ± 9.93	66.00 ± 10.82	61.21 ± 10.19	−8.380	<0.001
Age groups (years)					
45–54	687 (29.60)	40 (12.90)	727 (27.63)	79.245	<0.001
55–64	865 (37.27)	105 (33.87)	970 (36.87)		
65–74	540 (23.27)	91 (29.35)	631 (23.98)		
≥75	229 (9.87)	74 (23.87)	303 (11.52)		
Sex					
Male	905 (38.99)	88 (28.39)	993 (37.74)	13.089	<0.001
Female	1,416 (61.01)	222 (71.61)	1,638 (62.26)		
Educational level					
Illiterate	770 (33.18)	157 (50.65)	927 (35.23)	39.193	<0.001
Less than elementary school	1,389 (59.84)	144 (46.45)	1,533 (58.27)		
High school	96 (4.14)	6 (1.94)	102 (3.88)		
Above vocational school	66 (2.84)	3 (0.97)	69 (2.62)		
Marital status					
Single	1963 (84.58)	244 (78.71)	2,207 (83.88)	6.961	0.008
Married	358 (15.42)	66 (21.29)	424 (16.12)		
Current residence					
Rural	2,128 (91.68)	293 (94.52)	2,421 (92.02)	2.985	0.084
Urban	193 (8.32)	17 (5.48)	210 (7.98)		
Alcohol drinking					
No	1,686 (72.64)	253 (81.61)	1939 (73.70)	12.458	0.002
Less than once a month	164 (7.07)	19 (6.13)	183 (6.96)		
More than once a month	471 (20.29)	38 (12.26)	509 (19.35)		
Smoking status					
No	1,534 (66.09)	221 (71.29)	1755 (66.70)	5.351	0.069
Former smoke	206 (8.88)	30 (9.68)	236 (8.97)		
Current smoke	581 (25.03)	59 (19.03)	640 (24.33)		
Taking activities					
No	1,155 (49.76)	187 (60.32)	1,342 (51.01)	12.202	<0.001
Yes	1,166 (50.24)	123 (39.68)	1,289 (48.99)		
Physical exercise					
No physical exercise	191 (8.23)	127 (40.97)	318 (12.09)	280.613	<0.001
Less than regular physical exercise	1,020 (43.95)	106 (34.19)	1,126 (42.80)		
Regular physical exercise	1,110 (47.82)	77 (24.84)	1,187 (45.12)		
Chronic diseases (counts)	1.70 ± 1.44	2.37 ± 1.76	1.78 ± 1.50	−6.502	<0.001
Chronic diseases groups (counts)					
0	520 (22.40)	40 (12.90)	560 (21.28)	42.331	<0.001
1–2	1,209 (52.09)	139 (44.84)	1,348 (51.24)		
3–14	592 (25.51)	131 (42.26)	723 (27.48)		
BMI (kg/m^2)	23.75 ± 4.02	23.25 ± 4.49	23.69 ± 4.08	1.850	0.065
BADL disability					
No	2,238 (96.42)	231 (74.52)	2,469 (93.84)	227.154	<0.001
Yes	83 (3.58)	79(25.48)	162 (6.16)		

(Continued)

TABLE 1 (Continued)

Variables	No- frailty (2321)	Frailty (310)	All participants (2631)	$t/\chi 2$	*p*-value
IADL disability					
No	2027 (87.33)	138 (44.52)	2,165 (82.29)	343.989	<0.001
Yes	294 (12.67)	172 (55.48)	466 (17.71)		
ADL disability					
No	1980 (85.31)	129 (41.61)	2,109 (80.16)	328.305	<0.001
Yes	341 (14.69)	181 (58.39)	522 (19.84)		

groups, educational level, current residence, smoking status, taking activities, physical exercise, chronic diseases, and BMI exhibited significant differences among components of ADL.

Table 3 demonstrates baseline characteristics categorized based on the subsequent onset of frailty in short-term period (2011–2013) and long-term period (2011–2015) in BADL, IADL, and ADL cohorts. In short-term period, the likelihood of developing frailty was higher among individuals aged 65–74, residing in rural areas, having chronic diseases, and with a BMI ranging from 18.5 to 24 kg/m^2. In long-term period, the likelihood of developing frailty was higher among individuals aged 65–74, educational level in illiterate, and having chronic diseases.

Table 4 reports baseline characteristics classified according to the subsequent onset of BADL, IADL, and ADL disability in short-term period (2011–2013) and long-term period (2011–2015). In short-term period, the likelihood of developing BADL disability was higher among individuals aged 65–74, male, single, never smoking, having less than regular physical exercises, and having 1–2 chronic diseases. The likelihood of developing IADL disability was higher among individuals single, aged 55–64, educational level less than elementary school, having regular physical exercises, and having 1–2 chronic diseases. They tended to take no activities. The likelihood of developing ADL disability was higher among individuals aged 55–64, female, single, educational level less than elementary school, having regular physical exercises, and having 1–2 chronic diseases. They tended to never smoke and take no activities. In long-term period, the likelihood of developing BADL disability was higher among individuals aged 65–74, educational level less than elementary school, having less than regular physical exercises, and having 1–2 chronic diseases. The likelihood of developing IADL disability was higher among individuals aged 55–64, educational level less than elementary school, residing in rural areas, having less than regular physical exercises, having 1–2 chronic diseases, and with a BMI ranging from 18.5 to 24 kg/m^2. The likelihood of developing ADL disability was higher among individuals aged 55–64, educational level with illiterate or above vocational school, residing in rural areas, having less than regular physical exercises, having 1–2 chronic diseases, and BMI ranging from 18.5 to 24 kg/m^2.

Table 5 presents the cross-sectional relationship between ADL in baseline and frailty, frailty as the dependent variable. Both BADL (OR = 6.660, 95% CI 4.519–9.815), IADL (OR = 5.950, 95% CI 4.490–7.886), and ADL (OR = 5.658, 95% CI 4.278–7.483) disability were associated with frailty significantly after controlling for covariates of sex, age, educational level, marital status, current residence, alcohol drinking, smoking status, taking activities, physical exercise, chronic diseases, and BMI (adjusted model 4).

Table 6 presents the cross-sectional relationship between baseline frailty and ADL, ADL as the dependent variable. Frailty was significantly associated with BADL (OR = 6.741, 95% CI 4.574–9.933), IADL (OR = 6.042, 95% CI 4.555–8.016) and ADL (OR = 5.735, 95% CI 4.333–7.591) disability after controlling for covariates of sex, age, marital status, educational level, current residence, alcohol drinking, smoking status, taking activities, physical exercise, chronic diseases, and BMI (adjusted model 4).

Table 7 reports the prospective associations between baseline ADL and frailty after 2 years and 4 years of follow-up in the individuals without frailty at baseline. First, in crude analysis, IADL and ADL disability showed a significant association with incident frailty during the short-term [IADL disability: HR = 2.603 (1.563, 4.335); ADL disability: HR = 2.499 (1.533, 4.072)]. After controlling for covariates of age, sex, marital status, educational level, current residence, alcohol drinking, smoking status, taking activities, physical exercise, chronic diseases, and BMI, IADL disability [HR = 1.971 (1.150, 3.379)] and ADL disability [HR = 1.920 (1.146, 3.215)] showed a significant association with incident frailty during the short-term. Second, in crude analysis, IADL and ADL disability showed a significant association with incident frailty during the long-term [IADL disability: HR = 2.685 (1.472, 4.898); ADL disability: HR = 2.111 (1.165, 3.826)]. After controlling for covariates of age, sex, educational level, marital status, and current residence, IADL and ADL disability showed significant association with incident frailty [IADL disability: HR = 2.498 (1.349, 4.626); ADL disability: HR = 1.873 (1.018, 3.448)] (adjusted model 2). After adjusting for all covariates, IADL disability [HR = 2.056 (1.085, 3.895)] still showed a significant association with incident frailty, but the ADL disability [HR = 1.556 (0.830, 2.917)] did not show significant association with incident frailty (adjusted model 4).

Table 8 reports the prospective associations between frailty in baseline and ADL after 2 years and 4 years of follow-up in individuals without ADL disability in baseline. First, in crude analysis, frailty showed a significant association with incident BADL disability [frailty: HR = 2.044 (1.256, 3.327)], IADL disability [frailty: HR = 2.069 (1.348, 3.177)] and ADL disability [frailty: HR = 1.865(1.209, 2.876)] during the short-term. After controlling for covariates of age, sex, marital status, educational level, and current residence, frailty was significantly associated with incident BADL disability [frailty: HR = 2.008 (1.210, 3.334)], IADL disability [frailty: HR = 1.740 (1.110, 2.725)], and ADL disability [frailty: HR = 1.703 (1.085, 2.671)] (adjusted model 2). After adjusting for all covariates, frailty was not significantly associated with incident BADL disability [frailty: HR = 1.573 (0.912, 2.712)], IADL disability [frailty: HR = 1.437 (0.901, 2.291)], and ADL disability [frailty: HR = 1.393 (0.873, 2.225)] during the short-term (adjusted

10.3389/fpubh.2024.1382384

TABLE 2 Baseline characteristics of participants according to the level of BADL, IADL and ADL in CHARLS Waves 2011 (*N*, %).

Variables	BADL disability (162)	IADL disability (466)	ADL disability (522)
Age groups(years)			
45–54	26 (16.05)	89 (19.10)	101 (19.35)
55–64	50 (30.86)	146 (31.33)	164 (31.42)
65–74	44 (27.16)	145 (31.12)	158 (30.27)
≥75	42 (25.93)	86 (18.45)	99 (18.97)
$\chi 2$ (p)	42.057 (<0.001)	58.091 (<0.001)	63.518 (<0.001)
Sex			
Male	71 (43.83)	154 (33.05)	180 (34.48)
Female	91 (56.17)	312 (66.95)	342 (65.52)
$\chi 2$ (p)	2.742 (0.098)	5.206 (0.023)	2.944 (0.086)
Educational level			
Illiterate	75 (46.30)	233 (50.00)	256 (49.04)
Less than elementary school	83 (51.23)	220 (47.21)	251 (48.08)
High school	2 (1.23)	9 (1.93)	10 (1.92)
Above vocational school	2 (1.23)	4 (0.86)	5 (0.96)
$\chi 2$ (p)	11.821 (0.008)	59.048 (<0.001)	60.170 (<0.001)
Marital status			
Single	135 (83.33)	379 (81.33)	430 (82.38)
Married	27 (16.67)	87 (18.67)	92 (17.62)
$\chi 2$ (p)	0.045 (0.832)	3.025 (0.082)	1.097 (0.295)
Current residence			
Rural	151 (93.21)	440 (94.42)	494 (94.64)
Urban	11 (6.79)	26 (5.58)	28 (5.36)
$\chi 2$ (p)	0.323 (0.570)	4.532 (0.033)	6.076 (0.014)
Alcohol drinking			
No	118 (72.84)	363 (77.90)	399 (76.44)
Less than once a month	13 (8.02)	32 (6.87)	36 (6.90)
More than once a month	31 (19.14)	71 (15.24)	87 (16.67)
$\chi 2$ (p)	0.293 (0.864)	6.396 (0.041)	3.083 (0.214)
Smoking status			
No	95 (58.64)	301 (64.59)	333 (63.79)
Former smoke	26 (16.05)	54 (11.59)	64 (12.26)
Current smoke	41 (25.31)	111 (23.82)	125 (23.95)
$\chi 2$ (p)	11.488 (0.003)	4.991 (0.082)	8.727 (0.013)
Taking activities			
No	96 (59.26)	280 (60.09)	309 (59.20)
Yes	66 (40.74)	186 (39.91)	213 (40.80)
$\chi 2$ (p)	4.685 (0.030)	18.679 (<0.001)	17.471 (<0.001)
Physical exercise			
No physical exercise	46 (28.40)	108 (23.18)	115 (22.03)
Less than regular physical exercise	59 (36.42)	177 (37.98)	203 (38.89)
Regular physical exercise	57 (35.19)	181 (38.84)	204 (39.08)
$\chi 2$ (p)	43.344 (<0.001)	65.893 (<0.001)	60.858 (<0.001)
Chronic diseases(counts)			
t (p)	−6.117 (<0.001)	−8.450 (<0.001)	−9.145 (<0.001)

(Continued)

TABLE 2 (Continued)

Variables	BADL disability (162)	IADL disability (466)	ADL disability (522)
Chronic diseases categories			
0	11 (6.79)	56 (12.02)	60 (11.49)
1–2	80 (49.38)	218 (46.78)	247 (47.32)
3–14	71 (43.83)	192 (41.20)	215 (41.19)
$\chi 2$ (p)	34.008 (<0.001)	66.055 (<0.001)	75.804 (<0.001)
BMI (kg/m^2)			
<18.5	17 (10.49)	55 (11.80)	59 (11.30)
18.5–24	75 (46.30)	228 (48.93)	251 (48.08)
24–28	44 (27.16)	134 (28.76)	151 (28.93)
≥28	26 (16.05)	49 (10.52)	61 (11.69)
$\chi 2$ (p)	3.814 (0.282)	16.285 (0.001)	12.951 (0.005)

model 4). Second, in crude analysis, frailty was significantly associated with incident BADL disability [frailty: HR = 3.042 (1.982, 4.669)], IADL disability [frailty: HR = 2.364 (1.560, 3.582)] and ADL disability [frailty: HR = 1.840 (1.187, 2.852)] during the long-term. After adjusting for all covariates, frailty was significantly associated with incident BADL disability [frailty: HR = 1.820 (1.126, 2.939)] and IADL disability [frailty: HR = 1.724 (1.103, 2.694)]. However, frailty did not show a significant association with incident ADL disability [frailty: HR = 1.351 (0.846, 2.158)] during the long-term (adjusted model 4).

Discussion

The study based on a representative sample from CHARLS reveals ADL disability and frailty are common among middle-aged and older individuals in China (6). There is a positive, reciprocal, time-varying association between ADL disability and frailty. The present study provides the comprehensive analysis of the reciprocal associations between ADL/IADL/BADL and frailty, both longitudinally and cross-sectionally. First, there was a confirmed correlation between baseline ADL/IADL/BADL disability and frailty, as well as between baseline frailty and ADL/BADL/IADL disability. Second, ADL/IADL disability at baseline was reported to be associated with the onset of frailty significantly after a two-year follow-up. However, no significant associations were found between baseline frailty and the onset of ADL/BADL/IADL disability after a two-year follow-up. Last, Baseline IADL disability was significantly associated with the onset of frailty after a four-year follow-up. In contrast, the baseline frailty was significantly associated with the onset of BADL and IADL disability after a four-year follow-up.

The meta-analysis study (9) including cross-sectional and cohort studies, comprehensive analysis showed that frailty increased the likelihood of developing IADL and BADL disabilities. In terms of follow-up time, frailty was significantly associated with an elevated risk of disability onset in BADL and IADL after 2-5 years and above 5 years of follow-up, which was in line with our results after 4 years of follow-up; but no relevant data was found at 1–2 years of follow-up. Thus, further studies during short-term and long-term follow-up are needed to explore the dynamic association between frailty and incidence of ADL disability in middle-aged and older adults. Previous meta-analysis (30, 31) including studies from United States, the United Kingdom, Europe, Australia, Mexico, Korea and China revealed that during 1–15 years of follow-up, frailty individuals had a higher risk of both ADL and IADL disability compared to those without frailty among middle-aged and older people. In contrast, there was no significant association between frailty in baseline and the onset of ADL/BADL/IADL disability after a short-term (2-year) period in our study. The occurrence can be elucidated by the cumulative effect, demonstrating significant association between frailty and the longitudinal onset of BADL and IADL disability over a long-term (4-year) period.

Similarly, previous studies have also reported that disability in ADL/BADL/IADL is associated with frailty in cross-section (6, 34, 54, 55), which aligns with our results. Other research reported that BADL and IADL disability at baseline did not serve as predictors for the occurrence of frailty after one-year follow-up in community-dwelling older adults (1). This study is conducted in middle-aged and older people, IADL and ADL disability at baseline serve as predictors for the occurrence of frailty after short-term follow-up, IADL disability at baseline serves as predictors for the onset of frailty after long-term follow-up among middle-aged and older individuals. The occurrence can be ascribed to the cumulative effect.

In theory, two directions of this relationship are reasonable according to middle-aged and older individuals. Through various potential mechanisms, frailty can exert an impact on ADL disability. For instance, frailty individuals commonly had a higher prevalence of chronic diseases than non-frailty people (56). People with chronic conditions demonstrated higher incidence rates of disability across all ADL items (57–59), our results also supported this view. Over time, the decline of BADL such as bathing, walking, toileting, dressing, transferring and eating, as well as IADL such as performing housework, shopping, cooking, taking medicine and financial management will increase. IADL represent the functional competence required for complex everyday tasks, such as shopping or meal preparation, and are recognized to decline before BADL associated with self-care (60). Besides, frailty phenotype demonstrated independent predictability for ADL disability. The presence of frailty syndrome may serve as an etiologic factor and physiological precursor in the development of disability, owing to its primary characteristics encompassing weakness, exhaustion, weight loss,

TABLE 3 Baseline characteristics classified according to subsequent onset of frailty.

Variables	2011 → 2013						2011 → 2015					
	BADL disability Incidence rate (*N* = 92, %)	*p1*	IADL disability Incidence rate (*N* = 92, %)	*p2*	ADL disability Incidence rate (*N* = 92, %)	*p3*	BADL disability |Incidence rate (*N* = 60, %)	*p1*	IADL disability Incidence rate (*N* = 60, %)	*p2*	ADL disability Incidence rate (*N* = 60, %)	*p3*
Age(years)		0.008		0.005		0.007		0.033		0.030		0.032
45–54	1.54		1.53		1.55		1.92		1.89		1.93	
55–64	2.72		2.69		2.73		2.88		2.84		2.89	
65–74	3.00		2.96		3.01		3.69		3.63		3.69	
≥75	1.09		1.08		1.09		1.12		1.10		1.12	
Sex		0.911		0.886		0.898		0.199		0.221		0.206
Male	3.09		3.05		3.10		2.40		2.37		2.41	
Female	5.27		5.21		5.28		7.21		7.10		7.22	
Educational level		0.001		0.001		0.001		0.018		0.022		0.019
Illiterate	4.09		4.04		4.10		4.97		4.89		4.98	
Less than elementary school	4.27		4.22		4.28		4.17		4.10		4.17	
High school	0.00		0.00		0.00		0.16		0.16		0.16	
Above vocational school	0.00		0.00		0.00		0.32		0.32		0.32	
Marital status		0.175		0.158		0.179		0.372		0.343		0.375
Single	6.81		6.73		6.83		8.01		7.89		8.03	
Married	1.54		1.53		1.55		1.60		1.58		1.61	
Current residence		0.021		0.021		0.021		0.100		0.105		0.099
Rural	8.17		8.08		8.20		9.46		9.31		9.47	
Urban	0.18		0.18		0.18		0.16		0.16		0.16	
Alcohol drinking		0.137		0.148		0.142		0.146		0.157		0.149
No	6.90		6.82		6.92		8.01		7.89		8.03	
Less than once a month	0.45		0.45		0.46		0.16		0.16		0.16	
More than once a month	1.00		0.99		1.00		1.44		1.42		1.44	
Smoking status		0.631		0.641		0.626		0.550		0.596		0.560
No	5.54		5.48		5.56		7.37		7.26		7.38	
Former smoke	0.54		0.54		0.55		0.48		0.47		0.48	
Current smoke	2.27		2.24		2.28		1.76		1.74		1.77	

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TABLE 3 (Continued)

Variables	2011 → 2013						2011 → 2015					
	BADL disability Incidence rate (*N* = 92, %)	*p1*	IADL disability Incidence rate (*N* = 92, %)	*p2*	ADL disability Incidence rate (*N* = 92, %)	*p3*	BADL disability |Incidence rate (*N* = 60, %)	*p1*	IADL disability Incidence rate (*N* = 60, %)	*p2*	ADL disability Incidence rate (*N* = 60, %)	*p3*
Taking activities		0.389		0.374		0.384		0.070		0.078		0.073
No	4.54		4.49		4.55		6.09		5.99		6.10	
Yes	3.81		3.77		3.83		3.53		3.47		3.53	
Physical exercise		0.190		0.202		0.188		0.452		0.469		0.454
No physical exercise	0.64		0.63		0.64		0.64		0.63		0.64	
Less than regular physical exercise	4.45		4.40		4.46		4.97		4.89		4.98	
Regular physical exercise	3.27		3.23		3.28		4.01		3.94		4.01	
Chronic diseases(counts)		0.005		0.004		0.006		0.016		0.013		0.016
0	1.09		1.08		1.09		1.12		1.10		1.12	
1–2	3.63		3.59		3.64		4.01		3.94		4.01	
3–14	3.63		3.59		3.64		4.49		4.42		4.49	
BMI (kg/m^2)		0.018		0.013		0.016		0.114		0.109		0.102
<18.5	1.36		1.35		1.37		1.28		1.26		1.28	
18.5–24	3.36		3.32		3.37		4.81		4.73		4.82	
24–28	2.63		2.60		2.64		2.08		2.05		2.09	
≥28	1.00		0.99		1.00		1.44		1.42		1.44	

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TABLE 4 Baseline characteristics classified according to subsequent onset of BADL, IADL, and ADL disability.

Variables	2011 → 2013						2011 → 2015					
	Frailty→ BADL disability Incidence rate (*N* = 123,%)	*p1*	Frailty→ IADL disability Incidence rate (*N* = 290,%)	*p2*	Frailty→ ADL disability Incidence rate (*N* = 307,%)	*p3*	Frailty→ BADL disability Incidence rate (*N* = 143,%)	*p1*	Frailty→ IADL disability Incidence rate (*N* = 331,%)	*p2*	Frailty→ ADL disability Incidence rate (*N* = 348,%)	*p3*
Age(years)		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001
45–54	1.00		2.32		3.00		0.88		3.83		4.69	
55–64	1.62		5.17		6.75		2.09		5.64		7.42	
65–74	2.41		4.49		5.87		3.14		5.53		7.16	
≥75	1.41		3.00		3.56		1.76		2.61		3.39	
Sex		<0.001		0.380		0.033		0.885		0.337		0.733
Male	3.46		6.10		8.00		2.70		6.17		7.75	
Female	2.99		8.88		11.18		5.17		11.44		14.91	
Educational level		0.559		<0.001		<0.001		0.023		<0.001		<0.001
Illiterate	2.51		6.71		8.43		3.69		8.04		11.39	
Less than elementary school	3.61		7.85		10.18		4.02		8.94		0.52	
High school	0.26		0.31		0.44		0.17		0.48		0.20	
Above vocational school	0.05		0.10		0.12		0.00		0.16		11.39	
Marital status		0.003		0.027		<0.001		0.272		0.163		0.295
Single	4.87		12.19		15.05		6.38		14.80		18.88	
Married	1.57		2.79		4.12		1.49		2.82		3.78	
Current residence		0.994		0.182		0.240		0.751		0.001		0.012
Rural	5.97		14.10		17.99		7.26		17.03		21.68	
Urban	0.47		0.88		1.19		0.61		0.59		0.98	
Alcohol drinking		0.558		0.245		0.677		0.746		0.776		0.929
No	4.56		11.52		14.62		5.89		13.20		17.12	
Less than once a month	0.47		0.88		1.06		0.66		1.06		1.50	
More than once a month	1.41		2.58		3.50		1.32		3.35		4.04	
Smoking status		<0.001		0.093		0.017		0.525		0.463		0.298
No	3.14		9.87		12.37		5.17		11.92		15.43	
Former smoke	1.00		1.70		2.31		0.61		1.60		2.08	

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TABLE 4 (Continued)

Variables	2011 → 2013						2011 → 2015					
	Frailty→ BADL disability Incidence rate (*N* = 123,%)	*p1*	Frailty→ IADL disability Incidence rate (*N* = 290,%)	*p2*	Frailty→ ADL disability Incidence rate (*N* = 307,%)	*p3*	Frailty→ BADL disability Incidence rate (*N* = 143,%)	*p1*	Frailty→ IADL disability Incidence rate (*N* = 331,%)	*p2*	Frailty→ ADL disability Incidence rate (*N* = 348,%)	*p3*
Current smoke	2.30		3.41		4.50		2.09		4.10		5.14	
Taking activities		0.978		<0.001		<0.001		0.120		0.133		0.187
No	3.25		8.88		11.06		4.51		9.31		11.91	
Yes	3.20		6.10		8.12		3.36		8.30		10.74	
Physical exercise		0.002		0.010		0.002		<0.001		0.047		0.033
No physical exercise	1.31		2.07		2.81		1.65		2.08		2.67	
Less than regular physical exercise	2.67		6.35		8.12		3.58		8.09		10.55	
Regular physical exercise	2.46		6.56		8.24		2.64		7.45		9.44	
Chronic diseases(counts)		0.001		<0.001		0.001		0.006		0.001		0.030
0	0.84		2.48		3.12		1.27		3.57		4.56	
1–2	2.83		7.49		9.56		3.52		8.41		11.07	
3–14	2.78		5.01		6.50		3.08		5.64		7.03	
BMI (kg/m^2)		0.226		0.106		0.138		0.061		0.001		0.019
<18.5	0.63		1.39		1.81		0.88		1.81		2.15	
18.5–24	2.51		7.64		9.43		3.36		8.83		11.46	
24–28	2.36		4.29		5.68		2.20		4.52		5.92	
≥28	0.94		1.65		2.25		1.43		2.45		3.13	

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TABLE 5 Odds ratios (ORs) and 95% confidence interval (CIs) for frailty at baseline associated with BADL, IADL, and ADL disability at baseline.

N = 2,631	Model 1 OR (95% CI)	Wald, df	*p*-value	Model 2 OR (95% CI)	Wald, df	*p*-value	Model 3 OR (95% CI)	Wald, df	*p*-value	Model 4 OR (95% CI)	Wald, df	*p*-value
BADL disability												
No (2469)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
Yes (162)	9.221 (6.586, 12.911)	167.395, 1	<0.001	8.288 (5.817, 11.808)	137.070, 1	<0.001	6.588 (4.478, 9.693)	91.563, 1	<0.001	6.660 (4.519, 9.815)	91.815, 1	<0.001
IADL disability												
No (2165)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
Yes (466)	8.593 (6.658, 11.092)	272.880, 1	<0.001	7.231 (5.560, 9.404)	217.697, 1	<0.001	6.025 (4.547, 7.984)	156.399, 1	<0.001	5.950 (4.490, 7.886)	153.997, 1	<0.001
ADL disability												
No (2109)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
Yes (522)	8.147 (6.323, 10.497)	263.255, 1	<0.001	6.860 (5.283, 8.907)	208.913, 1	<0.001	5.714 (4.322, 7.556)	149.546, 1	<0.001	5.658 (4.278, 7.483)	147.638, 1	<0.001

Model 1: unadjusted.
Model 2: adjusted for age, sex, educational level, marital status, current residence.
Model 3: adjusted for age, sex, educational level, marital status, current residence, alcohol drinking, smoking status, taking activities, physical exercise, chronic diseases.
Model 4: adjusted for age, sex, educational level, marital status, current residence, alcohol drinking, smoking status, taking activities, physical exercise, chronic diseases, BMI.

TABLE 6 Odds ratios (ORs) and 95% confidence interval (CIs) for BADL, IADL, and ADL disability at baseline associated with frailty at baseline.

	N = 2,631	Model 1 OR (95% CI)	Wald, df	*p*-value	Model 2 OR (95% CI)	Wald, df	*p*-value	Model 3 OR (95% CI)	Wald, df	*p*-value	Model 4 OR (95% CI)	Wald, df	*p*-value
Frailty→BADL disability	No (2321)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
	Yes (310)	9.221 (6.586, 12.911)	167.395, 1	<0.001	8.367 (5.870, 11.925)	138.0391	<0.001	6.676 (4.536, 9.826)	92.712, 1	<0.001	6.741 (4.574, 9.933)	93.042, 1	<0.001
Frailty→IADL disability	No (2321)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
	Yes (310)	8.593 (6.658, 11.092)	272.880, 1	<0.001	7.248 (5.572, 9.429)	217.861, 1	<0.001	6.114 (4.609, 8.110)	157.720, 1	<0.001	6.042 (4.555, 8.016)	155.607, 1	<0.001
Frailty→ADL disability	No (2321)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
	Yes (310)	8.147 (6.323,10.497)	263.255, 1	<0.001	6.878 (5.296, 8.932)	209.096, 1	<0.001	5.789 (4.374, 7.663)	150.683, 1	<0.001	5.735 (4.333, 7.591)	149.099, 1	<0.001

Model 1: unadjusted.
Model 2: adjusted for age, sex, educational level, marital status, current residence.
Model 3: adjusted for age, sex, educational level, marital status, current residence, alcohol drinking, smoking status, taking activities, physical exercise, chronic diseases.
Model 4: adjusted for age, sex, educational level, marital status, current residence, alcohol drinking, smoking status, taking activities, physical exercise, chronic diseases, BMI.

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TABLE 7 Association between BADL, IADL, and ADL disability and incident frailty without frailty at baseline.

Follow-up period			Model 1 HR (95% CI)	Wald, df	*p*-value	Model 2 HR (95%CI)	Wald, df	*p*-value	Model 3 HR (95%CI)	Wald, df	*p*-value	Model 4 HR (95%CI)	Wald, df	*p*-value
2011 → 2013	*N* = 1,101	BADL disability												
		No (1060)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
		Yes (41)	1.942 (0.794, 4.745)	2.117, 1	0.146	1.865 (0.750, 4.639)	1.799, 1	0.180	1.625 (0.641, 4.116)	1.048, 1	0.306	1.632 (0.644, 4.134)	1.065, 1	0.302
	N = 1,114	IADL disability												
		No (975)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
		Yes (139)	2.603 (1.563, 4.335)	13.524, 1	<0.001	2.246 (1.333, 3.786)	9.236, 1	0.002	1.985 (1.159, 3.398)	6.245, 1	0.012	1.971 (1.150, 3.379)	6.094, 1	0.014
	N = 1,098	ADL disability												
		No (935)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
		Yes (163)	2.499 (1.533, 4.072)	13.514, 1	<0.001	2.134 (1.295, 3.517)	8.852, 1	0.003	1.930 (1.153, 3.230)	6.256, 1	0.012	1.920 (1.146, 3.215)	6.149, 1	0.013
2011 → 2015	*N* = 624	BADL disability												
		No (600)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
		Yes (24)	0.399 (0.053, 3.006)	0.796, 1	0.372	0.346 (0.045, 2.628)	1.054, 1	0.305	0.315 (0.041, 2.411)	1.238, 1	0.266	0.318 (0.042, 2.435)	1.216, 1	0.270
	N = 634	IADL disability												
		No (537)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
		Yes (97)	2.685 (1.472, 4.898)	10.376, 1	0.001	2.498 (1.349, 4.626)	8.473, 1	0.004	2.094 (1.109, 3.956)	5.187, 1	0.023	2.056 (1.085, 3.895)	4.888, 1	0.027
	N = 623	ADL disability												
		No (510)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
		Yes (113)	2.111 (1.165, 3.826)	6.068, 1	0.014	1.873 (1.018, 3.448)	4.068, 1	0.044	1.583 (0.845, 2.963)	2.059, 1	0.151	1.556 (0.830, 2.917)	1.899, 1	0.168

Model 1: unadjusted.
Model 2: adjusted for age, sex, educational level, marital status, current residence.
Model 3: adjusted for age, sex, educational level, marital status, current residence, alcohol drinking, smoking status, taking activities, physical exercise, chronic diseases.
Model 4: adjusted for age, sex, educational level, marital status, current residence, alcohol drinking, smoking status, taking activities, physical exercise, chronic diseases, BMI.

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TABLE 8 Association between frailty and incident BADL, IADL and ADL disability without disability at baseline.

Follow-up period			Model 1 HR (95% CI)	Wald, df	*p*-value	Model 2 HR (95% CI)	Wald, df	*p*-value	Model 3 HR (95% CI)	Wald, df	*p*-value	Model 4 HR (95%CI)	Wald, df	*p*-value
2011 → 2013	BADL disability	Frailty (*N* = 1909)												
		No (1715)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
		Yes (194)	2.044 (1.256, 3.327)	8.271, 1	0.004	2.008 (1.210, 3.334)	7.268, 1	0.007	1.507 (0.877, 2.590)	2.202, 1	0.138	1.573 (0.912, 2.712)	2.658, 1	0.103
	IADL disability	Frailty (*N* = 1936)												
		No (1815)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
		Yes (121)	2.069 (1.348, 3.177)	11.047, 1	0.001	1.740 (1.110, 2.725)	5.844, 1	0.016	1.449 (0.909, 2.310)	2.425, 1	0.119	1.437 (0.901, 2.291)	2.318, 1	0.128
	ADL disability	Frailty (*N* = 1,601)												
		No (1493)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
		Yes (108)	1.865 (1.209, 2.876)	7.948, 1	0.005	1.703 (1.085, 2.671)	5.365, 1	0.021	1.401 (0.878, 2.235)	1.995, 1	0.158	1.393 (0.873, 2.225)	1.930, 1	0.165
2011 → 2015	BADL disability	Frailty (*N* = 1818)												
		No (1641)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
		Yes (177)	3.042 (1.982, 4.669)	25.887, 1	<0.001	2.311 (1.473, 3.624)	13.302, 1	<0.001	1.807 (1.121, 2.912)	5.902, 1	0.015	1.820(1.126, 2.939)	5.983, 1	0.014
	IADL disability	Frailty (*N* = 1879)												
		No (1767)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
		Yes (112)	2.364 (1.560, 3.582)	16.441, 1	<0.001	1.963 (1.274, 3.024)	9.348, 1	0.002	1.732 (1.108, 2.707)	5.817, 1	0.016	1.724 (1.103, 2.694)	5.715, 1	0.017
	ADL disability	Frailty (*N* = 1,536)												
		No (1439)	Ref (1.000)			Ref (1.000)			Ref (1.000)			Ref (1.000)		
		Yes (97)	1.840 (1.187, 2.852)	7.436, 1	0.006	1.544 (0.978, 2.438)	3.484, 1	0.062	1.361 (0.852, 2.173)	1.662, 1	0.197	1.351 (0.846, 2.158)	1.585, 1	0.208

Model 1: unadjusted.
Model 2: adjusted for age, sex, educational level, marital status, current residence.
Model 3: adjusted for age, sex, educational level, marital status, current residence, alcohol drinking, smoking status, taking activities, physical exercise, chronic diseases.
Model 4: adjusted for age, sex, educational level, marital status, current residence, alcohol drinking, smoking status, taking activities, physical exercise, chronic diseases, BMI.

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slowness, and low physical activity. Frailty was likely to primarily impact functions reliant on energy expenditure and speed of execution (e.g., mobility), frailty initially affected mobility tasks before manifesting difficulties in BADL and IADL (9, 35, 56). Additionally, a 2-year longitudinal study revealed that individuals with weakness faced a significantly incidence risk of ADL disability compared to those without weakness individuals at baseline in the older (61). A cohort study indicated that frailty acts as a significant negative factor in the recovery process of disability in ADL among newly disabled Chinese older people (62). Furthermore, frailty is characterized by a decline in the body's reserve capacity, implying physiological decrements and adverse health outcomes can be anticipated (63). The underlying mechanism involves a multifaceted interaction, including a lower activity level, malnutrition, sarcopenia, weight loss, and difficulty maintaining homeostasis (35). This multiorgan system imbalance manifests as impaired energy metabolism and neuromuscular alterations (64), along with the growth of age, potentially leading to a decline in physical functioning as well as an increased occurrence of ADL (65). Simultaneously, existing research has reported that engagement in physical activities can reduce the risk of ADL disability and functional limitations among older individuals (66, 67), our findings also support this view, one of the characteristics of frailty is a decrease in physical activity, which would increase the risk of ADL disability.

Similarly, previous studies have also demonstrated that disability in ADL is a necessary predictor of frailty (6, 34). Individuals who had difficulty with ADL were more likely to show having frailty (55). Through a variety of underlying mechanisms, ADL disability can affect frailty. For example, having more difficulties with BADL and IADL increases the risk of frailty by limiting older people's social participation and physical activity. People with higher levels of ADL functioning tend to experience more social participation (68), and individuals with ADL disabilities experience the opposite pattern. Disability in BADL, e.g., eating, bathing, dressing, and toileting, etc., as well as IADL, e.g., shopping, taking medicine and financial management, etc., can act as a hindrance that causes or exacerbates low level of social participation (69), may results social isolation and loneliness (70), accordingly promoting the frailty progression (71, 72). Low physical activity poses a significant risk factor for the development of frailty (73, 74). Difficulties in ADL can impede mobility and hinder flexibility, inevitably leading to insufficient levels of physical activity and reduced function of extremities, and therefore increasing the risk of physical frailty as people age (75, 76). People with ADL difficulties tend to experience more negative affect (68), which is a risk factor for frailty (77). Disability in ADL, such as continence control, housework and cooking, can serve as a stressor due to the loss of independence and decline in self-care abilities, causing or exacerbating high level of negative affect (69), and increasing the incidence risk of frailty (21, 72). The inability to perform essential ADL leads to dependence on others and/or mechanical aids, and negatively affects daily activities, safe conditions and quality of life (78), all those increase slowness, weakness, low physical activity, and exhaustion resulting in frailty (79, 80). In addition, the middle-aged and older participants with disability in ADL often suffer from chronic diseases (59), and the ability to take medicine in IADL may be restricted, which is not conducive to disease control, thus aggravating physical weakness and presenting frailty (3, 6).

Frailty is characterized by a condition of increased vulnerability to both exogenous and endogenous stressors, impacting the quality of life and raising the risk of adverse health-related outcomes for individuals (81, 82), and frailty is significantly associated with mortality (3). Frailty is described as a transition state between ADL disability and successful aging (83). Identifying potential frailty in middle-aged and older population is essential for early prevention and management. Special attention should be given to middle-aged and older person with ADL disability to prevent the incidence of their frailty. Besides, ADL disability is one independent risk factor for 7 years mortality in middle-aged and older adults in China (84), and ADL skills can facilitate successful aging (85). Frailty serves as a strong predictor for disability in ADL, while disability in ADL is also a strong predictor of frailty among middle-aged and older population. The findings of our research demonstrate that middle-aged and older individuals with ADL disability and frailty are both at high risk and require increased attention. The present study just examines the bivariate bidirectional association between frailty and ADL disability. Further studies are necessary to determine the impact of this relationship in order to break this vicious cycle.

Strengths and limitations of the study

This study possesses several strengths. It is based on a nationwide representative cohort with a relatively large sample size, which includes individuals aged ≥45 years. It explores the bidirectional association between frailty and ADL disability across two different time intervals and provides help to understand the short-term and long-term effects further. Certain limitations should be noted in the current study. Some predictors in our study, such as ADL, frailty, and disease history, were self-reported and potentially introduced partial information bias. The exclusion of some participants with incomplete data resulted in a reduced sample size and would affect the analysis results. This study did not investigate how certain lifestyles might relate to ADL disabilities, which should be carried out in the follow-up study.

Conclusion

In summary, this study established bidirectional cross-sectional and longitudinal associations between frailty and ADL using a nationwide representative sample in China. This study suggested that disability in ADL increased the risk of frailty and vice versa. They may create a vicious circle, negatively reinforcing each other. Early interventions targeting ADL disability or frailty for middle-aged and older adults will be beneficial to improving their health status. Accordingly, in the context of increasing aging, the interaction between ADL disability and frailty should be explored to prevent the development of a vicious cycle.

Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession

number(s) can be found at: https://charls.charlsdata.com/pages/data/111/zh-cn.html.

Author contributions

XiaopL: Writing – original draft, Writing – review & editing. XiaogL: Writing – review & editing. LS: Writing – review & editing. LY: Writing – review & editing. CW: Writing – review & editing. TY: Writing – review & editing. YL: Writing – review & editing. JL: Writing – review & editing. ML: Writing – review & editing. DZ: Writing – review & editing. YH: Writing – review & editing. HL: Writing – review & editing. LZ: Writing – review & editing.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. CHARLS was supported by the NSFC (70910107022 and 71130002) and National Institute on Aging (R03-TW008358-01 and R01-AG037031-03S1) and World Bank (7159234).

Acknowledgments

We thank the members of the CHARLS as well as all participants for their contribution.

Conflict of interest

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

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frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 07 May 2024
DOI 10.3389/fpubh.2024.1309673

OPEN ACCESS

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RECEIVED 08 October 2023
ACCEPTED 10 April 2024
PUBLISHED 07 May 2024

CITATION
Liu L, Zhang Y, Shi Y, Wu L, Meng L and Zhao T (2024) The bidirectional relationship between sarcopenia and disability in China: a longitudinal study from CHARLS. *Front. Public Health* 12:1309673. doi: 10.3389/fpubh.2024.1309673

The bidirectional relationship between sarcopenia and disability in China: a longitudinal study from CHARLS

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Objectives: Sarcopenia and disability represent significant concerns impacting the health of older people. This study aimed to explore the bidirectional relationship between sarcopenia and disability in Chinese older people.

Methods: This study recruited older people ≥60 years old from the China Health and Retirement Longitudinal Study. In phase I, the study analyzed the relation between disability and subsequent sarcopenia using multinomial logistic regression models. Conversely, in phase II, the study assessed whether sarcopenia was associated with future disability using binary logistic regression models.

