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Trabajo Original

Paciente anciano

Associations between dietary intake and sarcopenia: a Mendelian randomization study

Relación entre el consumo alimentario y la sarcopenia: estudio de aleatorización mendeliana

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Abstract

Background: sarcopenia, typified by the progressive diminution of skeletal muscle mass and functionality, represents a substantial public health challenge, particularly among the geriatric population. Dietary intake, as a modifiable determinant, has elicited considerable interest due to its prospective role in preventing and alleviating sarcopenia.

Methods: this investigation employed Mendelian randomization (MR) analysis, a robust statistical method, to investigate the causal associations between dietary consumption and sarcopenia-associated phenotypes, including appendicular lean mass (ALM), hand grip strength, and walking pace. Genetic variants extracted from the extensive UK Biobank cohort served as instrumental variables for a comprehensive set of 26 dietary elements.

Results: our MR analysis unveiled that the ingestion of oily fish and cheese was significantly correlated with augmented ALM, diminished risk of low hand grip strength, and enhanced walking pace. In addition, cooked vegetables, fresh fruit, dried fruit, cereal, and raw vegetables were protective of one or both of the sarcopenia-associated phenotypes. These findings were robust to potential confounding influences owing to the sophisticated MR design.

Conclusions: our results underscore that specific dietary constituents play a pivotal protective role against sarcopenia, underscoring the necessity for tailored nutritional strategies to bolster muscle health in the elderly. Further investigations are requisite to corroborate these findings across heterogeneous populations and to unravel the underlying biological mechanisms.

Keywords:

Sarcopenia. Diet. Mendelian randomization. Appendicular lean mass. Hand grip strength. Walking pace.

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Artificial intelligence: the authors declare not to have used artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

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Resumen

Introducción: la sarcopenia, caracterizada por la disminución progresiva de la masa muscular esquelética y la funcionalidad, representa un importante desafío de salud pública, particularmente entre la población geriátrica. La ingesta alimentaria, como determinante modificable, ha suscitado un interés considerable debido a su posible papel en la prevención y el alivio de la sarcopenia.

Métodos: en esta investigación se emplea el análisis mendeliano de aleatorización (MR), un método estadístico sólido, para investigar las relaciones causales entre el consumo alimentario y los fenotipos relacionados con la sarcopenia, como la masa magra apendicular (ALM), la fuerza de agarre manual y el ritmo de marcha. Las variantes genéticas extraídas de la extensa cohorte del biobanco del Reino Unido sirvieron como variables instrumentales para un amplio conjunto de 26 elementos dietéticos.

Resultados: nuestro análisis de MR reveló que la ingestión de pescado graso y queso estaba significativamente correlacionada con el aumento de la ALM, la disminución del riesgo de baja fuerza de agarre manual y el aumento del ritmo al caminar. Además, las verduras cocidas, la fruta fresca, las frutas secas, los cereales y las verduras crudas protegieron uno o ambos fenotipos relacionados con la sarcopenia. Estos hallazgos fueron robustos frente a posibles influencias de confusión debido al sofisticado diseño de la MR.

Conclusiones: nuestros resultados ponen de relieve que los componentes dietéticos específicos desempeñan un papel protector fundamental contra la sarcopenia y subrayan la necesidad de estrategias nutricionales adaptadas para reforzar la salud muscular en los ancianos. Se necesitan más investigaciones para corroborar estos hallazgos en poblaciones heterogéneas y para desentrañar los mecanismos biológicos subyacentes.

Palabras clave:

Sarcopenia. Dieta. Aleatorización mendeliana. Masa magra apendicular. Fuerza de agarre manual. Ritmo de marcha.

INTRODUCTION

Sarcopenia, characterized by the progressive loss of skeletal muscle mass and function, has emerged as a significant public health concern, particularly among the aging population (1). Sarcopenia not only leads to physical frailty and decreased quality of life but also increases the risk of falls, fractures, and mortality (2). Despite its substantial impact on health, the underlying causes of sarcopenia remain multifactorial and not fully understood. Among the various factors contributing to sarcopenia, diet has attracted considerable attention due to its modifiable nature and potential for preventive interventions (3).

Dietary intake influences muscle health through various pathways, including the provision of essential nutrients necessary for muscle protein synthesis, modulation of inflammatory responses, and maintenance of overall metabolic health (4). Effective strategies for preventing and managing sarcopenia emphasize a healthy lifestyle, particularly through high-quality nutrition and regular physical activity, highlighting the role of specific dietary interventions and their mechanisms in combating age-related muscle loss (5). Additionally, previous observational studies have suggested associations between specific dietary components and muscle mass or function (6). For instance, Bo et al. demonstrated that supplementation with whey protein, vitamin D, and E significantly improves muscle mass, strength, and anabolic markers in older adults with sarcopenia (7). However, these studies often face challenges, such as confounding factors and reverse causation, subsequently limiting their ability to establish causal relationships.

