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Association between nut consumption and mortality risk: a 20-year cohort study in Korea with a stratified analysis by health-related variables

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Abstract

Background Although nuts are a well-known healthy food group, the relationship between nut consumption and mortality remains unclear, particularly among Asians. This prospective cohort study examined the association between nut consumption and the risk of all-cause, cardiovascular disease (CVD), and cancer mortality in Korean adults.

Methods Data from two cohorts (the Ansan-Ansung and Health-Examinees) from the Korean Genome and Epidemiology Study were used. A total of 114,140 individuals aged 40–79 years were included in the data analyses. Nut consumption was assessed using a validated semi-quantitative food frequency questionnaire and categorized into four groups: non-consumers, less than 1 serving/week, 1–2 servings/week, and 2 or more servings/week (one serving was 15 g of nuts). Mortality outcomes were determined based on the 2001–2021 death records from Statistics Korea. Cox proportional hazard regression analysis was used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for mortality across nut consumption categories. A stratified subgroup analysis by health-related variables was also performed.

Results During a mean follow-up of 12.3 years, 4,559 deaths were recorded. After adjusting for covariates, the HR for all-cause mortality was 0.877 (95% CI = 0.772–0.996, p for trend = 0.006) in individuals with a nut consumption of 2 or more servings/week compared with that in non-consumers. Multivariable HRs for CVD mortality were 0.800 (95% CI = 0.681–0.939) in individuals consuming less than 1 serving/week, 0.656 (95% CI = 0.469–0.918) in those consuming 1–2 servings/week, and 1.009 (95% CI = 0.756–1.347) in those consuming 2 or more servings/week compared with that in non-consumers (p for trend = 0.080). No association was observed between nut consumption and cancer mortality. Stratified analysis identified significant interactions in the association between nut consumption and all-cause mortality by age, body mass index, and physical activity.

Conclusions Nut consumption was linearly associated with the reduced risk of all-cause mortality and showed a non-linear dose-response relationship with CVD mortality in Koreans, but had no association with cancer mortality.

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The effects of nut consumption, which have been inadequately investigated in this population, varied across different subgroups. These findings suggest that incorporating nuts into the diet should be encouraged for long-term health of Korean adults.

Keywords Nuts, Mortality, Cardiovascular disease, Diet, Korean

Background

Noncommunicable diseases (NCDs) are the leading cause of death worldwide, with cardiovascular disease (CVD) and cancer, in particular, posing a significant public health burden [1]. NCDs are increasingly likely to occur because of lifestyle changes, and unhealthy diets play a particularly important role in their development [2]. Dietary regimens widely recommended for the prevention and management of NCDs include the Dietary Approaches to Stop Hypertension and Mediterranean diet patterns [3]. These healthy dietary regimens have nuts in common, as one of the key food components, since nuts are a good source of monounsaturated and polyunsaturated fatty acids, dietary fiber, carotenoids, vitamin E, vitamin K, and minerals such as magnesium, copper, potassium, and selenium [4–6].

Nuts are well known to offer protective benefits against CVD and its risk factors, such as obesity [7], hypertension [8], and type 2 diabetes [9]. However, the results regarding their effect on cancer remain inconsistent. Similar discrepancies are also observed in studies related to mortality. Most studies have shown a significant effect on reducing CVD mortality associated with nut consumption [10, 11], while the evidence on cancer mortality reduction is controversial [12, 13]. In addition, most of the studies included in the meta-analysis regarding the long-term health benefits of nut consumption were conducted in Western populations. Although Asian adults have considerably different dietary practices, including nut consumption patterns, compared with adults in Western countries [10–13], relatively few studies have been conducted in Asian regions to explore the association between nut consumption and mortality. Therefore, additional research is necessary to clarify the overall link between nut consumption and all-cause and cause-specific mortality, particularly among Asians.

Recent studies conducted in Asian populations on nut intake and mortality have reported findings that differ from those in Western populations. These studies also investigated stratified associations by sociodemographic and lifestyle factors, such as sex, age, body mass index (BMI), and physical activity, as nut consumption is closely linked to these factors [14, 15]. A Japanese study found that increased total nut intake was associated with lower all-cause mortality in men, but not in women [16]. In contrast, a higher peanut intake was inversely associated with CVD mortality only in women, with no significant association in men [16]. A Chinese study showed that for participants engaging in normal activities, nut consumption was not related to mortality (hazard ratio [HR] = 0.923; 95% confidence interval [CI] = 0.841–1.013), whereas for participants with impaired activities of daily living, nut intake was significantly associated with a decrease in mortality (HR = 0.884; 95% CI = 0.839–0.931) [17].

Investigating the role of nut consumption in the risk of mortality among Asians, particularly in relation to mortality by specific subgroups, is necessary to understand the association of nut intake with mortality and to improve the long-term health status of individuals. Therefore, the aims of this study were to explore the association of nut consumption with all-cause, CVD, and cancer mortality, and to examine the association between nut consumption and all-cause mortality stratified by health-related variables using data from Korean prospective cohort studies.

Methods

Data and study participants

The Korean Genome and Epidemiology Study (KoGES), which includes the Ansan-Ansung and Health Examinees (HEXA) cohort studies, is a large-scale population-based prospective study conducted in Korea by the National Institute of Health, Korea Disease Control and Prevention Agency, aimed at investigating the risk factors of NCDs among Koreans. The baseline investigations for the Ansan-Ansung cohort were conducted between 2001 and 2002 and focused on residents in small to medium-sized cities, examining lifestyle, dietary, and environmental impacts on chronic diseases. The baseline study for the Ansan-Ansung cohort included 10,030 participants aged 40–69 years. The HEXA cohort involved medical institutions, public health centers, and healthcare facilities across large and smaller cities, emphasizing the identification of both environmental and genetic risk factors for prevalent chronic diseases in diverse urban settings. The baseline study for the HEXA cohort was conducted between 2004 and 2013, and included 173,195 participants aged 40–79 years. The design and protocol of the KoGES are described in the literature and on the KoGES website [18].