Results: In phase I, 65 (16.80%) new cases of possible sarcopenia, 18 (4.65%) cases of sarcopenia, and 9 (2.33%) cases of severe sarcopenia were observed in the disabled older people and 282 (10.96%) new cases of possible sarcopenia, 97 (3.77%) cases of sarcopenia, 35 (1.36%) cases of severe sarcopenia were observed in the older people without disability. The OR (95% CI) for sarcopenia in older disabled individuals compared to those without disability was 1.61 (1.25–2.07). Adjusting for all covariates in 2011, the OR (95% CI) value for disabled individuals vs. those without disability was 1.35 (1.02–1.79). Subgroup analyses showed that disabled participants aged <80 years were more likely to have sarcopenia (OR = 1.42, 95% CI: 1.07–1.89), and the risk of sarcopenia did not differ significantly between sex subgroups. In phase II, 114 cases (33.83%) in the possible sarcopenia patients, 85 cases (28.91%) in the sarcopenia patients, 23 cases (35.94%) in the severe sarcopenia patients, and 501 cases (16.10%) in the individuals without sarcopenia showed symptoms of disability. The OR (95% CI) for disability was 2.66 (2.08–3.40) in the possible sarcopenia patients, 2.12 (1.62–2.77) in the sarcopenia patients, and 2.92 (1.74–4.91) in the severe sarcopenia patients compared with the no sarcopenia patients. After adjusting for all covariates in 2011, the OR (95% CI) values were 2.21 (1.70–2.85) in the possible sarcopenia patients, 1.58 (1.14–2.19) in the sarcopenia patients, and 1.99 (1.14–3.49) in the severe sarcopenia patients, as compared to the older people without sarcopenia. Subgroup analyses showed that compared with men, women with possible sarcopenia had a higher risk of disability (OR = 2.80, 95% CI: 1.98–3.97). In addition, participants aged <80 years with sarcopenia or severe sarcopenia s were more likely to have disability (OR = 2.13, 95% CI: 1.52–2.98; OR = 2.98, 95% CI: 1.60–5.54).

Conclusion: The occurrence of disability increase the risk of sarcopenia in the older people, and baseline sarcopenia predicts the future disability in older people.

KEYWORDS

sarcopenia, disability, bidirectional relationship, CHARLS, older people

Introduction

With the increasing aging of the population, the prevalence of sarcopenia is on the rise. Currently, ~50 million older persons worldwide suffer from sarcopenia, and this number is expected to reach 500 million by 2050 (1, 2). In Japan, the prevalence of sarcopenia among older individuals is 11.5–16.7% (3), while in China, it is 26.6% (4). Older people with sarcopenia experience significantly lower quality of life in terms of physical function, health status, and social function (5), and they are at a higher risk for falls, disability, death, cognitive impairment, and depression (6–12). Additionally, sarcopenia can either cause or exacerbate other conditions such as osteoporosis (13) and coronary heart disease (14). Therefore, it is crucial to identify the risk factors for sarcopenia in order to develop effective prevention programs. Furthermore, disability is also a significant issue in the aging population. In China, the number of disabled older people is projected to exceed 42 million in 2020 and reach 137 million by 2030 (15, 16). Disability negatively impacts the quality of life of the older people, and adds to the burden of care for their families and society (17). Therefore, it is important to study the factors influencing disability and work toward preventing disability in older people.

Several studies have analyzed the relationship between sarcopenia and disability, Xu et al. (7) found that sarcopenia was independently associated with disability in community-dwelling older people in China, with those suffering from sarcopenia being approximately twice as likely to be disabled in ADLs compared to those without sarcopenia. Kitamura et al. (3) demonstrated that older Japanese sarcopenia patients had an increased risk of disability, and there was no significant increase in disability risk for those with possible sarcopenia and those with only low muscle mass. However, no relevant studies have explored the interrelationship between the two. Considering the shared influencing factors and pathophysiological mechanisms between sarcopenia and disability, such as age, physical activity, inflammatory responses, and levels of oxidative stress, it is possible that they may interact with each other.

This study aims to analyze the relation between sarcopenia and disability based on the findings of the China Health and Retirement Longitudinal Study (CHARLS). In phase I, the study assessed disability and future sarcopenia's connection. In phase II, the study analyzed the relation between the presence of sarcopenia and disability.

Methods

Data sources

In this study, we utilized data from CHARLS (18). The data set is a longitudinal, nationally representative cohort survey with people in China aged 45 years and older, aiming at collecting information related to social, economic and health conditions. The national baseline assessment was conducted in 2011, involving ~17,000 participants, and follow-up assessments were carried out in 2013, 2015, and 2018, and there were studies described CHARLS in more detail (18, 19). The data of 2011 and 2015 were used for this study. In phase I, we focused on individuals without sarcopenia in 2011, dividing them into disability and no disability groups, and then followed up to 2015 to assess the development of possible sarcopenia, sarcopenia, and severe sarcopenia. In phase II, we studied individuals without disability in 2011, categorizing them into no sarcopenia, possible sarcopenia, sarcopenia, and severe sarcopenia groups, and followed them up to 2015 to assess disability status.

Participants

Phase I participants must meet the following requirements: (1) aged ≥60 years, (2) without possible sarcopenia and sarcopenia, (3) collected the information related to ADL, (4) successfully followed up in 2015. A total of 2,961 participants were included in the follow-up analysis (Figure 1). Phase II participants were required to (1) aged ≥60 years, (2) without disability, (3) collected the information related to sarcopenia, (4) successfully followed up in 2015. Ultimately, 3,806 participants were included in the follow-up analysis (Figure 1). Less than 5% of the data were missing covariable information, we imputed missing data based on mean imputation.

Sarcopenia

In this study, we adopted the AWGS 2019 standard to define and evaluate sarcopenia using three indexes: appendicular skeletal muscle mass (ASM), muscle strength and physical function (20). Sarcopenia is characterized by decreased muscle mass, accompanied by reduced physical function and/or muscle strength. In addition, the 2019 Asian Sarcopenia Working Group pointed out that if older people have normal muscle mass and decreased muscle strength, regardless of whether the physical function is decreased, they are called possible sarcopenia patients.

ASM is calculated using anthropometric equation developed and verified for China population (21). ASM = 0.193 * weight (kg) + 0.107 * height (cm) – 4.157 * sex (male = 1, female = 2) – 0.037 * age – 2.631. Studies have shown strong agreement between dual X-ray absorptiometry (DXA) and the ASM equation model (21, 22). The critical value of muscle mass reduction is determined according to the sex-specific lowest 20% of the height (Ht)-adjusted muscle mass [skeletal muscle mass index (SMI) = ASM/Ht2] within the study population (22–24). In this study, the SMI value of women is <5.38 kg/m^2, and that of men is <7.08 kg/m^2, which indicates that muscle mass is reduced. Muscle strength was measured using a grip strength meter, and values below 28 kg for males and below 18 kg for females indicate decreased muscle strength. Decline in physical function in this study was defined as a decline in lower limb mobility in the older person, which was assessed using the chair stand test, if an individual takes longer than 12 s to complete the task for five-times, it indicates a decline in physical function.

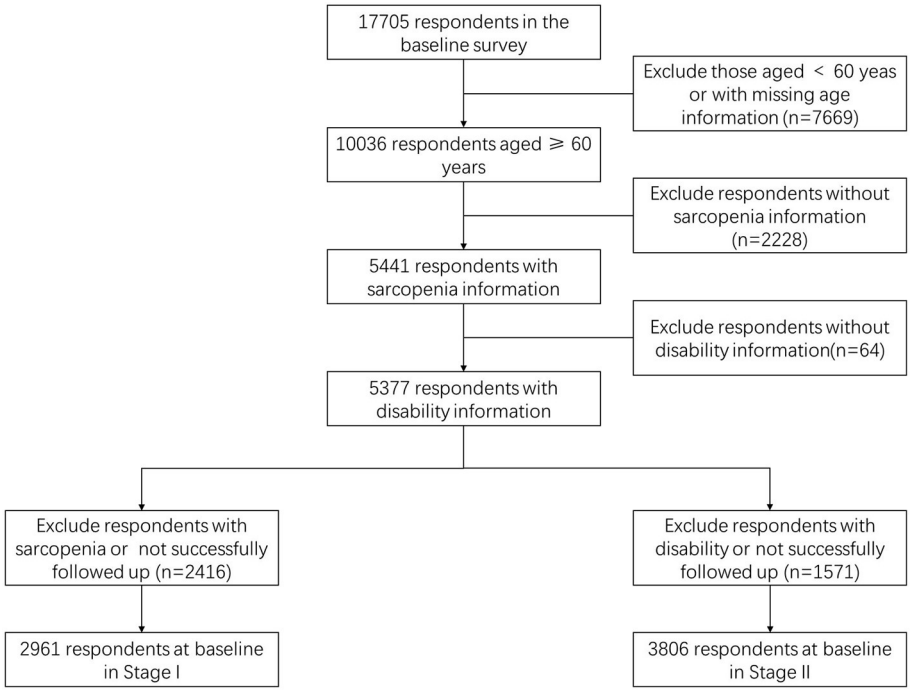

FIGURE 1
Flowchart of sample screening.

Disability

In this study, disability refers to the decreased ability of older people to perform activities of daily living assessed using the basic activities of daily living (BADL) and instrumental activities of daily living (IADL) scales (25). BADLs includes six questions: dressing, getting out of bed, eating, bathing, toileting and continence. IADLs includes five problems: doing housework, taking medication, shopping, cooking and handling finances. Each question includes four answer options: no difficulty; difficult but achievable; some difficulties and need help; unable to complete. The older people are considered to have a disability if they lack complete independence in any question (26, 27).

Covariates

Other covariates collected included sex (females and males), age, residence (rural and urban), marital status (married/cohabitated and separated/divorced/widowed/never married), educational level (illiterate/primary school, middle school, high school/vocational high school, and junior college or above), smoking status (still smoking, ever smoking, and never smoking), drinking status (drink more than once a month, drink but less than once a month, no drinking), body mass index (BMI $<$ 18.5, 18.5 $\leq$ BMI $<$ 24, BMI $\geq$ 24), and annual household expenditure level (in tertiles), whether accompanied by other chronic diseases [high blood sugar (HBS)/diabetes, lung disease, hypertension, heart disease, cancer, stroke, dyslipidemia, digestive disease, kidney disease, liver disease, emotional, nervous, or psychiatric problems, memory-related disease, arthritis or rheumatism and asthma].

Statistical analyses

We conducted statistical analyses to assess the normality of continuous variables using Skewness-Kurtosis tests. Since the age did not follow a normal distribution ($P < 0.05$), its description was based on the median (p25–p75), and the comparison of baseline characteristics between groups utilized the Wilcoxon rank sum test and Kruskal-Wallis rank sum test. Categorical variables were described with frequency (percentage), and the differences in baseline characteristics between groups were compared using the chi-square test. In phase I, we utilized binary logistic regression models to estimate the odds ratio (ORs) and confidence intervals (CIs) between baseline disability and subsequent sarcopenia. In phase II, binary logistic regression models were also used to investigate whether baseline sarcopenia was associated with an increased risk of disability in older people. Both models were adjusted for potential confounding factors (adjusted Model 1 adjusted for gender and age; adjusted model 2 adjusted all covariates in this study). Finally, sex and age ($<$80, $\geq$80) were analyzed in subgroups. In order to explore whether other chronic diseases will affect the results, we conducted a sensitivity analysis. In addition, we performed additional *post-hoc* power analysis for each of the two phases. Statistical analyses were carried out using STATA version 17 software, with the significance level set at 0.05.

TABLE 1 Characteristics of the participants.

Characteristics		Phase I ($n = 2,961$)[a]			Phase II ($n = 3,806$)[b]				
		No disability	Disability	*P*-value	No sarcopenia	Possible sarcopenia	Sarcopenia	Severe sarcopenia	*P*-value
Number of participants		2,574	387	-	3,111	337	294	64	-
Sex *n* (%)	Male	1,396 (54.23)	156 (40.31)	<0.001	1,664 (53.49)	171 (50.74)	126 (42.86)	39 (60.94)	0.002
	Female	1,178 (45.77)	231 (59.69)		1,447 (46.51)	166 (49.26)	168 (57.14)	25 (39.06)	
Age		65 (62–69)	66 (62–70)	0.0092	65 (62–69)	67 (63–73)	71 (66–76)	75 (70–78.5)	0.0001
Residence *n* (%)	Rural	2,119 (82.32)	352 (90.96)	<0.001	2,485 (79.88)	285 (84.57)	268 (91.16)	60 (93.75)	<0.001
	Urban	455 (17.68)	35 (9.04)		626 (20.12)	52 (15.43)	26 (8.84)	4 (6.25)	
Marital status *n* (%)	Married/cohabitated	412 (16.01)	336 (86.82)	0.153	511 (16.43)	84 (24.93)	90 (30.61)	22 (34.38)	<0.001
	Separated/divorced/widowed/never married	2,162 (83.99)	51 (13.18)		2,600 (83.57)	253 (75.07)	204 (69.39)	42 (65.63)	
Educational level *n* (%)	Illiterate/primary school	2,055 (79.87)	344 (88.89)	<0.001	2,464 (79.23)	297 (88.13)	263 (90.07)	58 (90.63)	<0.001
	Middle school	366 (14.22)	33 (8.53)		443 (14.24)	29 (8.61)	22 (7.53)	4 (6.25)	
	High school/vocational high school	106 (4.12)	9 (2.33)		144 (4.63)	10 (2.97)	7 (2.40)	2 (3.13)	
	Junior college or above	46 (1.79)	1 (0.26)		59 (1.90)	1 (0.30)	0 (0.00)	0 (0.00)	
Smoking status *n* (%)	Still smoking	886 (34.42)	103 (26.61)	0.008	1,043 (33.53)	99 (29.38)	99 (33.67)	19 (29.69)	0.008
	Ever smoking	276 (10.72)	51 (13.18)		344 (11.06)	36 (10.68)	15 (5.10)	12 (18.75)	
	Never smoking	1,412 (54.86)	233 (60.21)		1,724 (55.42)	202 (59.94)	180 (61.22)	33 (51.56)	
Drinking status *n* (%)	Drink more than once a month	693 (26.92)	82 (21.19)	0.027	818 (26.29)	75 (22.26)	70 (23.81)	19 (29.69)	0.079
	Drink but Less than once a month	182 (7.07)	23 (5.94)		227 (7.30)	22 (6.53)	10 (3.40)	4 (6.25)	
	No drinking	1,699 (66.01)	282 (72.87)		2,066 (66.41)	240 (71.22)	214 (72.79)	41 (64.06)	
BMI *n* (%)	<18.5	146 (5.67)	23 (5.94)	0.193	180 (5.79)	1 (0.30)	147 (50)	25 (39.06)	<0.001
	18.5–24	1,455 (56.53)	200 (51.68)		1,719 (55.26)	219 (64.99)	147 (50)	39 (60.94)	
	≥24	973 (37.80)	164 (42.38)		1,212 (38.96)	117 (34.72)	0 (0.00)	0 (0.00)	
Household expenditure *n* (%)	Tertile 1	591 (23.94)	67 (18.06)	0.015	829 (26.65)	101 (29.97)	127 (43.20)	29 (45.31)	<0.001
	Tertile 2	1,250 (50.63)	215 (57.95)		1,507 (48.44)	158 (46.88)	124 (42.18)	21 (32.81)	
	Tertile 3	628 (25.44)	89 (23.99)		775 (24.91)	78 (23.15)	43 (14.63)	14 (21.88)	

(Continued)

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TABLE 1 (Continued)

Characteristics		Phase I ($n = 2,961$)[a]			Phase II ($n = 3,806$)[b]				
		No disability	Disability	*P*-value	No sarcopenia	Possible sarcopenia	Sarcopenia	Severe sarcopenia	*P*-value
High Blood Sugar (HBS)/diabetes *n* (%)	Yes	147 (5.71)	37 (9.56)	0.003	184 (5.91)	20 (5.93)	9 (3.06)	2 (3.13)	0.178
	No	2,427 (94.29)	350 (90.44)		2,927 (94.09)	317 (94.07)	285 (96.94)	62 (96.88)	
Lung disease *n* (%)	Yes	298 (11.58)	69 (17.83)	0.001	356 (11.44)	44 (13.06)	44 (14.97)	10 (15.63)	0.211
	No	2,276 (88.42)	318 (82.17)		2,755 (88.56)	293 (86.94)	250 (85.03)	54 (84.38)	
Hypertension *n* (%)	Yes	737 (28.63)	140 (36.18)	0.002	893 (28.70)	99 (29.38)	51 (17.35)	10 (15.63)	<0.001
	No	1,837 (71.37)	247 (63.82)		2,218 (71.30)	238 (70.62)	243 (82.65)	54 (84.38)	
Heart disease *n* (%)	Yes	326 (12.67)	79 (20.41)	<0.001	414 (13.31)	40 (11.87)	31 (10.54)	7 (10.94)	0.486
	No	2,248 (87.33)	308 (79.59)		2,697 (86.69)	297 (88.13)	263 (89.46)	57 (89.06)	
Cancer *n* (%)	Yes	18 (0.70)	5 (1.29)	0.216	20 (0.64)	2 (0.59)	4 (1.36)	1 (1.56)	0.442
	No	2,556 (99.30)	382 (98.71)		3,091 (99.36)	335 (99.41)	290 (98.64)	63 (98.44)	
Stroke *n* (%)	Yes	48 (1.86)	15 (3.88)	0.011	59 (1.90)	9 (2.67)	4 (1.36)	3 (4.69)	0.266
	No	2,526 (98.14)	372 (96.12)		3,052 (98.10)	328 (97.33)	290 (98.64)	61 (95.31)	
Dyslipidemia *n* (%)	Yes	254 (9.87)	49 (12.66)	0.091	311 (10.00)	24 (7.12)	7 (2.38)	3 (4.69)	<0.001
	No	2,320 (90.13)	338 (87.34)		2,800 (90.00)	313 (92.88)	287 (97.62)	61 (95.31)	
Digestive disease *n* (%)	Yes	555 (21.56)	113 (29.20)	0.001	674 (21.67)	71 (21.07)	67 (22.79)	19 (29.69)	0.451
	No	2,019 (78.44)	274 (70.80)		2,437 (78.33)	266 (78.93)	227 (77.21)	45 (70.31)	
Kidney disease *n* (%)	Yes	150 (5.83)	41 (10.59)	<0.001	179 (5.75)	27 (8.01)	10 (3.40)	3 (4.69)	0.098
	No	2,424 (94.17)	346 (89.41)		2,932 (94.25)	310 (91.99)	284 (96.60)	61 (95.31)	
Liver disease *n* (%)	Yes	96 (3.73)	23 (5.94)	0.039	127 (4.08)	10 (2.97)	8 (2.72)	1 (1.56)	0.378
	No	2,478 (96.27)	364 (94.06)		2,984 (95.92)	327 (97.03)	286 (97.28)	63 (98.44)	
Emotional, nervous, or psychiatric problems *n* (%)	Yes	28 (1.09)	14 (3.62)	<0.001	36 (1.16)	3 (0.89)	1 (0.34)	1 (1.56)	0.585
	No	2,546 (98.91)	373 (96.38)		3,075 (98.84)	334 (99.11)	293 (99.66)	63 (98.44)	

(Continued)

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TABLE 1 (Continued)

Characteristics		Phase I ($n = 2,961$)[a]			Phase II ($n = 3,806$)[b]				
		No disability	Disability	*P*-value	No sarcopenia	Possible sarcopenia	Sarcopenia	Severe sarcopenia	*P*-value
Memory-related disease *n* (%)	Yes	37 (1.44)	15 (3.88)	0.001	41 (1.32)	5 (1.48)	8 (2.72)	1 (1.56)	0.293
	No	2,537 (98.56)	372 (96.12)		3,070 (98.68)	332 (98.52)	286 (97.28)	63 (98.44)	
Arthritis or rheumatism *n* (%)	Yes	873 (33.92)	202 (52.20)	<0.001	1,078 (34.65)	143 (42.43)	106 (36.05)	21 (32.81)	0.040
	No	1,701 (66.08)	185 (47.80)		2,033 (65.35)	194 (57.57)	188 (63.95)	43 (67.19)	
Asthma *n* (%)	Yes	117 (4.55)	31 (8.01)	0.004	135 (4.34)	13 (3.86)	15 (5.10)	2 (3.13)	0.843
	No	2,457 (95.45)	356 (91.99)		2,976 (95.66)	324 (96.14)	279 (94.90)	62 (96.88)	

BMI, body mass index.
Tertile 1, High level of household expenditure; Tertile 2, Medium level of household expenditure; Tertile 3, Low level of household expenditure.
[a]Missing data: 1 for educational level, 121 for household expenditure.
[b]Missing data: 3 for educational level.

Results

Baseline characteristics of the participants

The results showed that in phase I, out of 2,961 participants, 387 (13.07%) had disability, while in phase II, out of 3,806 older persons, 337 (8.85%) participants had possible sarcopenia, 294 (7.72%) had sarcopenia, and 64 (1.68%) had severe sarcopenia. Table 1 presents the baseline characteristics of the two phases.

Phase I: the relationship between baseline disability and follow-up sarcopenia

During the 4-year follow-up, 65 (16.8%) new cases of possible sarcopenia, 18 (4.7%) new cases of sarcopenia, and 9 (2.3%) new cases of severe sarcopenia were reported in disabled patients, additional information is shown in Table 2. Those considered disabled had a higher risk of subsequent sarcopenia (crude OR = 1.61; 95% CI = 1.25–2.07). After adjusting for all covariates in 2011, the OR (95% CI) values for older people with disability was 1.35 (1.02–1.79) compared with individuals without disability (Table 3). Subgroup analyses showed that participants with disability aged <80 years had a higher risk of sarcopenia (OR = 1.42, 95% CI: 1.07–1.89), but the risk of sarcopenia did not differ significantly between sex subgroups (Supplementary Table 1). In addition, as a sensitivity analyses, we excluded patients with concomitant comorbidities of other chronic diseases, and the results did not change substantially, suggesting that the relationship between sarcopenia and disability is unlikely to be influenced by these diseases (Supplementary Table 2). After *post-hoc* power analysis, we found that with the group size, at alpha=0.5 the expected power to detect the difference seen is 96%. If we look for a detectable difference between no sarcopenia, sarcopenia and possible or severe sarcopenia, the power is 95%.

Phase II: association of baseline sarcopenia with follow-up disability

At this phase, 114 patients with possible sarcopenia, 85 patients with sarcopenia, 23 patients with severe sarcopenia, and 501 individuals with no sarcopenia showed symptoms of disability (Table 4). Compared to patients without sarcopenia, the OR (95% CI) for disability was 2.66 (2.08–3.40) for patients with possible sarcopenia, 2.12 (1.62–2.77) for patients with sarcopenia, and 2.92 (1.74–4.91) for patients with severe sarcopenia. After adjusting for all covariates at baseline, the OR (95% CI) in patients with possible sarcopenia compared with patients without sarcopenia was 2.21 (1.70–2.85), for patients with sarcopenia was 1.58 (1.14–2.19), and for patients with severe sarcopenia, the OR (95% CI) was 1.99 (1.14–3.49; Table 5). Subgroup analysis shows older female patients who may have sarcopenia are at higher risk of disability than men (OR = 2.80, 95% CI: 1.98–3.97), and patients with sarcopenia or severe sarcopenia aged <80 years had a higher risk of disability (OR = 2.13, 95% CI: 1.52–2.98; OR = 2.98, 95% CI: 1.60–5.54; Supplementary Table 3). In addition, the results did not change after sensitivity analyses (Supplementary Table 4). *Post-hoc* power

TABLE 2 New case of sarcopenia in phase I.

	Total	Possible sarcopenia	Sarcopenia	Severe sarcopenia	No sarcopenia
		n (%)	*n* (%)	*n* (%)	*n* (%)
Disability	387	65 (16.8)	18 (4.7)	9 (2.3)	295 (76.2)
No disability	2,574	282 (11.0)	97 (3.8)	35 (1.4)	2,160 (83.9)
Total	3,961	347	115	44	2,455

TABLE 3 Logistic regression of disability for sarcopenia.

Disability	Crude		Adjusted 1		Adjusted 2	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
No	1 (reference)	-	1 (reference)	-	1 (reference)	-
Yes	1.61 (1.25–2.07)	<0.001	1.45 (1.12–1.88)	0.006	1.35 (1.02–1.79)	0.038

OR, odds ratio; 95% CI, 95% confidence interval.
Adjusted 1 adjusted for sex, age.
Adjusted 2 adjusted for sex, age, residence, marital status, educational level, smoking status, drinking status, body mass index, and annual household expenditure level, whether accompanied by other chronic diseases [high blood sugar (HBS)/diabetes, lung disease, hypertension, heart disease, cancer, stroke, dyslipidemia, digestive disease, kidney disease, liver disease, emotional, nervous, or psychiatric problems, memory-related disease, arthritis or rheumatism and asthma].

TABLE 4 New case of disability in phase II.

	Total	Disability	No disability
		n (%)	*n* (%)
Possible sarcopenia	337	114 (33.8)	223 (66.2)
Sarcopenia	294	85 (28.9)	209 (71.1)
Severe sarcopenia	64	23 (35.9)	41 (64.1)
No sarcopenia	3,111	501 (16.1)	2,610 (83.9)
Total	3,806	723	3,083

analysis shows that with the group size, at alpha = 0.05 the expected power to detect the difference seen is 100%.

Discussion

In our study, we observed a bidirectional relationship between disability and sarcopenia. Specifically, disability in older people increases the risk of developing sarcopenia, while possible sarcopenia, sarcopenia, and severe sarcopenia also increase the risk of subsequent disability. Even after adjusting for sex, age, or other confounders, the relation still existed. Furthermore, the connection between disability and sarcopenia exhibited some variation in subgroup analyses based on age and sex.

Several scholars in the field have analyzed the impact of sarcopenia on disability. For instance, Phillips et al. noted that sarcopenia results in higher disability scores in older people, and the 3-year incidence of disability was ~32.7% (28). Moreover, in a cross-sectional analyses of 27,924 participants in the Canadian Longitudinal Study (29), sarcopenia was associated with an increased risk of ADL disability. It is worth noting that studies have indicated that older individuals with sarcopenia exhibit lower levels of basic and instrumental activities of daily living compared to those without sarcopenia (30, 31), suggesting that both may be influenced by sarcopenia.

Sarcopenia as a risk factor for subsequent disability is confirmed by the fact that sarcopenia is associated with future disability, even after adjusting for sex, age, and other covariates. Proactively preventing and managing sarcopenia has been shown to effectively reduce the risk of disability (32, 33), therefore, it is recommended that sarcopenia should be included when screening for disability. Additionally, our study found that the ORs for increased risk of disability did not progressively increase by severity of sarcopenia. Patients with possible sarcopenia and severe sarcopenia displayed a higher risk of disability, while patients with sarcopenia had a relatively lower risk, it is an interesting phenomenon. This may because that a higher number of patients with possible sarcopenia had reduced physical function and therefore a higher risk of subsequent disability, whereas all patients with severe sarcopenia had reduced physical function. Therefore, patients with possible sarcopenia (especially with reduced physical function) need to be given equivalent attention as patients with severe sarcopenia when it comes to preventing disability in the older person. We are currently unaware of studies investigating the impact of disability on sarcopenia. In our study, disability remained positively associated with subsequent sarcopenia even after adjustment for covariables. Older people who are impaired in physical activity (34) and spend most of their time in a sedentary state (35) are at increased risk for sarcopenia, which may contribute to the results of the study.

Several explanations may elucidate the bidirectional relation between disability and sarcopenia. Firstly, sarcopenia may lead to an increased number of falls (6) and reduced exercise participation (36) in older people, consequently increasing the risk of disability. Similarly, decreased mobility (37) and heightened risk of malnutrition (38) in disabled older people may also contribute to the onset of sarcopenia. If the energy intake is low and cannot match the energy expenditure level, it will lead to weight loss and loss of muscle mass in the older people. In addition, as

TABLE 5 Logistic regression of sarcopenia for the odds of disability.

Sarcopenia	Crude		Adjusted 1		Adjusted 2	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
No	1 (reference)	-	1 (reference)	-	1 (reference)	-
Possible sarcopenia	2.66 (2.08–3.40)	<0.001	2.34 (1.82–3.01)	<0.001	2.21 (1.70-2.85)	<0.001
Sarcopenia	2.12 (1.62–2.77)	<0.001	1.45 (1.09–1.94)	0.010	1.58 (1.14-2.19)	0.006
Severe sarcopenia	2.92 (1.74–4.91)	<0.001	1.86 (1.09–3.20)	0.024	1.99 (1.14-3.49)	0.016

OR, odds ratio; 95% CI, 95% confidence interval.

the amount of food consumed by the older people decreases, it may lead to difficulties in meeting nutritional needs, especially micronutrients, which will also increase the risk of sarcopenia in the older people (39). Secondly, aging will leads to heightened inflammation levels, which directly impacts the metabolism of muscle tissue and bone (40), ultimately causing declining physical function or disability. Elevated inflammation levels may play a role in the bidirectional correlation between sarcopenia and disability in the older people. One study has indicated (41) that increased levels of superoxide dismutase (SOD), the main antioxidant enzyme, reduce the risk of disability in older individuals. Moreover, higher levels of oxidative stress are associated with an increased risk of sarcopenia, indicating that oxidative stress levels may influence the relationship between sarcopenia and disability (42). Finally, it is important to note that older individuals with chronic diseases, such as diabetes (43) and COPD (44), are at an increased risk of developing sarcopenia. Similarly, diabetes (45) and COPD (46) can elevate the risk of disability.

In the subgroup analyses, we found a higher risk of subsequent sarcopenia in disabled persons aged <80 years, as well as a higher prevalence of disability in individuals aged <80 years with sarcopenia and severe sarcopenia. This could be attributed to the higher occurrence of malnutrition, reduced physical activity, and decreased physical function in older individuals aged ≥80 years, thereby weakening the relationship between the two conditions. Consequently, in the prevention of sarcopenia and disability, greater attention should be directed toward disabled or sarcopenia patients < 80 years of age, and all older people ≥80 years of age. Furthermore, in a subgroup analysis by sex, women with possible sarcopenia are more susceptible to disability than men. This may be due to women having less time for physical activity (47) and poorer health status (48) compared to men, and the allocation of social and family roles that negatively affects their access to healthcare and health protection based on traditional Chinese cultural beliefs. Additionally, previous studies have also indicated that older women are more severely disabled than men (49, 50), which could be related to the above reasons. Taken together, our study results advocate for the consideration of sex and age effects when formulating intervention strategies for sarcopenia or disability.

The study used a nationally representative cohort survey to reflect the general health status of Chinese older adults, it has large sample size and a long follow-up period. Second, it may be the first study to examine the bidirectional relationship between disability and sarcopenia using a single cohort. In addition, this study adjusted for confounding variables including gender, age, education level, and other baseline characteristics. However, we should also note the limitations of this study. First, some disease-related data were self-reported, and these diseases may generate measurement errors. In addition, there may be other unmeasured confounders influencing the association between disability and sarcopenia, but it is difficult to avoid this issue in most observational studies. Finally, the follow-up interval in this study was 4 years, and future studies need to conduct longer follow-ups to analyze whether the bidirectional association between disability and sarcopenia can be sustained over a longer period of time.

Conclusions

In conclusion, we found a bidirectional relation between disability and sarcopenia. Disability can influence subsequent sarcopenia, and sarcopenia can also predict the incidence of subsequent disability. Screening and timely management of sarcopenia should be enhanced to prevent disability in older people. Furthermore, when assessing the relationship between disability and sarcopenia, we should be mindful of the impact of gender and age to help clinical staff develop more targeted and applicable interventions to promote healthy aging.

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 authors.

Ethics statement

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

Author contributions

LL: Writing – review & editing, Writing – original draft, Conceptualization. YZ: Writing – review & editing, Writing – original draft, Validation. YS: Methodology, Software, Writing – original draft, Writing – review & editing. LW: Writing – original draft, Methodology. LM: Writing – review & editing, Software. TZ: Writing – review & editing, Investigation.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. This work was supported by the 2023 Henan Province Social Science Joint Committee Research Topic (Grant No. SKL-2023-569).

Acknowledgments

We are grateful to the CHARLS research team and every respondent.

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.2024.1309673/full#supplementary-material

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frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 09 May 2024
DOI 10.3389/fpubh.2024.1303958

OPEN ACCESS

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RECEIVED 28 September 2023
ACCEPTED 22 March 2024
PUBLISHED 09 May 2024

CITATION
Yang C-C, Chen P-H, Yang C-H, Dai C-Y, Luo K-H, Chen T-H, Chuang H-Y and Kuo C-H (2024) Physical frailty identification using machine learning to explore the 5-item FRAIL scale, Cardiovascular Health Study index, and Study of Osteoporotic Fractures index.
Front. Public Health 12:1303958.
doi: 10.3389/fpubh.2024.1303958

Physical frailty identification using machine learning to explore the 5-item FRAIL scale, Cardiovascular Health Study index, and Study of Osteoporotic Fractures index

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Background: Physical frailty is an important issue in aging societies. Three models of physical frailty assessment, the 5-Item fatigue, resistance, ambulation, illness and loss of weight (FRAIL); Cardiovascular Health Study (CHS); and Study of Osteoporotic Fractures (SOF) indices, have been regularly used in clinical and research studies. However, no previous studies have investigated the predictive ability of machine learning (ML) for physical frailty assessment. The aim was to use two ML algorithms, random forest (RF) and extreme gradient boosting (XGBoost), to predict these three physical frailty assessment models.

Materials and methods: Questionnaires regarding demographic characteristics, lifestyle habits, living environment, and physical frailty assessment were answered by 445 participants aged 60 years and above. The RF and XGBoost algorithms were used to assess their scores for the three physical frailty indices. Furthermore, feature importance and Shapley additive explanations (SHAP) were used to determine the important physical frailty factors.

Results: The XGBoost algorithm obtained higher accuracy for predicting the three physical frailty indices; the areas under the curve obtained by the XGBoost algorithm for the 5-Item FRAIL, CHS, and SOF indices were 0.84. 0.79, and 0.69, respectively. The feature importance and SHAP of the XGBoost algorithm revealed that systolic blood pressure, diastolic blood pressure, age, and body mass index play important roles in all three physical frailty models.

Conclusion: The XGBoost algorithm has a more accurate predictive rate than RF across all three physical frailty assessments. Thus, ML can be a useful tool for the early detection of physical frailty.

KEYWORDS
machine learning, physical frailty, model, prediction, XGBoost

Introduction

Physical frailty has become an important issue in the geriatric population of super-aging societies. It is a condition wherein susceptibility to stressors increases, especially in the older adults population, (1) resulting in undesirable health consequences, such as falling, stroke, disability, hospitalization, institutionalization, and death (2–5). The prevalence of physical frailty ranges from 3.9–51.4%, (6–8) influenced by different nationalities, socioeconomic conditions, and, most importantly, the assessment tool. Currently, there is no gold-standard diagnostic tool for assessing physical frailty. Several assessments have been established, including Fried's phenotype model (9) and the physical frailty index in Rockwood's cumulative deficit model (10). These assessments help identify persons with physical frailty who are at high risk of adverse consequences and provide an opportunity to counteract the evolution of adverse sequelae (11).

Machine learning (ML), a subset of artificial intelligence (AI), is a method of self-learning to provide solutions (12, 13). According to scholars such as Arthur Samuel, ML provides computers with the ability to learn without explicit programming. Therefore, ML can be classified as a computer science (14). Nevertheless, ML algorithms can be classified as "supervised" or "non-supervised" (15). Supervised ML involves training the model on predictions of relationships between features and outputs from data, whereas non-supervised ML involves searching for relevant structures within a dataset (15). The advantage of supervised ML is that it can achieve a high classification rate using a large amount of labeled data (16). Random forest (RF), initially published by Breiman, is a non-parametric learning algorithm wherein classification results are determined through voting on multiple decision trees (17). It has the advantage of reducing outliers and is less susceptible to overfitting, resulting in higher classification accuracy in many applications (18). RF is widely used in mass spectrometry, soil mapping, eye-state estimation, and remote sensing imaging (19). The extreme gradient boosting (XGBoost) algorithm, proposed by Chen, (20) randomly selects subsets to iteratively fit a single predictor and obtain a minimized loss function, and introduces a stochastic gradient boosting procedure. Through regularization, Boost can reduce the risk of overfitting and improve generalisability (21). It has been applied to detect abnormal satellite engineering parameters, personal credit risk assessment, and urban water resources (22).

However, there are a limited number of studies on using ML for predicting health conditions of the older adults, and there are no studies on predicting their physical frailty status. We aimed to employ two supervised ML methods, RF and XGBoost, to explore three physical frailty assessment indices and construct prediction models. The physical frailty assessment indices were the 5-Item fatigue, resistance, ambulation, illness, and loss of weight (FRAIL) scale; Cardiovascular Health Study (CHS) index; and Study of Osteoporotic Fractures (SOF) index.

Abbreviations: 5-Item FRAIL, 5-Item fatigue, resistance, ambulation, illness and loss of weight; CHS, Cardiovascular Health Study; SOF, Study of Osteoporotic Fractures; RF, Random Forest; XGBoost, extreme gradient boosting; SHAP, Shapley additive explanations.

Materials and methods

Participants

The participants were included after obtaining informed consent and approval from the Institutional Review Board. We randomly selected community residents from three urban districts in Kaohsiung City, and randomly selected participants according to the proportion of the population over 60 years old. Participants were included to this study after informed consent. The inclusion criteria were: (1) aged 60 years and above, (2) ability to respond to a questionnaire, and (3) allowing for a physical assessment. The exclusion criteria were: (1) suffering from a mental disability or psychological disease, (2) unwillingness to provide informed consent and inability to cooperate with the study, and (3) acute hospitalization within the 3 months prior to the study. From April–October 2022, 445 participants were recruited for the study. This study was approved by the Kaohsiung Medical University Hospital Institutional Review Board [IRB number: KMUHIRB-E(I)-20220048].

Measurements and questionnaire

All the participants were assessed through one-to-one interviews. After they completed the questionnaire and physical frailty assessment, we obtained their demographic characteristics, including sex, age, living environment, education level, and smoking and drinking habits. Elementary school education or no education was considered "low education." The participants' past histories were documented using their medical records obtained from their National Health Insurance cards. Physical examinations of height, weight, and blood pressure were also performed. The assessment indices for physical frailty included the (1) 5-Item FRAIL, (23) (2) CHS (Fried's Frailty Phenotype), (24) and (3) SOF (25). Two researchers independently entered the data and confirmed their accuracy.

Three tools for physical frailty assessment

The Geriatric Advisory Panel developed the 5-Item FRAIL scale, which comprises five items: (1) exhaustion, (2) weakness, (3) slowness while walking, (4) low activity, and (5) weight loss. Two items—fatigue and weight loss—were considered biological factors; another two—resistance and ambulation—were considered functional factors; and the last item was considered to involve deficit accumulation because of illness. The 5-Item FRAIL scale categorizes participants' health

statuses based on their scores as physical frail (3–5), physical pre-frail (1–2), and physical non-frail (0) (23).

The CHS index, a biological model of physical frailty, comprises five components: (1) unintentional weight loss, (2) feeling of exhaustion, (3) decreased physical activity, (4) slow walking speed, and (5) weakness, which are also used to classify health statuses based on scores as physical frail (3–5), physical pre-frail (1–2), and physical non-frail (0) (9, 24).

The SOF index comprises two factors with three components: (1) inability to complete five chair rises or suffering from weight loss, representing biological factors, and (2) reduced energy levels, representing a functional factor, which are also used to classify health statuses based on scores as physical frail (2–3), physical pre-frail (1), and physical non-frail (0) (25).

Machine learning

The RF algorithm, developed by Breiman in 2001, (17) is an ensemble learning bagging algorithm (26). RF involves random sampling of the original training dataset, creating a new classifier for each sample, (27) and voting on the results generated by each classifier. The result is determined by voting on the results generated by each classifier, and the category with the largest number of votes constitutes the final result (28). RF requires minimal pruning and has no overfitting risk. Furthermore, it has high tolerance for outliers and noise, high adaptability to new samples, and good stability. Therefore, RF is suitable for parallel computing, even for high-dimensional data, with faster training speed and higher computing performance (29). The RF decision tree is built by selecting a feature at the root node and partitioning the training dataset into subsets of values of the selected feature (30). The information gain (IG) for partitioning training data y into subsets (y_i) is calculated as follows Equation (1):

$$IG = -\sum_i \frac{|y_i|}{|y|} E(y_i) \tag{1}$$

where $E(y_i)$ is the entropy of set $y_i$and is calculated as Equation (2):

$$E(y_i) = -\sum_{j=1}^{n} P_j \log_2(P_j) \tag{2}$$

The XGBoost algorithm, developed by Chen, (20) can be applied to handle regression and classification problems (31). It originated from the gradient boosting decision tree algorithm, which was modified to improve its generalisability and convergence rate (32). Boosting is an ensemble learning algorithm that converts weak classifier iterative learning into a strong classifier algorithm (32). It produces a new decision tree at each iteration based on the residuals of the previous one (33). XGBoost enhances the regularization of the loss function as a whole to create an objective function and improve the performance of the algorithm, (34) which is described in Equation (3).

$$J(\theta) = L(\theta) + R(\theta) \tag{3}$$

where θ is the parameter for data training, L is the loss function, and R is the regularization. Because the decision tree is the base model, the output of model y_i is an ensemble of k decision trees and is computed as follows Equation (4):

$$\hat{y_i} = \sum_{i=1}^{k} f_k(\chi_i), f_k \in F \tag{4}$$

where χ_i is the ith sample in the training set and F is the decision tree value.

Loss function L is calculated as follows Equation (5):

$$L = \sum_i^n \left(\hat{y_i}, y_i \right) + \sum_k \Omega(f_k) \tag{5}$$

$$\Omega(f_k) = \mathrm{YT} + \frac{1}{2}\lambda |w|^2 \tag{6}$$

where T is the number of trees in the leaf and w is the leaf weight in Equation (6).