Mendelian randomization (MR) analysis offers a robust approach to infer causality by utilizing genetic variants as instrumental variables (IVs) for exposures of interest (8). This method mitigates confounding and reverse causation issues by utilizing the random allocation of genes at conception, which mimics the randomization process in controlled trials (9). MR analysis allowed researchers to infer causal relationships without the biases inherent in observational studies. This method also helped to overcome issues such as reverse causation and confounding, making it a powerful tool for investigating the effects of exposures on outcomes in a more robust and reliable manner (10). As a result, MR analysis can provide more reliable evidence of the causal effects of dietary intake on sarcopenia-related traits. Recent MR studies, such as Park et al., highlight the causal impact of lifestyle factors like tobacco smoking on aging-related traits, demonstrating the effectiveness of MR in identifying genetic influences on sarcopenia and guiding preventive strategies (11). And, Ye et al. demonstrate the causal link between sarcopenia-related traits and cardiometabolic diseases, including Alzheimer's disease, highlighting insulin resistance as a significant mediator and the importance of targeting sarcopenia and insulin resistance in disease prevention strategies (12). By using genetic variants as proxies for dietary intake, MR can help isolate the direct effects of diet on muscle health from other confounding variables, leading to a clearer understanding of the underlying biological mechanisms (13). Despite the potential of MR analysis, to our knowledge, no studies have yet applied this method to investigate the causal relationship between dietary intake and sarcopenia.

Therefore, this study intended to utilize MR analysis to investigate the causal relationship between dietary intake and the risk of sarcopenia. Strategically, genetic variants related to dietary intake were derived from the UK Biobank cohort, including 26 dietary elements. Single nucleotide polymorphisms (SNPs) were selected based on stringent criteria to serve as IVs. The study outcomes were sarcopenia-related traits, including appendicular lean mass (ALM), low hand grip strength, and walking pace, with data drawn from the UK Biobank and other Genome-wide Association Study (GWAS) meta-analyses. A MR analysis was performed using several methods to ensure robustness and multiple sensitivity analyses were conducted to assess the stability of the results and to address potential issues, such as horizontal pleiotropy and heterogeneity. The explorations of the causal links between dietary intake and sarcopenia-related traits, are beneficial for providing potential dietary modifications that could prevent sarcopenia risk. Understanding these relationships is crucial for developing effective nutritional strategies to enhance muscle health and prevent sarcopenia, ultimately improving the quality of life and health outcomes for the aging population.

MATERIALS AND METHODS

STUDY OVERVIEW

We performed a MR analysis to investigate the causal impact of diet on sarcopenia. MR analysis uses SNPs as IVs of dietary intake to infer causality between dietary intake and sarcopenia. In theory, SNPs are less susceptible to potential reverse causality and confusion bias, improving the reliability of inferred results. The graphical flow of the study design was shown in figure 1. The MR analysis design was mainly based on three key assumptions: assumption 1, the selected IV is strongly associated with dietary intake; assumption 2, the selected IV is not associated with any confounding factors that could bias estimates of causal effects; and assumption 3, IV influences results only through its effect on exposure (14).

GWAS SUMMARY DATA OF DIETARY INTAKE

The GWAS data for dietary intake was obtained from the UK Biobank GWAS database, which contained a cohort of about 500,000 European individuals. The exposure factor, dietary intake, was obtained by asking participants about the frequency of dietary intake in a questionnaire. The data for each dietary pattern included both integer variables, such as the average daily consumption of coffee in cups, and categorical variables, such as the frequency of poultry consumption. Prior to analysis, any unreasonable responses were carefully screened and excluded during the data submission process. Detailed information regarding the dietary habit assessment questions and specific units of measurement utilized in our study can be accessed through the publicly available resources on the UK Biobank website. The GWAS data for 26 types of dietary intakes, including milk (n = 64,949 participants), yogurt (n = 64,949 participants), salted peanuts (n = 64,949 participants), unsalted peanuts (n = 64,949 participants), salted nuts (n = 64,949 participants), unsalted nuts (n = 64,949 participants), bacon (n = 64,949 participants), lamb (n = 460,006 participants), beer/cider (n = 327,634 participants), red wine (n = 327,026 participants), coffee (n = 428,860 participants), tea (n = 447,485 participants), cheese (n = 451,486 participants), cereals (n = 441,640), bread (n = 452,236 participants), oily fish (n = 460,443 participants), non-oily fish (n = 460,880 participants), beef (n = 461,053 participants), pork (n = 460,162 participants), processed meat (n = 461,981 participants), cooked vegetable (n = 448,651 participants), raw vegetable (n = 435,435 participants), fresh fruit (n = 446,462 participants), dried fruit (n = 421,764 participants), saturated fatty acids (n = 114,999 participants) and polyunsaturated fatty acids (n = 114,999 participants), were collected and used for MR analysis.

