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Association of nut consumption and sarcopenia in Chinese older adults

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Sarcopenia emerges as a predominant health concern among the older adults, it makes the identification of relational factors crucial. Nut, a universally consumed dietary component, is posited to confer benefits to the musculoskeletal system. This study aimed to elucidate the association between nut consumption and sarcopenia in Chinese older adults. Data concerning nut consumption and sarcopenia were sourced from the 2018 wave of the Chinese Longitudinal Healthy Longevity Survey (CLHLS). The analysis incorporated 14,281 participants furnishing valid responses. This research employed logistic regression to investigate the association between nut consumption and sarcopenia. A total of 14,181 older adults (mean age = 84.86 ± 11.47 years and 55.08% were female) were included in this study. This study found an inverse association between nut consumption and sarcopenia in Chinese older adults, with higher nut consumption associated with a lower prevalence of sarcopenia, even after controlling for confounders. Compared with the nut consumption group of occasionally/rarely or never, the adjusted ORs of sarcopenia for at least once per month, at least once per week, and almost every day were 0.78 (95% CI: 0.66, 0.91), 0.81 (95% CI: 0.69, 0.95), and 0.62 (95% CI: 0.51, 0.77), respectively. Moreover, the result also displayed there is a significant interaction of nut consumption with gender (P-value = 0.016). This study identified an inverse association between nut consumption and sarcopenia. Introducing nut into the dietary regimen might present an accessible approach to bolster musculoskeletal health among the older adults.

Keywords Nut, Sarcopenia, Older adults, China, Chinese

With the increase in the proportion of older adults and the improvement of people's living standards, the expectation of healthy aging increases accordingly[1]. Given that China hosts the largest aging demographic in world, it inevitably amplifies concerns the health of older adults[2]. Sarcopenia, typified by the depletion of skeletal muscle mass, diminished muscle strength, and/or reduced physical performance, is occurred with advancing age and has become increasingly prevalent[3–5]. It represents a pressing public health challenge in today's aging societies[6].

Emerging evidence increasingly suggests that sarcopenia holds a strong association with diverse adverse outcomes such as falls, functional impairment, frailty, and mortality[7,8]. An epidemiological investigation from Asian nations, utilizing the Asian Working Group for Sarcopenia 2014 criteria, has reported sarcopenia prevalence rates ranging between 5.5% and 25.7% among different Asian countries[4]. Hence, it is more and more vital to comprehend and related factors of sarcopenia in China. Identifying the relational factors that associate with the incidence of sarcopenia can lead to marked improvements in the health and living standards of the older adults.

The factors associate with sarcopenia are multifaceted. Research has indicated that aging, suboptimal nutritional status, smoking, and a decreased BMI are among the risk factors for its onset[9,10]. Furthermore, numerous studies have substantiated the association between sarcopenia and diet[11]. Similarly, Berrazaga et al.

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noted that protein is positively related to sarcopenia[12]. A study by Remelli et al. also found that lack of vitamin D in older adults can greatly increase the risk of sarcopenia[13]. There was evidence to suggest that nut was rich in protein, fatty acid, fiber, vitamins, minerals, phytosterols and phenolics[14]. Nevertheless, in previous studies, the association between nut consumption and sarcopenia has not been specifically examined.

Consequently, we employed the 2018 dataset from the Chinese Longitudinal Healthy Longevity Survey (CLHLS) to investigate the association between nut consumption and sarcopenia.

Methods

Study population

The CLHLS is a nationwide, community-based study designed to examine the health status and factors affecting longevity among Chines older adults (The data from CLHLS survey already obtained the ethical approval and informed consent, and was approved by research ethics committees of Peking University (IRB00001052-13074). Each participant signed an informed consent form and all methods in our study were performed in accordance with the guidelines and regulations of Declaration of Helsinki). By using a multi-stage cluster random sampling technique, the CLHLS assessed older adults across 23 of 31 provinces/autonomous regions/municipalities in mainland China. In this study, trained interviewers conducted face-to-face interviews with participants at their residences to collect data. To ensure comprehensive data collection, participants were encouraged to provide extensive responses. The CLHLS implemented a rigorous quality control system to maintain data reliability and consistency. These procedures included pretesting of survey instruments, training of survey staff, and regular monitoring of data quality[15]. The specifics pertaining to this survey have been previously report[16].