Evaluation metrics

To evaluate the performances of the RF and XGBoost algorithms for classifying the participant assessments on the 5-Item FRAIL, CHS, and SOF indices into robust, pre-frail, and frail, we employed the common evaluation indicators for ML classification: Accuracy (Equation 7), Precision (Equation 8), Recall (Equation 9), and F1 score (Equation 10): (35).

$$Accuracy = \frac{TP + TN}{TP + FP + TN + FN} \times 100 \tag{7}$$

$$Precision = \frac{TP}{TP + FP} \times 100 \tag{8}$$

$$Recall = \frac{TP}{TP + FN} \times 100 \tag{9}$$

$$F1 - score = \frac{(Precision \times Recall) \times 2}{Precision + Recall} \tag{10}$$

Shapley additive explanations (SHAP)

SHAP, proposed by Lundberg and Lee in 2017, (36) is a framework for a unified interpretation of different ML prediction models (37). It is a Shapley value based on game theory (38) that explains the impact of each feature on an ML prediction (39). It is useful for both single- and full-feature interpretability; therefore, it can be used for the entire dataset to explain the influence of each feature on the prediction (39).

Statistics

Descriptive statistics were used to analyse the mean and dispersion of continuous variables, including age and physical frailty scores. Numbers and proportions were used to evaluate categorical variables such as sex, smoking, and alcohol consumption. Furthermore, the participants were divided into groups according to their physical frailty status. The scores for the 5-Item FRAIL, CHS, and SOF indices were classified into physical non-frail, physical pre-frail, and physical frail groups. Statistical analyses were performed using IBM SPSS version 20 and Python (version 3.8.8).

Results

Demographic characteristics

In total, 445 participants satisfied the inclusion criteria. They were classified into physical non-frail, physical pre-frail, and physical frail groups according to their scores on the three indices and their demographic characteristics were determined, as listed in Table 1. According to the 5-Item FRAIL scale, 196 (44.04%), 184 (41.35%), and 65 (14.61%) participants were classified into physical non-frail, physical pre-frail, and physical frail groups, respectively. According to the CHS index, 144 (32.36%), 145 (32.58%), and 156 (35.06%) participants were classified into physical non-frail, physical pre-frail, and physical frail groups, respectively. According to the SOF index, 230 (51.69%), 152 (34.16%), and 63 (14.15%) participants were classified into physical non-frail, physical pre-frail, and physical frail groups, respectively. The average age of the participants was 68.75 years, and their average body mass index (BMI) was 25.39. They comprised 163 men (36.63%) and 282 women (63.37%). Moreover, 38.20% (170) had low levels of education (elementary school only or no education), 9.66% (40) lived alone, 4.49% (19) were smokers, and 10.11% (41) consumed alcohol.

ML algorithms: RF and XGBoost

The XGBoost and RF predictions were compared based on accuracy, recall, precision, and F1 score. Compared with RF, XGBoost predicted the 5-Item FRAIL scale, CHS index, and SOF index with higher accuracy (Table 2). The receiver operating characteristic (ROC) curve was used to estimate model performance, with the ordinate and abscissa representing the frequencies of true and false positives, respectively. For the 5-Item FRAIL scale, the area under the ROC curve (AUC) of the RF algorithm was 0.78, and that of the XGBoost algorithm was 0.84, as shown in Figure 1A. For the CHS index, AUC of RF was 0.76, and that of the XGBoost was 0.79, as shown in Figure 1B. For the SOF index, AUC of RF was 0.62, and that of XGBoost was 0.69, as shown in Figure 1C. In summary, XGBoost had a better predictive ability than RF.

Feature importance

Feature importance was determined using the XGBoost algorithm. The F-score indicates the number of times a feature is split during model training (42). The higher the score, the more important the feature and the greater its impact on the classification results (43). Figures 2A–C show the feature importance in the 5-Item FRAIL, CHS, and SOF indices, respectively. In all three, systolic blood pressure, diastolic blood pressure, age, and BMI have the top four F-score values.

SHAP

SHAP shows the contribution of important features across the dataset. The x-axis represents the Shapley value and the y-axis represents the important features in the dataset, which are sorted according to their Shapley values. In the SHAP graph, the red points indicate that the value of the data is higher, and blue points indicate that the value of the data is lower. Figure 3A shows the SHAP values of the top 20 features in the 5-Item FRAIL scale, wherein the eigenvalues of age, diastolic blood pressure, systolic blood pressure, and BMI all affected the predicted value to some extent, and polypharmacy showed a positive correlation, indicating that the larger the feature value, the higher its contribution to the prediction. Figure 3B shows the SHAP values of the top 20 characteristics of the CHS index, where the eigenvalues of age, diastolic blood pressure, systolic blood pressure, and BMI affect the predicted value to some extent, and polypharmacy and urology disorders are positively correlated, indicating that the characteristics with larger values contribute more to the model prediction. Figure 3C shows the SHAP values of the top 20 SOF features. The eigenvalues of age, systolic blood pressure, BMI, and diastolic blood pressure affected the predicted value.

Post-stratification of HTN

Table 3 shown the proportion of HTN or non-HTN in the three frailty assessments. Compared with physical non-frail population, HTN take significantly larger proportion in physical frail population in all three assessment classifications.

Discussion

To compare RF and XGBoost, the same data were used for the training and testing evaluation. Overall, XGBoost performed better than RF. A significant difference was observed between high recall and low precision, as shown in Table 2. The recall rate is calculated by dividing the true positives by anything that should have been predicted as positive. Precision refers to the number of actual positives among the positive predictions, and a high recall rate indicates that the number of false positives are low, which is generally desirable. In summary, the XGBoost algorithm achieved a better prediction rate.

The exceptional predictive accuracy of XGBoost compared to Random Forest is the result of several unique techniques and features integral to XGBoost's approach. Notably, its Gradient Boosting Framework allows for systematic improvements in predictions by specifically addressing errors from previous training rounds, employing gradient descent to reduce loss with each new addition (40). Additionally, XGBoost incorporates a regularization term in its objective function, which serves to prevent overfitting by penalizing

TABLE 1 Demographic characteristics for model prediction according to the three physical frailty indices: 5-Item FRAIL, CHS, and SOF.

	5-Item FRAIL scale			CHS index			SOF index		
	Physical non-frail (*n* = 196)	Physical pre-frail (*n* = 184)	Physical frail (*n* = 65)	Physical non-frail (*n* = 144)	Physical pre-frail (*n* = 145)	Physical frail (*n* = 156)	Physical non-frail (*n* = 230)	Physical pre-frail (*n* = 152)	Physical frail (*n* = 63)
	n(%)/ Mean ± SD	*n*(%)/ Mean ± SD	*n*(%)/ Mean ± SD	*n*(%)/ Mean ± SD	*n*(%)/ Mean ± SD	*n*(%)/ Mean ± SD	*n*(%)/ Mean ± SD	*n*(%)/ Mean ± SD	*n*(%)/ Mean ± SD
Sex (male)	74	60	29	54	47	62	88	52	23
Age (years)	65.80 ± 5.30	69.20 ± 6.59	76.28 ± 8.38	66.04 ± 4.35	66.00 ± 6.49	73.78 ± 7.38	65.87 ± 4.84	70.96 ± 7.82	73.88 ± 8.40
elementary school or no education	39	84	46	22	46	102	56	75	39
Live alone (yes)	17	19	7	13	14	16	19	17	7
No elevator in the house (yes)	167	158	56	121	125	136	196	131	55
No religion (yes)	25	18	7	20	20	10	28	16	6
Smoke (yes)	11	6	3	9	5	6	13	4	3
Alcohol (yes)	26	14	5	16	16	13	31	10	4
Lack of exercise (yes)	8	11	3	5	9	8	10	11	1
Hypertension (yes)	69	103	44	47	59	110	87	90	39
Diabetes mellitus (yes)	49	74	33	32	47	77	61	63	32
Hyperlipidemia (yes)	47	68	23	36	45	57	62	50	26
Cerebral vascular disease (yes)	5	12	5	5	3	14	8	10	4
Heart disease (yes)	24	27	22	18	17	39	30	30	14
Pulmonary disease (yes)	32	25	22	21	22	36	33	27	19
Liver disease (yes)	19	22	4	14	19	12	22	17	6
Urology disease (yes)	11	22	27	6	10	44	16	24	20
Malignancy (yes)	13	13	5	11	4	16	13	8	10
Sleep disorder (yes)	27	44	21	27	21	44	39	37	16
Neurological disease (yes)	1	5	1	1	2	5	1	5	2
Thyroid disease (yes)	25	25	3	19	20	14	26	20	7
Gastrointestinal disease (yes)	33	43	13	25	29	35	38	36	15
Hematological disease (yes)	2	1	2	2	0	3	3	0	2
Arthritis (yes)	22	36	14	16	25	31	33	22	17
Osteoporosis (yes)	17	28	8	15	17	21	23	17	13
Spine disorder (yes)	14	22	10	9	15	22	18	14	14

(Continued)

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TABLE 1 (Continued)

	5-Item FRAIL scale			CHS index			SOF index		
	Physical non-frail ($n = 196$)	Physical pre-frail ($n = 184$)	Physical frail ($n = 65$)	Physical non-frail ($n = 144$)	Physical pre-frail ($n = 145$)	Physical frail ($n = 156$)	Physical non-frail ($n = 230$)	Physical pre-frail ($n = 152$)	Physical frail ($n = 63$)
	n(%)/ Mean ± SD	*n*(%)/ Mean ± SD	*n*(%)/ Mean ± SD	*n*(%)/ Mean ± SD	*n*(%)/ Mean ± SD	*n*(%)/ Mean ± SD	*n*(%)/ Mean ± SD	*n*(%)/ Mean ± SD	*n*(%)/ Mean ± SD
Rheumatic disease (yes)	3	4	0	4	1	2	5	2	0
Gout (yes)	3	4	11	3	3	12	6	5	7
Polypharmacy (yes)	5	23	24	3	9	41	16	22	15
Systolic blood pressure (mmHg)	142.29 ± 19.82	141.04 ± 19.63	150.37 ± 23.49	140.49 ± 18.81	143.28 ± 22.59	144.87 ± 19.76	141.09 ± 20.37	145.06 ± 20.81	144.53 ± 19.70
Diastolic blood pressure (mmHg)	82.39 ± 9.36	79.21 ± 10.10	79.00 ± 12.12	81.59 ± 9.32	82.30 ± 10.19	78.05 ± 10.54	81.67 ± 9.67	80.23 ± 10.34	77.44 ± 11.11
Body mass index (kg/m^2)	25.13 ± 3.77	25.56 ± 3.80	25.64 ± 4.04	24.60 ± 3.46	25.72 ± 3.80	25.82 ± 4.07	25.08 ± 3.88	25.92 ± 3.77	25.22 ± 3.64

FRAIL, Fatigue, Resistance, Ambulation, Illness and Loss of Weight; CHS, Cardiovascular Health Study; SOF, Study of Osteoporotic Fracture; SD, standard deviation.

overly complex models, thus fostering more generalizable and robust predictions. It also employs a sophisticated tree pruning method, which ensures the retention of only the most beneficial structures. Furthermore, XGBoost's built-in routine for handling missing values, which intelligently decides the best course of action to minimize loss, significantly enhances its predictive capabilities (44). These combined features not only enhance XGBoost's efficiency but also establish it as a formidable tool in machine learning competitions and applications where prediction accuracy is paramount.

The uniqueness of this study is that it employed ML to explore and address the characteristics of physical frailty predictions. The RF algorithm is a widely used ML algorithm in many fields (41) and has high accuracy, robustness, and the ability to handle high-dimensional data (30). It has been applied to the Minnesota Multiphasic Personality Inventory scale, and resulted in better classification and prediction (45). The XGBoost algorithm is a new ensemble learning method with an excellent implementation performance. Compared to other classifiers, XGBoost is anti-overfitting, highly efficient, entails low computational cost, and has better generalisability and accuracy compared to other ML algorithms (46, 47). The XGBoost algorithm has been previously applied to mental health prediction. Six ML algorithms were used to predict mental health using electronic medical records, of which XGBoost obtained the highest AUC value (48). Therefore, ML, especially the XGBoost algorithm, is better for classification and prediction of the three physical frailty indices: 5-Item FRAIL, CHS, and SOF.

Our study suggests that the 5-Item FRAIL is more aligned or similar to the SOF Index when it comes to classifying individuals who are physically frail. This implies that both tools might share common criteria or assess similar aspects of frailty, making them more interchangeable or comparable for identifying frail individuals. When it comes to classifying physical pre-frailty, the CHS Index is said to be closer to the SOF Index (49). This means that for identifying individuals who are not fully frail but have some signs of frailty (pre-frail), the CHS Index and SOF Index might share more similarities or provide more consistent classifications compared to other combinations of indices or scales. The result implies a comparison of the effectiveness or similarity of different frailty assessment tools, which is crucial for research, clinical practice, and policy-making, as identifying and managing frailty can help improve quality of life, reduce healthcare costs, and delay or prevent the progression to disability.

In this study, we used the SHAP tool and XGBoost algorithm to determine feature importance for a better understanding of these predictors. Figures 2, 3 show that among the top 20 important features, the influences of age, diastolic blood pressure, systolic blood pressure, and BMI on the prediction of the ML algorithms can be clearly understood. This indicates that a higher age is associated with higher physical frailty. For glioma grading, Cheng et al. applied the deep neural network model and SHAP tool, which not only shows the importance of every feature on the outcome but also indicates the influences of the associations between features on the predictions (50). For patients with severe COVID-19 intubation, Fleuren et al. applied the SHAP and found predictors of extubation failure, including ventilatory settings, inflammatory parameters, neurological status, and BMI (51). Hathaway et al. (52) conducted supervised learning through SHAP by identifying the most relevant and novel cardiac biomarkers for forecasting diabetes mellitus development, and

TABLE 2 Scores for the three physical frailty indices, 5-Item FRAIL, CHS, and SOF predicted using RF and XGBoost.

	RF	XGBoost
5-Item FRAIL scale		
Accuracy (%)	70.78	76.40
Recall (%)	75.31	73.48
Precision (%)	66.55	73.01
F1 score (%)	66.73	72.76
CHS index		
Accuracy (%)	68.53	70.78
Recall (%)	69.89	74.44
Precision (%)	68.04	70.38
F1 score (%)	64.23	68.22
SOF index		
Accuracy (%)	56.17	68.53
Recall (%)	52.59	62.72
Precision (%)	46.86	59.94
F1 score (%)	47.34	60.37

FRAIL, Fatigue, Resistance, Ambulation, Illness and Loss of Weight; CHS, Cardiovascular Health Study; SOF, Study of Osteoporotic Fracture; RF, random forest; XGBoost, extreme gradient boosting.

discovered that this approach may be a potential guideline for investigating disease pathogenesis and discovering novel biomarkers in the future. For predicting infant autopsy outcome, Booth et al. used three models for model training, including decision tree, RF, and gradient boosting. Fundamental data items associated with determining the medical cause of death, including the most important items, such as age at death and cardiovascular and respiratory histological findings, were recognized using model feature importance, with the XGBoost algorithm being the most effective (53). The SHAP method and its feature importance classification can further assist clinicians in expanding their knowledge of the fundamental mechanisms by which predictors affect the output of ML models for health outcomes.

In our study, hypertension is recognized as one of the important predictive factors in the frailty among older adults. Studies have shown that hypertension can contribute to the development of frailty by affecting cardiovascular health, leading to impairments in physical function and an increased risk of adverse health outcomes (54). Research by Fried et al. (9) in the criteria for frailty, highlight the relationship between hypertension and frailty, suggesting that managing hypertension could be crucial in preventing or mitigating frailty in the older population. Our study represents the first instance of utilizing ML techniques to explore this domain, and remarkably, we have found results that align closely with those of previous studies.

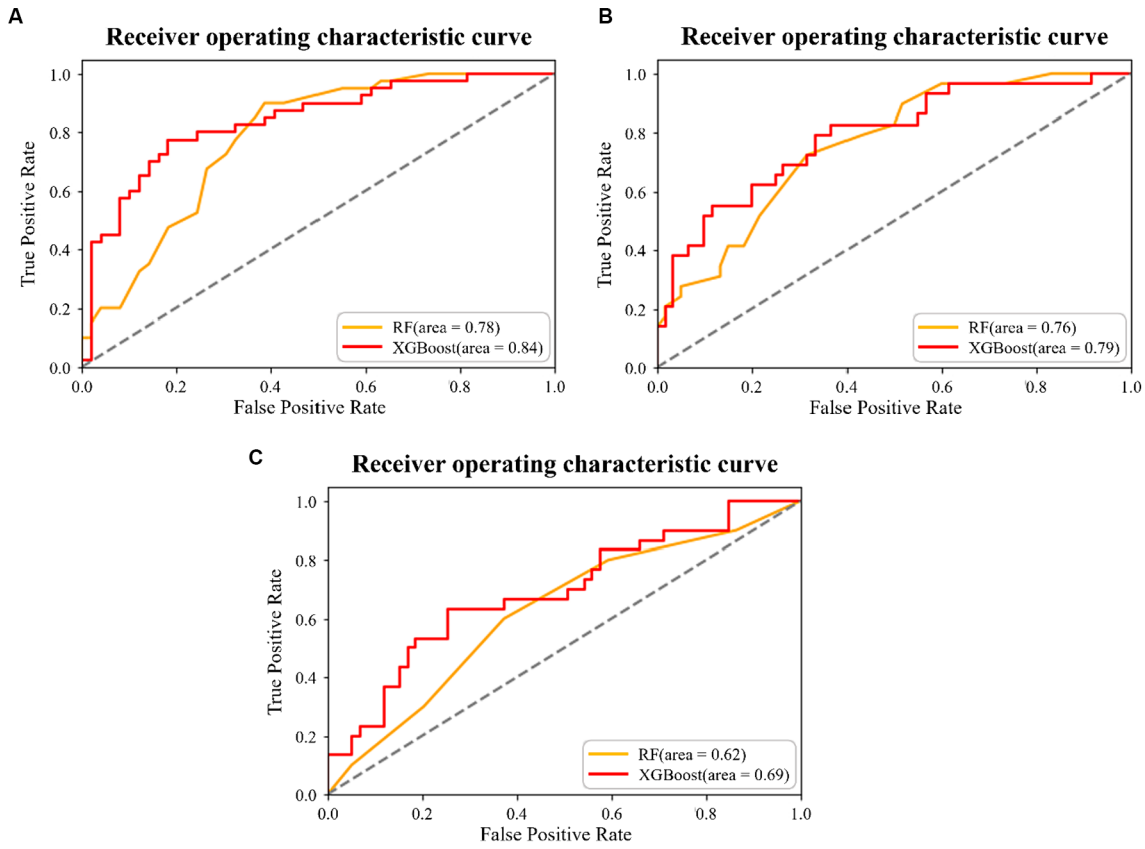

FIGURE 1
Results of the two machine learning algorithms for the **(A)** 5-Item Fatigue, Resistance, Ambulation, Illness, and Loss of Weight (FRAIL) scale prediction, **(B)** Cardiovascular Health Study (CHS) index prediction, and **(C)** Study of Osteoporotic Fracture (SOF) index prediction.

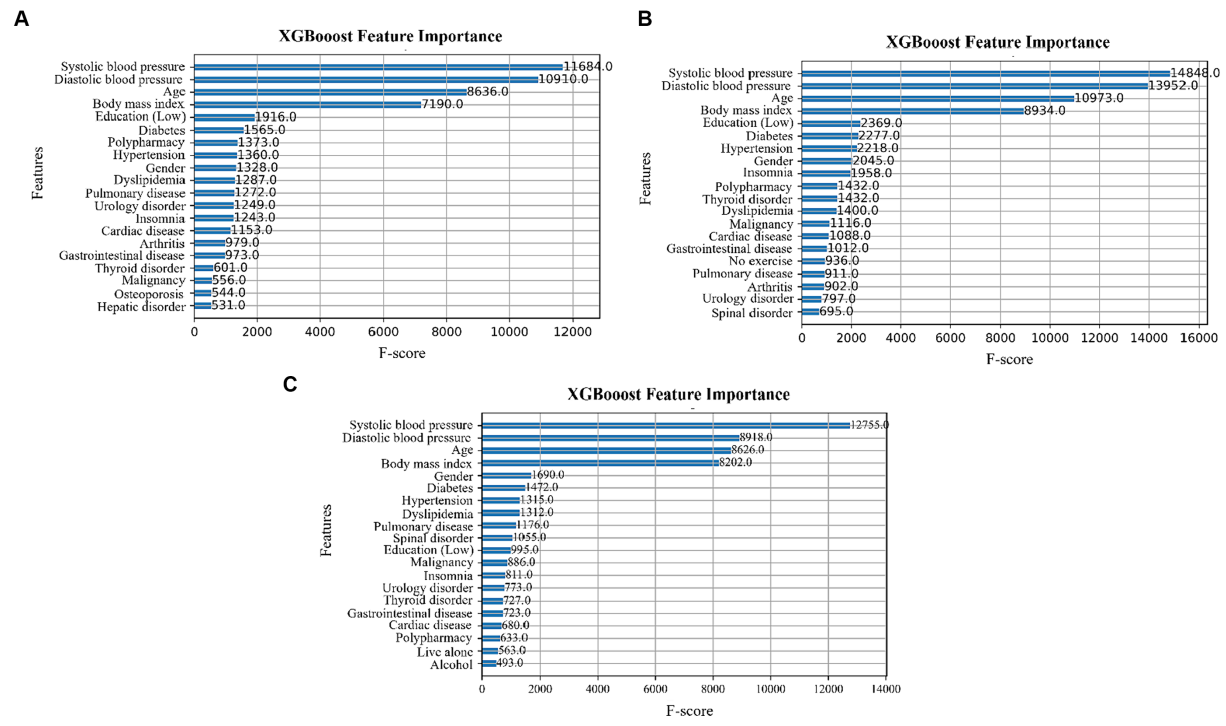

FIGURE 2
Feature importance for the **(A)** 5-Item FRAIL scale, **(B)** CHS index, and **(C)** SOF index.

This study had several limitations. First, it was a cross-sectional study that could only demonstrate associations and not infer causality. Further longitudinal studies are required to determine the causality between the possible risk factors and physical frailty. Second, we used self-reported questionnaires, and the results may have been influenced by recall biases such as memory, mood, or cognition. Third, ML models require a large amount of historical data for training to ensure that the model is not biased, (55) and it must be combined with datasets from other medical institutions to improve their predictive ability (56), such as Goh's study, which aim to develop a predictive model for bacteremia in septic patients using machine learning methods, analysing data from an emergency department (57). Fourthly, the economic factor, a critical determinant that could significantly influence physical frailty through insufficient access to nutrition and healthcare, was omitted from the machine learning models. This oversight highlights the necessity of integrating economic considerations into future research. Incorporating this factor into subsequent studies will allow for a more comprehensive analysis, potentially uncovering deeper insights into the dynamics between economic status and physical frailty. Fifth, because the dataset is inherently predictive, when the sample size is small, models may face challenges. One of these challenges is the high sensitivity to outliers, which may overly emphasize anomalies in the samples, leading the ML model to believe that these outliers have a greater impact (52). Due to limitations in the dataset, the model may overfit to the training data, especially when using derived models like classification trees. This means that during training, the model may generate a branch for each patient sample, and such a complex model may not generalize well to new, (58) unseen data because it overly caters to the details and noise in the training data. Furthermore, training ML models is costly, and stakeholders, such as governments and major hospitals, must be persuaded, trained, and educated on ML applications; therefore, the adoption of ML algorithms is another challenge. These issues must be addressed to obtain the optimal gains in predictive accuracy (55). In light of these limitations encountered in this study, there are several promising avenues for deepening future research. Primarily, undertaking longitudinal studies emerges as a critical next step to establish causality between risk factors and physical frailty, moving beyond the associations observed in a cross-sectional framework. Additionally, future studies should consider employing objective measures alongside or in place of self-reported questionnaires to mitigate the impact of recall bias and enhance the reliability of data. The integration of economic factors into ML models is another vital area for exploration, aiming to capture the nuanced impacts of socioeconomic status on physical frailty. This inclusion promises a more rounded analysis and could reveal intricate dynamics that have been previously overlooked. Expanding the datasets for ML training by incorporating data from a variety of medical institutions will also be crucial in improving the models' predictive accuracy and reducing bias. Lastly, addressing the challenges related to the cost and complexity of ML model training, as well as fostering stakeholder engagement, are essential steps for the broader adoption and application of ML in healthcare research. These focused directions not only aim to rectify the limitations of the current study but also pave the way for more comprehensive and impactful future research on physical frailty.

Conclusion

This study demonstrated that two machine learning models are used for physical frailty assessing by the 5-item FRAIL scale, CHS

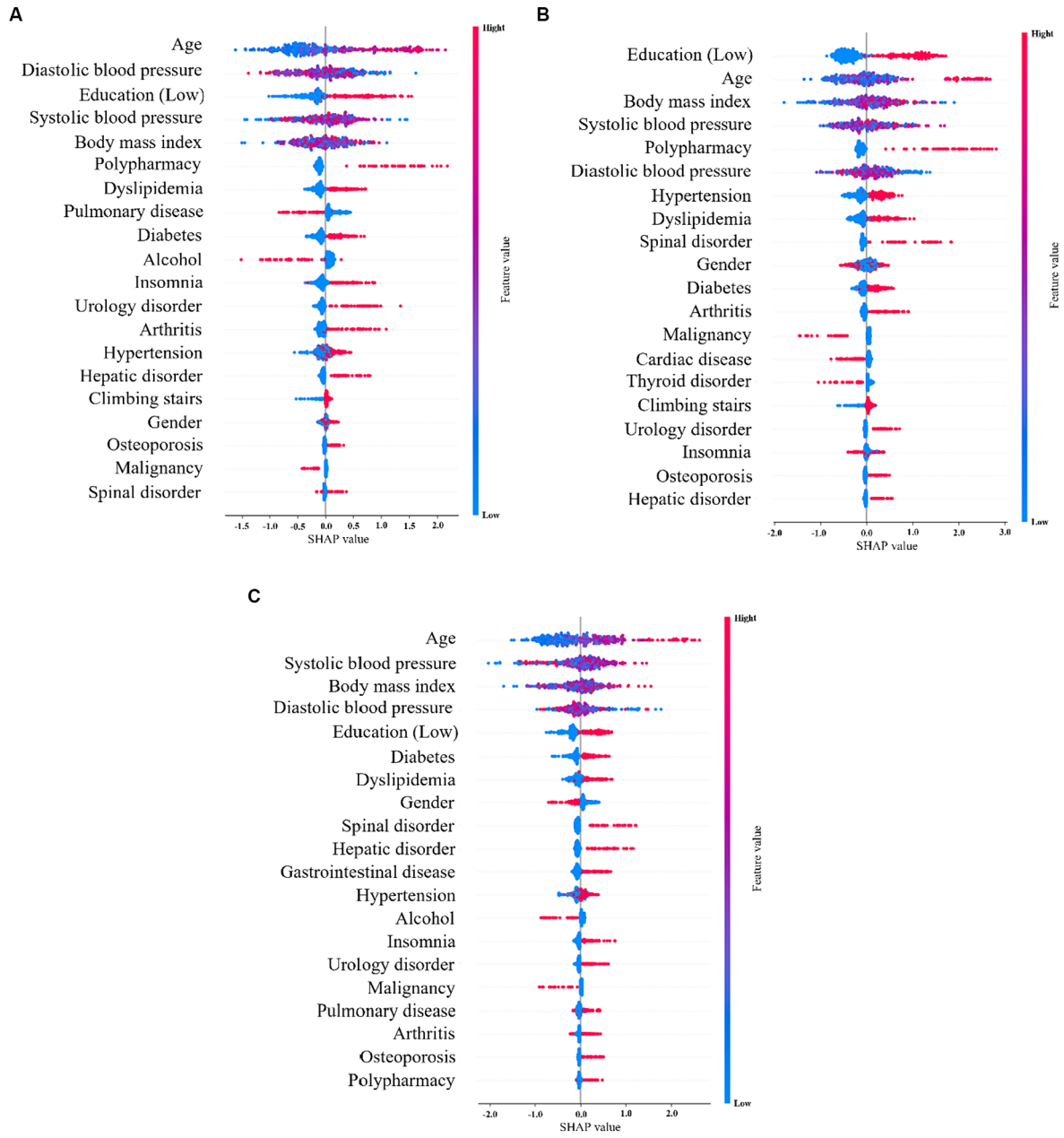

FIGURE 3
SHAP values for the **(A)** 5-Item FRAIL scale, **(B)** CHS index, and **(C)** SOF index.

index, and SOF index. XGBoost model is more precise predictive rate than RF model in all the three physical frailty models. Machine learning might be a useful instrument for early detection of physical frailty in the future. Furthermore, this study highlights the transformative potential of machine learning, especially the XGBoost algorithm's efficacy in frailty assessments, for advancing early detection practices in healthcare. By integrating the XGBoost model, this research not only promises significant improvements in health care but also emphasizes the importance of such findings in informing health policy development. Furthermore, it offers practical guidance for healthcare professionals on leveraging these insights to enhance frailty management strategies for the aging population.

Data availability statement

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

Ethics statement

The studies involving humans were approved by Kaohsiung Medical University Hospital Institutional Review Board. 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.

TABLE 3 The post-stratification of HTN and non-HTN in the three frailty assessments, 5-Item FRAIL scale, CHS index, and SOF index.

	5-Item FRAIL scale			*p*-value
	Physical non-frail	Physical pre-frail	Physical frail	
Non-HTN	127 (64.8%)	81 (44.0%)	21 (32.3%)	<0.001*
HTN	69 (35.2%)	103 (56.0%)	44 (67.7%)	
	CHS index			
	Physical non-frail	Physical pre-frail	Physical frail	
Non-HTN	97 (67.4%)	86 (59.3%)	46 (29.5%)	<0.001*
HTN	47 (32.6%)	59 (40.7%)	110 (70.5%)	
	SOF index			
	Physical non-frail	Physical pre-frail	Physical frail	
Non-HTN	143 (62.2%)	62 (40.8%)	24 (38.1%)	<0.001*
HTN	87 (37.8%)	90 (59.2%)	39 (61.9%)	

FRAIL, Fatigue, Resistance, Ambulation, Illness and Loss of Weight; CHS, Cardiovascular Health Study; SOF, Study of Osteoporotic Fracture.
*p-value < 0.05.

Author contributions

C-CY: Conceptualization, Data curation, Funding acquisition, Writing – original draft. P-HC: Formal analysis, Methodology, Software, Writing – original draft. C-HY: Conceptualization, Formal analysis, Methodology, Resources, Writing – review & editing. C-YD: Investigation, Writing – review & editing. K-HL: Formal analysis, Investigation, Writing – review & editing. T-HC: Investigation, Writing – review & editing. H-YC: Conceptualization, Formal analysis, Supervision, Writing – review & editing. C-HK: Supervision, Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research, authorship, and/or publication of this article. This work was supported by the National Science and Technology Council, R.O.C., Taiwan (grant number 112-2314-B-037-038), by Kaohsiung Medical University (grant number N-N112227, NSYSU-KMU-113-P25), by Kaohsiung Municipal Siaogang Hospital, Kaohsiung Medical University (grant number R-11101, S-11103), and by Kaohsiung Municipal Siaogang Hospital, Kaohsiung Medical University (grant number O-11217) from the Occupational Injury and Disease Diagnosis and Treatment Medical Institutions Accreditation Management Subsidy from the Occupational Safety and Health Administration of the Ministry of Labor, R.O.C., Taiwan.

Acknowledgments

We would like to thank all the participants, Kaohsiung Municipal Siaogang Hospital, and Kaohsiung Medical University.

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

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frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 16 May 2024
DOI 10.3389/fpubh.2024.1362268

OPEN ACCESS

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RECEIVED 28 December 2023
ACCEPTED 29 April 2024
PUBLISHED 16 May 2024

CITATION
Qing Z, Wu C and Gao T (2024) The impact of social participation on Subjective Wellbeing in the older adult: the mediating role of anxiety and the moderating role of education.
Front. Public Health 12:1362268.
doi: 10.3389/fpubh.2024.1362268

The impact of social participation on Subjective Wellbeing in the older adult: the mediating role of anxiety and the moderating role of education

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Introduction: The study aims to examine the mediating role of anxiety in the relationship between social participation and Subjective Wellbeing among Chinese older adults. Additionally, it investigates the moderating ed of education in this relationship.

Methods: The data came from the Chinese Longitudinal Healthy Longevity Survey (CLHLS) published by peking University, with a sample size of 10,626 individuals aged 60 years and above. SPSS 21.0 was used for the statistical analysis of the data, and Mplus 8.0 was used for the statistical processing of the mediating and moderating effects analysis.

Results: (1) The social participation significantly and positively predicated Subjective Wellbeing; (2) Anxiety partially mediated the eect between social participation and Subjective Wellbeing. The mediating eect value was 0.103; (3) Education plays a moderating role in the impact of social participation on subjective Wellbeing.

Discussion: In summary, social participation can reduce the anxiety and enhance their Subjective Wellbeing. Meanwhile, the eet of social participation on Subjective Wellbeing was the greatest for the older adult with high education. The findings suggest that community-led activities can be initiated to improve social participation in the older adult. Furthermore, educational courses could be to support the healthy aging of older adults in China.

KEYWORDS

social participation, subjective Wellbeing, education, Chinese older adult, mediating role, moderating role

1 Introduction

The aging of the population is a worldwide social phenomenon. With the proportion of aging population continually on the rise, aging has become a fundamental national concern in China. By 2050, it is estimated that China's older adult population aged 65 and above will account for 25.6% of the total population, and society will reach a stage of deep aging (1). As the older adult population continues to expand, their need for health services has become increasingly urgent. The older adult's living conditions, quality of life, and other factors have received widespread attention from all sectors of society. The older adult population is generally more susceptible to diseases and requires more care. Therefore, as population aging accelerates, the government has proposed the strategic goal of active aging to improve the existing policy protection with the perspective of healthy aging (2, 3). Healthy aging is mainly assessed by the quality of life in the older adult, and the Subjective Wellbeing of the older adult is an important indicator to evaluate the healthy aging process. Helping the older adult improve their quality of life has become a salient social phenomenon (4, 5).

Subjective Wellbeing, also known as psychological Wellbeing, is primarily an individual's overall assessment of their quality of life based on their self-set criteria (6). It is reflected in the individual's life satisfaction, the acquisition of positive emotions, and the disappearance of negative emotions, and it is characterized by subjectivity, wholeness, and relative stability (7). According to existing studies, higher Subjective Wellbeing is associated with reduced risks of cardiovascular disease, cognitive decline, physical frailty, and mortality in the older adult (8, 9). Therefore, studying the Subjective Wellbeing of the older adult and improving their quality of life bear great social and practical significance.

Social participation is a contributing factor to healthy aging. It refers to a pattern of behavior in which participants realize their own values in the process of social interaction in the form of social work or social activities (10). As per the theory of the older adult subcultural group, the older adult fulfill their inner psychological needs in the process of social participation and promote communication among them. The older adult feel relaxed in the subcultural group, can obtain happiness, form a positive mindset, and obtain a sense of satisfaction in life (11). Social participation can reduce the older adult's frailty, improve their memory, and reduce depression. By participation, the older adult can create social value and enhance their own sense of Wellbeing (12–14). Therefore, this study proposes hypothesis 1: Social participation would positively predict the older adult's Subjective Wellbeing, Social participation may increase the older adult's Subjective Wellbeing.

Anxiety significantly impacts the Wellbeing of the older adult. Research has shown that there is a significant negative correlation between anxiety and happiness. The greater the severity of anxiety experienced by the older adult, the lower the level of happiness they perceive (15). As they age, older adult individuals experience degenerative physiological changes that affect their daily living and self-care abilities. Moreover, coupled with the onset of their diseases, retirement, social disconnection, and fear of death, all make the older adult feel lonely, helpless, and anxious (16, 17). These negative emotions can affect the older adult individuals' feelings and evaluation of their lives, thus affecting their perceived Wellbeing. The Activity Theory posits that the older adult should actively participate in society to replace the social roles they have lost due to retirement, and so on. This can alleviate negative emotions caused by the interruption of social roles, thereby reducing their societal disconnect (18). There have been studies that found that social participation was able to reduce anxiety in the older adult (19). Therefore, the second hypothesis was raised:

Hypothesis 2: Anxiety mediates the relationship between social participation and Subjective Wellbeing.

Hypothesis 2a: Social participation would negatively predict the anxiety of the older adult.

Hypothesis 2b: Anxiety would negatively predict subjective Wellbeing of the older adult.

The educational level of the older adult affects their Subjective Wellbeing, and numerous scholars have argued that education has a beneficially enhances the Wellbeing of the older adult (20, 21). The older adult who is educated is more willing to participate in social activities after retirement, such as physical exercise, leisure activities, etc. The cognitive enrichment hypothesis suggests that education is an important factor in the construction of socio-spiritual resources (22). Compared to individuals with low education level, the older adult with high education are more capable of building social support networks. They increase the frequency of socializing with others in their lives, gain more human capital and development opportunities in society, and display a great willingness to participate in social activities (23). While participating in social activities, they can release stress and negative emotions, maintain a good psychological condition, and increase Subjective Wellbeing (24, 25). Additionally, some studies have revealed that education moderates the relationship between social status and the older adult's Wellbeing (26). To some extent, social participation also reflects the older adult's level of social status. Here we put forward the third hypothesis:

Hypothesis 3: education plays a moderating role in the relationship between social participation and the older adult's Subjective Wellbeing. Education may function as a positive moderator which amplifies the enhancing effect of social participation on subjective Wellbeing.

In conclusion, this study aimed to investigate the mechanisms of social participation on the older adult Subjective Wellbeing, including the mediating role of anxiety and the moderating role of education, in order to provide a scientific basis for enhancing the healthy aging of the older adult.

2 Methods

2.1 Study population and data source

The data used in this paper were all obtained from the 2018 data from the Chinese Longitudinal Healthy Longevity Survey (CLHLS) published by Peking University. The CLHLS survey's covered 23 provinces and regions, and the total population of the regions involved accounted for approximately 85% of the national. The questionnaire contained information on various aspects, including demographic and sociological characteristics, family background, economic status, health status, and living conditions, which provided better data support for this study. In our pursuit of robust and reliable data, any instances featuring randomly occurring missing values were eliminated from the study. This resulted in a final sample size of 10,626, exclusively composed of individuals aged 60 and above, aligning with our focus on geriatric psychology. The age range within the sample is quite substantial, extending from 60 to 117 years, with an average age of 83.39 years.

2.2 Measurements

2.2.1 Social participation

Under the social participation condition, the CLHLS questions on social participation included: outdoor activities (including tai chi, square dancing, hanging out, living with friends, and other outdoor activities), playing cards or mahjong, watching TV or listening to radio, reading books and newspapers, and participating in organized social activities. For each activity, there were five options: almost every day, at least once a week, at least once a month, sometimes, and not at all. The questions were reverse coded

TABLE 1 Baseline characteristics for the study participants.

Variables	Overall ($N = 10,626$)	Male ($N = 4,821$)	Female ($N = 5,805$)	X^2	p
Household registration				236.53	<0.001
Urban areas	3,248 (30.6%)	1,110 (23.0%)	2,138 (36.8%)		
rural areas	7,378 (69.4%)	3,711 (77.0%)	3,667 (63.2%)		
Place of residence				331.22	<0.001
City	2,680 (25.2%)	811 (16.80%)	1,869 (32.20%)		
Town	3,514 (33.1%)	1,797 (37.30%)	1,717 (29.60%)		
Rural	4,432 (41.7%)	2,213 (45.90%)	2,219 (38.20%)		
Age				1.179	0.143
60–79	4,301 (40.5%)	1,924 (39.9%)	2,377 (40.9%)		
More than 80	6,325 (59.5%)	2,987 (60.1%)	3,428 (59.1%)		
Marital status				3.41	0.03
Married	5,898 (55.5%)	2,723 (56.50%)	3,175 (54.70%)		
Unmarried, divorced, or widowed	4,728 (44.5%)	2,098 (43.50%)	2,630 (45.30%)		
Education year				1,305.98	<0.001
0	4,751 (44.70%)	1,889 (39.20%)	2,862 (49.30%)		
1–6	3,620 (34.10%)	2,432 (50.40%)	1,188 (20.50%)		
7–12	1,823 (17.20%)	477 (9.90%)	1,346 (23.20%)		
13+	432 (4.10%)	23 (0.50%)	409 (7.00%)		
Co-residence				10.70	0.005
With household member(s)	8,517 (80.20%)	3,917 (81.20%)	4,600 (79.20%)		
Alone	1,732 (16.30%)	760 (15.80%)	972 (16.70%)		
In an institution	377 (3.50%)	144 (3.00%)	233 (4.00%)		

TABLE 2 Correlation analysis between variables.

Variables	1	2	3	4	5	6	7	8
1. Gender	1							
2. Household type	−0.149**	1						
3. Place of residence	−0.143**	0.666**	1					
4. Age	0.018	0.048**	−0.009	1				
5. Subjective Wellbeing	0.172**	−0.156**	−0.123**	−0.163**	1			
6. Social participation	0.142**	−0.208**	−0.183**	−0.186**	0.509**	1		
7. Anxiety	−0.312***	0.116**	0.058**	0.048**	−0.571**	−0.350**	1	
8. Education	0.157**	−0.369**	−0.361***	−0.320**	0.296**	0.392***	−0.129**	1
M	1.55	1.69	2.16	83.39	16.34	17.36	1.55	3.66
SD	0.498	0.461	0.801	11.357	5.074	7.707	2.874	4.369

*** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$.

and scored on a 5-point scale, with 1 = not participating and 5 = almost every day. The scores for each item were summed to give a total score, with higher scores indicating higher levels of social participation. In the present study, the Cronbach α coefficient for the scale was 0.73.