GWAS SUMMARY DATA OF SARCOPENIA

According to the European Working Group on Sarcopenia in Older People (EWGSOP), sarcopenia was defined by three parameters: low muscle strength, low muscle quantity or quality, and low physical performance (15). Also, the consensus suggested that appendicular lean mass (ALM), grip strength, and walking speed could be used to measure sarcopenia.

The GWAS summary statistics for ALM were extracted from the UK Biobank GWAS database (n = 450,243). ALM was measured with bioelectrical impedance analysis. The GWAS summary statistics of walking pace were also obtained from the UK Biobank GWAS database (n = 459,915). The walking pace

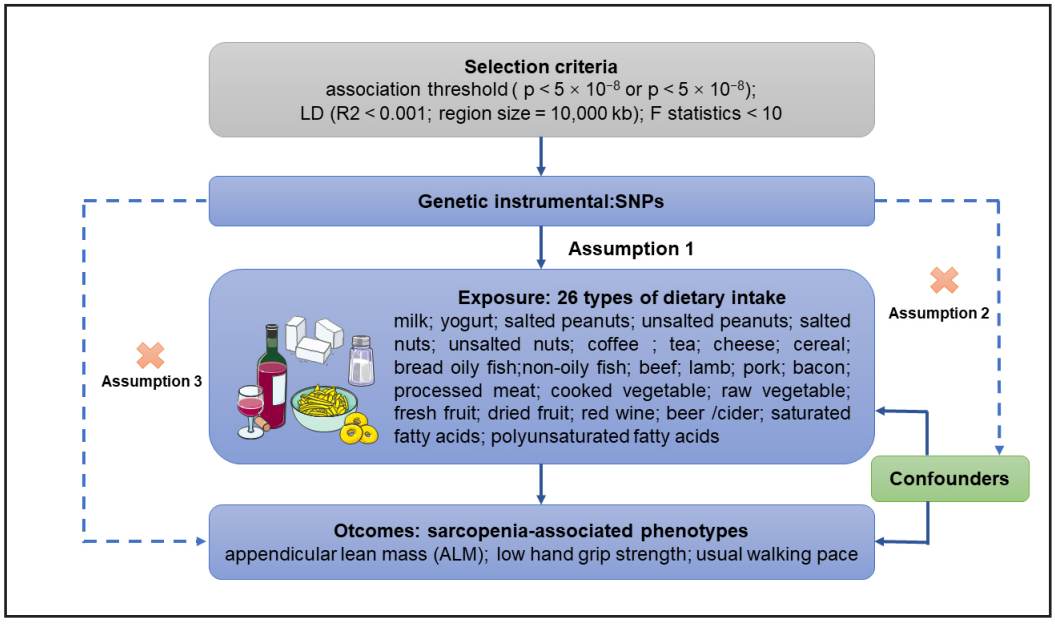

Figure 1.
Overview of the study design for MR analysis exploring the causal relationship between dietary intake and sarcopenia-associated phenotypes.

data were captured through a questionnaire by asking the question "How would you describe your usual walking speed?" The summary data for low hand grip strength were derived from the GWAS meta-analysis comprising cohorts with 20335 cases and 236,188 controls. Low grip strength was defined depending on the Foundation for the National Institutes of Health (FNIH) criteria (male: < 26 kg, female: < 16 kg).

GENETIC INSTRUMENTAL VARIABLES SELECTION

In Mendelian randomization, the basic principle behind using SNPs as IVs is the random assortment of genetic variants during meiosis, which mimics the random assignment of individuals to different levels of the exposure (10). This randomization process helps to overcome confounding and reverse causation biases that are common in observational studies, making Mendelian randomization a powerful tool for inferring causal relationships. According to assumption 1 of MR analysis, SNPs at the genome-wide significant level ($p < 5 \times 10^{-8}$) were selected as IVs. Then, SNPs in linkage disequilibrium ($R2 < 0.001$; region size = 10,000 kb) were removed. For milk, yogurt, salted nuts, unsalted nuts, salted peanuts, bacon, lamb, beer, red wine, and unsalted peanuts we did not select more than 5 SNPs with the strict threshold ($p < 5 \times 10^{-8}$). To explore the potential associations between those 9 dietary intakes and sarcopenia, we used a relatively relaxed threshold ($p < 1 \times 10^{-5}$, $R2 < 0.001$; region size = 10,000 kb) to select SNPs. Finally, F statistics were calculated to eliminate weak instruments using the formula: $F = R2 \times (N - 2)/(1 - R2)$, where N represents the sample size and R2 refers to the variance of exposure explained by IVs. IVs with low F statistics (< 10) were considered as weak instruments and removed.