This study utilized the 2018 wave of CLHLS, which surveyed 15,874 participants. The study excluded participants who were younger than 65 years old ($n = 95$), missed information of sarcopenia ($n = 1297$), and missed information of nut consumption ($n = 201$). The final analysis consisted of 14,281 participants (Fig. 1).

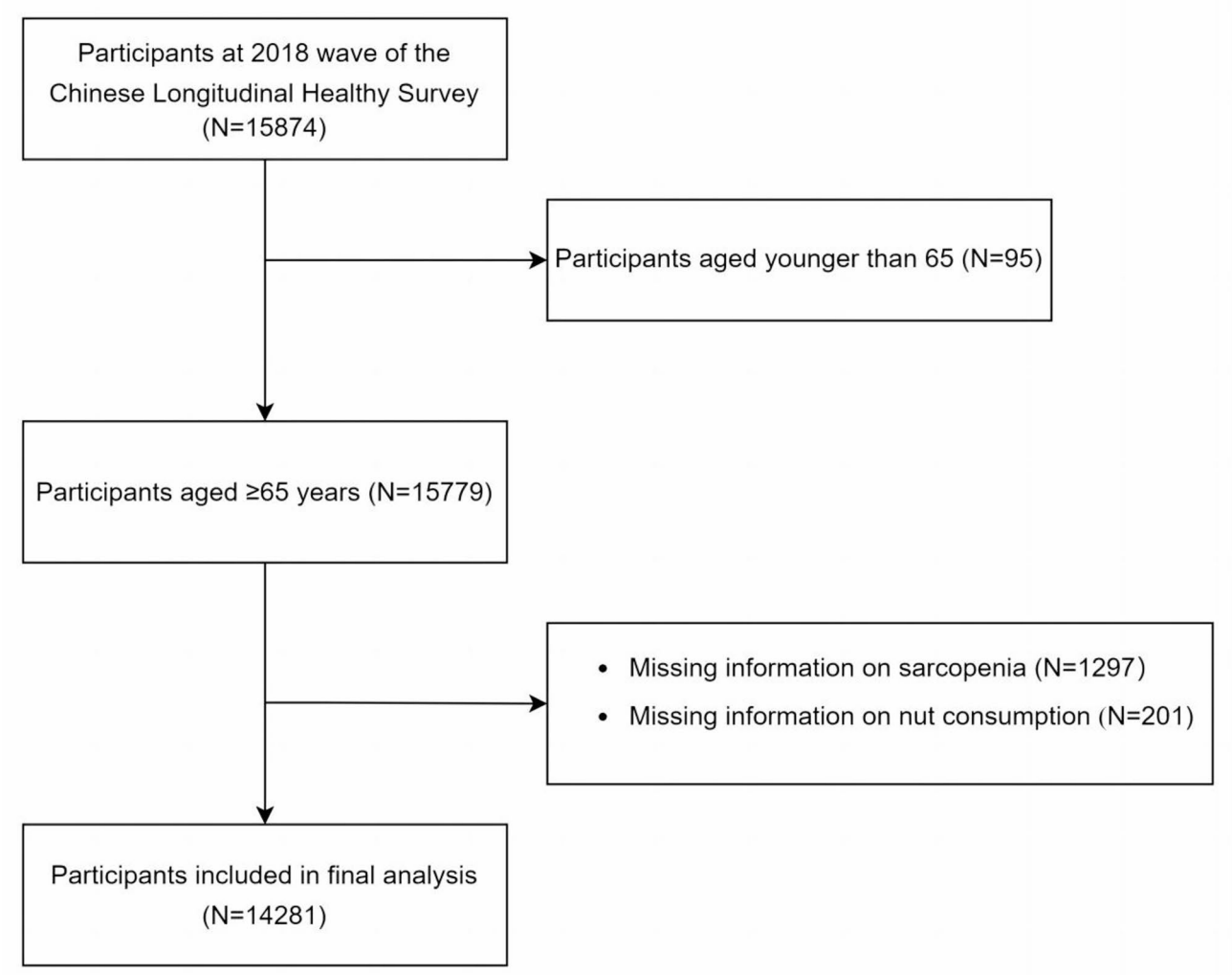

Fig. 1. Flow chart of participants selection from the Chinese Longitudinal Healthy Longevity Survey.