2.2.2 Generalized anxiety disorde-7

The GAD-7 (27) is a self-rating scale that assesses the frequency of symptoms in the last 2 weeks and can be used to screen for generalized anxiety and its severity. The GAD-7 consists of 7 items, each of which is scored on a 4-point scale. A score of 0 was assigned to "never," and a score of 3 was assigned to "almost every day." The total score (0–21) is calculated by adding the scores of each item, with higher scores indicating more severe anxiety. A total score of <5 was considered as no anxiety symptoms (negative), and ≥5 was considered as having anxiety symptoms (positive), and the Cronbach α coefficient of this scale in this study was 0.92.

2.2.3 Subjective Wellbeing

Some scholars suggest that Subjective Wellbeing should include an emotional component (mainly the presence of positive

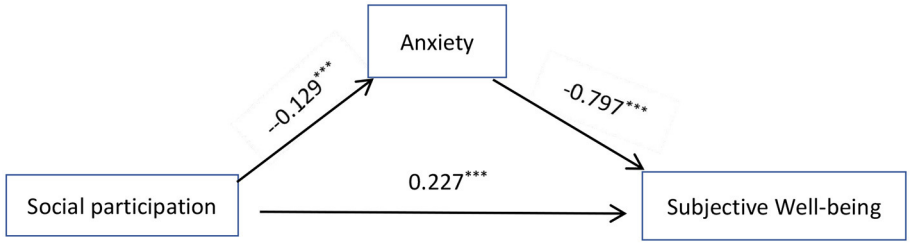

FIGURE 1
The mediating role of anxiety.

TABLE 3 The mediation effect of anxiety.

Effect	Paths	Effect value	Effect amount	95% confidence interval
Direct effect	Social participation ⟶ Subjective Wellbeing	0.227	62.73%	
Intermediary effect	Social participation ⟶ Anxiety ⟶ Subjective Wellbeing	0.103	31.23%	(0.096, 0.109)
Total effect		0.330		

emotions and the absence of negative emotions) and an evaluative component (life satisfaction) (6, 28, 29). This paper addresses six questions in the CLHLS regarding the evaluation of the older adult's life and the older adult's emotional state. The questions were, "In general, how do you think you are living your life?" "Are you hopeful about your future life?" "Are you as happy now as you were when you were younger?" "Do you often feel nervous or scared?" "Do you often feel lonely?" "Do you feel less and less useful as you get older?" Each of the six questions had five options in the order of 1 to 5, with 1 being very happy or always and 5 being very unhappy or never. The above six questions were reverse coded, with questions one to three showing positive emotion scores and questions four to six showing negative emotion scores, both of which were distributed between 3 and 15. Based on the relevant definition of Subjective Wellbeing, the composite score of Subjective Wellbeing for each sample was calculated by subtracting the negative emotion score from the positive emotion score, and the range of the composite score was −12 to 12. For the convenience of calculation, a constant of 12 was added, and the range of scores was 0 to 24. The higher the score, the happier the self-perception, and the Cronbach α coefficient of the scale in this study was 0.71.

2.2.4 Education level

According to the CLHLS questionnaire, "How many years of schooling have you attended in total?" is measured as years of formal education received. This was the moderating variable for the present study.

2.3 Data analysis

SPSS 21.0 was used for the statistical analysis of the data, and Mplus 8.0 was used for the statistical processing of the mediating and moderating effects analysis.

3 Results

3.1 Sample characteristics

Table 1 presents the characteristics of the entire study population. This study included 10,626 older adults (mean age: 83.39 ± 11.35 years). Among participants, there were 4,821 (45.4%) males and 5,805 (54.6%) females. There were 7,378 (69.4%) people with household registration in rural areas. There were 2,680 people (25.2%) currently living in the city, 3,514 people (33.1%) living in the town, and 4,432 people (41.7%) living in the countryside. Four thousand three hundred and one (40.5%) were aged 60–79 years, 5,898 (55.5%) were married, 8,517 (80.2%) lived with family members, 4,751 (44.7%) had not received education.

3.2 Common method deviation test

Because the data sources in this study were all derived from self-reported by participants, in order to avoid common methodology bias, Harman's single-factor test was used to perform unrotated exploratory factor analysis for all variables in this study (30). It was found that there were five common factors with characteristic roots >1, and the variance explained by the first common factor was 25.82%, which was much less than the critical value of 40%, indicating that there was no significant common method bias in this study.

3.3 Analysis of the correlation between variables

The older adult Subjective Wellbeing was significantly positively correlated with social participation and significantly negatively correlated with anxiety, as shown in Table 2.

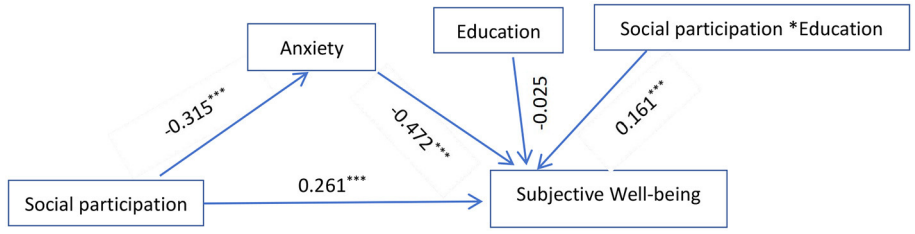

FIGURE 2
Moderating role of education.

TABLE 4 Moderated mediation model testing.

Predictive variable	M1 (Anxiety)			M2 (Subjective Wellbeing)		
	β	*SE*	*t*	*β*	*SE*	*t*
Gender	−0.269	0.007	−36.841***	−0.034	0.008	−4.382***
Age	−0.01	0.009	−1.097	−0.060	0.008	−7.547***
Household types	0.072	0.012	6.134***	0.013	0.012	1.082
Residence	0.095	0.013	7.499***	−0.009	0.018	−0.498
Social participation	−0.315	0.008	−38.389***	0.261	0.015	17.608***
Anxiety				−0.472	0.015	−56.837***
Social participation *Education				0.161	0.024	6.821***
R	0.443			0.430		
R^2	0.196			0.185		
F	518.132			1,166.99		

*** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$.

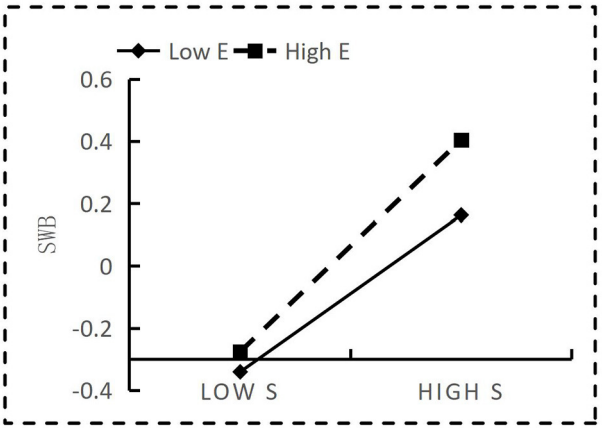

FIGURE 3
Moderating effect of education on social participation and Subjective Wellbeing (SWB, Subjective Wellbeing; E, education; S, social participation).

3.4 The mediating role of anxiety

Structural equation modeling was constructed with Mplus 8.0 to examine the mediating role of anxiety between social participation and the older adult Subjective Wellbeing (see Figure 1). Gender, age, household types, and residence were used as control variables. The fit indices of the model were: χ^2 = 103.807, df = 4, CFI = 0.969, TLI = 0.916, SRMR = 0.03, and RMSEA = 0.05, indicating that the model fits well. Bias-corrected non-parametric percentile Bootstrap tests were used to test the significance of mediating effects with 1,000 replicate samples. The results indicated that the 95% confidence interval for the mediating effect of anxiety between social participation and the older adult Subjective Wellbeing was (0.096, 0.109), excluding 0, indicating a significant mediating effect. The total effect of social participation on the older adult Subjective Wellbeing was 0.330, and the direct effect was 0.227, accounting for 62.73% of the total effect. The mediating effect of anxiety between social participation and Subjective Wellbeing was 0.103, accounting for 31.23% of the total effect, as detailed in Table 3.

3.5 The moderating effects of education

The mediating effect model with adjustment was constructed by including gender, age, household types, and residence as control variables and education as moderating variables (see Figure 2). The fit indices of the model were: χ^2 = 24.396, df = 2, CFI = 0.993, TLI = 0.976, SRMR = 0.017, RMSEA = 0.032, indicating that the model fits well. The results showed that the interaction term of education and social participation significantly predicted Subjective Wellbeing in the older adult (β = 0.161, $p < 0.001$). This indicated a significant moderating effect of education on

the pathway of social participation and Subjective Wellbeing (see Table 4).

Further simple slope analysis demonstrated that social participation was a stronger predictor of Subjective Wellbeing for highly educated individuals, as shown in Figure 3 ($b_{simple} = 0.175$ $p < 0.001$) with a 95% confidence interval of [0.161, 0.175]. For low-educated individuals, social participation had a greater effect on the prediction of Subjective Wellbeing ($b_{simple} = 0.162$, $p < 0.001$) with a 95% confidence interval of [0.144, 0.178]. This result means that education positively moderates the relationship between social participation and Subjective Wellbeing by playing an amplifying role, indicating that when education is high, social participation enhancing impact on Subjective Wellbeing can increase.

4 Discussion

Using a large-scale sample, this study investigated the mechanisms of social participation on the Subjective Wellbeing of the older adult in China, the mediating role of anxiety, and the moderating role of education from the perspective of healthy aging. This research provides a foundation for promoting healthy living among the older adult.

In this study, it was found that social participation significantly predicts the Subjective Wellbeing of the older adult, which is consistent with previous results (13, 14). Active participation in various social activities can enhance the Subjective Wellbeing of the older adult. Social identity theory suggests that individuals can obtain an identity of being a member of a team through social participation, and this identity not only affects individual mental and health behaviors but also facilitates individuals to obtain social support in the team, thus enhancing the older adult's Subjective Wellbeing (31). The older adult's active participation in social activities such as playing cards, exercising, or engaging in leisure activities enhances their mental agility, maintains their physical fitness, and fosters life satisfaction through interaction with others (32). Ponce's study found that social participation promotes social integration and enhances life satisfaction among the older adult (33). Additionally, a study by Liao et al. on the older adult in China found that both high and low levels of social participation enhanced the older adult's Wellbeing. Social participation promoted the older adult's social interactions, helped made more friends, and increased their sense of social integration (34). This study further proved that the active participation of the older adult in social activities is a key factor in improving their Wellbeing.

This study revealed that anxiety was partially mediated between social participation and Subjective Wellbeing in the older adult in China, with a mediated effect value of 0.043, accounting for 13.48% of the total effect. High social participation can reduce anxiety in the older adult. The older adult without anxiety may face their old age in an optimistic way, and their Subjective Wellbeing will be higher. In the process of social participation, the older adult maintains interactions with friends and relatives, maintain harmonious interpersonal relationships, actively participate in social work or group activities, and realize their own value through social interaction and interpersonal communication. These activities can effectively reduce anxiety in the older adult (35). Social participation can also improve the older adult's social adaptation ability. Obtaining more social support from different channels, rationally understanding and accepting new social roles, and reducing anxiety due to withdrawal from the social stage or physical aging have positive effects on the physical and mental health of the older adult (36, 37). This study found that social participation is a protective factor against anxiety in the older adult. Subjective Wellbeing has two dimensions: emotional Wellbeing and life satisfaction. Emotional Wellbeing is a profound and stable long-lasting emotional experience closely related to the level of individual mental health (38). Social participation provides the older adult with stable, strong social interactions and emotional refuge, which is an important foundation for maintaining positive emotions and psychological Wellbeing late in life. On the basis of psychological health, the older adult is more likely to reap the benefits of happiness.

This study found that education moderated the pathway between social participation and the older adult Subjective Wellbeing. Specifically, the educated older adult social participation was a strong predictor of Subjective Wellbeing than the uneducated older adult. First, education can improve individuals' knowledge and cognitive ability. In old age, they are more willing to communicate with others, build a rich social support network, and participate in social activities, thus accumulating their social and spiritual resources. In turn, these spiritual resources can protect individuals' mental health and improve their Subjective Wellbeing (24). Second, highly educated individuals tend to be more receptive to healthy lifestyles, such as being physically active and engaging in leisure activities (39). They are able to construct high Subjective Wellbeing through these activities. Third, the educated older adult are likely to have higher social status and better social resources before retirement. This typically results in better social support when they need to talk or require assistance, higher self-efficacy, hope for life, and a sense of joy in life. This study examines the effects of social participation on the older adult Subjective Wellbeing, the mediating role of anxiety, and the moderating role of education from a healthy aging perspective.

This study found that anxiety partially mediates the relationship between social participation and the older adult Subjective Wellbeing and that education moderates the relationship between social participation and the older adult Subjective Wellbeing. After the older adult retires from the formal labor market, their emotional state will definitely be affected. Here are some implications for policy and practice. We can rely on the community to create more social participation opportunities for the older adult and organize various cultural and recreational activities and volunteer services so that the older adult can find social activities that meet their personal interests in their familiar living areas, enhance the diversity of their life in their old age, and thus improve their sense of Wellbeing and satisfaction. On the other hand, the community can also increase financial investment in education. For example, they can develop skill courses such as the use of electronic devices, knowledge courses such as the introduction of social hotspots and mental health knowledge, and interest courses such as sports and art instruction. By improving

the educational level of the older adult, this can promote their social participation, enhance their sense of Wellbeing, and help maintain a healthy and happy life in their older adult years.

There are limitations in this study as follows: first, because this study is a cross-sectional study, there is no way to explore the causal relationship, and a longitudinal study can be added later to discuss the causal relationship between social participation and the older adult Subjective Wellbeing. Second, the study results were based on the self-reports from the participants, and recall bias or reporting bias for some questions could not be controlled.

Data availability statement

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

Author contributions

ZQ: Writing – original draft. CW: Writing – original draft, Formal analysis, Data curation. TG: Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research, authorship, and/or publication of this article. This study was supported by Scientific Research Youth Project, Hunan Provincial Department of Education, China (21B0835).

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

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frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 28 May 2024
DOI 10.3389/fpubh.2024.1392581

OPEN ACCESS

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RECEIVED 27 February 2024
ACCEPTED 17 May 2024
PUBLISHED 28 May 2024

CITATION
Wang R, Shi W, Zhou W, Xu Y and Wang J (2024) Associations between peak expiratory flow and frailty in olderly individuals: findings from the China health and retirement longitudinal study. *Front. Public Health* 12:1392581. doi: 10.3389/fpubh.2024.1392581

Associations between peak expiratory flow and frailty in olderly individuals: findings from the China health and retirement longitudinal study

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Purpose: Peak Expiratory Flow (PEF) is associated with a variety of adverse health outcomes in older adults; however, the relationship between PEF and frailty remains uncertain, and this study investigated the relationship between PEF and frailty within an olderly Asian demographic.

Methods: Data were sourced from the Chinese Health and Retirement Longitudinal Study (CHARLS). Individuals in the study, all 60 years or older, underwent baseline PEF assessments quantified as standardized residual (SR) percentile values. The evaluation of frailty was conducted based on the criteria established by Fried. Participants without frailty at the outset were tracked over a four-year period, during which the relationships between PEF and frailty were examined through logistic regression and discrete-time Cox regression analyses.

Results: Among 5,060 participants, cross-sectional analysis revealed that the prevalence of frailty was 2–3 times higher in the lower 10–49th and < 10th SR percentile groups compared to the 80–100th SR percentile group. The longitudinal study corroborated these results, showing an adjusted hazard ratio (HR) of 2.01 (95% CI, 1.15–3.51) for PEF SR percentiles below the 10th, in contrast to those between the 80th and 100th percentiles.

Conclusion: PEF independently predicts and determines frailty in older adults. Declines in PEF greater than expected are associated with the development of frailty. Subsequent studies are encouraged to delve deeper into the connection between respiratory function and frailty in diverse contexts.

KEYWORDS

respiratory function, peak expiratory flow, frailty, older adults, CHARLS

1 Introduction

Population aging is now a global phenomenon, with China experiencing the largest aging population worldwide. As per the 2020 national census data, China has over 260 million individuals aged 60 and above, presenting a significant challenge to the healthcare system (1). Among the various issues arising from population aging, the clinical condition of frailty stands out as particularly problematic (2, 3).

Frailty primarily denotes a non-specific state characterized by multiple functional abnormalities or diminished physiological reserves, leading to heightened vulnerability and reduced stress resilience in individuals (2, 4). This condition escalates dependence, fragility, and mortality risk (5). Compared to their non-frail counterparts, frail olderly individuals are more susceptible to adverse health outcomes, including falls, disability, delirium, emergency hospital admissions, and even death (6). Hence, early screening and diagnosis of frailty in olderly adults are crucial for averting these negative consequences. Age-related declines in lung function and respiratory strength, associated with health issues like diminished physical capacity and increased mortality risk (7, 8), may serve as indicators of frailty and its implications. However, the gold standard for lung function assessment, spirometry, necessitates specialized training and equipment (9, 10).

Peak expiratory flow (PEF), the maximum instantaneous flow achieved during forced expiration at maximal lung inflation, is notably simple and cost-effective (11, 12). Its measurements can be easily obtained even by untrained individuals, making it a practical tool for large-scale studies involving older adults. Prior research has identified a two-way relationship between frailty and respiratory illnesses, particularly those characterized by restrictive and obstructive patterns (13). However, there is limited evidence linking lung function, specifically PEF, with frailty in older adults (14, 15). Furthermore, while PEF has been associated with frailty in older adults in prospective cohorts, there is a notable gap in such data from Asian populations.

Our hypothesis posits that PEF values lower than anticipated could be linked to both the presence and progression of frailty in older adults. To explore this, our study utilizes data from the China Health and Retirement Longitudinal Study (CHARLS) to examine these hypotheses. This research marks the first instance of investigating the relationship between low PEF and the onset of frailty in community-dwelling older adults in China.

2 Methods

2.1 Study population

Our study's data was sourced from the China Health and Retirement Longitudinal Study (CHARLS), a project aimed at collecting detailed and nationally representative data on households and individuals over the age of 45 in China, primarily to examine the dynamics of aging within the country. Detailed information about the CHARLS design and methods has been previously described in detail (16). In brief, CHARLS initiated a national baseline survey in 2011 (wave 1), followed by subsequent follow-up visits in 2013 (wave 2), 2015 (wave 3), and 2018 (wave 4). This baseline survey encompassed 450 villages and urban residences across 150 counties and districts, successfully interviewing 17,708 individuals who broadly represent China's middle-aged and olderly adults. CHARLS received ethical approval from the Ethics Review Committee of Peking University (IRB0000105211015), and all participants provided written informed consent.

In our study, we utilized data exclusively from wave 1, wave 2, and wave 3, as the collection of frailty information in wave 4 was incomplete. To specifically target the frail olderly demographic, we included only individuals aged 60 years and older. We excluded data from individuals who either lacked PEF information or whose frailty status could not be ascertained in the baseline analysis. Additionally, participants identified as frail at baseline were excluded from the analysis predicting the development of frailty, based on follow-up data from wave 2 and wave 3 (refer to Figure 1).

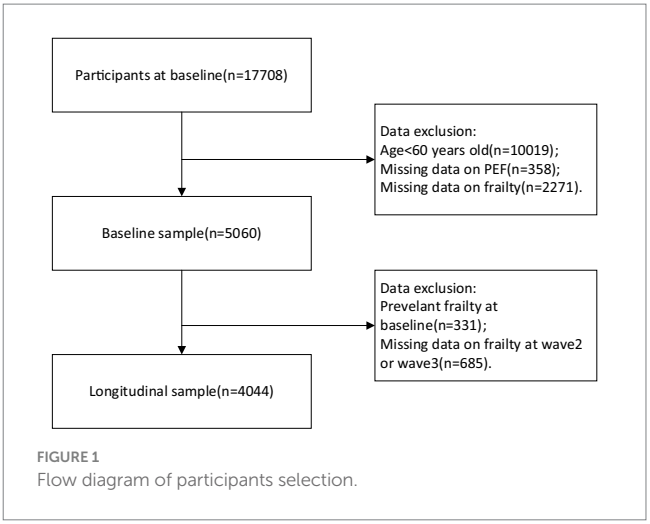

FIGURE 1
Flow diagram of participants selection.

2.2 Measures

2.2.1 Frailty

Frailty assessment in this study was conducted using the revised Physical Frailty Phenotype (PFP) scale (17, 18). This scale includes five criteria: weakness, slow walking speed, exhaustion, weight loss, and low physical activity (19, 20). Individuals meeting three or more of these criteria were classified as frail, while those meeting fewer were categorized as non-frail.

(1) Weakness: This was assessed using the highest value from two grip strength tests performed with either hand while standing. Participants were classified as exhibiting weakness if their grip strength was at or beneath the 20th percentile, with adjustments made for gender and body mass index.
(2) Slow Walking Speed: Defined as the average of two walking tests over a distance of 2.5 meters. Walking velocities that were at or under the 20th percentile, once adjusted for gender and height, were classified as reduced.
(3) Exhaustion: Evaluated using two components from the Center for Epidemiologic Studies Depression Scale (CESD) (21). Participants were identified as meeting the exhaustion criterion if they indicated feeling "Occasionally or a moderate amount of time (3–4 days)" or "Most or all of the time (5–7 days)"when answering either of these questions: "I feel everything I did was an effort" or "I could not get going."
(4) Weight Loss: Participants self-reporting a loss of 5 kg or more over the past year during wave 1 and wave 2 were considered to have experienced significant weight loss. In wave 3, this criterion was met if there was a weight loss of 5 kg or more between wave 2 and wave 3.

(5) Low Physical Activity: Defined based on participants' responses to three questions. Participants were classified as having low physical activity if they answered "no" to all of the following questions: "During a usual week, did you do any vigorous activities for at least 10 min continuously," "Did you do any moderate physical effort for at least 10 min continuously," and "Did you do any walking for at least 10 min continuously."

2.2.2 PEF

PEF assessments were carried out with the use of a peak lung flow meter (EverpureTM, Shanghai, China). Participants were directed to stand, inhale deeply, securely enclose the mouthpiece with their mouths, and then exhale forcefully and rapidly. This procedure was repeated thrice, with 30-s intervals between each attempt. The highest reading from these three attempts, expressed in liters per minute, was used for analysis (22). Previous studies indicate that PEF naturally declines with age and varies among individuals due to factors like gender and height (11). Consequently, a reference group was formed by choosing a healthy subset from the same demographic, comprising individuals who had never smoked and had no history of diagnosed respiratory disorders, cardiovascular diseases, cancer, and similar conditions. This allowed us to use age, gender, and height-standardized PEF values to estimate the expected PEF values. PEF was defined in terms of:

(1) PEF Residuals: Defined as the variance between the observed PEF and the anticipated PEF, these residuals were classified into groups with 10 L/min decrement intervals.
(2) Percent Predicted: This metric was derived from the ratio of the actual measured PEF to the expected PEF. Predicted percentages were categorized at 10% intervals of decrease, and grouped into thresholds of 50, 80, and 100%.
(3) PEF Standardized Residual (SR) Percentiles: Calculated by standardizing the ratio (measured PEF – expected PEF)/standard deviation of the residuals. An SR of 0 was equated to the 50th percentile. Percentiles were regarded as continuous variables and were grouped into categories decreasing by 10 percentage points, further divided into the following ranges: below 10th, 10th to 49th, 50th to 79th, and 80th to 100th percentiles.

2.3 Covariates

The study's covariates included both demographic and health and functioning variables. Demographic variables comprised age, gender, residence (urban or rural), education level (uneducated, did not complete elementary school, elementary school, middle school, high school, and above), and marital status (married, widowed, or other). Health and functioning variables encompassed smoking status (never smoked, former smoker, current smoker), alcohol consumption (never, occasional, or regular), number of chronic conditions, cognitive functioning, and depression (yes or no). Occasional drinking was characterized as consuming alcohol fewer than once per month over the previous year, while regular consumption meant drinking more than once a month. Chronic diseases were identified based on self-reported histories of conditions like hypertension, diabetes mellitus, malignant neoplasms, chronic lung disease, liver disease, heart disease, kidney disease, stomach or digestive disease, stroke, arthritis, or rheumatism. Participants were grouped based on the number of chronic conditions (0, 1, and >1). Cognitive functioning was evaluated using memory and mental state scores (23, 24), where the total cognitive score, ranging from 0 to 21, is the sum of these scores, with higher scores indicating better cognitive performance. Depression was assessed using the CESD-10 scale (25), with a score of 12 or more indicating depression (26).

2.4 Data analyses

Descriptive analyses were presented as means ± standard deviation for continuous variables and as frequencies and percentages for categorical variables. The baseline characteristics related to frailty status and covariates were categorized based on PEF SR percentile intervals. Interindividual characteristics were compared using the Kruskal–Wallis test and chi-square tests, as appropriate. Logistic regression analysis was utilized to assess the correlation between PEF and initial frailty, whereas discrete-time Cox regression analysis was applied to determine the connection between PEF and frailty in subsequent follow-up data. In this analysis, participants who completed the follow-up without becoming frail served as the reference group. The multivariate analysis comprised three models: Model 1 was unadjusted; Model 2 adjusted for age and gender; and Model 3 further adjusted for place of residence, education level, marital status, smoking status, alcohol consumption, number of chronic diseases, cognitive functioning, and depression.

To investigate whether baseline chronic lung disease or smoking habits influenced the relationship between peak expiratory flow (PEF) and frailty, participants were stratified into two subgroups in the fully adjusted model for a sensitivity analysis. Based on this stratification, interactions were assessed by integrating PEF and its corresponding multiplicative interaction factors into a comprehensively adjusted Cox regression model.

Each statistical test was two-sided, with a p-value of less than 0.05 indicating statistical significance. All statistical analysis was performed retrospectively with Stata 18 (Stata Corp, College Station, TX).

3 Results

3.1 Baseline sample characteristics

Table 1 displays the initial characteristics of the study cohort. Following the preliminary screening, a total of 5,060 individuals were enrolled in the study. Of these, 1,055 (20.8%) were classified in the 100th–80th PEF SR percentile, 1,544 (30.5%) in the 79th-50th percentile, 1970 (38.9%) in the 49th-10th percentile, and 491 (9.7%) in the <10th percentile. The average age of the participants was 67.6 ± 6.4 years, with 49.2% being female. Participants in the lower PEF SR percentiles, compared to those in the highest percentile group, were more likely to live in rural areas and have current smoking habits and regular alcohol consumption. Regarding health status, lower PEF SR percentiles were associated with a greater number of chronic diseases and a higher prevalence of depression. A total of 331 individuals were identified with debilitation at baseline, with the prevalence of debilitation increasing progressively with decreasing PEF SR percentiles (2.8, 5.9, 8.4, and 9.0%, respectively, $p < 0.001$).

TABLE 1 Baseline characteristics of study sample grouped by peak expiratory flow (PEF) standardized residual percentiles ($N = 5,060$).

Characteristics		All	Peak expiratory flow SR percentiles				*p*-value
		($n = 5,060$)	80th–100th ($n = 1,055$)	50th–79th ($n = 1,544$)	10th–49th ($n = 1970$)	<10th ($n = 491$)	
Age, mean ± SD		67.6 ± 6.4	67.9 ± 6.6	67.5 ± 6.4	67.9 ± 6.4	65.9 ± 5.1	<0.001
Gender, *n* (%)	Male	2,572 (50.8)	580 (55.0)	664 (43.0)	940 (47.7)	388 (79.0)	<0.001
	Female	2,488 (49.2)	475 (45.0)	880 (57.0)	1,03 0(52.3)	103 (21.0)	
marital status, *n* (%)	Married	4,061 (80.3)	874 (82.8)	1,192 (77.2)	1,579 (80.2)	416 (84.7)	<0.001
	Widowed	925 (18.3)	168 (15.9)	330 (21.4)	367 (18.6)	60 (12.2)	
	Others	74 (1.5)	13 (1.2)	22 (1.4)	24 (1.2)	15 (3.1)	
Residential area, *n* (%)	Rural	3,177 (62.8)	613 (58.1)	982 (63.6)	1,275 (64.7)	307 (62.5)	0.004
	Urban	1883 (37.2)	442 (41.9)	562 (36.4)	695 (35.3)	184 (37.5)	
Education, *n* (%)	No formal education illiterate	1784 (35.3)	284 (28.3)	585 (39.4)	776 (37.9)	139 (26.9)	<0.001
	Did not finish elementary school	1,058 (20.9)	101 (20.6)	436 (22.1)	322 (20.9)	199 (18.9)	
	Elementary school	1,270 (25.1)	149 (30.4)	471 (23.9)	358 (23.2)	292 (27.7)	
	Middle school	637 (12.6)	70 (14.3)	209 (10.6)	192 (12.4)	166 (15.7)	
	High school or above	311 (6.2)	32 (6.5)	78 (4.0)	87 (5.6)	114 (10.8)	
Smoking, *n* (%)	Never smoked	2,890 (57.1)	610 (57.8)	967 (62.6)	1,129 (57.3)	184 (37.5)	<0.001
	Have quit	597 (11.8)	149 (14.1)	139 (9.0)	214 (10.9)	95 (19.4)	
	Current smoker	1,573 (31.1)	296(28.1)	438(28.4)	627(31.8)	212(43.2)	
Drinking, *n* (%)	Never	3,457 (68.3)	689 (65.3)	1,114 (72.2)	1,363 (69.2)	291 (59.3)	<0.001
	Occasionally	357 (7.1)	104(9.9)	95(6.2)	123(6.2)	35(7.1)	
	Regularly	1,246 (24.6)	262 (24.8)	335 (21.7)	484 (24.6)	165 (33.6)	
Number of chronic diseases, *n* (%)	0	1,363 (26.9)	312 (29.6)	423 (27.4)	513 (26.0)	115 (23.4)	0.002
	1	1,534 (30.3)	335 (31.8)	490 (31.7)	573 (29.1)	136 (27.7)	
	>1	2,163 (42.8)	408 (38.7)	631 (40.9)	884 (44.9)	240 (48.9)	
Cognition score, median (IQR)		9.5 (6.0, 13.0)	11.0 (8.0, 14.5)	9.5 (6.0, 13.0)	8.5 (5.0, 12.0)	10.0 (6.5, 13.0)	<0.001
Depression, *n* (%)	No	3,614 (71.4)	822 (77.9)	1,134 (73.5)	1,306 (66.3)	352 (71.7)	<0.001
	Yes	1,446 (28.6)	233 (22.1)	410 (26.6)	664 (33.7)	139 (28.3)	
Frailty, *n* (%)	No-frail	4,729 (93.5)	1,025 (97.2)	1,453 (94.1)	1804 (91.6)	447 (91.0)	<0.001
	Frail	331 (6.5)	2.8	91 (5.9)	166 (8.4)	44 (9.0)	

SD, standard deviation; IQR, interquartile range.

3.2 Cross-sectional association between PEF and frailty

The fully adjusted cross-sectional regression analysis model illustrates this point: When PEF was analyzed as SR percentile (OR = 1.14, 95% CI: 1.09–1.19) or percent predicted (OR = 1.13, 95% CI: 1.08–1.18), the risk of frailty increased by approximately 14% for each 10-unit decrease in PEF. In comparison to the group with the highest PEF SR percentiles, individuals in the lower percentile groups (10th to 49th and below 10th SR percentiles) exhibited a 2–3 fold increase in the number of frail participants, as shown in Table 2, Model 3.

3.3 Correlation between PEF and frailty in subsequent follow-up studies

Table 3 demonstrates the association between PEF and the development of frailty during the four-year follow-up period. Out of

TABLE 2 Cross-sectional correlation between peak expiratory flow and frailty.

PEF measures	*n*	Odds ratios and 95% confidence intervals of frailty					
		Model 1	*p*-value	Model 2	*p*-value	Model 3	*p*-value
PEF residual							
Per each 10 L/min decrease	5,060	1.02 (1.01–1.02)	<0.001	1.02 (1.01–1.02)	<0.001	1.02 (1.01–1.02)	<0.001
PEF SR percentile							
Per each 10th decrease	5,060	1.14 (1.10–1.19)	<0.001	1.18 (1.13–1.23)	<0.001	1.14 (1.09–1.19)	<0.001
80th–100th	1,055	Reference		Reference		Reference	
50–79th	1,544	2.14 (1.24–3.04)	<0.001	2.21 (1.27–3.16)	<0.001	2.13 (1.18–3.07)	0.01
10th–49th	1970	3.14 (1.90–4.40)	<0.001	3.25 (1.94–4.55)	<0.001	2.52 (1.46–3.57)	<0.001
<10th	491	3.36 (1.76–4.97)	<0.001	4.86 (2.47–7.24)	<0.001	3.82 (1.85–5.80)	<0.001
PEF percent predicted							
Per each 10% decrease	5,060	1.16 (1.11–1.21)	<0.001	1.17 (1.13–1.22)	<0.001	1.13 (1.08–1.18)	<0.001
>100%	2,312	Reference		Reference		Reference	
80–100%	942	1.28 (0.85–1.71)	0.154	1.36 (0.89–1.83)	0.078	1.16 (0.75–1.58)	0.408
50–79%	1,223	1.81 (1.29–2.33)	<0.001	1.89 (1.34–2.43)	<0.001	1.54 (1.07–2.02)	0.006
<50%	583	3.10 (2.14–4.07)	<0.001	3.24 (2.21–4.28)	<0.001	2.39 (1.58–3.20)	<0.001

Model 1 is unadjusted. Model 2 is adjusted for age and sex. Model 3 is also adjusted for educational level, marital status, smoking habits, residential area, drinking, number of chronic diseases, cognition score and depression. PEF stands for peak expiratory flow; SR represents standardized residual.

TABLE 3 Longitudinal correlation between peak expiratory flow and frailty.

PEF measures	*n*	Hazard ratios and 95% confidence intervals of frailty					
		Model 1	*p*-value	Model 2	*p*-value	Model 3	*p*-value
PEF residual							
Per each 10 L/min decrease	4,044	1.01 (1.01–1.02)	<0.001	1.01 (1.01–1.02)	<0.001	1.01 (1.00–1.01)	0.002
PEF SR percentile							
Per each 10th decrease	4,044	1.09 (1.04–1.14)	<0.001	1.11 (1.06–1.16)	<0.001	1.08 (1.03–1.31)	0.002
80th–100th	895	Reference		Reference		Reference	
50–79th	1,251	1.74 (1.13–2.66)	0.011	1.75 (1.14–2.69)	0.01	1.62 (1.06–2.50)	0.028
10th–49th	1,514	2.29 (1.53–3.43)	<0.001	2.31 (1.54–3.45)	<0.001	1.89 (1.26–2.84)	0.002
<10th	384	1.91 (1.11–3.29)	0.019	2.41 (1.39–4.18)	0.002	2.01 (1.15–3.51)	0.014
PEF percent predicted							
Per each 10% decrease	4,044	1.10 (1.05–1.15)	<0.001	1.11 (1.06–1.17)	<0.001	1.07 (1.03–1.12)	0.003
>100%	1971	Reference		Reference		Reference	
80–100%	765	1.37 (0.96–1.96)	0.081	1.44 (1.01–2.05)	0.046	1.31 (0.92–1.87)	0.141
50–79%	935	1.72 (1.25–2.35)	0.001	1.75 (1.28–2.40)	0.001	1.49 (1.09–2.05)	0.014
<50%	427	1.83 (1.22–2.75)	0.003	1.91 (1.27–2.87)	0.002	1.53 (1.01–2.31)	0.044

Model 1 is unadjusted. Model 2 is adjusted for age and sex. Model 3 is also adjusted for educational level, marital status, smoking habits, residential area, drinking, number of chronic diseases, cognition score, and depression. PEF, peak expiratory flow; SR, standardized residual.

all participants, 236 (5.8%) developed frailty. For each 10-unit reduction in PEF SR percentile, there was a roughly 8% rise in the likelihood of developing frailty. Moreover, individuals in the 10th–49th and < 10th percentile groups had over twice the odds ratio (OR) of developing frailty compared to those in the highest PEF SR percentile group. When PEF was calculated as a percent of the predicted value, the 10th-49th and < 10th percentile groups showed about a 1.5-fold increase in frailty risk compared to the reference group.

3.4 Sensitivity analysis

After stratifying participants based on the presence of chronic lung disease, a significant association was observed between peak expiratory flow (PEF) and frailty in participants without chronic lung disease, compared to those with the condition ($p = 0.001$; Table 4). Similarly, when analyzing the data stratified by smoking status, the results indicated comparable associations between PEF and frailties

10.3389/fpubh.2024.1392581

TABLE 4 Stratification of participants based on the presence or absence of chronic lung disease and their associated peak expiratory flow and frailty.

PEF measures	No chronic lung disease	*p*-value	Chronic lung disease	*p*-value
	Odds ratios and 95% confidence intervals of frailty			
Cross-sectional analysis				
n	4,366		680	
PEF residual				
Per each 10 L/min decrease	1.016(1.010–1.022)	<0.001	1.011(0.997–1.025)	0.114
PEF SR percentile				
Per each 10th decrease	1.144(1.086–1.202)	<0.001	1.116(0.978–1.254)	0.081
PEF percent predicted				
Per each 10% decrease	1.138(1.083–1.193)	<0.001	1.101(0.977–1.225)	0.094
	Hazard ratios and 95% confidence intervals of frailty			
Longitudinal analysis				
n	3,541		503	
PEF residual				
Per each 10 L/min decrease	1.010 (1.004–1.016)	0.001	1.001 (0.984–1.018)	0.911
PEF SR percentile				
Per each 10th decrease	1.092 (1.037–1.149)	0.001	1.011 (0.868–1.177)	0.89
PEF percent predicted				
Per each 10% decrease	1.088 (1.035–1.144)	0.001	0.993 (0.864–1.142)	0.926

Model is adjusted for age, sex, educational level, marital status, smoking habits, residential area, drinking, number of chronic diseases, cognition score, and depression. PEF, peak expiratory flow; SR, standardized residual.

(Supplementary Table S1). Furthermore, the addition of a multiplicative interaction term between PEF SR percentile and chronic lung disease or smoking status to examine changes in the relationship between baseline PEF and follow-up frailty revealed no statistically significant interaction (p interaction >0.05).

4 Discussion

Previous research has identified a link between frailty and PEF and has utilized PEF as a predictive indicator of frailty in older populations (11, 15, 27). Nonetheless, there is some controversy, as highlighted by the study of Charles et al., which did not find a correlation between PEF and frailty after adjusting for covariates (14). Moreover, most prior studies have been confined to cross-sectional designs and specific settings, such as nursing homes, with a notable lack of data from Asian populations, thus limiting the applicability of PEF in detecting frailty in these groups. This study, therefore, stands as the first to investigate the association between PEF and frailty using both cross-sectional and longitudinal approaches within a generalized Asian population, utilizing CHARLS data. Our findings indicate that lower-than-expected PEF values are independently associated with both the development and presence of frailty in olderly adults.

Various mechanisms, such as sarcopenia – a widespread reduction in skeletal muscle mass and function associated with aging, help elucidate the link between PEF and frailty (28–30). This condition leads to weakened muscles throughout the body, including the respiratory muscles (31–33), and plays a crucial role in the frailty indicators of the FRAIL scale, such as low grip strength and slow walking speed (34). Additionally, sarcopenia-induced respiratory muscle weakness significantly impacts peak respiratory flow rates. Studies have shown a longitudinal link between decreased PEF and sarcopenia (35, 36). Moreover, low physical activity and impaired respiratory function due to sarcopenia exacerbate fatigue, further increasing frailty risk and perpetuating a vicious cycle. Inflammation is another key mechanism contributing to respiratory impairment and frailty. Chronic inflammation drives age-related declines in physical functioning, leading to reduced mobility, cognitive impairment, and the development of both physical and cognitive frailty (37, 38). This inflammation not only weakens muscle strength but also impairs lung function (39, 40), which in turn increases the risk of lung infections and frailty in individuals with lower PEF. Furthermore, decreased lung function is linked to impaired cognitive function and a heightened risk of dementia (41, 42). Indications are that ongoing deterioration in lung capacity could lead to a state of inflammation driven by reduced oxygen supply to the brain (43), making individuals with low PEF more prone to developing frailty.

While the mechanisms discussed above indicate a bidirectional relationship between frailty and respiratory function, our longitudinal analysis excluded individuals already frail at baseline. Our results indicate that reduced PEF could act as an early indicator and contributing factor to frailty. The results of this study demonstrate that the impact of PEF on frailty in olderly adults remains consistent, irrespective of whether it is assessed at a single time point or observed over a period. This consistency suggests that the mechanisms linking these two variables are stable, and these determinants do not undergo significant changes over time.

Previous research often indicates that certain relationships are enduring (12, 35). Our findings align with these studies and exhibit similar patterns in both cross-sectional and longitudinal analyses. Prior studies have indicated an increased association between frailty and PEF in the presence of chronic lung disease (7, 44). However, in this study, the fully adjusted model and subsequent sensitivity analysis revealed no significant findings. Furthermore, upon including interaction terms, no significant interactions between PEF and chronic lung disease were observed. This could be due to other covariates in our study that are closely linked with chronic lung disease, obscuring potential interactions. Additionally, despite the known impact of smoking on respiratory impairment, our study did not find any interaction between smoking status and PEF. This underscores the need for future research to further explore these associations in different contexts and populations, taking into account various symptoms related to respiratory disorders.