STATISTICAL ANALYSIS

All statistical analyses were conducted using the R 4.3.0 software. The inverse variance weighted (IVW) method was used as the main statistical approach to evaluate the causal relationship between dietary intake and sarcopenia. The IVW method, known for its accuracy in estimating causal relationships, is often considered the gold standard when there is no clear evidence of directional pleiotropy, as indicated by a non-significant *p*-value for the MR-Egger intercept ($p > 0.05$). In cases where there is evidence of heterogeneity among the selected IVs, the random-effects model in the IVW method is typically employed. In this study, we mainly used the random-effects model in the IVW method to evaluate the causal relationship between dietary intake and sarcopenia-associated phenotypes. Additionally, MR-Egger, weighted median, simple mode, and weighted mode methods were utilized as supplementary analyses. The MR-PRESSO method was used to detect outliers by testing the heterogeneity of IVs. Cochrane's *Q* test was performed to evaluate heterogeneity across IVs. The MR pleiotropy test was employed to evaluate horizontal pleiotropy.

RESULTS

DIETARY INTAKE AND APPENDICULAR LEAN MASS (ALM)

Supplementary Table I (https://www.nutricionhospitalaria.org/files/8552/ADMA1-05487-02.pdf) showed the IVs that were significantly associated with the 26 types of dietary intake. Among all dietary factors studied, 9 dietary intakes were found significantly associated with ALM in the IVW analysis. Cooked vegetables [odds ratio (OR), 1.694; 95 % confidence interval (CI), 1.232-2.331; $p = 0.001$], coffee [OR, 1.376; CI, 1.059-1.788; $p = 0.017$], fresh fruit [OR, 1.738; CI, 1.335-2.263; $p < 0.001$], oily fish [OR, 1.271; CI, 1.114-1.451; $p < 0.001$], dried fruit [OR, 1.587; CI, 1.261-1.998; $p < 0.001$], cereals [OR, 1.278; CI, 1.009-1.619; $p = 0.042$], and cheese [OR, 1.257; CI, 1.080-1.463; $p = 0.003$] were positively related to ALM. But, saturated fatty acids [OR, 0.935; CI, 0.880-0.994; $p = 0.031$] and polyunsaturated fatty acids [OR, 0.942; CI, 0.894-0.991; $p = 0.022$] were negatively related to ALM (Fig. 2).

DIETARY INTAKE AND LOW HAND GRIP STRENGTH

Subsequently, a MR analysis was performed with low hand grip strength as the outcome. The results showed that 5 dietary intakes were associated with low hand grip strength. Among them, cooked vegetables [OR, 0.459; CI, 0.272-0.776; $p = 0.004$], oily fish [OR, 0.790; CI, 0.625-0.997; $p = 0.047$], dried fruit [OR, 0.673; CI, 0.464-0.977; $p = 0.037$], and cheese [OR, 0.701; CI, 0.552-0.890; $p = 0.004$] were significantly associated with the reduced risk of low hand grip strength. Red wine [OR, 1.174; CI, 1.019-1.352; $p = 0.027$] was significantly associated with the increased risk of low hand grip strength (Fig. 3).

DIETARY INTAKE AND WALKING PACE

The IVW results showed that a total of 9 dietary intakes were linked with the usual walking pace. Among them, processed meat [OR, 0.914; CI, 0.842-0.992; $p = 0.031$], pork [OR, 0.786; CI, 0.674-0.917; $p = 0.002$], and bacon [OR, 0.973; CI, 0.948-0.999; $p = 0.045$] were negatively related to walking pace. Fresh fruit [OR, 1.125; CI, 1.014-1.248; $p = 0.026$], oily fish [OR, 1.118; CI, 1.057-1.182; $p < 0.001$], raw vegetable [OR, 1.187; CI, 1.045-1.347; $p = 0.008$], dried fruit [OR, 1.276; CI, 1.189-1.368; $p < 0.001$], cereals [OR, 1.129; CI, 1.062-1.200; $p < 0.001$], and cheese [OR, 1.187; CI, 1.130-1.247; $p < 0.001$] were positively related to walking pace (Fig. 4).