Assessment of nut consumption

Nut consumption was assessed using a specific question, "How often do you normally eat nut?" The frequency of nut consumption was documented as "almost every day", "not every day, but at least once a week", "not every week, but at least once a month", and "occasionally/rarely or never"[17].

Assessment of sarcopenia

This study used the diagnostic method recommended by Asian Working Group for Sarcopenia in 2019 to define sarcopenia: low muscle mass plus low muscle strength, or low physical performance[4]. According to this standard, low muscle mass plus low physical performance ware used to identified sarcopenia. Low muscle mass is defined as Skeletal Muscle Mass Index (SMI) < 5.08 kg/m^2 for female and < 6.88 kg/m^2 for male[18]. SMI = Appendicular Skeletal Muscle Mass (ASM)/height (m)^2; ASM = 0.193 × body weight (kg) + 0.107 × height (cm) − 4.157 × sex (male = 1; female = 2) − 0.037 × age (year) − 2.631[19]. Physical performance was assessed with the question "how do you stand up after sitting on a chair?" Respondents were asked to choose from three responses: "no problem," "with problem," and "not able to do it." Responses of "with problem" or "not able to do it" indicated low physical performance[20].

Assessments of covariates

Based on previous studies[11,21,22], the covariates we included the continuous variables of age, years of education, and calf circumference; the categorical variables of gender (male vs. female), area of residence (urban vs. rural), marital status (having a spouse vs. not having a spouse), smoking status (yes vs. no), alcohol consumption (yes vs. no), annual family income (< 30000 Yuan, 30000–50000 Yuan, > 50000 Yuan) (1 Yuan = 0.15124 US dollars in 2018), and heart disease (yes vs. no).

Statistical analyses

Firstly, this study used the Kolmogorov–Smirnov test to assess the normality of continuous variables. The Q–Q plots indicated that age followed a normal distribution, while education years and calf circumference did not follow a normal distribution. Secondly, the baseline characteristics of the study participants which were stratified according to their nut consumption were presented by mean that followed a normal distribution, and by median and interquartile range (IQR) that did not follow a normal distribution (for continuous variables) or frequency distribution (for categorical variables). To analyze variations in the covariates across four nut consumption categories, the Kruskal–Wallis test was used for continuous variables, and the chi-square test for categorical ones. Thirdly, binary logistic regression analyses were used to investigate the association between nut consumption and sarcopenia. This study employed three models for binary logistic regression analysis: Model 1 was the unadjusted model; Model 2 was adjusted for gender, age, and annual family income; and Model 3 was adjusted for gender, age, annual family income, marital status, area of residence, education years, smoking status, alcohol consumption, calf circumference, and heart disease. Additionally, to explore the dose-response association between nut consumption and sarcopenia, this study performed a linear trend test using an ordinal categorical variable for nut consumption frequency. The categories included rarely or never, at least once per month, at least once per week, and almost every day. A chi-square test for trend was conducted to assess whether increasing frequency of nut consumption was associated with a linear decrease in the risk of sarcopenia. The P-value for trend was calculated for each model to test the hypothesis of a linear association. Finally, stratified and interaction analyses were carried out on categorical variables to evaluate potential effect of modifications. To account for potential inflation of type I error due to multiple subgroup comparisons, we applied the Bonferroni correction (Bonferroni correction = 0.05/number of subsamples)[23]. The significance threshold for interaction terms was set at $P < 0.0071$ (0.05/7) accordingly.

In addition, a sensitivity analyse was performed. Missing values were multiply-imputed using the "chained equations" method. Five imputations were performed. The imputation models included all variables used in the final analytical model, including: age, gender, annual family income, marital status, years of education, area of residence, smoking status, alcohol consumption, calf circumference, and heart disease status.

This study uses double tailed P-value < 0.05 as the standard for statistical significance. The statistical software used in this study are R statistical package (http://www.R-project.org; version3.6.3), Empower (R) software (www.empowerstats.com, X&Y Solutions, Inc., Boston, MA, USA), and STATA version 17.0 (Stata Corp, College Station, TX, USA).