This study has certain limitations, including the exclusion of part of the sample due to missing information. This excluded subset may have been older and in poorer health, potentially leading to an underestimation of frailty prevalence. Additionally, while we controlled for numerous relevant covariates, unaccounted confounding factors might still exist, introducing potential bias. Furthermore, due to limitations inherent in the CHARLS database, our study exclusively employed the Revised Physical Frailty Phenotype (PFP) scale for frailty assessment and employed only PEF to evaluate respiratory function. This approach represents a potential bias. Future research could explore variations in outcomes derived from different frailty assessment methods, providing a detailed analysis of the relationship between individual frailty components and the Respiratory function assessment. However, the study also possesses notable strengths. As far as we are aware, this is the inaugural long-term study in Asia examining the link between PEF and the risk of frailty, utilizing a large, nationally representative sample from the CHARLS dataset, which includes community-dwelling older adults in China. Furthermore, the assessment of PEF through various methods enhances the reliability of our findings.

5 Conclusion

In conclusion, through both cross-sectional and longitudinal analyses, this study has established a clear relationship between decreased PEF and frailty in an Asian population. We have demonstrated that PEF can serve as an independent predictor of frailty among older adults, with lower-than-expected PEF values being notably associated with the development of frailty. Future research should focus on further exploring the impact of chronic respiratory diseases on the correlation between PEF and frailty.

Data availability statement

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

Ethics statement

The studies involving humans were approved by Peking University Biomedical Ethics Committee. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

Author contributions

RW: Data curation, Writing – original draft, Writing – review & editing. WS: Software, Writing – review & editing. WZ: Methodology, Software, Writing – review & editing. YX: Software, Writing – review & editing. JW: Supervision, Writing – review & editing.

Funding

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

Acknowledgments

The data for this study came from CHARLS, and we thank all the researchers and respondents interviewed and all the team members involved.

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.2024.1392581/full#supplementary-material

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frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 06 June 2024
DOI 10.3389/fpubh.2024.1356878

OPEN ACCESS

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RECEIVED 26 January 2024
ACCEPTED 17 May 2024
PUBLISHED 06 June 2024

CITATION
Hu F, Zhang G, Xu Z, Zuo Z, Huang N, Ge M, Liu X and Dong B (2024) The diagnostic agreement of sarcopenic obesity with different definitions in Chinese community-dwelling middle-aged and older adults.
Front. Public Health 12:1356878.
doi: 10.3389/fpubh.2024.1356878

The diagnostic agreement of sarcopenic obesity with different definitions in Chinese community-dwelling middle-aged and older adults

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Background: In 2022, the European Society for Clinical Nutrition and Metabolism (ESPEN) and the European Association for the Study of Obesity (EASO) launched a consensus on the diagnostic methods for sarcopenic obesity (SO). The study aimed to identify the prevalence and diagnostic agreement of SO using different diagnostic methods in a cohort of subjects from West China aged at least 50 years old.

Methods: A large multi-ethnic sample of 4,155 participants from the West China Health and Aging Trend (WCHAT) study was analyzed. SO was defined according to the newly published consensus of the ESPEN/EASO. Furthermore, SO was diagnosed as a combination of sarcopenia and obesity. The criteria established by the Asian Working Group for Sarcopenia 2019 (AWGS2019) were used to define sarcopenia. Obesity was defined by four widely used indicators: percent of body fat (PBF), visceral fat area (VFA), waist circumference (WC), and body mass index (BMI). Cohen's kappa was used to analyze the diagnostic agreement of the above five diagnostic methods.

Results: A total of 4,155 participants were part of the study, including 1,499 men (63.76 ± 8.23 years) and 2,656 women (61.61 ± 8.20 years). The prevalence of SO was 0.63–7.22% with different diagnostic methods. The diagnosis agreement of five diagnostic methods was poor-to-good (κ: 0.06–0.67). The consensus by the ESPEN/EASO had the poorest agreement with other methods (κ: 0.06–0.32). AWGS+VFA had the best agreement with AWGS+WC ($\kappa = 0.67$), and consensus by the ESPEN/EASO had the best agreement with AWGS+ PBF ($\kappa = 0.32$).

Conclusion: The prevalence and diagnostic agreement of SO varies considerably between different diagnostic methods. AWGS+WC has the highest diagnostic rate in the diagnosis of SO, whereas AWGS+BMI has the lowest. AWGS+VFA has a relatively good diagnostic agreement with other diagnostic methods, while the consensus of the ESPEN/EASO has a poor diagnostic agreement. AWGS+PBF may be suitable for the alternative diagnosis of the 2022 ESPEN/EASO.

KEYWORDS

sarcopenic obesity, prevalence, diagnostic agreement, WCHAT, obesity

Introduction

Sarcopenia is an age-related skeletal muscle disorder characterized by a decrease in muscle mass, strength, and function. Sarcopenic obesity (SO) is a condition characterized by the coexistence of sarcopenia and obesity (1). Obesity and sarcopenia have synergistic and reinforcing effects (2). Patients with sarcopenia experience a decrease in total energy expenditure, which promotes ectopic fat deposition. In addition, obesity can lead to oxidative stress, inflammation, increased insulin resistance, and the exacerbation of muscle metabolism and breakdown (3, 4). SO is associated with increased body fat and decreased muscle volume and function, which reduces the likelihood of an individual with SO engaging in exercise. A lack of exercise is both the cause and the result of SO (5). However, most treatments for obesity, including factors such as diet, surgery, and imbalanced nutritional structure, inevitably lead to a loss of skeletal muscle mass (SMM), resulting in weight loss characterized by a decrease in SMM (6–8). In addition, having high body fat may lead to a decrease in relative SMM (skeletal muscle mass/body weight, SMM/W) in individuals with obesity, but due to their greater body mass, these individuals exert more physical effort during daily activities, which may preserve absolute SMM (9). Similarly, overall muscle function and muscle contractile quality are conserved in individuals with mild obesity (10). This has made the diagnosis, treatment, and standard formulation of SO difficult.

In previous research, SO was diagnosed by the combination of sarcopenia and obesity. Generally, the standard criteria for sarcopenia established by the Asian Working Group for Sarcopenia (AWGS) or the European Working Group on Sarcopenia in Older People are used to define sarcopenia. However, the diagnostic criteria for SO vary as a result of different methods for diagnosing obesity, such as body mass index (BMI), waist circumference (WC), percent of body fat (PBF), and visceral fat area (VFA) (11, 12). Due to the absence of unified standards for obesity-related diagnosis, it is difficult to correlate the results of various research teams. The establishment of diagnostic criteria for SO assessment is important for identifying patients with SO, the precise treatment of SO, and the evaluation of SO-related results. In 2022, the European Society for Clinical Nutrition and Metabolism (ESPEN) and the European Association for the Study of Obesity (EASO) launched a consensus of SO diagnostic methods based on skeletal muscle function and body composition (12). The consistency of traditional diagnostic methods and newly released consensuses remain unclear, with important implications for the diagnosis/monitoring of SO.

This article aimed to compare the prevalence and consistency of different assessment methods in a natural population cohort of individuals aged over 50 years. In addition, we further explored the basal metabolic profiles of each group of patients with SO, which may provide a basis for exploring the optimal diagnosis for SO. We hypothesized that the new SO consensus would yield the best diagnostic efficiency.

Methods

Study population

This study used the baseline data from the West China Health and Aging Trend (WCHAT) study. Previous studies have published details of the study design and questionnaires used to generate data (13). In this study, 7,536 participants were enrolled at first. Out of these, only 4,500 participants aged 50 years and above finished sarcopenia assessment. Furthermore, 32 subjects were excluded as they did not have information on handgrip strength (HS), PBF, or SMM /W. In addition, 313 subjects were excluded as they did not have information on obesity measurements like BMI, WC, PBF, or VFA. Finally, 4,155 participants were included in the current study (Figure 1).

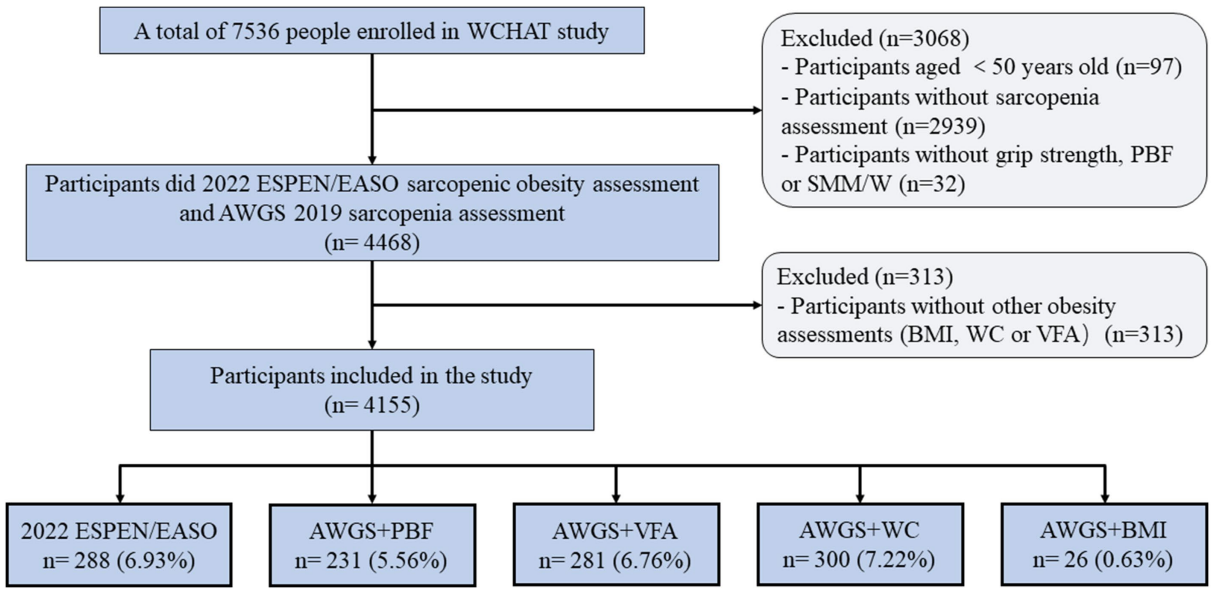

FIGURE 1
Study flow.

Measurements of sarcopenia

According to the Asian Working Group for Sarcopenia 2019 (AWGS2019) consensus criteria, sarcopenia was defined as low muscle mass in the presence of either low HS or slow gait speed (14). The Inbody 770 instrument (Biospace, Seoul, Korea) was used to assess the muscle mass. The cut-off values of appendicular skeletal muscle mass index (ASMI) were 7.0 kg/m^2 for males and 5.7 kg/m^2 for females. The HS was measured with a grip dynamometer (EH101; Camry, Zhongshan, China). The test was repeated twice and the highest value was recorded (15). Low muscle strength was defined as HS <28 kg in males and < 18 kg in females. The four-meter gait speed was tested using an infrared sensor (16). During the test, participants were required to walk at their usual pace. The acceleration and deceleration phases were excluded. The cut-off value of gait speed was 1.0 m/s (17).

Measurements of obesity

The indicators of obesity included PBF, VFA, WC, and BMI. PBF and VFA were measured using Bioelectric Impedance Analysis. WC was measured with a flexible, non-elastic tape at the midpoint between the ribs and ilium in the standing position. BMI was calculated by dividing weight by the square of height (CSTF-ST, Qinghuatongfang, China). The cutoff values of obesity indicators were as follows: (1) PBF ≥ 41% for females and PBF ≥ 29% for males; (2) VFA > 100 cm^2 (18); (3) WC ≥ 80 cm for females and WC ≥ 90 cm for males (19), and (4) BMI ≥ 28 kg/m^2 (20).

Definitions of SO

According to the 2022 ESPEN/EASO consensus, participants with decreased muscle strength (HS < 28 kg for males and < 18 kg for females), low muscle mass (SMM/W < = 37% for males, ≤ 27.6% for females), and high-fat mass (>29% for male, > 41% for female) were defined as SO (12). Further, SO was also diagnosed as a combination of the above four different diagnostic criteria of obesity and sarcopenia.

Laboratory examinations

Fasting blood samples were obtained from the antecubital vein after an overnight fast. Complete blood count, blood glucose, and lipid profile were tested. Inflammatory biomarkers were further calculated, including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII). SII was calculated using the following formula: SII = peripheral platelets* neutrophils/ lymphocyte counts (21).

Statistical analysis

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as numbers (percentages). Differences between groups were evaluated with the unpaired t-test and Mann–Whitney U test for continuous data with a normal and non-normal distribution, respectively. A comparison of categorical variables was conducted with chi-square tests. We also assessed the sex-stratified and age-stratified prevalence of SO. Binary logistic regression analysis was used to examine the association of age and sex with SO. A diagnostic agreement of SO between different diagnostic methods was evaluated using Cohen's kappa score. The interpretations of κ value were as follows: poor agreement = 0.00–0.20, fair agreement = 0.21–0.40, moderate agreement = 0.41–0.60, good agreement = 0.61–0.80, and very good agreement = 0.81–1.00 (22). Statistical analyses were performed using Stata v16.0 (Stata Corp, College Station, TX, USA) software programs. Two-sided *p*-values of <0.05 were considered statistically significant.

Results

Characteristics of participants

The characteristics of our participants are presented in Table 1. A total of 4,155 participants were included in our study, including 1,499 men (63.76 ± 8.23 years) and 2,656 women (61.61 ± 8.20 years). Indicators related to obesity, including BMI, PBF, and VFA, were all significantly higher in women than in men ($p < 0.05$). However, the indicators related to sarcopenia, including ASMI, HS, and gait speed, were all significantly higher in men than in women ($p < 0.05$). As compared to women, men had a higher WC and weight-adjusted SMM ($p < 0.05$).

Prevalence of SO

The prevalence of SO varied across different diagnostic methods, with rates of 6.93, 5.56, 6.76, 7.22, and 0.63% according to the 2022 ESPEN/EASO, AWGS+PBF, AWGS+VFA, AWGS+WC, and AWGS+BMI criteria, respectively (see Table 2). In particular, the prevalence of SO diagnosed by AWGS+BMI was much lower than with other diagnostic methods. Except for AWGS+BMI ($p = 0.159$), the prevalence of SO diagnosed by other methods was significantly different among four age groups ($p < 0.05$), and the prevalence increased with age. Stratified by sex, according to the 2022 ESPEN/EASO and AWGS+PBF, the prevalence of SO was significantly higher in men (14.81 and 10.41%) than in women (2.48 and 2.82%). However, when using AWGS+VFA and AWGS+WC as diagnostic criteria, the prevalence of SO in males was 4.94 and 3.80%, and in females was 7.79 and 9.15%, respectively. In the case of AWGS+BMI, the detection rate of SO in men (0.93%) was similar to that in women (0.45%).

The correlations between SO and age/sex are shown in Supplementary Table S1. Participants were divided into 4 groups based on age: 50–59, 60–69, 70–79, and ≥ 80 years. Compared with the youngest age group, the odds ratio (OR) for SO diagnosed by 2022 ESPEN/EASO was 2.35 (95%CI: 1.67–3.32), 5.05 (95%CI: 3.46–7.36), and 10.04 (95%CI: 5.57–18.12) for 60–69, 70–79, and ≥ 80 years groups, respectively. Similar correlations between age groups and SO diagnosed by AWGS+PBF, AWGS+VFA, and AWGS+WC were detected. Female was negatively associated with SO when diagnosed by 2022 ESPEN/EASO (OR = 0.17, 95%CI: 0.12–0.22) and AWGS+PBF (OR = 0.28, 95%CI: 0.21–0.38). In contrast, a positive association between females and SO was detected according to AWGS+VFA (OR = 1.92, 95%CI: 1.45–2.53) and AWGS+WC (OR = 3.06, 95%CI: 2.26–4.14).

TABLE 1 Baseline characteristics of study participants ($N = 4,155$).

Characteristics	Total	Men	Women	*p* value
	$N = 4,155$	$N = 1,499$	$N = 2,656$	
Age (years)	62.38 (8.27)	63.76 (8.23)	61.61 (8.20)	<0.001
Ethnicities (%)				<0.001
Han	1815 (43.70)	590 (39.39)	1,225 (46.14)	
Zang	1,063 (25.60)	456 (30.44)	607 (22.86)	
Qiang	1,012 (24.37)	356 (23.77)	656 (24.71)	
Yi	201 (4.84)	72 (4.81)	129 (4.86)	
Others	62 (1.49)	24 (1.60)	38 (1.43)	
BMI (kg/m^2)	25.28 (3.79)	25.04 (3.66)	25.42 (3.86)	0.011
ASMI (kg/m^2)	6.62 (0.94)	7.36 (0.79)	6.21 (0.73)	<0.001
SMM/W (%)	35.71 (4.61)	39.24 (3.93)	33.72 (3.68)	<0.001
Grip strength (kg)	22.07 (8.67)	28.56 (9.36)	18.41 (5.57)	<0.001
Gait speed (m/s)	0.85 (0.27)	0.87 (0.27)	0.84 (0.27)	<0.001
WC (cm)	87.23 (10.84)	88.35 (10.91)	86.60 (10.75)	<0.001
PBF (%)	33.76 (7.69)	28.37 (6.80)	36.81 (6.37)	<0.001
VFA (cm^2)	107.06 (41.15)	91.55 (36.96)	115.82 (40.81)	<0.001

Data are mean ± SD or numbers (percentages) indicated.
BMI, body mass index; ASMI, appendicular skeletal muscle mass index; SMM/W, total skeletal muscle mass adjusted by weight; WC, waist circumference; PBF, percent of body fat; VFA, visceral fat area.

TABLE 2 Prevalence of SO with different diagnostic methods.

Diagnosis methods	Total	50–59 years	60–69 years	70–79 years	≥80 years	*p* value
	$N = 4,155$	$N = 1,643$	$N = 1,668$	$N = 716$	$N = 128$	
Total						
2022 ESPEN/EASO	288 (6.93)	55 (3.35)	119 (7.13)	93 (12.99)	21 (16.41)	<0.001
AWGS+PBF	231 (5.56)	48 (2.92)	87 (5.22)	70 (9.78)	26 (20.31)	<0.001
AWGS+VFA	281 (6.76)	79 (4.81)	103 (6.18)	71 (9.92)	28 (21.88)	<0.001
AWGS+WC	300 (7.22)	74 (4.50)	105 (6.29)	87 (12.15)	34 (26.56)	<0.001
AWGS+BMI	26 (0.63)	11 (0.67)	6 (0.36)	7 (0.98)	2 (1.56)	0.159
Men						
2022 ESPEN/EASO	222 (14.81)	36 (7.58)	93 (14.46)	78 (23.42)	15 (31.25)	<0.001
AWGS+PBF	156 (10.41)	26 (5.47)	65 (10.11)	51 (15.32)	14 (29.17)	<0.001
AWGS+VFA	74 (4.94)	15 (3.16)	34 (5.29)	20 (6.01)	5 (10.42)	0.064
AWGS+WC	57 (3.80)	13 (2.74)	21 (3.27)	14 (4.20)	9 (18.75)	<0.001
AWGS+BMI	14 (0.93)	7 (1.47)	4 (0.62)	2 (0.60)	1 (2.08)	0.354
Women						
2022 ESPEN/EASO	66 (2.48)	19 (1.63)	26 (2.54)	15 (3.92)	6 (7.50)	0.002
AWGS+PBF	75 (2.82)	22 (1.88)	22 (2.15)	19 (4.96)	12 (15.00)	<0.001
AWGS+VFA	207 (7.79)	64 (5.48)	69 (6.73)	51 (13.32)	23 (28.75)	<0.001
AWGS+WC	243 (9.15)	61 (5.22)	84 (8.20)	73 (19.06)	25 (31.25)	<0.001
AWGS+BMI	12 (0.45)	4 (0.34)	2 (0.20)	5 (1.31)	1 (1.25)	0.027

Agreement between different SO diagnostic methods

The agreement between different diagnostic methods is shown in Table 3. The agreement between different diagnostic methods for SO varied, with poor agreement observed between 2022 ESPEN/EASO and AWGS+VFA ($\kappa = 0.16$), AWGS+WC ($\kappa = 0.06$), and AWGS+BMI ($\kappa = 0.09$), while fair agreement was found between 2022 ESPEN/EASO and AWGS+PBF ($\kappa = 0.32$). Among the other four diagnostic methods, AWGS+VFA and AWGS+WC showed good agreement

TABLE 3 Agreement between different diagnostic methods of SO.

SO definition		Men		Women		Total	
		Cohen's kappa	Magnitude	Cohen's kappa	Magnitude	Cohen's kappa	Magnitude
2022 ESPEN/EASO	AWGS+PBF	0.35	Fair	0.18	Poor	0.32	Fair
2022 ESPEN/EASO	AWGS+VFA	0.28	Fair	0.07	Poor	0.16	Poor
2022 ESPEN/EASO	AWGS+WC	0.11	Poor	0.05	Poor	0.06	Poor
2022 ESPEN/EASO	AWGS+BMI	0.04	Poor	0.20	Poor	0.09	Poor
AWGS+PBF	AWGS+VFA	0.62	Good	0.51	Moderate	0.55	Moderate
AWGS+PBF	AWGS+WC	0.39	Fair	0.38	Fair	0.37	Fair
AWGS+PBF	AWGS+BMI	0.14	Poor	0.22	Fair	0.17	Poor
AWGS+VFA	AWGS+WC	0.53	Moderate	0.71	Good	0.67	Good
AWGS+VFA	AWGS+BMI	0.26	Fair	0.08	Poor	0.13	Poor
AWGS+WC	AWGS+BMI	0.27	Fair	0.09	Poor	0.12	Poor

($\kappa = 0.67$). Meanwhile, AWGS+VFA was moderately consistent with AWGS+VFA ($\kappa = 0.55$). Stratified by sex, there was good agreement between AWGS+VFA and AWGS+PBF in males ($\kappa = 0.62$) and between AWGS+VFA and AWGS+WC in females ($\kappa = 0.71$).

Metabolic and inflammatory profiles of SO diagnosed by different methods

The fasting plasma insulin was significantly higher in the SO group diagnosed by the 2022 ESPEN/EASO (10.41 ± 14.69) as compared to the non-SO group (8.26 ± 8.88) (Table 4). Fasting glucose was significantly higher in SO groups diagnosed by the 2022 ESPEN/EASO and AWGS+BMI ($p < 0.05$ in both). Triglyceride and cholesterol were significantly higher in SO groups diagnosed by AWGS+VFA and AWGS+WC ($p < 0.05$ in both). High-density lipoprotein (HDL) in SO groups diagnosed by ESPEN/EASO and AWGS+BMI was significantly lower than that in control groups (both $p < 0.05$). Meanwhile, except for the SO group diagnosed by AWGS+BMI, the low-density lipoprotein (LDL) of all SO groups was significantly increased (all $p < 0.05$).

Indicators related to inflammation, including neutrophils ratio (GPR) and NLR were significantly higher in SO groups diagnosed by the 2022 ESPEN/EASO and AWGS+PBF (both $p < 0.05$). White blood cells (WBC) were significantly higher in SO groups diagnosed by the 2022 ESPEN/EASO, AWGS+PBF, and AWGS+WC (all $p < 0.05$). The lymphocyte ratio was significantly lower in SO groups diagnosed by the 2022 ESPEN/EASO and AWGS+PBF ($p < 0.05$ in both). Furthermore, SII was significantly higher in SO groups diagnosed by the 2022 ESPEN/EASO, AWGS+PBF, and AWGS+VFA (all $p < 0.05$).

Discussion

Using five different diagnostic methods, we compared the prevalence of SO among a multiethnic community-dwelling population of individuals over 50 years old living in western China. Our study revealed that AWGS+VFA had a relatively good diagnostic agreement, while the consensus of ESPEN/EASO had a poor diagnostic agreement with other diagnostic methods. Considering that the traditional diagnosis is the combination of sarcopenia and obesity, it is not surprising that the consistency between ESPEN/EASO and the other four traditional proposals using AWGS 2019 is not high. However, the traditional diagnostic criteria have been questioned, as growing evidence shows that SO is not only a combination of the two conditions but also a specific condition on its own (23). The unique metabolic and inflammatory profiles of patients with SO diagnosed by ESPEN/EASO further emphasized this issue.

Although BMI has been widely used to define SO, our findings indicated that BMI is considerably less sensitive than the other four identified criteria. This finding was in accordance with previous studies (11, 24). This suggests that BMI may not be suitable as an indicator of obesity according to the definition of SO in older Asian adults. According to previous studies, BMI cannot account for age-related changes in body fat composition, loss of lean body mass, or variations in body fat distribution (4). This is important because compared with peripheral fat deposition, central obesity could lead to increased mortality (25).

Our results on the prevalence of SO were consistent with those of previous studies. A previous study reported that the prevalence of SO among community-dwelling older adults in China varied greatly (0.1–7.9%) when different obesity diagnostic methods were combined with the AWGS 2019 criteria (11). Similarly, two other studies reported that the prevalence of SO ranged from 0.5 to 10.5% when using the AWGS 2014 criteria in combination with different obesity diagnostic methods (24, 26). Interestingly, in our study, we found that WC-defined obesity had the highest prevalence of SO, which was 7.22%. It is possible that most of the multiethnic population in western China, especially the Zang ethnic group, has central obesity resulting from their dietary habits. BMI-defined obesity was associated with the lowest prevalence of SO (0.63%). This might be because the cutoff value for obesity of 28 kg/m^2 was slightly high for older people diagnosed with sarcopenia. Furthermore, the proportion of body fat increases and decreases in muscle mass with age. However, these changes are not well reflected in height, weight, or BMI (27). Furthermore, when SO was diagnosed using AWGS+VFA and AWGS+PBF, the prevalence of SO was similar (6.76 and 5.56%, respectively), and the agreement between those measurements was

TABLE 4 Metabolism and inflammation characteristics of study participants (N = 4,155).

Characteristics	2022 ESPEN/EASO			AWGS + PBF			AWGS + VFA			AWGS + WC			AWGS + BMI		
	C	SO	*p* value	C	SO	*p* value	C	SO	*p* value	C	SO	*p* value	C	SO	*p* value
Insulin 0 (uU/mL)	8.26 (8.88)	10.41 (14.69)	<0.001	8.43 (9.57)	8.02 (6.29)	0.447	8.43 (9.63)	8.17 (5.72)	0.512	8.44 (9.66)	7.97 (5.20)	0.797	8.40 (9.44)	9.42 (5.40)	0.137
Fasting glucose (mmol/L)	5.56 (1.73)	5.87 (2.17)	0.025	5.56 (1.72)	5.89 (2.37)	0.199	5.57 (1.74)	5.64 (2.07)	0.403	5.57 (1.73)	5.73 (2.18)	0.823	5.57 (1.76)	6.59 (2.69)	0.010
Triglyceride (mmol/L)	1.86 (1.79)	1.68 (1.10)	0.635	1.85 (1.75)	1.85 (1.82)	0.498	1.85 (1.75)	1.91 (1.72)	0.010	1.84 (1.73)	2.01 (2.04)	0.004	1.85 (1.75)	1.79 (1.05)	0.727
Cholesterol (mmol/L)	4.78 (0.92)	4.80 (0.99)	0.579	4.77 (0.91)	4.90 (1.11)	0.139	4.76 (0.91)	5.07 (1.06)	<0.001	4.76 (0.91)	5.00 (1.05)	<0.001	4.78 (0.93)	4.80 (0.79)	0.786
HDL (mmol/L)	1.28 (0.31)	1.17 (0.25)	<0.001	1.27 (0.31)	1.24 (0.28)	0.115	1.27 (0.31)	1.29 (0.29)	0.158	1.27 (0.31)	1.28 (0.29)	0.375	1.27 (0.31)	1.15 (0.25)	0.041
LDL (mmol/L)	2.65 (0.87)	2.87 (0.85)	<0.001	2.66 (0.87)	2.82 (0.85)	0.024	2.65 (0.87)	2.91 (0.85)	<0.001	2.66 (0.87)	2.80 (0.92)	0.007	2.67 (0.87)	2.84 (0.76)	0.413
WBC (10^9/L)	5.83 (1.65)	6.24 (1.86)	<0.001	5.83 (1.64)	6.32 (1.96)	<0.001	5.85 (1.67)	5.91 (1.57)	0.303	5.84 (1.67)	6.04 (1.66)	0.023	5.86 (1.67)	5.70 (1.24)	0.920
GPR (%)	61.07 (8.60)	62.47 (8.94)	0.006	61.08 (8.63)	62.66 (8.62)	0.023	61.16 (8.63)	61.39 (8.65)	0.700	61.12 (8.58)	61.82 (9.31)	0.325	61.19 (8.63)	58.42 (8.09)	0.079
LPR (%)	31.58 (7.94)	30.10 (8.03)	0.004	31.55 (7.94)	30.10 (7.98)	0.023	31.48 (7.94)	31.42 (8.08)	0.902	31.50 (7.90)	31.10 (8.61)	0.545	31.46 (7.95)	33.89 (8.32)	0.080
NLR	2.20 (1.08)	2.45 (1.62)	0.006	2.21 (1.09)	2.46 (1.64)	0.025	2.22 (1.14)	2.22 (0.98)	0.763	2.21 (1.11)	2.34 (1.35)	0.424	2.22 (1.13)	1.93 (0.87)	0.083
PLR	103.07 (42.47)	107.05 (49.17)	0.554	103.29 (42.77)	104.36 (46.45)	0.922	103.03 (42.68)	107.79 (46.86)	0.116	103.15 (42.60)	105.87 (47.64)	0.653	103.34 (42.91)	104.58 (53.71)	0.608
SII	371.58 (228.10)	428.01 (315.16)	<0.001	372.56 (229.37)	425.73 (320.28)	0.007	374.24 (236.97)	393.31 (215.85)	0.045	373.10 (232.15)	406.90 (275.19)	0.105	375.73 (235.95)	343.32 (178.59)	0.612

Data are indicated as mean (standard deviation).

Insulin 0, fasting plasma insulin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; WBC, white blood cells; GPR, neutrophils ratio; LPR, lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index.

10.3389/fpubh.2024.1356878

moderate ($\kappa = 0.55$). These findings were consistent with those of previous studies (11, 24).

For gender differences, we found a large variation in the prevalence of SO between males and females. This might be related to hormonal changes. Gender-specific alterations in body composition are partly attributable to age-related changes in sex hormone levels. In women, menopause causes weight gain, which is characterized by an increase in fat mass, mostly located in the visceral area (28). This redistribution of fat leads to an increase in WC and a concomitant loss of muscle mass (29). In men, testosterone plays a crucial role in promoting muscle regeneration by activating satellite cells (30). In addition, testosterone enhances muscle protein synthesis and increases androgen receptor expression (31). Decreasing testosterone levels during aging may negatively affect muscle mass and fat distribution in older adults (32). Interestingly, in our study, we found that there was a negative association between females and SO when the 2022 ESPEN/EASO and AWGS+PBF diagnostic criteria were used. However, females were positively associated with SO when the AWGS+VFA and AWGS+WC diagnostic criteria were used, which was consistent with the findings of previous studies (11). Longitudinal studies are needed to confirm the relationship between sex and SO. Furthermore, given the large differences in the prevalence of SO between sexes when diagnosed using the 2022 ESPEN/EASO criteria, further studies are needed to identify the optimal cutoff points for diagnosing SO to be considered in research and clinical practice.

In addition, it seems that old age was a confirmed risk factor for developing SO according to all five diagnostic methods. With age, many factors are related to changes in body composition. Etiological factors including reduced physical activity, decreased mitochondrial volume, and diminished oxidative capacity, could lead to a decrease in the resting metabolic rate (33). Furthermore, reductions in the resting metabolic rate, the thermic effect of food, and participation in physical activity result in a reduction in total energy expenditure, which may lead to a progressive increase in body fat (34). Body fat has been reported to increase until the age of 70 years (35), while muscle mass decreases after 40 years of age, resulting in weight gain in older adults being primarily in the form of fat rather than lean mass (36). In addition, vertebral compression can lead to height loss, thereby affecting BMI (37). In other words, various factors could underlie the association between aging and SO.

It is well known that both muscle and adipose tissue play important roles in metabolic regulation. Previous studies have reported that SO is associated with metabolic syndrome (38–40), and an increased risk of developing metabolic syndrome may manifest decades before the development of SO (41). In our study, we observed that participants with SO were more likely to have metabolic dysfunction, characterized by increased fasting plasma insulin, fasting glucose, triglyceride, cholesterol, and LDL levels, and decreased HDL levels, which was consistent with previous evidence (40, 41). Insulin resistance serves as the central mechanism underlying the development of SO (42). As the largest insulin-sensitive tissue, skeletal muscle plays a crucial role in modulating insulin resistance. Thus, loss of muscle mass exacerbates insulin resistance. Furthermore, the accumulation of fat within muscle tissue triggers a proinflammatory cascade and oxidative stress, leading to mitochondrial dysfunction, impaired insulin sensitivity, and muscle atrophy (42). Therefore, emerging evidence suggests a link between SO and a hyperinflammatory state (43). Our study also revealed that patients diagnosed with SO using the 2022 ESPEN/EASO and AWGS+PBF criteria were more likely to exhibit dysfunctional inflammatory profiles, characterized by elevated WBC counts, GPR, NLR, and SII. Considering the diagnostic agreement and similar metabolic and inflammatory profiles between AWGS+PBF and 2022 ESPEN/EASO, AWGS+PBF may be suitable for the alternative diagnosis of 2022 ESPEN/EASO.

Several limitations should be noted when interpreting our results. First, our study design was cross-sectional, which limits our ability to establish causality. Second, our results included only people from western China, so the generalizability of our findings to other Asian populations may be limited. Third, the proportion of very old adults in our study was relatively small, and the majority of participants were in good health. Furthermore, we excluded 3,381 individuals from the 7,536 participants due to a lack of important diagnostic data. These may introduce some bias into the analysis and should be taken into consideration when interpreting the results. Future research should include non-Chinese populations and encompass more diverse and heterogeneous groups of older adults. Additionally, longitudinal studies that examine the trajectory of SO are necessary.

Conclusion

There is considerable variation in the prevalence of SO across definitions, with agreement between them ranging from low to good. Our results indicated that AWGS+WC has the highest diagnostic rate in diagnosing SO, while AWGS+BMI has the lowest. AWGS+VFA has a relatively good diagnostic agreement with other diagnostic methods, while the consensus of ESPEN/EASO has poor diagnostic consistency. Individuals with SO diagnosed by the 2022 ESPEN/EASO method were more likely to exhibit dysfunctional metabolic and inflammatory profiles. Sex-specific cutoffs of ESPEN/EASO should be further explored to enable accurate and early characterization of SO in older Asian populations.

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 authors.

Ethics statement

The studies involving humans were approved by the Ethics Committee of West China Hospital, Sichuan University. 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

FH: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Supervision, Visualization, Writing – original draft, Writing – review & editing. GZ: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Supervision, Visualization, Writing – original

draft, Writing – review & editing. ZX: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. ZZ: Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Writing – review & editing. NH: Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Writing – review & editing. MG: Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Writing – review & editing. XL: Conceptualization, Formal analysis, Funding acquisition, Methodology, Project administration, Resources, Supervision, Visualization, Writing – review & editing. BD: Conceptualization, Formal analysis, Funding acquisition, Methodology, Project administration, Resources, Supervision, Visualization, Writing – review & editing.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. This study was supported by the National Natural Science Foundation of China (No. 92248304, No. 82101653), the 1.3.5 project for disciplines of excellence, West China Hospital, Sichuan University (ZYGD20010), the China Postdoctoral Science Foundation (2021M692297, 2023M732473), and the National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University (Z2023YY003, Z2021JC003). The sponsors had no roles in the design of the study and collection, analysis, and interpretation of data or in writing the manuscript.

Acknowledgments

We thank all the volunteers for their participation and the personnel for their contribution to the WCHAT 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

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1356878/full#supplementary-material

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frontiers | Frontiers in Public Health

TYPE Systematic Review
PUBLISHED 08 July 2024
DOI 10.3389/fpubh.2024.1378462

OPEN ACCESS

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RECEIVED 29 January 2024
ACCEPTED 17 June 2024
PUBLISHED 08 July 2024

CITATION
Yang T-R, Ji P, Deng X, Feng X-X, He M-L, Wang R-R and Li X-H (2024) Ct-based diagnosis of sarcopenia as a prognostic factor for postoperative mortality after elective open-heart surgery in older patients: a cohort-based systematic review and meta-analysis.
Front. Public Health 12:1378462.
doi: 10.3389/fpubh.2024.1378462

Ct-based diagnosis of sarcopenia as a prognostic factor for postoperative mortality after elective open-heart surgery in older patients: a cohort-based systematic review and meta-analysis

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Background: Cardiac open-heart surgery, which usually involves thoracotomy and cardiopulmonary bypass, is associated with a high incidence of postoperative mortality and adverse events. In recent years, sarcopenia, as a common condition in older patients, has been associated with an increased incidence of adverse prognosis.

Methods: We conducted a search of databases including PubMed, Embase, and Cochrane, with the search date up to January 1, 2024, to identify all studies related to elective cardiac open-heart surgery in older patients. We used the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach to assess the certainty of evidence.

Results: A total of 12 cohort studies were included in this meta-analysis for analysis. This meta-analysis revealed that patients with sarcopenia had a higher risk of postoperative mortality. Furthermore, the total length of hospital stay and ICU stay were longer after surgery. Moreover, there was a higher number of patients requiring further healthcare after discharge. Regarding postoperative complications, sarcopenia patients had an increased risk of developing renal failure and stroke.

Conclusion: Sarcopenia served as a tool to identify high-risk older patients undergoing elective cardiac open-heart surgery. By identifying this risk factor early on, healthcare professionals took targeted steps to improve perioperative function and made informed clinical decisions.

Systematic review registration: https://www.crd.york.ac.uk/prospero/, identifier CRD42023426026.

KEYWORDS
sarcopenia, cardiac surgery, prognosis, skeletal muscle index, older patients

1 Introduction

With the global aging population, the increasing number of comorbidities and heterogeneity in patient activity have made clinical decision-making more challenging. Over the past few decades, there was a notable rise in the level of complexity among patients undergoing cardiac open-heart surgery, corresponding with an increase in surgical risk, which warranted careful consideration and attention from healthcare providers (1, 2). The medical procedure known as open-heart surgery frequently necessitates the use of cardiopulmonary bypass, which carries a heightened risk of acute or sustained organ injury resulting from systemic inflammatory response compared to other surgical approaches (3, 4). Thus, enhancing postoperative prognosis continues to be a major concern for cardiac surgeons. However, current cardiac surgical risk scores focus primarily on the presence of specific medical comorbidities in patients and do not take into account age-related factors, particularly muscle loss (5–7). In reality, the decline in muscle or muscle mass has a significant impact on the mortality rate of older cardiovascular patients and contributes to adverse events during the perioperative period (8).

Sarcopenia is a comorbidity characterized by a progressive decline in skeletal muscle mass and strength with advancing age, commonly referred to as physical weakness. This symptom is also highly prevalent among older patients, particularly associated with adverse consequences following cardiac surgery, and results in exacerbated functional decline and elevated mortality rates (9). Despite sarcopenia's severity, no single diagnostic criteria have been established, and most use a combination of muscle mass, muscle strength, and gait speed measurements. The most commonly used definitions are: the European Working Group on Sarcopenia in Older People [EWGSOP (2010)] (10), the revised EWGSOP2 (2019) (11), the Asian Working Group for Sarcopenia (AWGS) (12), as well as definitions using muscle mass only as a single criterion (e.g., Newman and Baumgartner definitions) (13, 14). For clinical purposes, frequently used computed tomography (CT) is an objective and quantitative diagnostic technique, which is considered as the gold standard for non-invasive assessment of muscle quantity/quality, and can quickly and easily identify sarcopenia. Some studies also believe that low muscle mass assessed by CT scan alone can diagnose sarcopenia (15–18). In patients with heart failure, skeletal muscle mass reduction can lead to reduced exercise capacity and weakness, ultimately undermining their quality of life and rehabilitation process (19). Hence, timely identification and intervention of muscle depletion are pivotal for enhancing patients' health condition and prognosis (20).

Sarcopenia has been widely studied in relation to surgical complications across different types of surgeries. Previous studies have shown that sarcopenia is associated with various adverse outcomes in patients undergoing lung transplantation, pancreaticoduodenectomy, colorectal surgery, and liver transplantation, including prolonged mechanical ventilation, increased risk of infection, and extended hospital stay (21–25). However, there is currently no consensus on the impact of sarcopenia on mortality rate and overall condition in patients after open-heart surgery.

Although previous literature has studied the association between cardiac surgery and sarcopenia, these studies often involved different surgical approaches, including transcatheter aortic valve implantation (TAVI) or emergency surgery, which may lead to biased and inconclusive research results (26). Furthermore, there is a dearth of literature reporting the impact of sarcopenia on older patients undergoing elective cardiac open-heart surgery. Therefore, we conducted further analysis to assess the impact of sarcopenia on postoperative in-hospital mortality, and postoperative complications in older patients undergoing elective cardiac open-heart surgery.

2 Methods

The systematic review and meta-analysis in this study were conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, and were registered on Prospero (registration number: CRD42023426026) (27). The whole research is quantitative analysis. Two researchers independently searched databases including PubMed, Embase, and Cochrane, with the search deadline being January 1, 2024. Furthermore, we conducted a search of the World Health Organization International Clinical Trials Registry and reviewed the bibliographies of relevant articles and reviews to identify any additional studies that potentially met the inclusion criteria, which we defined as other databases. The search was not restricted by language or region, and we have provided a PRISMA checklist. The search strategy was shown in Supplementary material 1. The review question of this manuscript was to discuss whether sarcopenia based on CT diagnosis was a prognostic factor for mortality in older patients after elective open-heart surgery.