exposure	outcome	nsnp	method	pval	OR(95% CI)
Cooked vegetable intake	ALM	17	MR Egger	0.259	8.282 (0.243 to 282.391)
		17	MR IVW	**0.001**	1.694 (1.232 to 2.331)
		17	Simple mode	**0.034**	1.602 (1.075 to 2.387)
		17	Weighted median	**0.007**	1.300 (1.075 to 1.572)
		17	Weighted mode	0.104	1.314 (0.963 to 1.794)
Coffee intake	ALM	39	MR Egger	0.491	0.838 (0.508 to 1.380)
		39	MR IVW	**0.017**	1.376 (1.059 to 1.788)
		39	Simple mode	0.157	1.145 (0.953 to 1.376)
		39	Weighted median	**<0.001**	0.864 (0.802 to 0.932)
		39	Weighted mode	**<0.001**	0.894 (0.841 to 0.950)
Fresh fruit intake	ALM	51	MR Egger	0.988	0.993 (0.400 to 2.463)
		51	MR IVW	**<0.001**	1.738 (1.335 to 2.263)
		51	Simple mode	**0.001**	1.535 (1.197 to 1.967)
		51	Weighted median	**<0.001**	1.350 (1.191 to 1.531)
		51	Weighted mode	**<0.001**	1.304 (1.136 to 1.497)
Oily fish intake	ALM	59	MR Egger	0.752	1.094 (0.629 to 1.900)
		59	MR IVW	**<0.001**	1.271 (1.114 to 1.451)
		59	Simple mode	0.338	1.077 (0.927 to 1.251)
		59	Weighted median	**<0.001**	1.140 (1.059 to 1.226)
		59	Weighted mode	0.176	1.097 (0.961 to 1.252)
Dried fruit intake	ALM	41	MR Egger	0.490	1.452 (0.509 to 4.140)
		41	MR IVW	**<0.001**	1.587 (1.261 to 1.998)
		41	Simple mode	**0.018**	1.208 (1.040 to 1.404)
		41	Weighted median	**<0.001**	1.261 (1.141 to 1.392)
		41	Weighted mode	**0.005**	1.222 (1.072 to 1.394)
Cereal intake	ALM	39	MR Egger	0.544	0.724 (0.258 to 2.031)
		39	MR IVW	**0.042**	1.278 (1.009 to 1.619)
		39	Simple mode	**0.003**	1.367 (1.124 to 1.663)
		39	Weighted median	**<0.001**	1.240 (1.117 to 1.377)
		39	Weighted mode	**0.033**	1.352 (1.035 to 1.765)
Cheese intake	ALM	63	MR Egger	0.298	1.407 (0.744 to 2.661)
		63	MR IVW	**0.003**	1.257 (1.080 to 1.463)
		63	Simple mode	**0.040**	1.198 (1.012 to 1.419)
		63	Weighted median	**0.003**	1.108 (1.037 to 1.184)
		63	Weighted mode	**0.007**	1.180 (1.050 to 1.325)
Saturated fatty acids	ALM	51	MR Egger	0.375	0.951 (0.853 to 1.061)
		51	MR IVW	**0.031**	0.935 (0.880 to 0.994)
		51	Simple mode	0.306	0.979 (0.940 to 1.019)
		51	Weighted median	0.379	0.989 (0.966 to 1.013)
		51	Weighted mode	0.637	0.995 (0.976 to 1.015)
Polyunsaturated fatty acids	ALM	58	MR Egger	0.599	1.026 (0.933 to 1.128)
		58	MR IVW	**0.022**	0.942 (0.894 to 0.991)
		58	Simple mode	0.300	0.981 (0.945 to 1.017)
		58	Weighted median	0.520	0.994 (0.974 to 1.013)
		58	Weighted mode	0.421	0.991 (0.971 to 1.012)

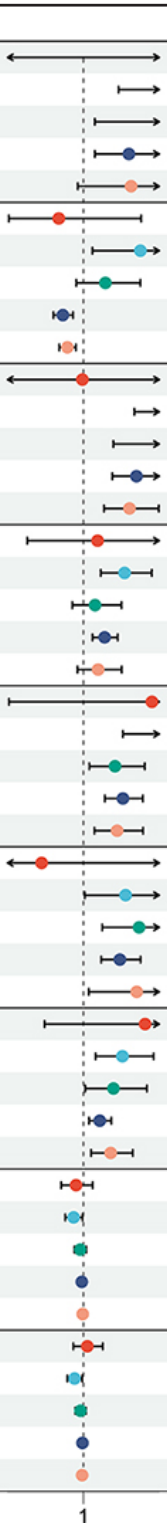

Figure 2.

Forest plot of MR results for dietary intake associated with ALM (nsnp: nonsynonymous single-nucleotide polymorphism; OR: odds ratio; CI: confidence interval).