Result

Characteristics of participants

Among the 14,281 participants, 8518 participants had sarcopenia. The mean age of participants is 84.86 years old. Of the participants, 55.08% were female and 83.60% resided in urban. Participants consuming nut almost everyday were more frequently observed to be advanced age, live in urban areas, have a spouse, and have a long education years (Table 1).

Association between nut consumption and sarcopenia

In Model 1, participants consuming nut almost everyday or at least once per week showed reduced likelihood of sarcopenia: at least once per week, OR = 0.47 (95% CI: 0.43, 0.52); almost everyday, OR = 0.36 (95% CI: 0.31, 0.41). In Model 2, the association was also existent: at least once a week, OR = 0.74 (95% CI: 0.65, 0.85); almost every day, OR = 0.57 (95% CI: 0.47, 0.68). In Model 3 when adjusting for all the study potential confounding risk factors, OR = 0.62 (95% CI:0.51, 0.77) (Table 2).

The results of the chi-square test for trend revealed a significant linear association between increasing frequency of nut consumption and a decreased risk of sarcopenia. The P-values for the trend tests were all less

Variables	Total (*N* = 14281)	Occasionally/rarely or never (*N* = 10113)	At least once per month (*N* = 1520)	At least once per week (*N* = 1765)	Almost everyday (*N* = 883)	*P*-value
Sarcopenia, n (%)						< 0.001
Yes	8518 (59.65)	6590 (65.16)	744 (48.95)	829 (46.97)	355 (40.20)	
No	5763 (40.35)	3523 (34.84)	776 (51.05)	936 (53.03)	528 (59.80)	
Gender, n (%)						< 0.001
Male	6415 (44.92)	4278 (42.30)	758 (49.87)	922 (52.24)	457 (51.76)	
Female	7866 (55.08)	5835 (57.70)	762 (50.13)	843 (47.76)	426 (48.24)	
Area of residence, n (%)						< 0.001
Rural	2010 (16.40)	1072 (12.53)	299 (22.38)	371 (23.68)	268 (33.50)	
Urban	10,247 (83.60)	7482 (87.47)	1037 (77.62)	1196 (76.32)	532 (66.50)	
Marital status, n (%)						< 0.001
Have a spouse	6086 (43.04)	3886 (38.82)	787 (52.19)	926 (53.04)	487 (55.66)	
Have no spouse	8054 (56.96)	6125 (61.18)	721 (47.81)	820 (46.96)	388 (44.34%)	
Smoking status, n (%)						0.300
Yes	2180 (15.41)	1513 (15.10)	240 (15.94)	293 (16.80)	134 (15.40)	
No	11,963 (84.59)	8510 (84.90)	1266 (84.06)	1451 (83.20)	736 (84.60)	
Alcohol consumption, n (%)						< 0.001
Yes	2072 (14.73)	1308 (13.12)	243 (16.16)	336 (19.42)	185 (21.46)	
No	11,992 (85.27)	8660 (86.88)	1261 (83.84)	1394 (80.58)	677 (78.54)	
Annual family income (Yuan), n (%)						< 0.001
< 30,000	6088 (44.33)	4615 (47.71)	573 (38.66)	626 (36.50)	274 (31.79)	
30,000–50,000	1895 (13.80)	1373 (14.19)	205 (13.83)	208 (12.13)	109 (12.65)	
> 50,000	5749 (41.87)	3685 (38.10)	704 (47.50)	881 (51.37)	479 (55.57)	
Heart disease, n (%)						< 0.001
Yes	2303 (17.87)	1448 (15.89)	301 (21.84)	356 (22.24)	198 (24.84)	
No	10,587 (82.13)	7666 (84.11)	1077 (78.16)	1245 (77.76)	599 (75.16)	
Age (years), mean (SD)	84.86 (11.47)	86.18 (11.40)	81.82 (10.85)	81.50 (11.04)	81.41 (11.05)	< 0.001
Calf circumference (cm), mean (SD)	31.22 (6.46)	30.67 (6.31)	32.39 (6.51)	32.45 (6.74)	33.08 (6.59)	< 0.001
Education years (years), median (IQR)	1.00 (0,6.00)	0 (0, 5.00)	4.00 (0, 8.00)	5.00 (0, 9.00)	6.00 (0, 9.00)	< 0.001

Table 1. Characteristics of the study participants. Total percentages within categories may not equal 100% due to rounding. *SD* standard deviation, *IQR* inter quartile range.