2.1 Study selection

This meta-analysis aimed to include studies comparing older patients with and without sarcopenia after elective cardiac open-heart surgery. The types of studies included in the systematic review were prospective or retrospective cohort studies. Inclusion and exclusion criteria were determined prior to the start of the study. Included studies followed the PICOTS criteria: (1) population: patients with mean or median age > 60 years who underwent elective open heart surgery; (2) intervention: patients with sarcopenia were diagnosed by preoperative CT scan; (3) comparator: patients were diagnosed with non-sarcopenia before operation; (4) outcomes: the study reported the occurrence of postoperative adverse events (such as in-hospital mortality and ICU admission); (5) Timing: the time after surgery; (6) setting: Include inpatients. Our exclusion criteria were: (1) The patient underwent emergency surgery; (2) The patient had the presence of a heart implant; (3) The diagnosis of sarcopenia was unclear; (4) article

types included case reports, reviews, expert opinions, or conference abstracts.

The two researchers imported the search results into citation management software (Endnote X9) and independently reviewed the titles and abstracts, selected studies that met the criteria for full-text reading, and had no knowledge of each other's results. Any discrepancies between the researchers were resolved by a third researcher.

2.2 Data extraction

Two researchers independently extracted data in Endnote from eligible studies based on the Checklist for critical Appraisal and data extraction for systematic Reviews of prediction Modeling Studies (CHARMS) (28) and collected the following information: first author's name, publication year, source of data, source of population, the characteristics of the included population, surgery type, measurement method of sarcopenia, sample size, postoperative outcome. Any discrepancies were resolved through discussion, and if necessary, another researcher was consulted.

We synthesized the data by directly extracting it from the original text. If the data was presented in the form of charts and could not be directly extracted, we used plot digitizers or contacted the corresponding author. If needed, we employed formulas provided by Hozo and other sources to convert the median and interquartile range into the mean and standard deviation (29, 30).

2.3 Quality assessment and risk of bias

Two researchers independently assessed the risk of bias, and disagreements were resolved through consultation with another researcher. We used the Newcastle-Ottawa Scale (NOS) to assess the quality and bias risk of cohort studies, which was a tool for critical evaluation of eligible cohort studies, mainly evaluating the quality and potential risk of bias from three aspects: selection of study population, comparability between groups, and measurement of outcomes. A score of ≥6 indicated high study quality and possible low risk of bias (31).

We utilized the GRADE approach to assess the quality of evidence for in-hospital mortality rate, complication rate, ICU length of stay, total length of hospitalization, and the number of patients requiring admission to healthcare facility after discharge. Considering factors such as risk of bias, inconsistency, imprecision, and intermittency, the evidence was categorized into high, moderate, low, and very low. We employed the GRADEpro GDT to generate the Summary of Finding (SoF) (32).

2.4 Outcome

The primary outcome was the in-hospital mortality of older patients after elective cardiac open-heart surgery, while the secondary outcomes included total length of hospital stay and ICU stay, the number of patients requiring admission to healthcare facility after discharge (for all causes), and outcome measures related to complications (such as the number of patients requiring continuous renal replacement therapy (CRRT), the incidence of atrial fibrillation, the incidence of pneumonia, the incidence of wound infection, the incidence of stroke, and the incidence of prolonged ventilation).

2.5 Data analysis

We conducted a meta-analysis using RevMan 5.3 and displayed the effect sizes of the studies using forest plots. Continuous variables were analyzed using mean differences (MD) and 95% confidence intervals, while binary variables were statistically analyzed using odds ratios. Given the heterogeneity in surgical types, surgical techniques, and operator experience, a random-effects model was employed for all the results in this study. I^2 was used in this meta-analysis to quantifies the proportion of the variation in point estimates due to between-study differences (33). If $I^2 \geq 50\%$, significant heterogeneity among studies was considered, and leave-one-out sensitivity analysis was conducted to identify potential sources of heterogeneity. Publication bias was analyzed and represented by a funnel plot, and funnel plot symmetry was assessed with Begg's test. It was considered that there was no publication bias among the included studies when the *p*-value was >0.05 (34).

3 Results

The flowchart in Figure 1 presents the process of study selection. A total of 799 studies were identified through systematic retrieval from the initial database. A total of 124 studies were excluded after removing duplicates, and after evaluating the titles and abstracts, 612 studies were excluded subsequently due to irrelevant content. Out of the remaining 63 studies, 4 articles were inaccessible in full text, leaving 59 studies for full-text reading. Following full-text screening, 47 studies were excluded due to unclear diagnosis, emergency surgery, or incompatible study types. Ultimately, a total of 12 articles were included in this study for further analysis. We conducted a quantitative analysis of the original research data reported in the 12 included studies.

Table 1 summarizes the main characteristics and details of the 12 articles that met the inclusion criteria (35–46). The total number of included patients was 4,749, with sample sizes ranging from 140 to 874, all of which were cohort studies. The majority of studies included both CABG and valve surgeries, with one study focusing on elective aortic arch replacement (38). Four studies included only valve surgeries (35, 40, 43, 44), while two studies only included patients undergoing CABG surgery (39, 46). In addition, various measurement methods for sarcopenia have been applied in different studies. A significant proportion of studies used the standardized total skeletal muscle mass normalized by the square of the height measured through CT images as the criterion for evaluating sarcopenia, known as skeletal muscle index (SMI). Moreover, certain studies employed the measurement of psoas muscle area (PMA) or psoas muscle index (PMI) to assess sarcopenia. Furthermore, one study measured grip strength and gait speed (36) while using SMI as a diagnostic criterion.

3.1 Risk of bias

All the studies included in this meta-analysis were cohort studies, and the quality assessment and bias risk were conducted according to NOS. Table 2 shows the bias risk of the 12 included studies, all of which were high-quality studies (NOS score ≥ 6), suggesting a low risk of bias in the included studies.

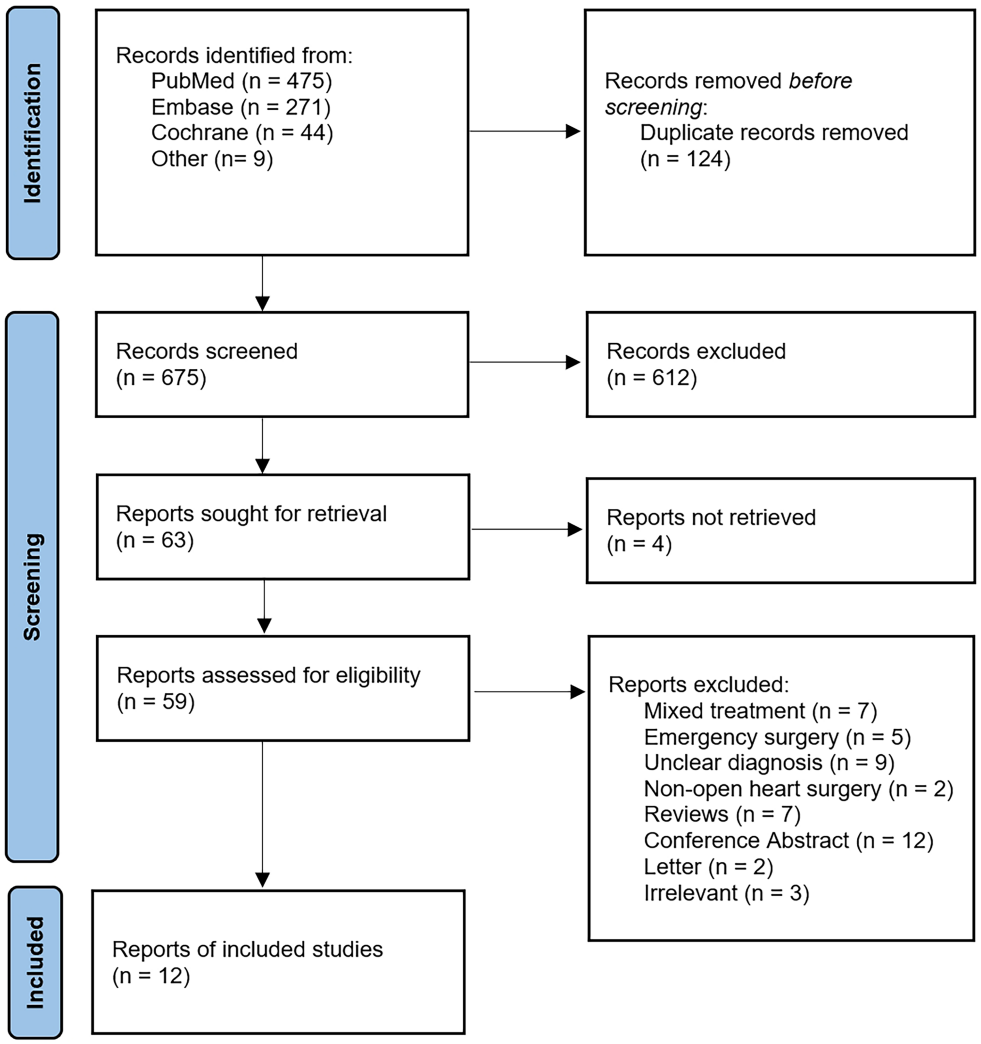

FIGURE 1
Flow chart showing selection of articles for review.

3.2 Quality of evidence

The SOF table in Figure 2 displays the quality of evidence and relevant details for each outcome measure. Based on the GRADE approach, we found that the evidence quality for the in-hospital mortality rate, and total length of hospital stay was moderate. The evidence quality for the occurrence rate of postoperative CRRT requirement, stroke occurrence, and post-discharge healthcare facility utilization rate was relatively low. Nevertheless, the evidence quality for the occurrence rate of postoperative pneumonia was exceptionally low.

3.3 Primary outcome

3.3.1 The relationship between sarcopenia and in-hospital mortality

We conducted a quantitative analysis of eight included articles that reported in-hospital mortality, and eight articles (26–30, 34–36) reported a total of 2,090 patients with in-hospital mortality after open heart surgery. Compared with patients without sarcopenia, patients with sarcopenia had a higher risk of postoperative hospital death (Figure 3; OR: 3.10 95% CI:1.80–5.34, $p < 0.0001$). There was no heterogeneity among the included literature types ($I^2 = 0\%$, $p = 0.83$). In addition, we performed a publication bias analysis for primary outcomes, and funnel plots can be seen in Supplementary material 2. The Begg's test was used for publication bias. A symmetrical appearance was checked in the funnel plot. The p-value of the Begg's test for the primary outcome was $0.083 > 0.05$, and no significant publication bias was found.

3.3.2 Subgroup analysis of in-hospital mortality

In order to investigate the sarcopenia in depth, we conducted subgroup analysis based on different clinical characteristics included in the articles. Table 3 presents the subgroup analysis data. When conducting subgroup analysis according to the measurement methods of sarcopenia, some studies evaluated sarcopenia at vertebral level by CT scan SMI (OR: 3.98, 95% CI: 1.77–8.94) (36, 40, 46), while five studies diagnosed sarcopenia using non-SMI measurement methods (OR: 2.53, 95% CI: 1.22–5.26) (37–39, 44, 45). After analyzing the subgroup analysis based on surgical types, we confirmed that patients with sarcopenia were associated with higher in-hospital mortality regardless of including multiple surgical

TABLE 1 Characteristics of included studies.

Author, year	Source of data	Source of population	Diagnose	Age	BMI	Surgery type	Muscle assessment method	CT measurement method	Total Sample	Sample	Postoperative outcome
Masashi 2017	Cohort study	Japan	Sarcopenia	65.5 ± 13.2	21.1 ± 3.5	CABG and Valve surgery	CT, gait speed, grip strength, 6MWD	SMI	*n* = 773	*n* = 386	Postoperative all-cause mortality
			No-sarcopenia	64.4 ± 13.1	23.4 ± 3.5					*n* = 387	
Ikeno 2017	Cohort study	Japan	Sarcopenia	76.2 ± 5.6	22.5 ± 3.1	Total arch replacement	CT, gait speed, grip strength	PMI	*n* = 266	*n* = 81	In-hospital mortality, Discharged to healthcare facility, Length of hospital stay, CRRT require, Atrial fibrillation, Pneumonia, Stroke, Prolonged ventilation
			No-sarcopenia	75.7 ± 5.7	23.8 ± 2.9					*n* = 185	
Okamura 2018	Cohort study	Japan	Sarcopenia	77.0 ± 4.6	19.6 ± 2.8	CABG and Valve surgery	CT	PMA	*n* = 428	*n* = 107	In-hospital mortality, Discharged to healthcare facility, Length of ICU stay, CRRT require, Atrial fibrillation, Stroke, Prolonged ventilation
			No-sarcopenia	76.0 ± 4.3	22.6 ± 3.5					*n* = 321	
Robert 2019	Cohort study	America	Sarcopenia	81 (8)	NA	Valve surgery	CT	PMI	*n* = 240	*n* = 60	Discharged to healthcare facility, Length of hospital stay, Length of ICU stay, CRRT require, Atrial fibrillation, Pneumonia, Wound infection, Stroke, Prolonged ventilation
			No-sarcopenia	80 (10)	NA					*n* = 180	
Yamashita 2019	Cohort study	Japan	Sarcopenia	70 ± 9.6	22.6 ± 4.0	CABG and Valve surgery or Aortic surgery	CT, gait speed, grip strength m, 6MWD	PMA	*n* = 664	*n* = 332	Postoperative all-cause mortality
			No-sarcopenia	61.5 ± 14.0	22.1 ± 3.4					*n* = 332	
Homare 2020	Cohort study	Japan	Sarcopenia	69.9 ± 8.9	21.6 ± 3.0	CABG	CT	PMI	*n* = 304	*n* = 76	In-hospital mortality, Discharged to healthcare facility, Length of ICU stay, CRRT require, Atrial fibrillation, Stroke, Prolonged ventilation
			No-sarcopenia	66.6 ± 9.7	24.1 ± 3.3					*n* = 228	

(Continued)

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TABLE 1 (Continued)

Author, year	Source of data	Source of population	Diagnose	Age	BMI	Surgery type	Muscle assessment method	CT measurement method	Total Sample	Sample	Postoperative outcome
Yuriko 2020	Cohort study	Japan	Sarcopenia	75.1 ± 5.5	22.7 ± 3.4	CABG and Valve surgery	CT	PMI	*n* = 206	*n* = 63	In-hospital mortality, Discharged to healthcare facility, Length of hospital stay, Length of ICU stay, CRRT require, Atrial fibrillation, Pneumonia, Wound infection, Stroke
			No-sarcopenia	73.9 ± 5.5	23.4 ± 3.7					*n* = 143	
Kondo 2021	Cohort study	Japan	Sarcopenia	81.0 ± 5.8	21.6 ± 4.2	Valve surgery	CT	PMI	*n* = 140	*n* = 29	In-hospital mortality, CRRT require, Atrial fibrillation, Wound infection, Stroke, Prolonged ventilation
			No-sarcopenia	77.3 ± 4.7	22.8 ± 3.7					*n* = 111	
Lee 2021	Cohort study	Korea	Sarcopenia	72.17 ± 5.46	22.60 ± 2.97	Valve surgery	CT	SMI	*n* = 874	*n* = 292	30-day in-hospital events
			No-sarcopenia	70.67 ± 5.47	25.29 ± 3.04					*n* = 582	
Ikuko 2022	Cohort study	Japan	Sarcopenia	73.8 ± 8.8	21.5 ± 3.0	CABG and Valve surgery	CT, gait speed, grip strength	SMI	*n* = 192	*n* = 72	In-hospital mortality, Discharged to healthcare facility, Length of hospital stay, Length of ICU stay
			No-sarcopenia	67.0 ± 10.1	24.5 ± 4.3					*n* = 120	
Liu 2022	Cohort study	China	Sarcopenia	63.5 (18)	19.94 (2.93)	Valve surgery	CT	SMI	*n* = 216	*n* = 36	In-hospital mortality, Length of hospital stay, Atrial fibrillation, Pneumonia, Wound infection, Stroke, Prolonged ventilation
			No-sarcopenia	63 (14)	24.29 (3.69)					n = 180	
Shen 2023	Cohort study	China	Sarcopenia	67 (10)	22.36 (5.63)	CABG	CT	SMI	*n* = 338	n = 44	In-hospital mortality, Length of hospital stay, Length of ICU stay, CRRT require, Atrial fibrillation, Pneumonia, Wound infection, Stroke, Prolonged ventilation
			No-sarcopenia	65 (11)	24.95 (3.88)					*n* = 294	

The number represents the mean ± standard deviation or median (interquartile range). BMI, body mass index; NA, Not afforded; CABG, coronary artery bypass grafting; PMI, psoas muscle index; SMI, skeletal muscle index; PMA; psoas muscle area; 6MWD, 6-min walking distance; CRRT, Continuous Renal Replacement Therapy; CT, Computed Tomography.

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TABLE 2 The NOS of included studies.

Study	Selection				Comparability	Outcome			Score
	Representativeness of the exposed cohort	Selection of the nonexposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of Cohorts on the Basis of the Design or Analysis	Assessment of outcome	Was follow-up long enough for out comes to occur	Adequacy of follow-up of cohorts	
Masashi 2017	☆	☆	☆	☆	☆	☆	☆		7
Ikeno 2017	☆	☆		☆	☆	☆		☆	6
Okamura 2018	☆	☆	☆	☆	☆☆	☆	☆		8
Robert 2019	☆	☆	☆	☆	☆	☆		☆	7
Yamashita 2019	☆	☆	☆	☆	☆	☆	☆		7
Homare 2020	☆	☆	☆	☆	☆☆		☆	☆	8
Yuriko 2020		☆	☆	☆	☆☆	☆	☆		7
Kondo 2021	☆	☆	☆	☆	☆	☆			6
Lee 2021	☆	☆	☆	☆	☆	☆	☆	☆	8
Ikuko 2022	☆	☆	☆		☆	☆		☆	6
Liu 2022	☆	☆	☆	☆	☆	☆	☆		7
Shen 2023	☆	☆	☆	☆	☆☆	☆	☆		8

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types or a single surgical type, with combined OR of 2.50 (95% CI: 1.04–6.01) and 3.54 (95% CI: 1.78–7.07), respectively. The population of the eight studies included are all from Asian countries, which was also consistent with the high aging society in Asian countries.

3.4 Secondary outcomes

3.4.1 Number of people discharged to healthcare facility

In a quantitative analysis of six articles, the number of people who returned to healthcare facilities after discharge was reported, and a total of 1,636 patients were recorded (36–39, 43, 45). It was true that more patients with sarcopenia need to be admitted to healthcare facilities after surgery due to poor functional status and physical independence (Figure 4; OR: 1.67, 95% CI: 1.02–2.73, $p = 0.04$). There was some heterogeneity among the included references ($I^2 = 48\%$, $p = 0.09$).

3.4.2 Length of hospital stay

A total of 1,458 patients reported total length of stay after surgery in six articles (36, 38, 40, 43, 45, 46). There was a significant difference in total length of hospital stay between the sarcopenia and non-sarcopenia groups (Figure 5A; MD: 2.61, 95% CI: 1.46–3.77, $p < 0.00001$), suggesting that patients with sarcopenia remained in the hospital longer after open heart surgery. There was acceptable heterogeneity among the included references ($I^2 = 20\%$, $p = 0.28$).

Summary of findings:

Sacropenic compared to Non-sarcopenic for elective open heart surgery in older patients

Patient or population: elective open heart surgery
Setting: Inpatient
Intervention: Sarcopenia
Comparison: Non-sarcopenia

Outcomes	Anticipated absolute effects* (95% CI) Risk with Non-sarcopenia	Risk with Sarcopenia	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
In-hospital mortality	21 per 1,000	**62 per 1,000** (37 to 102)	**OR 3.10** (1.80 to 5.34)	2090 (8 non-randomised studies)	⨁⨁⨁◯ Moderate	a,b,c
The length of hospital stay		MD **2.61 higher** (1.46 higher to 3.77 higher)	-	1458 (6 non-randomised studies)	⨁⨁⨁◯ Moderate	a,c
The need for CRRT	15 per 1,000	**44 per 1,000** (24 to 78)	**OR 3.01** (1.63 to 5.56)	1922 (7 non-randomised studies)	⨁⨁◯◯ Low	a,b,c,d
Incidence of pneumonia	38 per 1,000	**81 per 1,000** (38 to 166)	**OR 2.26** (1.00 to 5.10)	1266 (5 non-randomised studies)	⨁◯◯◯ Very low	a,c,e
Incidence of stroke	19 per 1,000	**37 per 1,000** (21 to 64)	**OR 1.92** (1.07 to 3.44)	2138 (8 non-randomised studies)	⨁⨁◯◯ Low	a,b,c
Incidence of discharge to healthcare facility	144 per 1,000	**219 per 1,000** (146 to 314)	**OR 1.67** (1.02 to 2.73)	1636 (6 non-randomised studies)	⨁⨁◯◯ Low	c,f

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. There are different ways to diagnose sarcopenia
b. Large effect (upgraded)
c. One study has different types of surgery
d. One study has different criteria for determining whether CRRT is needed
e. Less included studies
f. Statistical heterogeneity $I^2 = 48\%$ (not downgraded)

FIGURE 2
Certainty of the evidence and summary of findings.

3.4.3 Length of ICU stay

There were six articles documenting length of stay in the ICU, of which 1,708 cases were reported (36, 37, 39, 43, 45, 46). Patients in the sarcopenia group had longer ICU stays (Figure 5B; MD: 0.45, 95% CI: 0.00–0.91, $p = 0.05$) and there was acceptable heterogeneity between articles ($I^2 = 35\%$, $p = 0.18$).

3.5 Secondary outcomes associated with complications

3.5.1 Incidence of CRRT required

There were 1,922 patients, and a total of seven articles recorded patients who required CRRT after surgery (37–39, 43–46). The number of patients with sarcopenia who required CRRT after surgery was significantly higher than that of patients without sarcopenia (Figure 6A; OR: 3.01, 95% CI: 1.63–5.56, $p = 0.0004$), indicating that there was a higher incidence of renal failure in patients with sarcopenia after cardiac open-heart surgery. There was no heterogeneity between the articles ($I^2 = 0\%$, $p = 0.96$).

3.5.2 Incidence of postoperative atrial fibrillation

The incidence of complications after open heart surgery was quantitatively analyzed in 8 articles (37–40, 43–46), totaling 2,138 patients. There was heterogeneity among the included references ($I^2 = 48\%$, $p = 0.06$). Patients with sarcopenia did not have an increased incidence of new atrial fibrillation after open heart surgery (Figure 6B; OR: 1.04, 95% CI: 0.72–1.52, $p = 0.83$).

3.5.3 Incidence of postoperative pneumonia

Five articles reported the incidence of pneumonia after cardiac open-heart surgery (38, 40, 43, 45, 46), including a total of 1,266 patients. There was no statistically significant difference in the incidence of postoperative pneumonia between patients with sarcopenia and those without sarcopenia (Figure 6C; OR: 2.26, 95% CI: 1.00–5.10, $p = 0.05$). There was acceptable heterogeneity among the included studies ($I^2 = 43$, $p = 0.13$).

3.5.4 Incidence of postoperative wound infection

Five articles with a total of 1,140 patients of postoperative wound infections were quantitatively analyzed (40, 43–46). There was no difference in the incidence of wound infection between the sarcopenia group and the non-sarcopenia group (Figure 7A; OR: 2.27, 95% CI: 0.92–5.59, $p = 0.07$), and there was no heterogeneity between the articles ($I^2 = 0\%$, $p = 0.90$).

3.5.5 Incidence of postoperative stroke

Eight articles quantitatively reported the incidence of stroke in 2,138 patients after open heart surgery (37–40, 43–46). Compared with patients without sarcopenia, patients with sarcopenia had a higher risk of postoperative stroke (Figure 7B; OR: 1.92, 95% CI: 1.07–3.44, $p = 0.03$). There was no heterogeneity among the included literature types ($I^2 = 0\%$, $p = 0.51$).

3.5.6 Incidence of postoperative prolonged ventilation

There were seven articles quantitatively reporting the relationship between sarcopenia and the incidence of prolonged postoperative ventilation (37–40, 43, 44, 46). The results showed that patients with sarcopenia did not have an increased incidence of prolonged postoperative ventilation (Figure 7C; OR: 1.15, 95% CI: 0.76–1.75). The included original literature had low heterogeneity ($I^2 = 5\%$, $p = 0.39$).

4 Discussion

With increasing life expectancy and an aging population, the prevalence of sarcopenia has increased, and the proportion of patients with sarcopenia undergoing heart surgery is increasing (10, 47). However, there is a scarcity of studies investigating the effects of sarcopenia on open heart surgery. To address this gap, this study sought to investigate postoperative mortality in patients with preoperative sarcopenia. Through a rigorous systematic review and meta-analysis, we analyzed a total of 12 articles encompassing 4,749 patients. The results indicated that older patients with sarcopenia had higher postoperative mortality. Furthermore, patients with sarcopenia had longer stays in ICU, longer total hospital stays, increased need for postoperative CRRT, and heightened incidence of postoperative complications.

Patients diagnosed with sarcopenia prior to surgery were also associated with higher postoperative mortality, and there was no heterogeneity between studies. We performed a series of subgroup analyses based on the method of sarcopenia measurement, and type

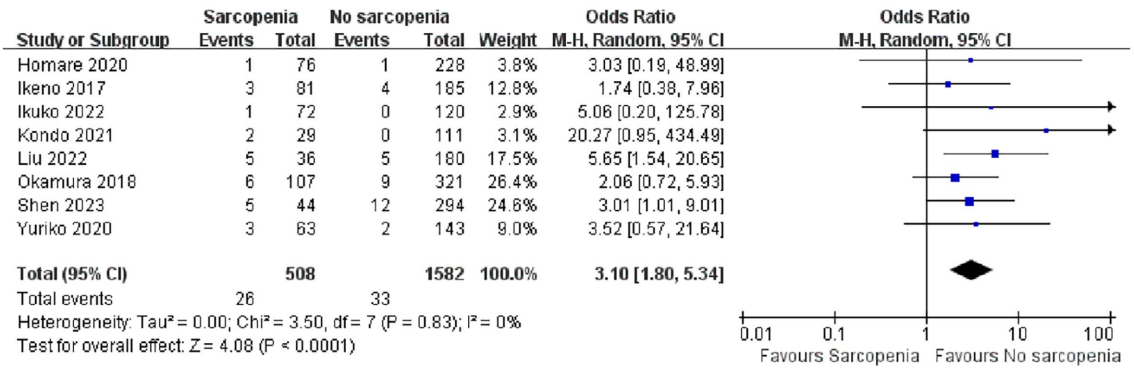

FIGURE 3
Forest plot showing the in-hospital mortality.

TABLE 3 The results of subgroup analysis for the In-hospital mortality.

Variable	Numbers of studies	Meta-analysis results OR (95% CI)	Heterogeneity
Measurement methods			
SMI	3	3.98 (1.77, 8.94)	$I^2 = 0\%$, $p = 0.008$
Non-SMI	5	2.53 (1.22, 5.26)	$I^2 = 0\%$, $p = 0.01$
Surgical types			
Single operation	5	3.54 (1.78, 7.07)	$I^2 = 0\%$, $p = 0.0003$
Multiple operations	3	2.50 (1.04, 6.01)	$I^2 = 0\%$, $P = 0.04$

SMI, skeletal muscle index; OR, Odds Ratio.

of surgery. Subgroup analysis showed that sarcopenia was significantly associated with higher postoperative mortality across different surgical modalities, and even subgroups of different sarcopenia measurement methods, which may have been due to the high negative impact of sarcopenia, which is associated with adverse outcomes in any subgroup. In certain subgroups, high heterogeneity could cause bias between aggregated results and actual results, which may need further confirmation.

Although previous studies have reported that preoperative sarcopenia defined from the psoas region was associated with a greater risk of long-term mortality and major unscrupulous cerebrovascular events in older patients undergoing heart surgery (48). However, there are still some cardiac studies, in order to predict the incidence of

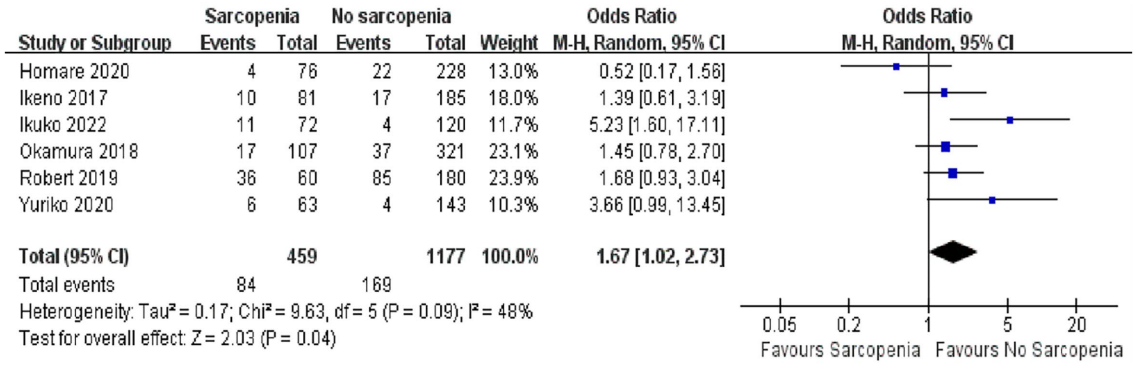

FIGURE 4
Forest plot showing the number of people discharged to healthcare facility.

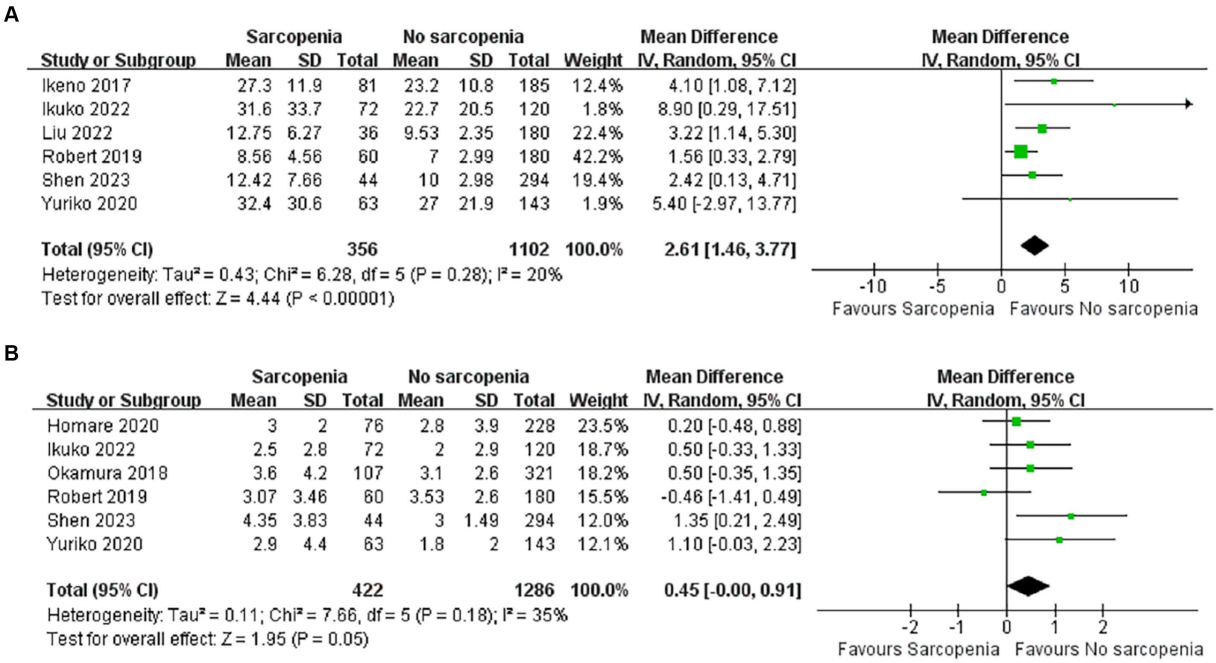

FIGURE 5
Forest plot showing the length of hospital stay and the length of ICU stay.

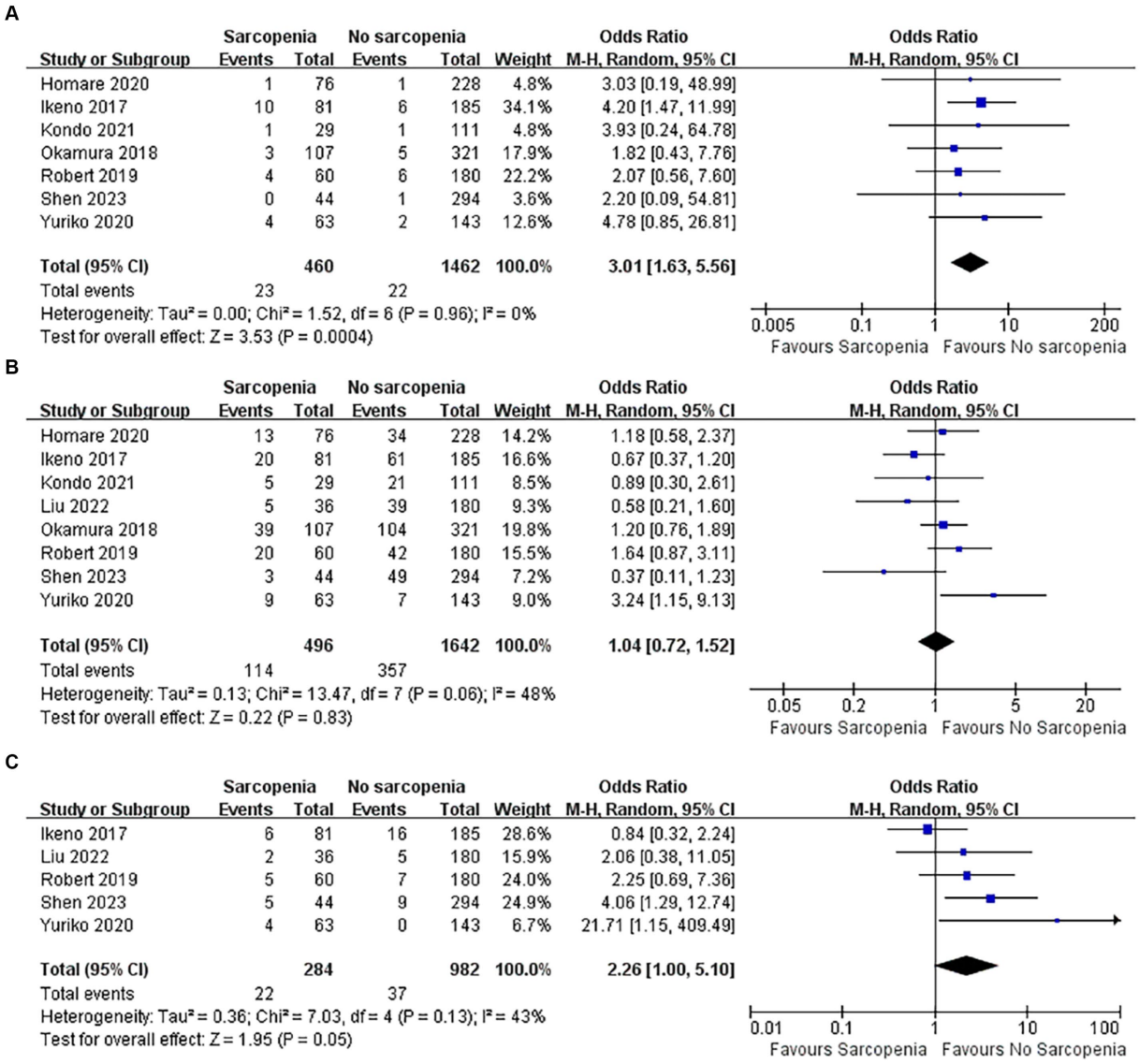

FIGURE 6
Forest plot showing the complications of part one.

postoperative pulmonary complications, the chest muscle is used to calculate the SMI index. This may be a possible source of heterogeneity in this study.

Our systematic review and meta-analysis independently investigated the association between sarcopenia and outcomes in older patients following elective cardiac open-heart surgery. Recently, the impact of sarcopenia on cardiac surgery has received extensive attention, and in cardiovascular surgery, sarcopenia is the most influential factor in slowing the progress of cardiac rehabilitation and increasing postoperative complications (49, 50). Previous studies on the effects of sarcopenia on TAVI have concluded that sarcopenia was closely associated with mortality and adverse outcomes after multiple surgeries, but no systematic article evaluated the relationship between sarcopenia and elective cardiac open-heart surgery. Cardiac open-heart surgery is always accompanied by cardiopulmonary bypass, which requires the opening of the chest for surgical procedures, and such patients are at a higher risk of acute or persistent sexual organ damage due to trauma and systemic inflammation than patients undergoing other surgeries. We therefore conducted a review of the topic and used GRADE to assess the quality of evidence in included studies. In our study, the research heterogeneity was low, the sample size was large, and the methodology was reliable, which increased the reliability and representativeness of the conclusions.

This meta-analysis included only older patients who had elective open-heart surgery. Therefore, in the conclusion of this study, the identification of sarcopenia before surgery may provide better medical management strategies and targets when it is found that sarcopenia may lead to adverse postoperative outcomes in patients undergoing this type of surgery. Introducing sarcopenia into a risk assessment can provide a better understanding of a patient's ability to tolerate surgery and help guide patients to more appropriate forms of treatment. For patients with sarcopenia, preoperative exercise training and nutritional supplements can be taken. Active

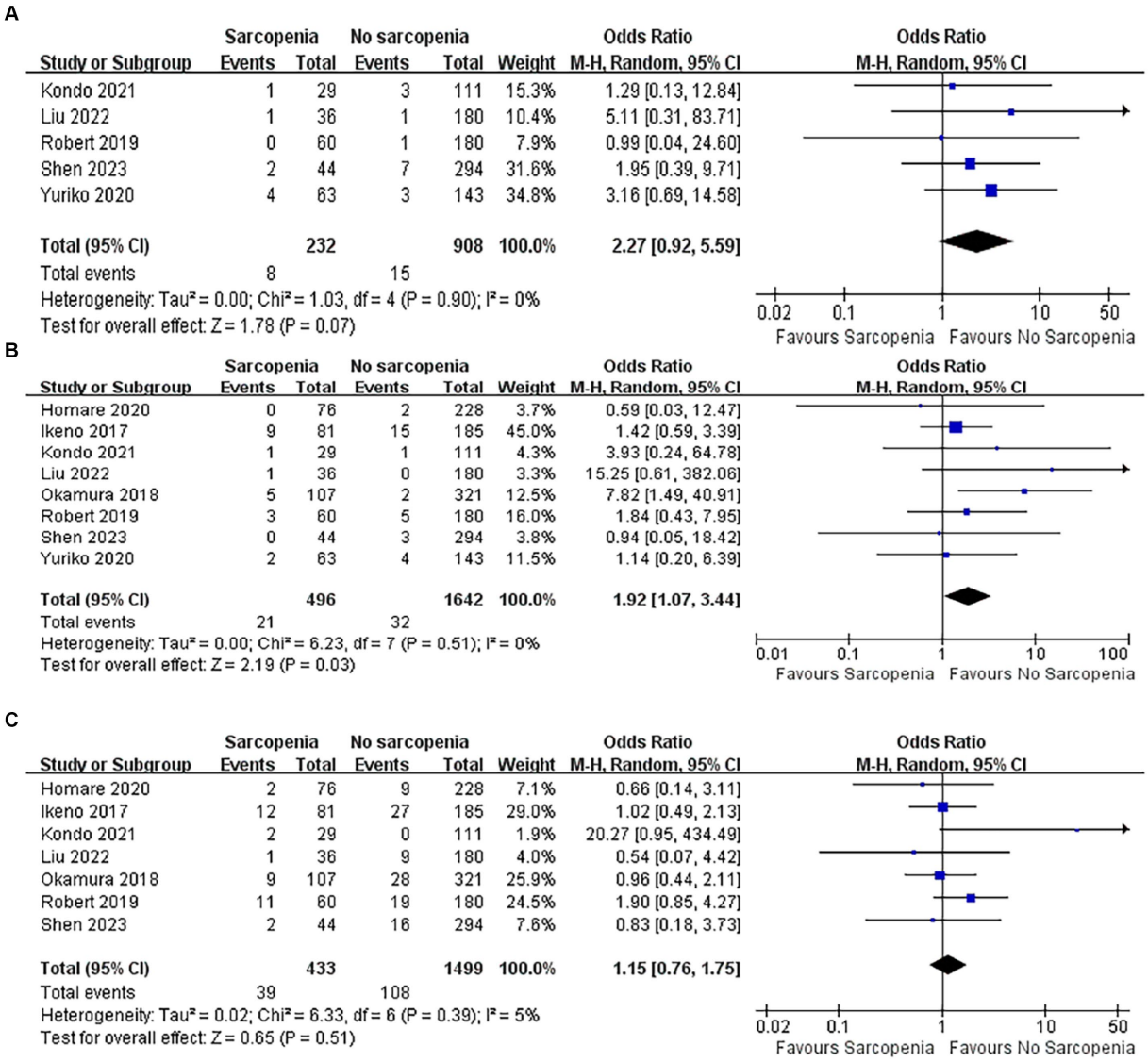

FIGURE 7
Forest plot showing the complications of part two.

rehabilitation programs can promote early postoperative activity, reduce the associated frequency of morbidity, and further improve activity throughout the life course.