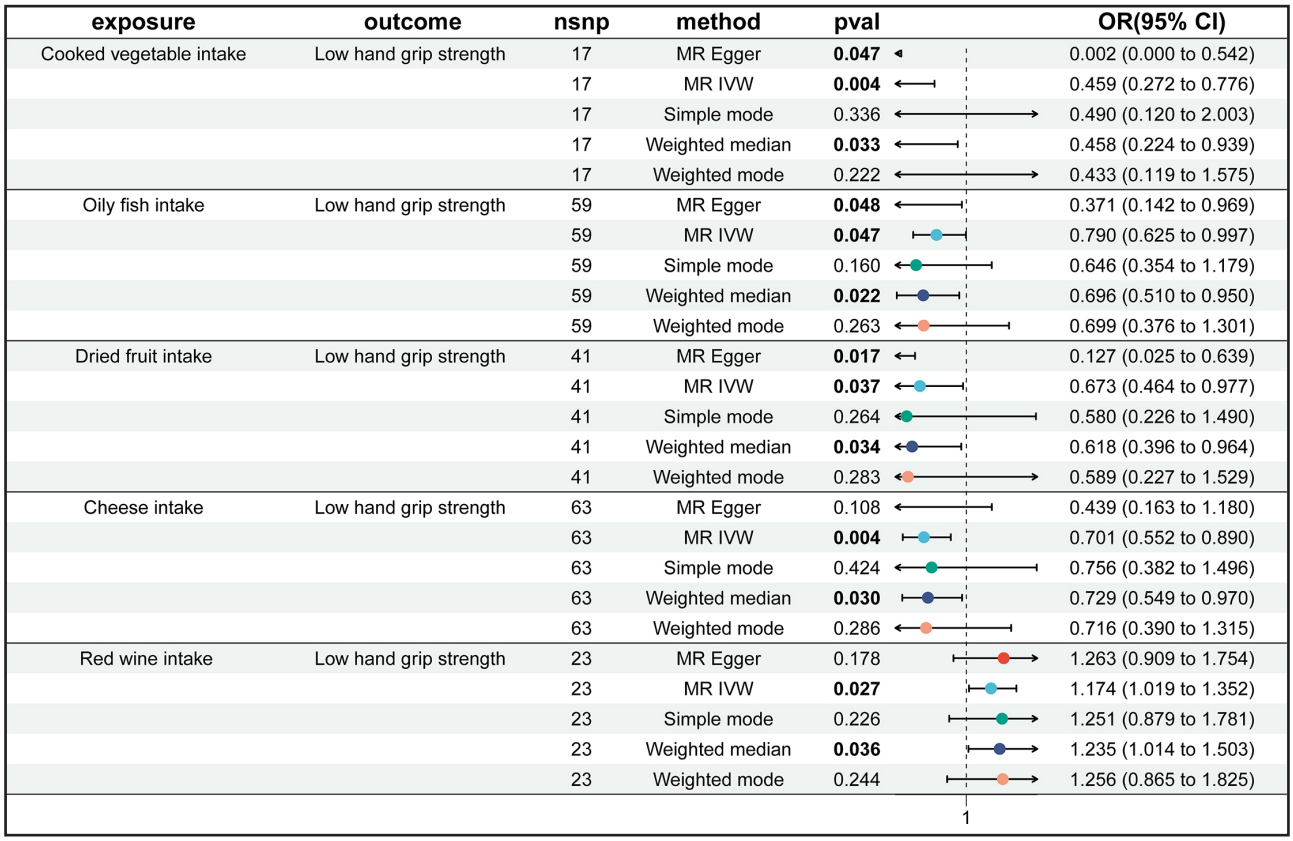

Figure 3.

Forest plot of MR results for dietary intake associated with low hand grip strength (nsnp: nonsynonymous single-nucleotide polymorphism; OR: odds ratio; CI: confidence interval).

SENSITIVITY ANALYSES

Heterogeneity was detected in all the positive studies except for the cooked vegetable intake and low hand grip strength study, oily fish intake and low hand grip strength study, red wine intake and low hand grip strength study, and bacon intake and usual walking pace (Supplementary Table II: https://www.nutricionhospitalaria.org/files/8552/ADMA2-05487-02.pdf). Therefore, a random-effects model in the IVW analysis was applied in our study. The MR-Egger intercept test results suggested that the IVs for the selected dietary intake showed no horizontal pleiotropy except for dried fruit intake and low hand grip strength study and coffee intake and ALM study (Supplemmentary Table III: https://www.nutricionhospitalaria.org/files/8552/ADMA3-05487-02.pdf). The presence of horizontal pleiotropy suggests that a single SNP has an effect on multiple phenotypes or traits in these studies, contrary to the MR hypothesis. So the results of dried fruit intake on low hand grip strength and coffee intake on ALM were excluded from our results.

Scatter plots and funnel plots are shown in supplemmentary figures 1 and 2 (https://www.nutricionhospitalaria.org/files/8552/ADMA4-05487-02.pdf), which underscores data stability. The leave-one-out analysis was performed to assess the influence of individual SNPs on MR findings (Supplemmentary Fig. 3: https://www.nutricionhospitalaria.org/files/8552/ADMA4-05487-02.pdf). The result suggested that individual SNPs for dietary intake have no significant impact on MR results.

DISCUSSION

The associations between diet and the incident risk of sarcopenia are critical and warrant significant research attention due to their potential implications for public health (16). MR studies have extensively explored associations between sarcopenia-related traits and various conditions, such as cardiometabolic diseases, Alzheimer's disease, osteoporosis, type 2 diabetes, and knee osteoarthritis (17-21). However, there remains a significant gap in MR research specifically addressing the causal relationship between sarcopenia and dietary factors, which our study aims to investigate. In this study, the present MR analysis has revealed significant associations between dietary intakes and sarcopenia-related traits, including appendicular lean mass (ALM), low hand grip strength, and walking pace. The intake of oily fish and cheese was consistently found to be beneficial,