Model	Rarely or never		At least once per month		At least once per week		Almost everyday		*P*-for-trend
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95%CI)	*P*-value	
Model 1	Ref.	Ref.	0.51 (0.46, 0.57)	< 0.001	0.47 (0.43, 0.52)	< 0.001	0.36 (0.31, 0.41)	< 0.001	< 0.001
Model 2	Ref.	Ref.	0.71 (0.62, 0.81)	< 0.001	0.70 (0.62, 0.79)	< 0.001	0.49 (0.41, 0.57)	< 0.001	< 0.001
Model 3	Ref.	Ref.	0.77 (0.66, 0.90)	0.001	0.78 (0.67, 0.91)	0.001	0.62 (0.50, 0.76)	< 0.001	< 0.001

Table 2. Association between nut consumption and sarcopenia. Model 1 was the unadjusted model. Model 2 was adjusted for gender, age, and annual family income. Model 3 was adjusted for gender, age, annual family income, marital status, education years, area of residence, education years, smoking status, alcohol consumption, calf circumference, and heart disease. *OR* odds ratios, *CI* confidence intervals, *Ref* Reference.

than 0.001 across all models, as nut consumption increased, the odds of developing sarcopenia significantly decreased, with the trend remaining highly significant (*P*-for-trend < 0.001) in each model. These results support a dose-response association between nut consumption and sarcopenia risk.

Stratified and interaction analyses

Subgroup analyses were conducted using nine categorical variables (gender, marital status, area of residence, smoking status, alcohol consumption, annual family income, and heart disease) (Supplementary Table 1). The positive association between nut consumption and sarcopenia was consistent across these subgroups. The interaction results showed that gender had significant interactions with nut consumption on sarcopenia (*P*-value for interaction = 0.016). However, after Bonferroni correction for multiple comparisons, the interaction between nut consumption and gender, which was initially statistically significant ($p = 0.016$), no longer met the corrected threshold (adjusted $p = 0.112$). Similar results were observed for other subgroup interactions. (Supplementary Table 1).

Sensitivity analysis

In the sensitivity analysis, we imputed the missing covariates for participants. The association of nut consumption and sarcopenia remained conherent (all *P*-values < 0.05) (Supplementary Table 2).

Discussion

This study is the first population-based study that explores the associations of nut consumption with sarcopenia. Our findings indicated a negative association between nut consumption and sarcopenia, with the association being significantly pronounced in male, suggesting a potential interaction between nut consumption and gender in the older adults.

Nut was rich of protein, fatty acid, fiber, vitamins, minerals, phytosterols and phenolics[14]. Previous studies have confirmed there is a negative association between protein and sarcopenia[24]. Reduced protein intake is correlate with the decreased muscle strength[25]. In addition, a low-quality restricted diet system of protein supply can exacerbates muscle function in older sarcopenic adults[24]. The possible reason for these results is that protein offers the amino acids required for muscle compound, so when protein intake decreases, the quantity and quality of muscle synthesis also decrease[6]. The nutrients contained in nut are not just proteins, previous studies have also shown that some components in nut such as vitamins, omega-3 fatty acids, and mineral are also associated with sarcopenia[26,27].

Previous studies have shown that have found low vitamin D levels can diminish muscle strength[26]. A study by Remelli et al. has proven that low levels of vitamin D intake are believed to reduce skeletal muscle mass, leading to the development of skeletal muscle atrophy[13]. In addition, frailty (a disease that overlaps with some skeletal muscle wasting disorders) is also associated with vitamin D absence[28]. Previous studies have revealed that vitamin D can be localized in the nucleus of human muscle cell lines, myoblasts[29], and adult skeletal muscle[30,31], which can promote muscle growth. Furthermore, chronic inflammation is a common cause of sarcopenia[32], however, the omega-3 fatty acids as a class of long-chain fatty acids in nut, they have long been hailed as having anti-inflammatory effects[27]. Smith et al. has also found omega-3 fatty acids significantly improving the efficiency of muscle synthesis rate induced by hyperaminoacidemia–hyperaminoacidemia[33]. Additionally, some minerals in nuts, such as phosphorus, zinc, have also been proven to contribute to reduce the incidence rate of sarcopenia[27].