Although these meta-analyses bring together evidence and illustrate that sarcopenia is a key factor of prognostic value in cardiac open-heart surgery, there are some limitations to this study. First, the 12 studies included were cohort studies, some of which measured sarcopenia differently. Some studies used the psoas muscle area or psoas muscle index to diagnose sarcopenia. Although psoas muscle has been recognized and recommended by some studies to diagnose sarcopenia (51–54), some literature has questioned this (55–57), and EWSOP2 still considers psoas as a small muscle, which may not reflect the state of the whole muscle (11). It is recommended to use the skeletal muscle index of the total lumbar muscle area (at the level of the third lumbar vertebra) to diagnose sarcopenia (58). Although the results of this study indicated that regardless of the measurement method used, the in-hospital mortality rate in the sarcopenia group was higher than the non-sarcopenia group, the inconsistency in measurement methods may pose a risk of inaccurately diagnosing sarcopenia using psoas muscle, potentially leading to biased results. Secondly, the definition of sarcopenia lacks a unified standard, which may be due to differences in human populations. Some original studies only use CT scans to diagnose sarcopenia without evaluating the patients' muscle strength, neglecting the potential impact of muscle strength, which could introduce bias in the diagnosis of sarcopenia and even lead to deviations in postoperative physical interventions for these patients, resulting in unfavorable outcomes. Future research should not only assess muscle mass/quantity reduction through CT scans but also include evaluations of patients' muscle strength to better and more accurately identify various aspects of sarcopenia. Furthermore, some patients in the included literature may have a history of cardiac open-heart surgery in the past, and multiple thoracotomies will increase the incidence of adverse

events in patients. In addition, positive results are more likely to be published, and there may be a risk of reporting bias. Therefore, more clinical studies in multiple centers are needed to confirm the value of sarcopenia in open heart surgery, and to conduct early targeted intervention for sarcopenia to improve the prognosis of patients.

5 Conclusion

This systematic review and meta-analysis found that sarcopenia diagnosed by preoperative CT scan was associated with higher rates of in-hospital mortality and complications in older patients after elective cardiac open-heart surgery, as well as significantly higher ICU and total length of stay.

We recommend that sarcopenia should be included in the routine evaluation of patients undergoing elective cardiac open-heart surgery, which may help clinicians refine treatment strategies and improve short - and long-term outcomes for patients.

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.

Author contributions

T-rY: Writing – original draft, Software, Methodology, Conceptualization. PJ: Writing – original draft, Validation, Software, Data curation. XD: Writing – original draft, Data curation. X-xF: Writing – original draft, Data curation. M-lH: Writing – original draft, Software. R-rW: Writing – review & editing, Supervision. X-hL: Writing – review & editing, Supervision, Methodology, Formal analysis, Conceptualization.

Funding

The author(s) declare that financial support was received for the research, authorship, and/or publication of this article. This work was funded by the Clinical research incubation project of West China Hospital, Sichuan University (No. 2022HXFH037 and No. 2022HXFH035) and the Sichuan University "From 0 to 1" innovation research project (No. 2023SCUH0039).

Acknowledgments

We would like to thank all our colleagues 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.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1378462/full#supplementary-material

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frontiers | Frontiers in Public Health

TYPE Study Protocol
PUBLISHED 24 July 2024
DOI 10.3389/fpubh.2024.1391383

OPEN ACCESS

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RECEIVED 25 February 2024
ACCEPTED 08 July 2024
PUBLISHED 24 July 2024

CITATION
Wang D, Zeng H, Wu P, Zhou Y, Chen H, Zhao F and Liu S (2024) Path analysis of the awareness status and influencing factors of sarcopenia in older adults in the community: based on structural equation modeling. *Front. Public Health* 12:1391383. doi: 10.3389/fpubh.2024.1391383

Path analysis of the awareness status and influencing factors of sarcopenia in older adults in the community: based on structural equation modeling

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Background: Sarcopenia is a progressive geriatric syndrome that impacts older adults' quality of life. Insufficient focus has been given to sarcopenia among Chinese residents, resulting in low level of sarcopenia awareness. This study aims to investigate awareness of sarcopenia and its influencing factors and the influencing pathways among older adults in Hangzhou.

Methods: A stratified random sample of 942 community-dwelling older adults was evaluated using the SARC-CalF screening tool, along with a questionnaire based on health ecology theory to assess awareness of sarcopenia and its influencing factors and the influencing pathways. Descriptive statistics, linear regression analysis, and path analysis were conducted using SPSS 25.0 and Amos 23.0 to analyze the data.

Results: The mean awareness score for sarcopenia was 60.26 ± 7.31. Self-rated physical health, daily intake of high-quality protein, exercise frequency, smoking status, self-efficacy, religious beliefs, social support, education level, occupation, participation in community free medical examinations, and awareness of nutrition policy were all factors affecting scores for sarcopenia awareness ($p < 0.05$). Except for negative effects observed in social support, smoking status, and self-rated physical health, all others exhibit positive effects.

Conclusion: Community healthcare institutions should target populations with low awareness of sarcopenia and focus on these key factors. Diverse health education programs and multi-channel screening activities can promote awareness, guide healthy lifestyles and prevent or delay the onset of sarcopenia in the older.

KEYWORDS

older adult, sarcopenia, awareness, influencing factors, pathway

1 Introduction

The global issue of population aging is currently a major concern. In China, the older adult population is growing rapidly, with an estimated 280 million individuals aged 60 and above by the end of 2022, accounting for 19.8% of the total population (1). As the aging process intensifies, there is growing attention towards sarcopenia, which is characterized by the

progressive loss of skeletal muscle mass, accompanied by a decline in muscle strength and/or muscle function associated with age (2, 3). Sarcopenia is influenced by several important risk factors, including aging, malnutrition, physical inactivity, smoking, alcohol abuse, and the presence of chronic diseases (4). Available data indicates that the prevalence of sarcopenia among individuals aged 65 and above in China varies from 14 to 33%, with a further increase to 50 to 60% among those aged 80 and above (5).

Sarcopenia is a progressive geriatric syndrome that detrimentally impacts physical function and capability. It has an insidious onset and can result in functional impairments, thereby increasing the risk of falls, disability, hospital readmission, and mortality among older adults (5). Studies have demonstrated that muscle mass declines at a rate of 2.5 to 3.0% per year after the age of 60 (6). A 10% reduction in muscle mass can compromise immune function and heighten the susceptibility to infections, whereas a 20% decrease can lead to muscle weakness, limited capacity for daily activities, and an elevated risk of falls (7).

In China, approximately 40 million individuals suffer from severe injuries caused by sarcopenia-related falls each year (8). This condition greatly compromises both their quality of life and overall health. In addition, sarcopenia is intricately linked to and reciprocally influences several chronic conditions including diabetes, cardiovascular diseases, chronic obstructive pulmonary disease, osteoporosis, and cognitive impairment (9–11). Given that both sarcopenia and chronic diseases are widespread among older adults, they impose substantial economic and caregiving burdens on families and society (12). According to reports, the hospitalization expenses for sarcopenia patients surged to a staggering $40.4 billion in the United States in 2014 (13). This substantial financial burden underscores the urgent need to address sarcopenia as a critical public health concern in an aging society.

Hence, early prevention and management of sarcopenia are crucial, emphasizing preventive approaches, enhancing older adults' awareness of sarcopenia, increasing their understanding of risk factors, and promoting preventive behaviors to mitigate the incidence and progression of sarcopenia from its roots (14). Studies have revealed inadequate attention towards sarcopenia among Chinese residents, with insufficient emphasis on its pathogenesis, risk factors, and potential harm. As a result, the overall awareness level regarding sarcopenia is low (15, 16). Disease awareness is influenced by various factors, including age, education level, occupation, and social environment. Thus, this study adopts the framework of ecological health theory, a significant theoretical model in public health practice. This theory highlights that individual health outcomes are the product of combined influences from genetic, psychological and behavioral, social and environmental, medical policy, cultural customs, and other factors (17).

This study conducted a comprehensive analysis on the factors and the pathways influencing the awareness of sarcopenia among older adults residing in the community. It evaluated the current status and identified existing issues regarding the awareness of sarcopenia in this population. The study also explored effective approaches to enhance the awareness of sarcopenia among older adults, presenting a foundation for conducting health education and research on sarcopenia in community-dwelling older adults.

This study puts forward the hypothesis that the current sarcopenia awareness among older adults is suboptimal. Furthermore, it postulates that disease awareness is influenced by various factors, including individual characteristics, psychological and behavioral lifestyles, family interpersonal networks, living and working environments, as well as policy and cultural contexts. And these influencing factors may interact with each other, collectively affecting older adults' awareness of sarcopenia.

2 Materials and methods

2.1 Study design and sample

This study investigated the awareness of sarcopenia among Chinese older adults from October and November 2022. The sampling method in this study comprised two stages. Initially, survey sites were chosen through stratified random sampling. Subsequently, older participants were selected via convenience sampling at the designated survey sites. The selected areas encompassed Gongshu District, Xihu District, Yuhang District, and Linping District in the central urban area of Hangzhou city, Zhejiang Province, China. From each district, two streets were randomly selected to sample the older adults. The sample size was determined using the Kendall sample size rough estimation method, which recommends a sample size of 10–20 times the number of survey indicators (18). The questionnaire consisted of 41 items. Considering the response rate and efficiency, the sample size was augmented by 10%, resulting in a final sample size of 902 participants.

From October 2022 to November 2022, 942 older adults were surveyed using a stratified random sampling method in Hangzhou, Zhejiang Province, China. The study enrolled older adults residing in Hangzhou city as participants. The inclusion criteria were as follows: ① aged 60 years and above; ② permanent residents of the community for more than six months; ③ possessing clear consciousness, self-reporting no hearing impairments, cognitive and memory-related disorders, reading and expressive ability issues, or difficulties in communication with the researchers; and ④ voluntary participation with signing of an informed consent form. The exclusion criteria included meeting any of the following conditions: self-reported lack of autonomy or presence of end-stage diseases.

2.2 Ethics statement

This research protocol received approval from the Institutional Review Board of Hangzhou Normal University (Hangzhou, China, Approval No. 2022-1117) and was conducted in accordance with the Helsinki Declaration and ethical guidelines. Written informed consent was obtained from all respondents, ensuring the protection of privacy and confidentiality of personal information for the older adult participants.

2.3 Measurements

This study designed a questionnaire based on relevant literature to evaluate the awareness levels of sarcopenia in the older adults, along with related influencing factors and their pathways of impact.

2.3.1 The questionnaire for assessing factors influencing awareness of sarcopenia

The questionnaire for assessing factors influencing awareness of sarcopenia in older adults was developed based on the health ecology theory. It consisted of five parts: (1) The personal characteristics considered in this study included gender, age, body mass index (BMI), waist circumference, presence of chronic diseases, self-rated health status, self-rated mental status, ability to perform daily living activities, and results of sarcopenia screening; (2) Psychological and behavioral lifestyle factors included smoking, alcohol consumption, exercise frequency, exercise duration, daily intake of high-quality protein, use of nutritional supplements, frequency of eating out, dietary regularity, and self-efficacy; (3) Family and interpersonal network factors included religious beliefs, marital status, living arrangement, and social support; (4) Living and working environment factors included occupation, education level, household monthly *per capita* income, availability of community life support services, and utilization of free community physical examination services; (5) Policy and cultural environmental factors included type of medical insurance, awareness of national nutrition policies such as the "Chinese Residents' Dietary Guidelines," and other relevant nutritional policies.

Sarcopenia screening in this study was conducted using the SARC-CalF (SARC-F combined with calf circumference) screening tool proposed by Barbosa-Silva et al. (19). A score of ≥11 points indicated a positive sarcopenia screening result. The SARC-CalF scale has demonstrated high sensitivity and specificity (20). Self-efficacy was assessed using the validated Chinese version of the General Self-Efficacy Scale, which has been widely utilized in the Chinese population. The scale demonstrated good reliability and validity, with a Cronbach's alpha coefficient of 0.89 (21). The scale comprised 10 items, and the total score ranged from 10 to 40, with higher scores indicating greater levels of self-efficacy. Social support was assessed using the Social Support Rating Scale developed by Shuiyuan Xiao, and the scale demonstrated good reliability and validity, with a Cronbach's alpha coefficient of 0.92 and a test-retest reliability coefficient of 0.89 (22). The Social Support Rating Scale consisted of a total score ranging from 12 to 66 points, with higher scores indicating greater levels of social support. Scores below 22 were classified as low, scores between 23 and 44 were moderate, and scores between 45 and 66 were high.

2.3.2 The questionnaire for sarcopenia awareness assessment

The questionnaire for sarcopenia awareness assessment in older adults was designed based on the "Expert Consensus on Diagnosis and Treatment of Sarcopenia in Chinese Older Adults (2021) (4)"and the "Core Information Consensus on Preventing Sarcopenia in Chinese Older Adults (5)." The questionnaire underwent a pretest among 240 community older adults to assess its effectiveness and ensure the readability and clarity of its content. It consists of 15 items, and each item is rated on a 5-point Likert scale ranging from "completely disagree" to "completely agree." Each item was scored on a 5-point Likert scale, with a maximum total score of 75. Higher scores were indicative of greater awareness. The awareness level was categorized as follows (23): a score ≥ 80% of the total possible score indicated good awareness level; a score ranging between 60 and 80% indicated moderate awareness level; and a score < 60% of the total possible score was considered poor awareness level. Awareness levels were classified based on the following criteria: scores of 60–75 were indicative of good awareness, scores of 45–59 indicated moderate awareness, and scores of 15–44 indicated poor awareness. The questionnaire was validated through investigation, with a Cronbach's alpha coefficient of 0.841, KMO = 0.865, Bartlett $p < 0.001$, indicating good reliability.

2.4 Data collection

The researchers conducted one-on-one interviews for questionnaire collection. Prior to distributing the questionnaire, they provided a comprehensive explanation of the research purpose, process, benefits, and potential risks to all participating older adults. Only after ensuring that the older adults had a full understanding and willingly agreed to participate, they were asked to sign the informed consent form. For survey participants with a primary school education or below, the researchers provided assistance in completing the survey questionnaire. All participants who fill out the questionnaire will be rewarded with a small gift.

2.5 Statistical analysis

The database was established and data were entered using Epidata 3.1 software, while Statistical analysis was performed using SPSS 25.0 and AMOS 23.0 software. Professional verification was conducted to ensure data completeness and accuracy. Frequency and percentage were used to describe count data, while normally distributed measurement data were presented as mean ± standard deviation $(\bar{x} \pm s)$. Stratified linear regression analysis was employed to identify influencing factors. The structural equation model (SEM) was applied to analyze the pathways between various factors and sarcopenia awareness. All results were considered statistically significant at $p < 0.05$.

3 Results

3.1 Social and demographic characteristics

A total of 984 questionnaires were distributed, and 942 valid questionnaires were collected, resulting in a valid response rate of 95.73%. Out of 942 community-dwelling older adults, 332 (35.24%) were male and 610 (64.76%) were female. The age group with the largest representation was 70–79 years, comprising 403 individuals (42.78%), followed by 60–69 years, which included 385 individuals (40.87%). A total of 794 individuals (84.29%) were married. The educational level of the majority of older adults was primary school or below, accounting for 53.08% ($n = 500$), while 243 individuals (25.80%) had completed junior high school. Regarding household monthly *per capita* income, 57.54% of older adults had an income between 2000 and 4,999 yuan, while 22.40% had an income below 2000 yuan (Table 1).

TABLE 1 General demographic information of the participants (n = 942).

Variables		n (%)
Gender	Male	332 (35.24)
	Female	610 (64.76)
Age	60–69	385(40.87)
	70–79	403 (42.78)
	80–89	138 (14.65)
	≧90	16 (1.70)
Marital Status	Married	794 (84.29)
	Widowed	129 (13.69)
	Divorced	3 (0.32)
	Unmarried	16 (1.70)
Educational level	Primary School and Below	500 (53.08)
	Junior High School	243 (25.80)
	High School/Junior College	123 (13.06)
	College and Bachelor's degree or above	76 (8.06)
Occupation type	Government employee, public sector worker	176 (18.68)
	Corporate/ Company personnel	232 (24.63)
	Service worker	32 (3.40)
	Farmer	306 (32.48)
	Laborer	141 (14.97)
	Self-employed individual	27 (2.87)
	Other	28 (2.97)
Religious belief or not	No	753 (79.94)
	Yes	189 (20.06)
Household monthly *per capita* income (RMB)	<2000	211 (22.40)
	2000–4,999	542 (57.54)
	5,000–6,999	126 (13.38)
	7,000–9,999	54 (5.73)
	>10,000	9 (0.95)
Type of medical insurance	Basic medical insurance for urban worker	484 (51.38)
	Basic medical insurance for urban and rural resident	412 (43.74)
	Public medical insurance	36 (3.82)
	Other	10 (1.06)
BMI (kg/m^2)	<18.5	31 (3.29)
	18.5–23.9	446 (47.35)
	24–27.9	347 (36.84)
	≥28	118 (12.52)
Waist circumference	Normal	577 (61.25)
	Abnormal	365 (38.75)
Whether you have chronic diseases	No	297 (31.53)
	Yes	645 (68.47)
	No	297 (31.53)
Self-assessed health status in the last 3 months	Poor	52 (5.52)
	Moderate	111 (11.78)
	Good	779 (82.70)

(Continued)

TABLE 1 (Continued)

Variables		*n* (%)
Self-assessed mental status in the last 3 months	Poor	16 (1.70)
	Moderate	57 (6.05)
	Good	869 (92.25)
Exercise frequency	Hardly exercise	161 (17.09)
	1–2 times/week	31 (3.29)
	3–5 times/week	39 (4.14)
	6–7 times/week	711 (75.47)
Exercise time per exercise (Minutes)	0–29	215 (22.82)
	30–59	328 (34.82)
	≥60	399 (42.36)
Do you smoke	No	859 (91.19)
	Yes	83 (8.81)
Do you consume alcohol	No	769 (81.63)
	Yes	173 (18.37)
Meal Regularity in the last 3 months	Irregular	5 (0.53)
	general	15 (1.59)
	Regular	922 (97.88)
Whether you can reach the nearest fitness facility/gym in your neighborhood within 15 min on foot	No	65 (6.90)
	Yes	877 (93.10)
Whether you can reach the nearest healthcare facility by walking for 15 min	No	71 (7.54)
	Yes	871 (92.46)
Whether you have used the free medical examination services provided by the community hospital in the last year	No	67 (7.11)
	Yes	875 (92.89)
Level of awareness of nutrition policies	Unfamiliar	847 (89.92)
	Moderate	39 (4.14)
	Familiar	56 (5.94)
SARC-CalF Classification	Non- sarcopenia	841 (89.28)
	Sarcopenia	101 (10.72)

TABLE 2 The level of awareness of sarcopenia in community-dwelling older adults ($n = 942$).

Grades	Number (%)	Scores ($\bar{x} \pm s$)
Poor (15 ~ 44points)	2 (0.21)	43.0 ± 1.41
Moderate (45 ~ 59points)	481 (51.06)	54.20 ± 3.33
Good (60 ~ 75points)	459 (48.73)	66.70 ± 4.10
Total	942(100.00)	60.26±7.31

Data are presented as n (%) or mean ± standard deviation.

3.2 Awareness of sarcopenia in community-dwelling older adults

The mean score for sarcopenia awareness among community-dwelling older adults surveyed was 60.26 ± 7.31. Insufficient awareness of sarcopenia was identified in 51.27% of the older adult population (Table 2).

3.3 Factors associated with awareness of sarcopenia in community-dwelling older adults

A stratified linear regression analysis method was employed in this study to examine the factors influencing sarcopenia awareness among community-dwelling older adults. The model fitness coefficients indicated a high fit for all models. Each additional level of the related factor resulted in a significant increase in the explanatory power of the regression model. Ultimately, after incorporating all relevant factors into the model, a total of 36.2% of the variance could be explained. The results indicated that the final model included 12 variables that demonstrated statistical significance. These variables encompassed self-rated physical health status, daily intake of high-quality protein, exercise frequency, smoking behavior, self-efficacy, religious beliefs, social support, education level, occupation, household monthly *per capita* income, participation in community free medical examinations, and knowledge of nutrition policies (Table 3).

TABLE 3 Regression results of factors influencing awareness of sarcopenia in community-dwelling older adults.

Dimensions	Variables	Model 1	Model 2	Model 3	Model 4	Model 5
		β (*SE*)	β (*SE*)	β (*SE*)	β (*SE*)	β (*SE*)
Personal	SARC-CalF questionnaire screening scores (ref.:<11)					
characteristics	Scores≥11	−0.095** (0.764)	−0.075* (0.716)	−0.021 (0.672)	−0.031 (0.677)	−0.025 (0.662)
	Self-assessed health status (ref: poor)					
	Moderate health	0.113* (1.231)	0.094 (1.153)	0.155** (1.075)	0.174*** (1.058)	0.156** (1.035)
	Good health	0.053 (1.092)	0.019 (1.029)	0.126* (0.969)	0.149** (0.955)	0.125* (0.936)
Psychological	Daily intake of good quality protein		0.152*** (0.487)	0.156*** (0.454)	0.104*** (0.467)	0.088** (0.460)
and	Weekly frequency of exercise (ref: no exercise)					
behavioral	Exercise 6–7 times/ week		0.159* (1.067)	0.118* (0.997)	0.150** (0.979)	0.141* (0.957)
lifestyle	Smoke (ref: No)					
	Yes		−0.084** (0.777)	−0.087** (0.721)	−0.085** (0.717)	−0.087** (0.704)
	Self-efficacy		0.272*** (0.040)	0.280*** (0.037)	0.256*** (0.038)	0.257*** (0.037)
Family	Religious belief (ref: No)					
interpersonal	Yes			0.200*** (0.533)	0.240*** (0.536)	0.224*** (0.527)
network	Social support			−0.265*** (0.030)	−0.263*** (0.031)	−0.245*** (0.030)
Living and	Educational level (ref: primary and below)					
working	Junior high school				0.091** (0.547)	0.083* (0.535)
environment	High school/ Junior college				0.072* (0.711)	0.050 (0.698)
	College and Bachelor's Degree or above				0.124** (0.972)	0.118** (0.952)
	Occupation Type (ref: other)					
	Service worker				0.117** (1.601)	0.097* (1.579)
	Household monthly *per capita* income (ref: < 2000 RMB)					
	2000–4,999 RMB				0.088* (0.537)	0.083* (0.525)
	Have you used free medical examination services provided by community hospitals in the last 1 year (ref: No)					
	Yes				0.079** (0.800)	0.070* (0.783)
Policy and	Level of awareness of nutrition policy (ref: Unfamiliar)					
cultural	Moderate awareness of nutrition policy					0.100*** (1.022)
environment	Familiar Nutrition Policy					0.167*** (0.869)
Regression	R2	0.029	0.163	0.283	0.331	0.362
model	ΔR2	0.029	0.134	0.119	0.048	0.032
	F	5.614	13.950	24.321	15.008	16.144
	p	<0.001	<0.001	<0.001	<0.001	<0.001

Stratified linear regression was performed with the awareness score of sarcopenia as the dependent variable. The regression model included the following stratified models: Model 1 Personal characteristics, Model 2 Psychological and behavioral lifestyle, Model 3 Family interpersonal network, Model 4 Living and working environment, and Model 5 Policy and cultural environment. For categorical variables, the "No" group was selected as the reference category. $P < 0.05$ represents statistical significance. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

3.4 Pathway analysis of awareness influencing factors of sarcopenia in community older adults

Based on the results of linear regression analysis and relevant professional knowledge, a structural equation model of awareness influencing factors of sarcopenia was constructed. The research data were validated using the maximum likelihood method (ML). After the modification and deletion of non-significant paths, the model fit well (Table 4). The standardized path coefficients of the modified structural equation model for the awareness influencing factors of sarcopenia in older adults are shown in Figure 1. The effects of each variable on the awareness of sarcopenia in older adults are divided into direct effects, indirect effects, and total effects. The order of the total effects of each variable on the awareness of sarcopenia is as follows: self-efficacy (0.262) > social support (−0.260) > religious beliefs (0.255) > understanding of nutritional policies (0.219) > exercise frequency (0.164) > level of education (0.135) > smoking status

TABLE 4 The revised model fit analysis.

Indices	$\chi 2$/df	RMSEA	GFI	AGFI	CFI	IFI	NFI	TLI
Model fit value	3.063	0.047	0.977	0.958	0.906	0.909	0.870	0.856
Evaluation criterion	<5	<0.08	>0.90	>0.90	>0.90	>0.90	>0.85*	>0.85*

*>0.85 acceptable and >0.90 goodness. RMSEA = root mean square error of approximation; GFI = goodness of fit index; AGFI = adjusted goodness of fit index; CFI = -comparative fit index; IFI = incremental fit index; NFI = normed fit index; TLI = Tucker-Lewis index; df = degree of freedom.

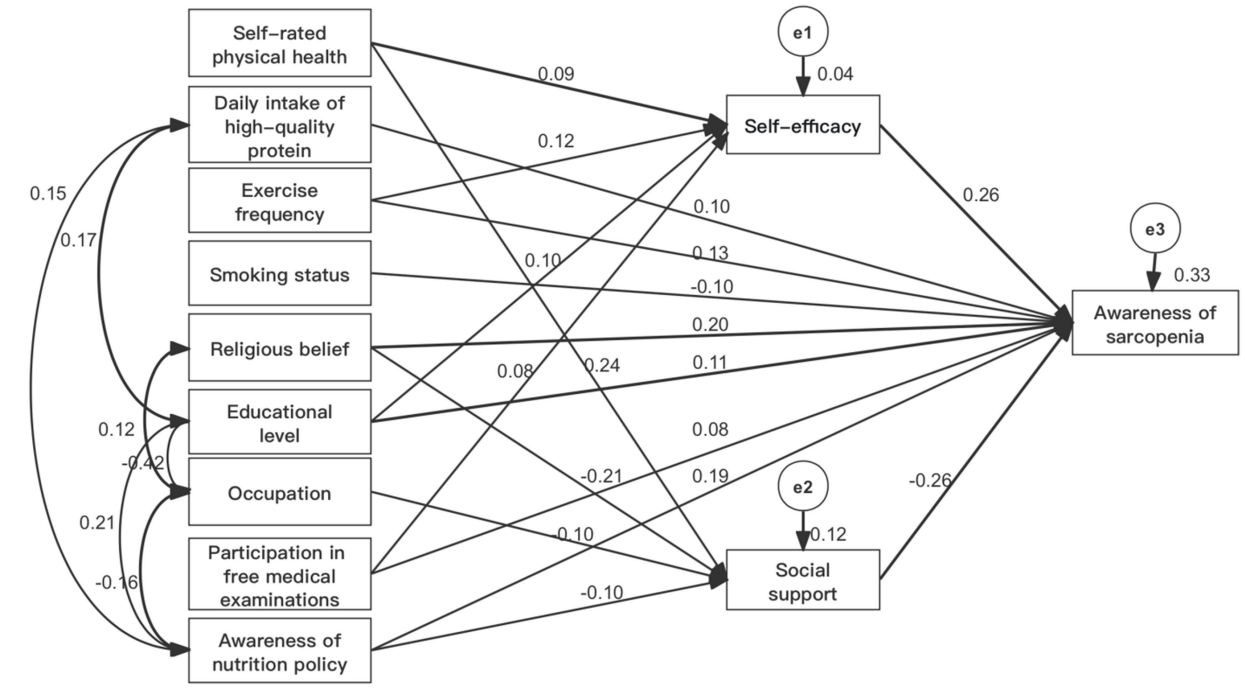

FIGURE 1
Standard path coefficients of the model.

(−0.099) > daily intake of high-quality protein (0.096) > use of free medical check-up services at the community hospital in the past year (0.095) > self-rated health status in the past 3 months (−0.037) > occupation (0.027). Except for social support, smoking status, and self-rated health status in the past 3 months, which have negative effects, the rest have positive effects (Table 5).

The Bootstrap method was used to test the mediating effects, and the results indicated that self-efficacy and social support partially mediated the relationship between self-rated health status in the past 3 months, exercise frequency, religious beliefs, level of education, occupation, use of free community medical check-up services in the past year, understanding of nutritional policies, and awareness of sarcopenia. The 95% confidence intervals of the mediating effects did not include 0 (Table 6).

4 Discussion

Among the surveyed participants, 48.73% demonstrated a good level of awareness regarding sarcopenia. A study by Soon Lean Keng et al. (24) on Malaysian residents aged 18 and above revealed that only 6.9% of the participants had a comprehensive understanding of the characteristics, consequences, and treatment of sarcopenia. Jeanine M. Van Ancum (25) discovered that merely 9% of Dutch residents were familiar with the concept of sarcopenia. Shu-Chun Lee (26) conducted a survey on older individuals aged 65 and above in Taipei, China, and found that their average score for sarcopenia awareness was 2.83 ± 0.82 (out of 5 score), indicating a limited level of familiarity with sarcopenia. At present, there is a scarcity of research regarding sarcopenia awareness, and the existing studies are in their preliminary stages. Researchers have utilized individually tailored assessment tools to conduct surveys, leading to discrepancies in both the tools employed and the demographics surveyed. Consequently, this has led to inconsistent research findings among different researchers.

However, a significant proportion (51.27%) of the older adult population exhibited insufficient awareness of sarcopenia, indicating the need for enhanced awareness, particularly considering its recent recognition as a disease by the World Health Organization (WHO) in 2016 (27). Sarcopenia is a geriatric disease with high prevalence and challenges associated with diagnosis (28). Currently, the social awareness of this disease remains relatively low. Based on reports, it was found that only 0.19% of the 1,056 nurses surveyed from 19 provinces in China possessed adequate knowledge of sarcopenia. Additionally, a significant majority (65.72%) of the nurses scored below passing grades in their assessment of sarcopenia knowledge (23). The inadequate level of disease awareness among healthcare

TABLE 5 Summary of the impact effects of various factors on awareness of sarcopenia.

Pathways	Direct effect	Indirect effect	Total effect
Self-rated health status in the past 3 months → Awareness	-	−0.037	−0.037
Daily high-quality protein intake ratio → Awareness	0.096	-	0.096
Exercise frequency → Awareness	0.132	0.031	0.164
Smoking → Awareness	−0.099	-	−0.099
Religious beliefs → Awareness	0.201	0.054	0.255
Educational level → Awareness	0.108	0.027	0.135
Occupation → Awareness	-	0.027	0.027
Free community hospital medical check-up services in the past year → Awareness	0.075	0.020	0.095
Level of understanding of nutrition policies → Awareness	0.194	0.025	0.219
Self-efficacy → Awareness	0.262	-	0.262
Social support → Awareness	−0.260	-	−0.260

TABLE 6 Results of the mediation analysis.

Pathways	Coefficient	95%CI		p
		Lower	Upper	
Self-rated health status in the past 3 months → self-efficacy/social support → Awareness	−0.037	−0.065	−0.01	0.007
Exercise frequency → self-efficacy → Awareness	0.031	0.016	0.048	0.001
Religious beliefs → social support → Awareness	0.054	0.037	0.074	0.001
Educational level → self-efficacy → Awareness	0.027	0.011	0.046	0.001
Occupation → social support → Awareness	0.027	0.01	0.045	0.001
Free community hospital health check-up service in the past year → self-efficacy → Awareness	0.020	0.007	0.032	0.005
Understanding of nutritional policies → social support → Awareness	0.025	0.01	0.042	0.003

professionals can impede the diagnosis and treatment of sarcopenia in clinical practice (29). Sarcopenia is characterized as a progressive disorder involving loss of muscle strength, muscle mass, or physical function (2, 3). However, these symptoms are often misconstrued as natural signs of aging. Additionally, in China, the absence of specialized geriatric departments in most hospitals has resulted in limited and inaccurate dissemination of knowledge concerning geriatric syndromes (23). While healthcare institutions place significant focus on preventing falls, their efforts primarily revolve around improving the physical environment and providing health education on medications that may induce falls. Consequently, sarcopenia, as an independent risk factor for falls tends to be overlooked (30). Therefore, it is crucial to increase public awareness of sarcopenia as an essential strategy for the effective prevention and treatment of both sarcopenia and its associated conditions (26).

In this study, Self-rated physical health has indirect effects on sarcopenia awareness through self-efficacy (0.024) and social support (−0.062). Older adults with good self-rated health tend to possess a stronger sense of control over their lives (31), strong sense of self-efficacy, enabling them to engage more actively with the outside world, acquire information, and consequently demonstrate higher levels of sarcopenia awareness. However, when individuals rate their own health as good, it reduces the motivation to seek medical and social support, weakening the potential informational function of social support, leading to decreased awareness of sarcopenia.

Older adults who maintain a healthy lifestyle and exhibit good psychological well-being demonstrate higher levels of sarcopenia awareness. The study results revealed that older adults who consumed high-quality protein on a daily basis, engaged in physical exercise 6–7 times per week, refrained from smoking, and demonstrated high self-efficacy exhibited higher scores of sarcopenia awareness. The effects of exercise frequency and daily high-quality protein intake on sarcopenia awareness are both positive (0.164, 0.096), while smoking status has a negative effect on sarcopenia (−0.099). This observation may be due to the greater emphasis placed by this group of older adults on their own health, as well as their heightened awareness of health-related issues and favorable daily habits (32). Prior research has demonstrated a positive correlation between disease knowledge and healthy lifestyle behaviors. Individuals possessing greater disease knowledge are more inclined to adopt healthy lifestyle behaviors, which can help prevent disease progression and associated complications (33). Previous research has identified a positive

correlation between protein intake and protein knowledge (34). In our study, older adults with higher scores of sarcopenia awareness have a greater understanding of protein nutrition knowledge and a relatively higher protein intake.

In this survey, it was found that 8.81% of the older population were smokers, and their awareness of sarcopenia was lower compared to non-smokers, which is in line with previous studies (24). Non-smokers exhibited higher levels of health literacy compared to smokers (35), and the lower health literacy observed in smokers was associated with their insufficient knowledge regarding health-related matters (36). This study revealed a lower level of sarcopenia awareness among smokers, potentially attributed to their limited access to education and health information, inadequate awareness of the hazards associated with smoking, and a lack of active involvement in acquiring and mastering health-related knowledge and skills (37).

The study found that self-efficacy has the greatest impact on sarcopenia awareness (0.262), and it is a positive influence. Self-efficacy plays a crucial role in influencing individuals' adoption of healthy lifestyles. Research has indicated that older adults with high self-efficacy are more confident in sustaining a healthy lifestyle and forming healthy habits (38). Additionally, there is a notable correlation between high self-efficacy and disease knowledge (39). Community healthcare institutions should prioritize the physical and mental well-being of the older adult and focus on fostering their self-efficacy. This approach can effectively enhance the impact of sarcopenia health education and facilitate older adults in modifying their unhealthy habits at an earlier stage.

We found that older individuals who hold religious beliefs exhibit higher scores of sarcopenia awareness. The influence of religious beliefs on sarcopenia awareness is positive (0.255). This may be attributed to their heightened social engagement compared to their non-religious counterparts (40). The problem-solving mechanisms and social support provided by their religious beliefs influence their daily behaviors and lifestyle, leading to enhanced mental well-being (41). Different religious beliefs advocate diverse dietary culture, inadequate protein intake is a significant risk factor for triggering sarcopenia. Therefore, people who choose vegetarianism because of their religious beliefs should consume sufficient additional plant-based protein to maintain muscle health (42). We also investigated the relationship between social support and sarcopenia awareness among older adults. In contrast to previous studies, this study found that older adults with low levels of social support had higher scores of sarcopenia awareness. The impact of social support on sarcopenia awareness is negative (−0.260). In traditional Chinese culture, the family holds a central role in social support (43), A strong family support system can expand the range of health-related information available to older adults (44) and provide them with enhanced healthcare resources (45). Nevertheless, research on sarcopenia in China is still at an early stage, with limited social awareness and public attention. Reliance solely on family support is inadequate for older adults to acquire sufficient knowledge about sarcopenia. Conversely, older individuals with lower levels of family support tend to rely more on medical services, presenting opportunities to obtain knowledge about sarcopenia from healthcare professionals during the treatment of associated chronic conditions. These findings highlight the importance for community healthcare institutions to not only foster self-health awareness among the older adults but also enhance the dissemination and accessibility of knowledge about sarcopenia. This can be achieved by raising public awareness and encouraging widespread attention to sarcopenia, while also leveraging the positive impact of the family support system to promote the health of older adults affected by sarcopenia.

The living and working environment has a significant impact on the awareness of sarcopenia in older adults. There is a positive correlation between their education level and scores of sarcopenic awareness. The effect of educational level on sarcopenia awareness is positive (0.135). Consistent with previous studies, individuals with higher levels of education possess a more comprehensive understanding of the disease (46), Furthermore, education is positively associated with the motivation to acquire knowledge, enhance awareness, and adopt healthier lifestyle choices (47). According to the Development Report on the Quality of Life for the older adults in China (2019) (48), compiled by the China Scientific Research Center on Aging, approximately 29.6% of older individuals in China have not received formal education, while approximately 41.5% have attained primary school education. The educational level of the older adults in China is generally low, therefore, we need to strengthen health education for the older adults even more. In this study, the occupation of older adults was found to influence their awareness of sarcopenia. The effect of occupation on sarcopenia awareness is positive (0.027). Specifically, older adults working in the catering service industry displayed the highest scores of sarcopenia awareness, potentially attributed to their occupation exposing them to a greater amount of nutrition-related information. This results in a positive impact on individuals' awareness of sarcopenia.

This study revealed that older adults who utilized community-based free physical examination services in the previous year exhibited higher scores of sarcopenia awareness compared to those who did not utilize such services. Whether the use of community free medical check-up services has a positive effect on sarcopenia awareness (0.095). As of 2015, a total of 118 million older adults aged 65 and above in China were benefiting from the provision of free medical examination services (49). This could be attributed to their heightened concern for personal health status, proactive engagement with community doctors in case of abnormal situations, and expression of health needs, leading to a greater acquisition of health knowledge. These findings imply the need for community healthcare institutions to enhance awareness among older adults regarding the significance of health checkups, promote active participation in such checkups, and advocate for the inclusion of sarcopenia screening as part of routine examinations. These measures aim to enhance older adults' awareness of and attention to sarcopenia.

Studies have revealed a positive correlation between the level of nutrition policy understanding among older adults and their scores of sarcopenia awareness. The overall effect of the level of understanding of nutrition policies on sarcopenia awareness is 0.219. This may be because older adults who pay more attention to policies have a better understanding of the risks and impacts of sarcopenia. As a result, they become more conscientious about their daily behaviors and lifestyle choices, aiming to prevent the onset of sarcopenia. These findings emphasize the importance of healthcare institutions reinforcing the promotion and dissemination of national nutrition-related policies, such as dietary guidelines for residents. By enhancing older adults' self-care awareness, improving their knowledge regarding sarcopenia, and enabling accurate assessments of their own health, these efforts can potentially delay the onset and progression of sarcopenia.

The level of sarcopenia awareness among older individuals in the community in Hangzhou city is inadequate. Given the critical role of

community settings in identifying and preventing sarcopenia, early screening and intervention (2, 3) are imperative to mitigate adverse health outcomes (50). Health education serves as a fundamental approach for community-based chronic disease management, playing a crucial role in enhancing health knowledge, fostering attitude change, improving skills, and facilitating the modification of unhealthy behaviors (51). Community healthcare institutions should focus on factors that affect sarcopenia awareness among older adults and implement specific health education and interventions. This includes actively promoting core information about sarcopenia prevention, guiding older adults to identify risk factors early (11), and encouraging healthy lifestyle habits to reduce negative health outcomes and alleviate the burden on healthcare resources.

5 Limitations

This study had certain limitations in sample selection, as it only focused on older individuals from specific areas in Hangzhou. To address this, future research can conduct comprehensive surveys across multiple regions and centers. Additionally, some variables in this study were evaluated based on self-reported data provided by the participants. Furthermore, being a cross-sectional study, this research cannot establish a causal relationship between healthy lifestyles and sarcopenia awareness in older adults. Therefore, further longitudinal studies are necessary to explore and understand these relationships in greater depth.

6 Conclusion

The current sarcopenia awareness among older individuals in the community in Hangzhou city requires improvement. The cultivation of sarcopenia awareness among older adults is intricately linked to their individual psychological and behavioral lifestyle, family interpersonal networks, as well as their living and working environments, along with policy environments. To address this issue, it is recommended to implement community-based diversified health education programs and multi-channel screening activities in the future. These endeavors will effectively enhance sarcopenia awareness among older adults in the community, guiding them towards the adoption of healthy lifestyle habits and the prevention and delay of sarcopenia occurrence.

Ethics statement

The studies involving humans were approved by the Institutional Review Board of Hangzhou Normal University (Hangzhou, China, Approval No. 2022-1117). 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

DW: Conceptualization, Funding acquisition, Resources, Supervision, Writing – review & editing. HZ: Data curation, Investigation, Software, Writing – original draft. PW: Data curation, Investigation, Writing – original draft. YZ: Investigation, Software, Writing – original draft. HC: Investigation, Writing – original draft. FZ: Formal Analysis, Methodology, Writing – review & editing. SL: Conceptualization, Funding acquisition, Project administration, Writing – original draft.

Funding

The author(s) declare that financial support was received for the research, authorship, and/or publication of this article. The research was supported by the National Natural Science Foundation of China (Grant number, 72304080, 2023 and 72074066, 2020) and by the Health Commission of Zhejiang Province (Grant number 2024KY240, 2024).

Acknowledgments

The author sincerely thanks the Zhejiang Registered Dietitian Working Committee for its support of 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

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1391383/full#supplementary-material

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frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 02 October 2024
DOI 10.3389/fpubh.2024.1337979

OPEN ACCESS

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RECEIVED 14 November 2023
ACCEPTED 20 September 2024
PUBLISHED 02 October 2024

CITATION
Su S, Zhou Y, Wang K, Liu A, Lei L, Ma H and Yang Y (2024) Effects of household solid fuel use on sarcopenia in middle-aged and older adults: evidence from a nationwide cohort study.
Front. Public Health 12:1337979.
doi: 10.3389/fpubh.2024.1337979

Effects of household solid fuel use on sarcopenia in middle-aged and older adults: evidence from a nationwide cohort study

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Background: Household solid fuel use is common in global households and has been linked to changes in handgrip strength and muscle mass. However, whether household solid fuel use results in sarcopenia over time is not well elaborated.