exposure	outcome	nsnp	method	pval	OR(95% CI)
Processed meat intake	Usual walking pace	23	MR Egger	0.403	1.182 (0.805 to 1.734)
		23	MR IVW	**0.031**	0.914 (0.842 to 0.992)
		23	Simple mode	0.106	0.828 (0.665 to 1.031)
		23	Weighted median	0.213	0.954 (0.886 to 1.027)
		23	Weighted mode	0.642	1.040 (0.884 to 1.224)
Pork intake	Usual walking pace	14	MR Egger	0.289	0.542 (0.184 to 1.600)
		14	MR IVW	**0.002**	0.786 (0.674 to 0.917)
		14	Simple mode	0.273	0.896 (0.744 to 1.081)
		14	Weighted median	0.052	0.886 (0.784 to 1.001)
		14	Weighted mode	0.346	0.924 (0.790 to 1.082)
Bacon intake	Usual walking pace	20	MR Egger	0.118	0.950 (0.893 to 1.010)
		20	MR IVW	**0.045**	0.973 (0.948 to 0.999)
		20	Simple mode	0.855	1.007 (0.933 to 1.087)
		20	Weighted median	0.371	0.983 (0.946 to 1.021)
		20	Weighted mode	0.860	1.007 (0.931 to 1.090)
Fresh fruit intake	Usual walking pace	51	MR Egger	0.396	0.856 (0.599 to 1.223)
		51	MR IVW	**0.026**	1.125 (1.014 to 1.248)
		51	Simple mode	0.957	1.005 (0.831 to 1.217)
		51	Weighted median	0.532	1.024 (0.951 to 1.103)
		51	Weighted mode	0.741	0.981 (0.876 to 1.098)
Oily fish intake	Usual walking pace	59	MR Egger	0.880	0.982 (0.778 to 1.240)
		59	MR IVW	**<0.001**	1.118 (1.057 to 1.182)
		59	Simple mode	0.070	1.149 (0.991 to 1.332)
		59	Weighted median	**<0.001**	1.116 (1.064 to 1.170)
		59	Weighted mode	0.088	1.115 (0.986 to 1.262)
Salad / raw vegetable intake	Usual walking pace	18	MR Egger	0.935	1.028 (0.535 to 1.977)
		18	MR IVW	**0.008**	1.187 (1.045 to 1.347)
		18	Simple mode	0.378	1.144 (0.855 to 1.532)
		18	Weighted median	**0.012**	1.152 (1.032 to 1.287)
		18	Weighted mode	0.516	1.096 (0.836 to 1.436)
Dried fruit intake	Usual walking pace	41	MR Egger	**0.031**	1.434 (1.045 to 1.969)
		41	MR IVW	**<0.001**	1.276 (1.189 to 1.368)
		41	Simple mode	**0.001**	1.364 (1.144 to 1.626)
		41	Weighted median	**<0.001**	1.285 (1.201 to 1.375)
		41	Weighted mode	**0.009**	1.333 (1.086 to 1.637)
Cereal intake	Usual walking pace	39	MR Egger	0.406	1.122 (0.858 to 1.466)
		39	MR IVW	**<0.001**	1.129 (1.062 to 1.200)
		39	Simple mode	0.343	1.074 (0.929 to 1.242)
		39	Weighted median	**0.001**	1.102 (1.040 to 1.168)
		39	Weighted mode	0.313	1.068 (0.941 to 1.212)
Cheese intake	Usual walking pace	63	MR Egger	0.376	1.098 (0.894 to 1.348)
		63	MR IVW	**<0.001**	1.187 (1.130 to 1.247)
		63	Simple mode	**0.002**	1.183 (1.066 to 1.313)
		63	Weighted median	**<0.001**	1.123 (1.078 to 1.170)
		63	Weighted mode	**0.011**	1.129 (1.031 to 1.237)

Figure 4.

Forest plot of MR results for dietary intake associated with low usual walking pace (nsnp: nonsynonymous single-nucleotide polymorphism; OR: odds ratio; CI: confidence interval).

positively impacting ALM, reducing the risk of low hand grip strength, and improving walking pace. Besides, cooked vegetables, fresh fruit, dried fruit, cereals, and raw vegetables were protective of one or two of the sarcopenia-associated phenotypes. This comprehensive dietary pattern suggests a protective role against various facets of sarcopenia, highlighting the multifaceted benefits of a balanced diet rich in these foods.

A primary advantage of our study is the application of MR analysis, which uses genetic variants as instrumental variables (IVs) to infer causality (22). This method addresses limitations in traditional observational studies, such as confounding and reverse causation (23). By employing SNPs associated with dietary intake as IVs, MR analysis ensures that the genetic variants are randomly allocated at conception, thereby mimicking the randomization process in controlled trials (24,25). This approach allows for a more reliable assessment of the causal relationship between dietary intake and sarcopenia-related traits. The use of summary-level data from GWAS further strengthens our findings, providing robust evidence for the dietary influences on muscle health.