From another perspective, frequent nut consumption may reflect a generally healthier dietary pattern. Previous studies have shown that individuals who consume more nuts also tend to have higher intakes of vegetables, fruits, fish, whole grains, and other high-quality foods[34,35], all of which are beneficial for muscle health and may contribute to a lower prevalence of sarcopenia[36]. In addition, people who frequently consume nuts may have greater health consciousness, as reflected in more regular physical activity and fewer unhealthy lifestyle behaviors such as smoking and excessive alcohol consumption, which may also jointly affect muscle health[37].Therefore, the observed association between nut consumption and sarcopenia may not be entirely attributable to the nutrients in nuts alone, but rather to a combination of dietary and lifestyle factors. Future studies should aim to adjust for overall dietary patterns and incorporate comprehensive lifestyle assessments to further disentangle the independent effects of nut consumption from those of broader health behaviors.

Several biological mechanisms have been proposed to clarify the association between nut consumption and sarcopenia. A potential mechanism is that essential amino acids are the most principal nutritional imports in muscle protein synthesis. In this regard, leucine in nut protein is supposed to a major nutritional modifier of muscle protein synthesis and metabolism, which can touch off the mammalian rapamycin target protein pathway and inhibit proteasomes, it can improve the quantity and quality of muscles[38]. Additionally, Vitamin D promotes cell proliferation by up-regulating follistatin and insulin-like growth factor 2. It influences cell differentiation by inducing multiple myogenic transcription factors, including fetal myosin, neural cell adhesion molecule, B-cell lymphoma 2, insulin-like growth factor-i, fibroblast growth factor, retinoblastoma protein, and myogenic differentiation protein 1[39,40]. Furthermore, Vitamin D initiates muscle regeneration, increasing the cross-sectional area of skeletal muscle fibers through generation cycle retardant, it is a crucial phase for myogenic onset[39,40]. Moreover, Vitamin D inhibits myostatin expression, a detractor of muscle growth, thereby preventing muscle deterioration and enhancing contractile filament functionality and muscle strength[41]. Another possible mechanism is omega-3 fatty acids can increase nerve conduction and muscle activation, then improve mitochondrial function (energy production) or compose a larger myofiber size[42]. In addition, trace element zinc has been proven to promote protein synthesis and slow down protein degradation[27].

The results of the interaction showed that gender had interactions with nut consumption on sarcopenia, significant association was observed among the male in older adults. Several studies had suggested that the absolute muscle loss rate in males was higher than that in females, so they are more likely to suffer from muscle-related diseases[43]. A study has shown that testosterone can interacts with androgen receptors in skeletal muscle, promoting the synthesis of skeletal muscle and thereby improving the quantity and quality of muscle[44]. However, Testosterone in older male decreases with age[45]. Therefore, the decrease of testosterone can lead to muscle dysfunction in older male. A study by Peng et al. also attested that among older adults, low serum myostatin levels only reduced the low skeletal muscle mass of male, but did not affect female[46]. There are significant differences in skeletal muscle composition between males and females. Studies have shown that male myofibers generally have a larger cross-sectional area than those in females, with this difference being particularly prominent in type II (fast-twitch) fibers[47]. Type II fibers play a critical role in rapid contraction and high-intensity activities, and they are more susceptible to age-related atrophy[48]. During the aging process, the accelerated degeneration of these fibers may render males more vulnerable to muscle deterioration and functional decline. In this physiological context, nut, which are rich in high-quality nutrients such as protein, unsaturated fatty acids, vitamin E, and antioxidants, may play a more important role in maintaining type II fibers health in males, thereby presenting a significant association between nut consumption and sarcopenia. Furthermore, Estrogen plays a vital role in muscle metabolism and repair in females. It possesses antioxidant

properties that help reduce oxidative stress in muscle cells and protect myofibers from damage[49]. In addition, estrogen promotes muscle regeneration by enhancing the activity of satellite cells and stabilizing the muscle cell membrane after injury[50]. Moreover, estrogen regulates the balance of muscle protein synthesis and degradation through pathways such as Akt/mTOR, thereby delaying muscle atrophy[51]. Therefore, the protective effects of estrogen may, to some extent, attenuate the significant association between nut consumption and sarcopenia in females. In contrast, due to the lack of similar hormonal protection in males, nut consumption may play a more critical role in maintaining muscle health, thereby exhibiting a stronger association. These sex-specific physiological differences underscored the importance of nut supplementation in men should be emphasized, while also considering the investigation of other dietary options that can help women increase muscle mass through nutrition.