Methods: This study employed data from the 2011–2015 China Health and Retirement Longitudinal Study (CHARLS) that recruited 4,932 participants ≥45 years. The Cox proportional hazards regression model was conducted to estimate the impact of household solid fuel use for cooking and heating on sarcopenia development. The analysis was further stratified based on geographic position. Mediation analysis was employed to estimate the potential mediating effects of cognitive function and depressive symptoms associated with household solid fuel use and sarcopenia.

Results: Over the 4-year follow-up, 476 cases of sarcopenia were reported (9.65%), with 254 in males (10.82%) and 222 in females (8.59%). Cooking and heating with solid fuels increased the risk of sarcopenia (Cooking: HR 1.401, 95% CI 1.138–1.724; Heating: HR 1.278, 95% CI 1.040–1.571). Crop residue/wood burning correlated with higher sarcopenia risk (Cooking: 1.420, 95% CI 1.147–1.758; Heating: 1.318, 95% CI 1.062–1.635). Switching to clean cooking fuels significantly reduced sarcopenia risk (HR 0.766, 95% CI 0.599–0.979). Heating with solid fuels was associated with higher sarcopenia risk only in southern China (HR 1.375, 95% CI 1.102–1.715). Additionally, cognitive function and depressive symptoms partially mediated the link between household solid fuel use and sarcopenia.

Conclusion: Household use of solid fuels is associated with an increased risk of sarcopenia. Restricting the use of solid fuels and focusing on cognitive function and depressive symptoms in solid fuel users can help decrease sarcopenia development.

KEYWORDS

sarcopenia, solid fuel use, indoor air pollution, cohort study, CHARLS

1 Introduction

Sarcopenia is a degenerative condition associated with aging in which skeletal muscle is progressively reduced in size, strength, and function (1, 2). As the global population ages, sarcopenia has become an increasingly pressing public health problem, especially in developing countries (3, 4). The approximate worldwide prevalence of sarcopenia among individuals over the age of 60 is 10% (5). Research has shown that skeletal muscle mass decreases by roughly 8% per decade beginning at the age of 40, with an accelerated decline observed among older individuals. After the age of 70, the decline rate further increases to 10–15% per decade (6). Notably, sarcopenia significantly increases the risk of adverse health consequences including falls, functional deterioration, frailty, and even mortality (1). Therefore, identifying contributing factors and implementing effective preventive measures for sarcopenia are vital concerns in public health.

The underlying mechanisms of sarcopenia are multifaceted, and in addition to established risk factors such as malnutrition, sedentary lifestyle, chronic diseases, and iatrogenic factors (1), recent studies have also revealed correlations between air pollutants and alterations in sarcopenia components (7–10). Previous evidence has demonstrated that exposure to air pollution can induce oxidative stress and inflammation (11), both of which have been identified as contributing factors to sarcopenia (12, 13). Indoor air pollution, resulting mainly from the burning of solid fuels in homes, is identified as one of the top 10 major risk factors for the global disease burden (14, 15). The burning of household solid fuels can generate harmful pollutants like particulate matter, nitrogen oxide, and sulfur oxides (16–18). Nearly 2.4 billion individuals depend on solid fuels to cook and/or heat, and indoor air pollution causes an estimated 3.2 million premature deaths annually (19). In a survey of 512,891 adults in 10 regions of China, a majority (52.1%) indicated the utilization of solid fuels for cooking or heating purposes, especially among rural residents (20). Numerous studies have demonstrated an association between exposure to indoor air pollution from the combustion of solid fuels and an increased risk of various health issues including arthritis (21), ischemic heart disease (22), depression (23), and cognitive decline (24, 25).

People spend the vast majority of their time indoors (88.9%), most of which is spent at home (26). Older adults tend to spend more time indoors (27), and their decline in overall physical health makes them more vulnerable to chronic health conditions and the negative effects of indoor air pollution (28). China, with the largest population of older adults (29), is experiencing an increasing burden of sarcopenia due to the rapidly aging demographic. To date, there is a lack of comprehensive longitudinal studies investigating the relationship between household solid fuel use and sarcopenia. Existing studies have ignored the large differences in fuel use between northern and southern China, as well as the potential influence of cognitive and psychological changes on the onset of sarcopenia.

In this study, we utilized a follow-up survey that included a nationally representative sample of Chinese adults aged 45 and above. The aim was to explore the association between household solid fuel use and sarcopenia, and to analyze the potential mediating effects of cognitive function and depressive symptoms within this association. The findings from this research will provide valuable evidence on the factors contributing to sarcopenia and support policy initiatives aimed at promoting the transition from inefficient and polluting solid fuels to cleaner alternatives. Additionally, addressing modifiable risk factors like cognitive decline and mental health concerns could help mitigate the burden of sarcopenia.

2 Methods

2.1 Data and sample

This study utilized follow-up data obtained from the China Health and Retirement Longitudinal Study (CHARLS). The CHARLS is a high-quality, nationally representative survey of Chinese individuals aged 45 and above. The individuals were recruited using a multistage probability sampling method in 28 provinces across China (30). After the 2011 baseline survey, follow-up surveys were performed every 2–3 years. Informed written consent was obtained from all subjects before participation, and the study gained ethical approval (approval numbers: IRB00001052-11015).

There were 17,708 participants successfully enrolled in 2011. As information about physical examination was not provided in 2018, the first three waves (from 2011 to 2015) were selected for our study. We excluded 4,654 individuals due to missing information on sarcopenia at baseline. Our sample was restricted to adults aged 45 years and older, with 268 participants excluded for not meeting the age criteria. We also excluded observations with missing values on household fuel use ($n = 1{,}100$), and covariates or mediators ($n = 1{,}296$). Additionally, we excluded participants with sarcopenia at baseline ($n = 1{,}635$) or incomplete sarcopenia information in the follow-up surveys ($n = 321$), as well as those lost to follow-up ($n = 3{,}522$). Finally, our longitudinal study enrolled a total of 4,932 participants. Figure 1 provides an illustrated depiction of the comprehensive selection process followed for enrolling these participants.

2.2 Assessment of household solid fuel use

Household solid fuel use for cooking and heating was collected through a self-reported survey. Respondents were required to report their main fuel source for cooking and heating. Solid fuels were classified as crop residue/wood burning or coal, while clean fuels encompassed natural gas, marsh gas, liquefied petroleum gas, electricity, solar energy, or other sources (21, 23). Notably, we restricted our assessment of the impact of fuel switching on sarcopenia risk to cooking fuels data only, due to the substantial amount of missing data on heating fuels in 2015. Fuel switching was defined as participants who transitioned from one fuel type to another. For instance, those who utilized solid fuels for cooking at baseline but transitioned to clean fuels during follow-up were classified as having switched from solid fuel to clean fuel.

2.3 Assessment of sarcopenia

The assessment of sarcopenia followed the criteria outlined by the 2019 Asian Working Group for Sarcopenia (AWGS 2019) (31). The criteria involved evaluating three key factors: muscle strength, muscle mass, and physical performance. Sarcopenia is determined when there

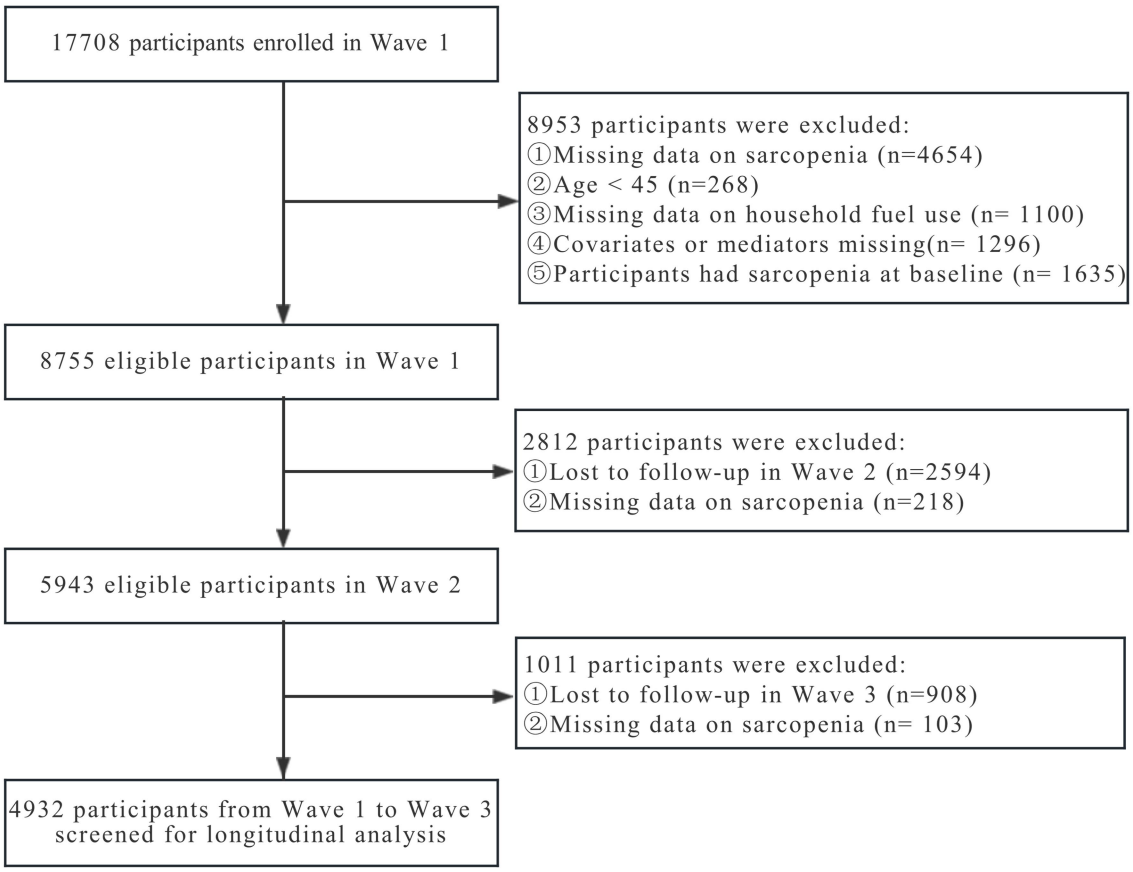

FIGURE 1
Flowchart of sample screened in the study.

is a combination of low muscle mass along with either low muscle strength or low physical performance.

2.3.1 Muscle strength

The study utilized grip strength measurements for determining overall muscle strength. Each participant's maximum values for both left and right hands were tested twice, and the resulting values were averaged. In cases where a hand could not measure grip strength due to health reasons, the measurement from the other hand was considered. Insufficient grip strength was defined as <18 kg in females and < 28 kg in males (31).

2.3.2 Muscle mass

The muscle mass was evaluated from appendicular skeletal muscle mass (ASM) using an anthropometric equation (32):

$$\begin{aligned}\text{ASM} = {} & 0.193 \times \text{body weight} + 0.107 \times \text{height} \\ & - 4.157 \times \text{gender} - 0.037 \times \text{age} - 2.631\end{aligned}$$

In this equation, body weight was measured in kilograms, height in centimeters, age in years, and gender was coded as 1 for male and 2 for female. ASM/Ht^2, which represents muscle mass adjusted for height, was obtained by dividing ASM by the square of height measured in centimeters. Low muscle mass was determined based on previous studies as ASM/Ht^2 values below the 20th percentile (33, 34). In the study, the thresholds indicating low muscle mass were < 5.29 kg/m^2 for females and < 7.01 kg/m^2 for males.

2.3.3 Physical performance

The physical performance of the participants was evaluated using the gait speed test and the five-time chair stand test. The gait speed test measured the participants' normal walking speed (m/s) over a 2.5-m distance, performed both forward and backward. The analysis was conducted using the average of the two records. The five-time chair stand test evaluated the participants' ability to stand and sit five consecutive times, with arms folded. Participants unable to complete the test were classified as having low physical performance. Low physical performance was determined as a gait speed less than 1.0 m/s or a five-time stand chair test lasting 12 s or longer (31).

2.4 Covariates and mediators

Based on previous studies, we selected potential covariates associated with household solid fuel use and sarcopenia, which have been categorized into two groups: sociodemographic variables and health-related factors. Sociodemographic variables included age (<60 or ≥ 60), gender (male or female), marital status (married/cohabited or others), residential area (rural or urban), geographic

position (north or south), education level (illiterate, primary school or below, middle school, or high school or above), and economic situation (good, fair, or poor). Health-related factors included smoking status (no or yes), drinking status (no or yes), and number of chronic diseases (0, 1, or ≥ 2). Additionally, we included baseline cognitive function and depressive symptoms as possible mediators in the mediation analysis.

In our study, the geographic position was determined using the Qinling-Huaihe line in China (35). The self-reported family economic situation was categorized into three groups: "very high" and "relatively high" were grouped as "good," "average" was classified as "fair," and "relatively poor" and "poor" were grouped as "poor" (36). The assessment of cognitive function involved measuring intelligence and episodic memory using a scoring system ranging from 0 to 31. A higher score on this assessment demonstrates better cognitive function (24, 25). The score for the assessment of depressive symptoms ranges from 0 to 30, with higher scores reflecting a greater presence of depressive symptoms (23).

2.5 Statistical analysis

In this study, means ± standard deviations (SDs) were used to present continuous variables, while categorical variables were reported as numbers (percentages). To analyze the differences in characteristics between different types of household solid fuel used for cooking and heating at baseline, *t*-tests were conducted for continuous data, and Chi-square tests were employed for categorical data.

To examine the association between household solid fuel use and sarcopenia, Cox proportional hazards regression models were utilized. We performed a stratified analysis based on geographic position, considering that northern China is classified as a central heating area during winter (37, 38). The results were presented as hazard ratios (HR) along with their corresponding 95% confidence intervals (CI). The endpoint of this study was the occurrence of sarcopenia, and the time scale used ranged from 0 to 4 (0, 2, and 4). Furthermore, we included cognitive function and depressive symptoms as potential mediators in the mediation analyses. These analyses were conducted using functions implemented in the R package "mediation" and employed the nonparametric bootstrap method simulation approach with 5,000 iterations.

The following variables were adjusted in all models to control for potential confounding factors: sociodemographic variables (age, gender, marital status, residential area, geographic position, education level, and economic situation) and health-related factors (smoking status, drinking status, and number of chronic diseases). All statistical analyses were performed utilizing Stata 17 and R 4.3.1 software. A significance level of $p < 0.05$ (two-tailed) was applied to determine statistical significance.

3 Results

3.1 Basic characteristics of the selected participants

There were 4,932 participants involved in this study, 52.41% of whom were females and 37.49% were aged 60 years or above. At baseline, 60.69 and 60.28% of individuals reported primary use of solid fuels for cooking and heating respectively, while 39.31 and 39.72% used clean fuels for cooking and heating, respectively. Participants who used solid fuels as their main energy for cooking/heating were more likely to live in rural regions and northern China, possess lower educational attainment, report worse economic status, do not smoke, and exhibit a higher burden of chronic disease. Additionally, those using solid cooking fuel attained lower scores on cognitive function and reported more depression symptoms. Additionally, we observed no significant differences in household fuel use types relative to gender, marital status, or drinking status (Table 1).

3.2 Association between household solid fuel use and sarcopenia

There were 297 (6.02%) new occurrences of sarcopenia in 2013, 179 (3.63%) in 2015, and a total of 476 (9.65%) incident cases of sarcopenia overall, with 254 (10.82%) occurring in males and 222 (8.59%) in females. Moreover, individuals who developed sarcopenia tended to be older, male, reside in southern regions or rural areas, smoke, exhibit a lower education level, lower cognitive function, and more depressive symptoms (Supplementary Table S1). During the 19,134 person-years of follow-up, the incidence rate of sarcopenia was higher among individuals who utilized solid fuels for cooking or heating compared to those who used clean fuels (Cooking: 28.85 vs. 18.84 per 1,000 person-years; Heating: 24.97 vs. 24.73 per 1,000 person-years). In the unadjusted model (model 1), the occurrence of sarcopenia was associated with the primary use of solid fuels for cooking, whereas heating demonstrated no association. However, after sociodemographic and health-related factors were taken into account (model 3), both the consumption of solid fuels for cooking (HR: 1.401; 95% CI: 1.138–1.724) and heating (HR: 1.278; 95% CI: 1.040–1.571) were found to be linked to an increased risk of developing sarcopenia (Table 2; Supplementary Figure S2). Different types of solid fuel use can also impact the development of sarcopenia. Participants who used crop residues or wood for cooking (HR: 1.420; 95% CI: 1.147–1.758) and heating (HR: 1.318; 95% CI: 1.062–1.635) had a significantly higher risk of developing sarcopenia than those who used coal (Table 2).

Among the participants surveyed at baseline, 1,939 used clean fuels and 2,993 used solid fuels to cook. In the subsequent follow-up, 303 individuals transitioned from clean to solid fuels, whereas 955 participants made the switch from solid to clean fuels (Supplementary Table S2). Participants with a persistent reliance on solid fuels for cooking displayed the highest incidence rate of sarcopenia, recording a rate of 30.98 per 1,000 person-years. Conversely, participants who consistently used clean fuels exhibited the lowest incidence rate at 17.77 per 1,000 person-years. After adjustment for all covariates, the final model (Model 3) revealed that transitioning from the persistent use of solid fuels for cooking to clean fuels decreased the risk of sarcopenia (HR: 0.766; 95% CI: 0.599–0.979). Conversely, transitioning from the persistent use of clean fuels to solid fuels potentially increased the risk of sarcopenia (HR: 1.367; 95% CI: 0.900–2.075), despite no statistical significance (Table 2).

TABLE 1 Baseline characteristics of enrolled participants.

Characteristics	Cooking fuels		*p*	Heating fuels		*p*
	Clean	Solid		Clean	Solid	
N	1,939 (39.31)	2,993 (60.69)		1,959 (39.72)	2,973 (60.28)	
Age			0.001			0.268
<60	1,265 (65.24)	1,818 (60.74)		1,243 (63.45)	1,840 (61.89)	
≥60	674 (34.76)	1,175 (39.26)		716 (36.55)	1,133 (38.11)	
Gender			0.874			0.476
Male	920 (47.45)	1,427 (47.68)		920 (46.96)	1,427 (48.00)	
Female	1,019 (52.55)	1,566 (52.32)		1,039 (53.04)	1,546 (52.00)	
Marital status			0.177			0.007
Married/Cohabited	1,752 (90.36)	2,738 (91.48)		1,757 (89.69)	2,733 (91.93)	
Others	187 (9.64)	255 (8.52)		202 (10.31)	240 (8.07)	
Residential area			<0.001			<0.001
Rural	1,416 (73.03)	2,842 (94.95)		1,522 (77.69)	2,736 (92.03)	
Urban	523 (26.97)	151 (5.05)		437 (22.31)	237 (7.97)	
Geographic position			<0.001			<0.001
North	668 (34.45)	1,564 (52.26)		289 (14.75)	1,943 (65.35)	
South	1,271 (65.55)	1,429 (47.74)		1,670 (85.25)	1,030 (34.65)	
Education level			<0.001			0.006
Illiterate	352 (18.15)	878 (29.34)		449 (22.92)	781 (26.27)	
Primary school or below	843 (43.48)	1,318 (44.04)		853 (43.54)	1,308 (44.00)	
Middle school	481 (24.81)	597 (19.95)		448 (22.87)	630 (21.19)	
High school or above	263 (13.56)	200 (6.68)		209 (10.67)	254 (8.54)	
Economic situation			<0.001			0.003
Good	59 (3.04)	60 (2.00)		60 (3.06)	59 (1.98)	
Fair	1,123 (57.92)	1,567 (52.36)		1,101 (56.20)	1,589 (53.45)	
Poor	757 (39.04)	1,366 (45.64)		798 (40.74)	1,325 (44.57)	
Smoking status			0.033			0.003
No	1,223 (63.07)	1,797 (60.04)		1,249 (63.76)	1,771 (59.57)	
Yes	716 (36.93)	1,196 (39.96)		710 (36.24)	1,202 (40.43)	
Drinking status			0.193			0.823

(Continued)

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TABLE 1 (Continued)

Characteristics	Cooking fuels		p	Heating fuels		p
	Clean	Solid		Clean	Solid	
No	1,274 (65.70)	2,020 (67.49)		1,312 (66.97)	1,982 (66.67)	
Yes	665 (34.30)	973 (32.51)		647 (33.03)	991 (33.33)	
Number of chronic diseases			0.005			0.012
0	672 (34.66)	983 (32.84)		660 (33.69)	995 (33.47)	
1	620 (31.98)	877 (29.30)		635 (32.41)	862 (28.99)	
≥2	647 (33.37)	1,133 (37.85)		664 (33.89)	1,116 (37.54)	
Cognitive function	15.52 ± 5.00	14.00 ± 5.04	<0.001	14.95 ± 5.15	14.36 ± 5.02	<0.001
Depressive symptoms	6.98 ± 5.54	8.85 ± 6.45	<0.001	14.95 ± 5.16	8.68 ± 6.35	<0.001
Handgrip strength (kg)	32.72 ± 9.58	31.98 ± 11.23	0.017	32.41 ± 9.31	32.18 ± 11.40	0.464
Gait speed (m/s)	0.80 ± 2.80	0.75 ± 2.38	0.692	0.79 ± 2.71	0.75 ± 2.42	0.751
5-time chair stand test (s)	9.86 ± 3.61	10.68 ± 3.86	<0.001	9.85 ± 3.56	10.70 ± 3.89	<0.001
ASM/Ht^2 (kg/m^2)	6.97 ± 1.02	6.90 ± 1.02	0.036	6.90 ± 1.03	6.95 ± 1.02	0.080

Values were means ± SD or *n* (percentages). Due to rounding, polytomous variable values may not add up to 100%. *p* values were calculated using analysis of *t*-test and Chi-square test for continuous and categorical variables, respectively.

3.3 Stratified analyses between household solid fuel use and sarcopenia

We performed stratified analyses based on geographic position. After adjusting for all covariates, our findings revealed significant associations between cooking with solid fuels and a higher risk of sarcopenia, irrespective of whether in the northern (HR: 1.646; 95% CI: 1.042–2.601) or southern (HR: 1.348; 95% CI: 1.065–1.707) regions. Notably, in the southern region, the use of solid fuels for heating was significantly associated with a higher risk of sarcopenia (HR: 1.375; 95% CI: 1.102–1.715), whereas no significant difference was observed in northern China (HR: 0.900; 95% CI: 0.537–1.506) (Table 3).

3.4 Mediation analyses between household solid fuel use and sarcopenia

In the mediation analyses, it was found that cognitive function and depressive symptoms played a partial mediating role in the association between household solid fuel use (including cooking and heating) and sarcopenia. Specifically, cognitive function mediated 5.31% ($p = 0.002$) of the effect of cooking solid fuels on sarcopenia and 5.87% ($p = 0.031$) of the effect of heating solid fuels on sarcopenia. Depressive symptoms, on the other hand, had a greater proportion of the mediation effects. For cooking solid fuels, depressive symptoms mediated 9.86% ($p = 0.003$) of the effect on sarcopenia, and for heating solid fuels, depressive symptoms mediated 15.03% ($p = 0.020$) of the effect on sarcopenia (Figure 2).

4 Discussion

In this population-based cohort study of Chinese individuals aged over 45 years, we identified a significant association between the use of solid fuels in households and an elevated risk of sarcopenia. Notably, the transition from solid fuels to clean fuels for cooking demonstrated a substantial impact on reducing the incidence rate of sarcopenia. Furthermore, the association between sarcopenia and household solid fuel use for heating was observed exclusively in southern China, likely due to regional variations in heating patterns. Additionally, cognitive function and depressive symptoms partially mediated the relationship between household solid fuel use and sarcopenia. These findings offer a unique environmental perspective that can inform public health authorities in their efforts to prevent and manage sarcopenia.

One important finding of our study indicated that the use of solid fuels for household cooking and heating increases the risk of sarcopenia, with potentially greater severity observed in the context of cooking with solid fuels. Our study is in accordance with these previous studies that have also highlighted the association between physical health issues and indoor air pollution (15, 21, 22, 36). Existing research has also suggested that exposure to ambient air pollution may contribute to a higher risk of sarcopenia and its associated components (7, 10, 39). The patterns and frequencies of solid fuel exposure differ significantly when households are engaged in cooking and heating activities (40, 41). Cooking represents an integral part of daily human life, leading to lifelong exposure, whereas combustion of solid fuels for heating occurs only in specific

TABLE 2 Incidence rates and hazard ratios with sarcopenia by household fuel types according to cooking and heating.

Exposure	Events	Incidence rate per 1,000 person-years	HR (95% CI)		
			Model 1	Model 2	Model 3
Cooking					
Household fuel use					
Clean fuel	143	18.84	Reference	Reference	Reference
Solid fuel	333	28.85	1.527 (1.255, 1.857)	1.400 (1.138, 1.722)	1.401 (1.138, 1.724)
Types of household fuel use					
Clean fuel	143	18.84	Reference	Reference	Reference
Coal	52	20.05	1.064 (0.774, 1.461)	1.303 (0.937, 1.812)	1.286 (0.925, 1.788)
Crop residue/Wood	281	31.40	1.660 (1.357, 2.031)	1.420 (1.147, 1.758)	1.425 (1.151, 1.765)
Heating					
Household fuel use					
Clean fuel	188	24.73	Reference	Reference	Reference
Solid fuel	288	24.97	1.010 (0.840, 1.213)	1.260 (1.026, 1.548)	1.278 (1.040, 1.571)
Types of household fuel use					
Clean fuel	188	24.73	Reference	Reference	Reference
Coal	111	17.79	0.720 (0.570, 0.911)	1.116 (0.840, 1.482)	1.133 (0.852, 1.505)
Crop residue/Wood	177	33.45	1.350 (1.099, 1.657)	1.318 (1.062, 1.635)	1.336 (1.076, 1.659)
Transition of cooking fuel					
Persistent clean fuel	114	17.77	Reference	Reference	Reference
Change from clean to solid	29	24.62	1.380 (0.920, 2.080)	1.414 (0.933, 2.143)	1.367 (0.900, 2.075)
Persistent solid fuel	243	30.98	Reference	Reference	Reference
Change from solid to clean	90	24.34	0.790 (0.620, 1.000)	0.772 (0.604, 0.987)	0.766 (0.599, 0.979)

HR, Hazard ratio; CI, Confidence interval. Model 1 was conducted without any adjustment; Model 2 was adjusted for the sociodemographic variables (age, gender, marital status, residential area, geographic position, educational level, and economic situation); Model 3 was further adjusted for health-related factors (smoking status, drinking status, and number of chronic diseases).

TABLE 3 Hazard ratios with sarcopenia by household fuel exposure stratified by geographic position at baseline.

Model	Geographic position	Cooking with solid fuel[a]		Heating with solid fuel[b]	
		HR (95% CI)	*p*	HR (95% CI)	*p*
Model 1	North	2.100 (1.353, 3.257)	0.001	1.088 (0.656, 1.807)	0.743
	South	1.647 (1.317, 2.060)	<0.001	1.578 (1.274, 1.955)	<0.001
Model 2	North	1.649 (1.044, 2.605)	0.032	0.892 (0.533, 1.490)	0.662
	South	1.340 (1.059, 1.696)	0.015	1.353 (1.085, 1.687)	0.007
Model 3	North	1.646 (1.042, 2.601)	0.033	0.900 (0.537, 1.506)	0.688
	South	1.348 (1.065, 1.707)	0.013	1.375 (1.102, 1.715)	0.005

[a]Reference group was cooking with clean fuel.
[b]Reference group was heating with clean fuel.
HR, Hazard ratio; CI, Confidence interval. Model 1 was performed without any adjustment; Model 2 was adjusted for the sociodemographic variables (age, gender, marital status, residential area, educational level, and economic situation); Model 3 was further adjusted for health-related factors (smoking status, drinking status, and number of chronic diseases).

circumstances, such as cold winters. Therefore, the regular use of solid fuels for cooking results in prolonged exposure to indoor pollution for household members, thereby increasing the susceptibility to sarcopenia. Over a 4-year follow-up period, we analyzed the occurrence of sarcopenia among participants who switched cooking fuels. The results revealed a significant reduction in the risk of sarcopenia when transitioning from solid to clean fuels. This finding is consistent with similar studies (25, 42). Conversely, transitioning from clean to solid fuels appears to increase the risk of sarcopenia, although there is no statistical significance. Possible reasons include the limited sample size of participants switching from clean to solid fuels and the fact that the

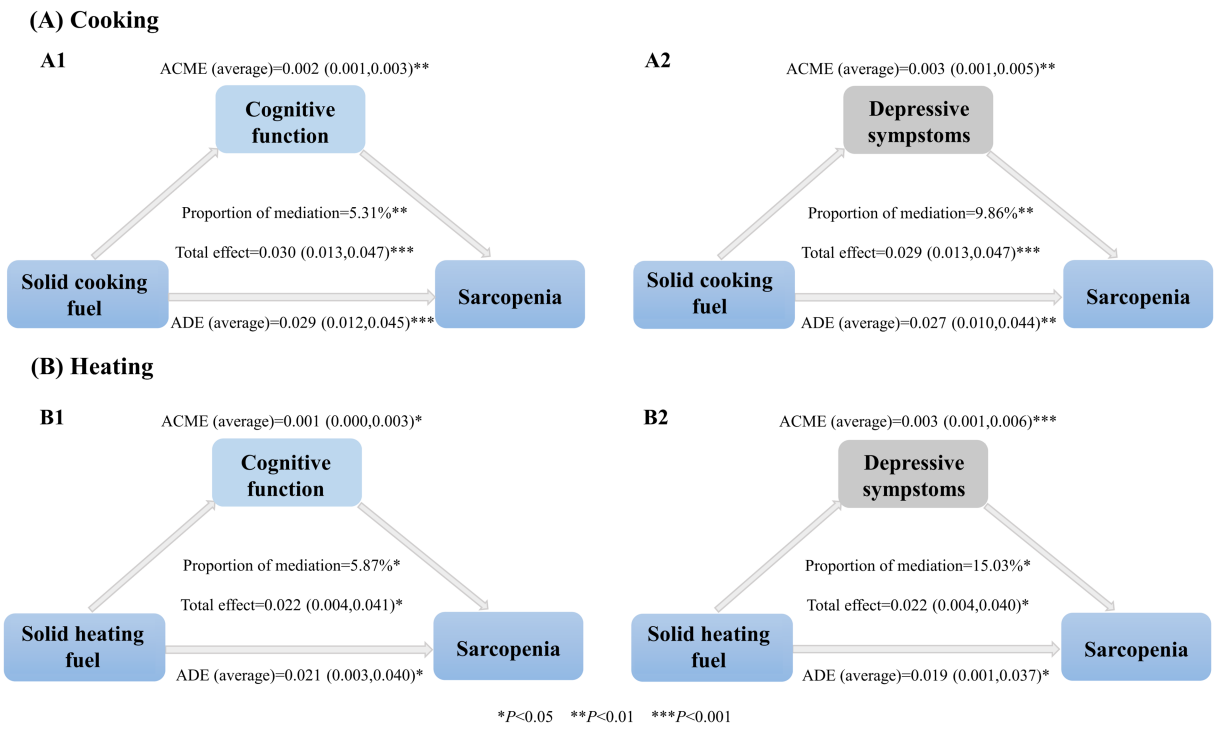

FIGURE 2
Association between household solid fuel use, mediation variables, and sarcopenia. ACME, The average causal mediation effect; ADE, The average direct effect. Proportion of mediation = ACME (average)/Total effect. ACME represents the effect of household solid fuel use on sarcopenia through mediators. ADE refers to the direct effect of household solid fuel use on sarcopenia. All mediation models were adjusted by sociodemographic variables (age, gender, marital status, residential area, geographic position, educational level, and economic situation) and health-related factors (smoking status, drinking status, and number of chronic diseases).

impact of air pollution on the body is a chronic and progressive process that manifests long-term health effects (43), a 4-year follow-up period may not be enough to observe a sufficient number of outcome events. In China, the Qinling-Huaihe Line divides the country into northern and southern regions (35, 37), the longer and colder winters in the northern region have led to the widespread adoption of centralized heating patterns, while traditional heating methods are still predominantly used in the southern region (37, 38). For most households in the northern region, indoor air pollution resulting from heating with solid fuels appears to be comparatively lower compared to the southern region, which potentially elucidates the association between the use of solid fuels for heating and the risk of sarcopenia that exists only in southern China. Our study findings highlight the effectiveness of promoting the use of clean fuels and adopting scientifically sound heating methods as an approach to reduce the occurrence of sarcopenia.

Another significant result from our analysis was the partial mediating effect of cognitive function and depressive symptoms in the association between household solid fuel use and sarcopenia. To our knowledge, few studies have examined the mediating role of cognitive functioning and depressive symptoms between household solid fuel use and sarcopenia. Previous research has shown that the burning of solid fuels is linked to decreased cognitive function (25) and increased depressive symptoms (23). A meta-analysis has identified depression and cognitive impairment as significant risk factors for sarcopenia (44). Depression may contribute to the occurrence of sarcopenia through reduced physical activity, upregulation of inflammatory cytokines, and dysregulation of the hypothalamic–pituitary–adrenal axis (45, 46). Sarcopenia and cognitive decline share common pathophysiological pathways, including oxidative stress and chronic inflammation (47). Impaired cognitive function can lead to decreased physical activity and reduced dietary intake, thereby accelerating the development of sarcopenia (33). Furthermore, a study conducted in China suggested that cognitive decline could serve as an early sensitive marker for gait speed, with poor baseline cognitive function predicting subsequent declines in gait speed after 4 years (48). Our findings present a novel perspective for preventing the occurrence of sarcopenia among long-term household solid fuel users by focusing on modifiable risk factors such as cognitive function and mental health, and implementing proactive measures to reduce the risk of sarcopenia to some extent. Nevertheless, the relationship between sarcopenia and depressive symptoms remains uncertain and may be bidirectional. Some studies suggest that sarcopenia may lead to depression (49, 50), while others propose that depression contributes to sarcopenia through behavioral and physiological changes (44, 45). Therefore, further studies are needed to clarify the causal pathways linking sarcopenia, cognitive function, and depressive symptoms, particularly in the context of long-term solid fuel use. Elucidating these mechanisms will be critical for developing effective interventions to mitigate the risk of sarcopenia.

The precise biological mechanisms underlying the link between indoor air pollution from solid fuel use and sarcopenia remain inadequately understood. Existing studies provide some clues: (1)

Air pollution has the potential to induce oxidative stress and mitochondrial dysfunction (11, 51), which can subsequently affect muscle function (4, 13); (2) Exposure to different air pollutants increases the production of pro-inflammatory mediators (52), potentially leading to muscle loss, decreased muscle mass, and reduced strength (12, 53); (3) Exposure to air pollution has been associated with modifications in DNA methylation patterns across an individual's lifespan (54). These alterations in the epigenetic regulation of genes have the potential to contribute to the development of impaired muscle function during later stages of life (55); and (4) Exposure to air pollution has been linked to a higher risk of insulin resistance (56), which is considered a contributing factor to the development of sarcopenia (13).

Cooking and heating with solid fuels are widely acknowledged as the primary contributors to indoor air pollution in developing countries. In this study, we found that participants who used solid fuels for cooking/heating were more prone to live in rural and northern China, and were associated with lower levels of education and poorer economic conditions. Previous studies have indicated that low income influences household fuel choices, with higher-income individuals being more inclined toward cleaner fuel options, while lower-income individuals are more likely to rely on solid fuels for cooking and heating purposes (57, 58). Furthermore, fuel choices differ due to various factors, including household size and composition, cooking and heating practices, geographical location, and the level of urbanization (57). Our study also found that for different types of solid fuels, burning traditional biomass fuels (e.g., crop residue/wood) was more harmful to sarcopenia than other fuels. This indicates the need for solid fuel users to switch from solid fuels to cleaner fuels. The utilization of polluting fuels necessitates extensive time investment in fuel collection and preparation, as well as the use of inefficient cooking devices. Without proactive policy actions, it is anticipated that by the year 2030, around 2.1 billion individuals will continue to lack access to clean fuels and technologies (19). Similarly, China faces a substantial public health risk due to the pollution caused by indoor solid fuel usage. Solid fuels are commonly used for cooking and heating purposes in rural Chinese households, particularly in western provinces such as Tibet, Qinghai, and Ningxia, where approximately 95% of rural families depend on traditional solid fuels for heating (59). Given these considerations, it is crucial to prioritize actions aimed at reducing the dependence on solid fuels, enhancing energy infrastructure, expanding access to clean energy sources, and implementing effective renewable energy policies. This is especially critical in economically underdeveloped rural areas.

This study makes several notable strengths in this field. Firstly, it utilizes a nationally representative prospective cohort dataset in China, enhancing the findings' reliability and generalizability. Secondly, multiple measurements of cooking fuel types were conducted to evaluate the effects of fuel transition on the risk of sarcopenia. Thirdly, the study compares the disparities in sarcopenia risk associated with cooking and heating fuel usage between the northern and southern regions of China. Furthermore, potential mediating factors were assessed, further supporting research on the underlying mechanisms. These findings provide robust evidence that supports the promotion of clean fuel policies. The findings underscore the significance of implementing clean fuel policies in safeguarding public health and reducing the prevalence of sarcopenia. However, this study has some limitations: (1) Rather than directly measuring indoor environmental pollutant concentrations, we relied on proxy variables by using self-reported primary fuel types for cooking and heating. This approach may introduce measurement errors and imprecision. (2) Due to the limitations of the CHARLS, recommended methods, such as dual-energy X-ray absorptiometry (DXA) or bioelectrical impedance analysis (BIA) (31), were not employed for estimating muscle mass. Nevertheless, a validated anthropometric equation specific to the Chinese population was utilized (32). (3) The study period was limited to 4 years, which may restrict the comprehensive assessment of alterations in muscle mass and function attributed to the use of household solid fuel. (4) Despite considering a relatively extensive range of confounding factors, residual confounding from variables like protein intake and physical activity may still have an impact due to insufficient or missing data in CHARLS. Future studies should employ longer-term and more comprehensive cohort designs to elucidate the mechanistic role of household consumption of solid fuel in the development of sarcopenia. Furthermore, there is an urgent imperative to conduct direct quantitative analyses to explore the association between various types of indoor air pollutants and the occurrence of sarcopenia.

5 Conclusion

In conclusion, our findings indicate an association between the use of household solid fuel and an increased risk of sarcopenia. Cognitive function and depressive symptoms may partially mediate this association. This suggests that mitigating the burden of sarcopenia can be achieved through modifiable risk factors, including the prevention of cognitive decline and addressing mental health concerns. Switching fuels from solid to clean has the potential to reduce the incidence of sarcopenia, underscoring the importance of promoting and disseminating the use of clean household fuels worldwide to promote health. Moving forward, research aimed at developing evidence-based policy recommendations to facilitate the adoption of clean fuels will be vital in reducing the health risks associated with household solid fuel use. Given the widespread use of solid fuels, our study makes substantial contributions to informing future policy and program development in the field of public health. These endeavors possess the potential to alleviate the detrimental consequences of indoor air pollution, improve physical and mental well-being, and mitigate associated health burdens both domestically and globally.

Data availability statement

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

Ethics statement

The studies involving humans were approved by Institutional Review Board at Peking University. 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. Written informed consent was obtained from

the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

SS: Conceptualization, Methodology, Software, Writing – original draft. YZ: Methodology, Software, Writing – review & editing. KW: Data curation, Writing – review & editing. AL: Writing – review & editing. LL: Writing – review & editing. HM: Writing – review & editing. YY: Conceptualization, Funding acquisition, Supervision, Writing – review & editing.

Funding

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

Acknowledgments

We sincerely acknowledge those who participated in the China Health and Retirement Longitudinal Study (CHARLS).

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 handling editor XL declared a shared affiliation with the authors at the time of review.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1337979/full#supplementary-material

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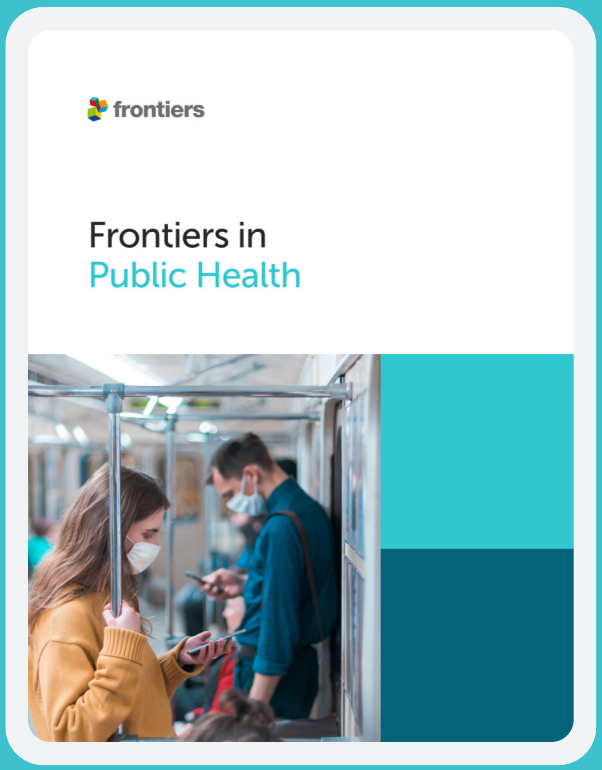

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