Specifically, the intake of oily fish and cheese was consistently linked to higher ALM, improved grip strength, and enhanced mobility. Oily fish, rich in omega-3 fatty acids, supports muscle cell integrity and reduces inflammation, aiding in muscle maintenance (26). Cheese, high in quality protein and calcium, supports muscle synthesis and bone health (27). These diverse dietary factors collectively emphasize the importance of a balanced diet in maintaining muscle mass and preventing sarcopenia. Additionally, diets rich in oily fish, cooked vegetables, and dairy products protect against decreased hand grip strength. Omega-3 fatty acids in oily fish have strong anti-inflammatory effects and enhance muscle protein synthesis, thus improving muscle strength (28). Cooked vegetables improve the bioavailability of essential nutrients, such as antioxidants and vitamins, through thermal processing, potentially reducing oxidative stress and inflammation, which are critical for muscle preservation (29). Dairy products, including cheese and yogurt, provide high-quality protein and calcium, essential for muscle function and bone health (30). These dietary components, through their combined effects on reducing inflammation, enhancing muscle synthesis, and providing essential nutrients, play a crucial role in preserving hand grip strength, a key indicator of overall muscle function. Furthermore, the intake of fresh fruits, raw vegetables, dried fruits, oily fish, and cheese is significantly associated with improved walking pace. Fresh fruits and vegetables, with their high antioxidant, vitamin, and mineral content, help mitigate oxidative damage and support overall muscle health (31). Dried fruits provide concentrated sources of potassium and fiber, crucial for muscle function and energy metabolism (32,33). Oily fish reduces inflammation and enhances physical performance, and cheese supports muscle maintenance and bone strength (34). These dietary intakes collectively enhanced mobility and overall physical function. These findings underscore the role of a varied diet in promoting healthy aging and preventing sarcopenia.

Based on the above, the findings of our study have significant implications for public health policy the elderly maintain muscle health. We recommend increasing the intake of omega-3-rich oily fish (e.g., salmon, sardines) and high-quality protein sources. Additionally, consuming more fresh fruits, nuts, grains, and raw vegetables, which are rich in vitamins, minerals, and antioxidants, can help protect muscle health (35). Personalized dietary guidelines can be developed to take into account the different nutritional needs of older persons based on age, sex, and health status. For instance, increasing calcium and vitamin D intake for those at risk of osteoporosis and reducing saturated fat intake for those at risk of cardiovascular diseases (36,37). Promoting healthy eating and regular physical activity can prevent sarcopenia and improve overall health and quality of life in older adults. We also propose collaborating with community health service organizations to conduct nutrition education and promotion activities, raising awareness about the relationship between diet and muscle health. Specific measures include hosting health seminars, creating easy-to-understand dietary guideline booklets, utilizing social media platforms to disseminate information, and establishing dietary consultation services to offer personalized advice and health guidance (38). These dietary recommendations can play a critical role in reducing the prevalence of sarcopenia and enhancing the quality of life for older adults.

Despite its valuable insights, the study is still limited by some specific issues. The study relies exclusively on data from the UK Biobank, which predominantly includes individuals of European descent (39). This limits the generalizability of the findings to other ethnic groups and populations with different genetic backgrounds and dietary habits. The dietary intake data were self-reported through questionnaires, which may introduce recall bias and inaccuracies in the reporting of actual consumption. This could affect the reliability of the associations identified between diet and sarcopenia-related traits. Despite the rigorous selection of instrumental variables and statistical adjustments, there may still be residual confounding factors that were not accounted for. These unmeasured confounders could bias the estimates of the causal effects between dietary intake and sarcopenia-related outcomes. Future studies should include diverse age groups, genders, ethnicities, and health statuses to validate the generalizability of the results, and should be designed as long-term longitudinal studies to observe the sustained effects of nutrients on muscle health. Additionally, conducting multicenter studies across various locations will enhance the reliability and generalizability of the findings (40). Beyond observational research, elucidating the exact biological mechanisms by which these dietary factors influence muscle health is essential. In-depth mechanistic studies are needed to explore how specific nutrients affect muscle health at the molecular and cellular levels, providing a theoretical basis for developing targeted nutritional strategies.

CONCLUSION

Our study's MR analysis demonstrated the significant role of dietary intake in influencing sarcopenia-related traits. Specifically, the consumption of oily fish and cheese was consistently associated with beneficial impacts on muscle mass, strength, and function. Cooked vegetables, fresh fruit, dried fruit, cereals, and raw vegetables were beneficial to at least one of the sarcopenia-associated phenotypes. These findings underscore the potential of dietary modifications as

a preventive and therapeutic strategy against sarcopenia. This study may contribute significantly to the advancement of public health outcomes in the field of sarcopenia and aging. In the future, there is a necessity to validate these associations in more diverse populations, using longitudinal studies and randomized controlled trials to explore the efficacy of dietary interventions for the prevention and treatment of sarcopenia.

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