Although subgroup analyses suggested potential heterogeneity in the association between nut consumption and sarcopenia across gender and other sociodemographic factors, these interaction effects were not statistically significant after Bonferroni correction for multiple comparisons. The results before and after Bonferroni correction were inconsistent, however, the non-significant findings after correction may reflect statistical outcomes rather than true null associations. Therefore, these results should not be totally interpreted as evidence negating potential gender differences. Previous studies have also pointed out that the Bonferroni correction imposes a stringent penalty during multiple comparisons, which may obscure potentially meaningful findings[52,53]. Thus, further investigation is warranted to explore these potential interactions in greater depth.

This study possesses several limitations that warrant acknowledgment. Firstly, due to the limitations of cross-sectional studies, causal association cannot be determined, therefore we cannot infer a causal relationship between nut consumption and sarcopenia. Hence, subsequent longitudinal studies are imperative to elucidate the relationship in question. Secondly, given that this study relies on self-reported data collection, there are certain limitations in the dietary frequency self-report, as it uses vague frequency descriptions such as "occasionally/rarely," which may lead to recall bias. Therefore, future studies will adopt more objective and systematic dietary assessment tools, such as 24-hour dietary recall or dietary frequency questionnaires. Thirdly, there are some confounding factors that have not been taken into account, such as physical activity, total dietary protein, dental health, esophageal and gastrointestinal digestive problems, which may associated with nut consumption. Future research will focus on collecting and adjusting for these related factors to more comprehensively assess the association between nut consumption and sarcopenia. Fourthly, in accordance with previous research, this study employed a combining "muscle mass and chair-stand performance" as the diagnostic criteria for analysis. However, prior studies have indicated that handgrip strength is also a widely accepted indicator for the assessment of sarcopenia. Future research may consider integrating multiple measurement methods, including handgrip strength, to validate and expand upon the current findings, thereby enhancing the robustness of the evidence and supporting further advancements in this field. Finally, although this study identified a significant inverse association between nut consumption and the risk of sarcopenia, practical implementation should consider the specific needs of older adults. For some individuals, especially those with chewing difficulties or dysphagia, consuming whole nuts may not be appropriate. In such cases, softer and safer alternatives are recommended, such as nut-based beverages (e.g., almond milk, walnut milk, peanut milk) or nut-based soft foods (e.g., almond tofu, peanut tofu). These options are easier to swallow and still provide similar nutritional benefits. Additionally, for individuals with nut allergies, consuming nuts or nut-based products may pose health risks. For them, other nutrient-rich substitutes such as avocado, soft tofu, or soft-textured fatty fish like salmon can be considered. These foods are also rich in unsaturated fatty acids and high-quality protein. Personalized dietary recommendations should account for swallowing ability and allergy history to maximize the preventive potential of nutritional strategies against sarcopenia.

Conclusions

This investigation centered on the association between nut consumption and sarcopenia in Chinese older adults, our findings provide significant empirical support for the protective role of nut in sarcopenia among older adults. The routine integration of nut into the diets of older adults might serve as a pragmatic and accessible approach to benefit musculoskeletal well-being.

Data availability

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

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Author contributions

S.Z. and D.L. are the corresponding authors of this work. Conceptualization: J.X. and D.L. Methodology: J.X., D.L. Data validation and analyses: J.X. Data interpretation: J.X., D.L., K.P., W.S., C.P., and S.Z. Writing—original draft preparation: J.X. Writing—review and editing: J.X., D.L., K.P., W.S., C.P., and S.Z. Supervision: J.X., D.L., S.Z., K.P., W.S., C.P., Final approval of manuscript: J.X., D.L., K.P., W.S., C.P., and S.Z.

Declarations

Competing interests

The authors declare no competing interests.

Ethical approval

The data from CLHLS survey already obtained the ethical approval and informed consent, and was approved by research ethics committees of Peking University (IRB00001052-13074).

Informed consent

Each participant signed an informed consent form and all methods in our study were performed in accordance with the guidelines and regulations of Declaration of Helsinki.

Additional information

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