Among the eligible individuals from the two cohort studies ($n = 183{,}225$), participants were excluded based on the following criteria: no linkage to death data ($n = 45{,}113$); absence of dietary data ($n = 1{,}756$); implausible energy intake (< 800 or ≥ 4,000 kcal/day for men, and < 500 or ≥ 3,500 kcal/day for women) (n = 1,996) [19]; lack of data on household income (n = 11,502), education (n = 400), alcohol drinking (n = 220), smoking (n = 174), physical activity (n = 93), and BMI (n = 115); and history of cancer diagnosis that could affect dietary habits (n = 7,716). Finally, 114,140 participants were included in the data analysis (Fig. 1). Before the commencement of the study, all participants voluntarily signed consent forms and the study received exemption approval from the Hannam University Institutional Review Board (approval number: 2023-E-01-09-0625).

Assessment of nut consumption

Dietary data obtained from a food frequency questionnaire (FFQ) were used to assess nut consumption. The reliability and validity of the FFQ used in the KoGES have been previously reported [20, 21]. The Ansan-Ansung cohort study used a 103-item FFQ and the HEXA cohort study used a 106-item FFQ at baseline. These FFQs were conducted through interviews with trained investigators. Both FFQs included the same question asking participants how often they had consumed peanuts, almonds, and pine nuts over the past year. The responses to this question comprised nine frequency options (rarely, 1 time/month, 2–3 times/month, 1–2 times/week, 3–4 times/week, 5–6 times/week, 1 time/day, 2 times/day, and 3 times/day), with three average serving sizes (0.5, 1, and 1.5 servings) representing the amount of nuts consumed by a participant. Peanuts, almonds, and pine nuts were included in the food list of FFQ as they were commonly consumed nuts in Koreans and the serving size of nuts was set in the FFQ (15 g) based on the median value of nut consumption determined from dietary data of the national nutrition survey [20, 21]. The daily intake of nuts for each participant was calculated by converting the reported frequency of consumption into a weekly intake based on one serving and multiplying it by the selected average serving size. Based on these responses, nut consumption was categorized into non-consumption, less than 1 serving/week, 1–2 servings/week, and 2 or more servings/week, considering the distribution of participants in each category of consumption frequency. Energy and nutrient intakes, calculated using dietary data obtained from the FFQs, were used in this study. The percentage of energy from macronutrients was calculated for carbohydrate, protein, and fat intakes.

Determination of mortality outcomes

To determine mortality outcomes, including all-cause and cause-specific mortality, this study analyzed the KoGES-linked National Death Index database provided by Statistics Korea. Participant deaths were monitored from the initial baseline survey to December 2021. The underlying causes of death were classified according to the Korean Standard Classification of Diseases, 7th edition, which is based on the 10th revision of the International Classification of Diseases. Deaths were classified as all-cause (A00-Z99), CVD (I00-I99), or cancer deaths (C00-D48) [22].

Measurement of covariates

This study considered potential confounding variables, including age, sex, BMI, household income, education, alcohol drinking, smoking, physical activity, and history of disease, as covariates. Covariates were assessed using self-administered questionnaires in the baseline examination of KoGES. BMI was calculated as measured weight divided by measured height squared (kg/m^2) and classified according to the guidelines of the Korean Society for the Study of Obesity as follows: non-overweight/obese (< 23 kg/m^2), overweight (23–25 kg/m^2), and obese (≥ 25 kg/m^2) [23]. Physical activity was categorized into "yes" (regularly exercised for ≥ 30 min once a day) or "no". Information on the participants' history of diseases was obtained from both participants' self-reported data and objective indicators provided by the health examinations. Previous diagnosis by a doctor or current use of medication or treatment of diabetes, CVD, hypertension, and metabolic syndrome were based on the self-reported data. The history criteria for diabetes included at least one of the following four criteria: a diagnosis of diabetes by a doctor, current consumption of anti-diabetic medication, a fasting plasma glucose ≥ 126 mg/dL, or a HbA1C ≥ 6.5% [24]. The history criteria for CVD included a diagnosis of or undergoing current treatment for conditions including myocardial infarction, congestive heart failure, coronary artery disease, peripheral vascular disease, cerebrovascular disease, stroke, transient ischemic attacks, or angina [25]. The history of hypertension was defined as a systolic blood pressure of ≥ 140 mmHg or a diastolic blood pressure of ≥ 90 mmHg, a diagnosis of hypertension, or currently under treatment for hypertension [26]. Metabolic syndrome was determined by the presence of three or more of the following conditions: abdominal obesity (waist circumference ≥ 90 cm in men and ≥ 85 cm in women), low HDL-cholesterol (< 40 mg/dL in men and < 50 mg/dL in women or medication use), elevated triglycerides (≥ 150 mg/dL or medication use), elevated blood pressure (systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg or medication use), and elevated fasting blood glucose (≥ 100 mg/dL or medication use) [27, 28].

Statistical analyses

All statistical analyses were conducted using SPSS version 25.0 (Armonk, NY: IBM Corp). A cumulative hazard graph was employed to estimate the cumulative mortality risk of all-cause, CVD, and cancer mortality across nut

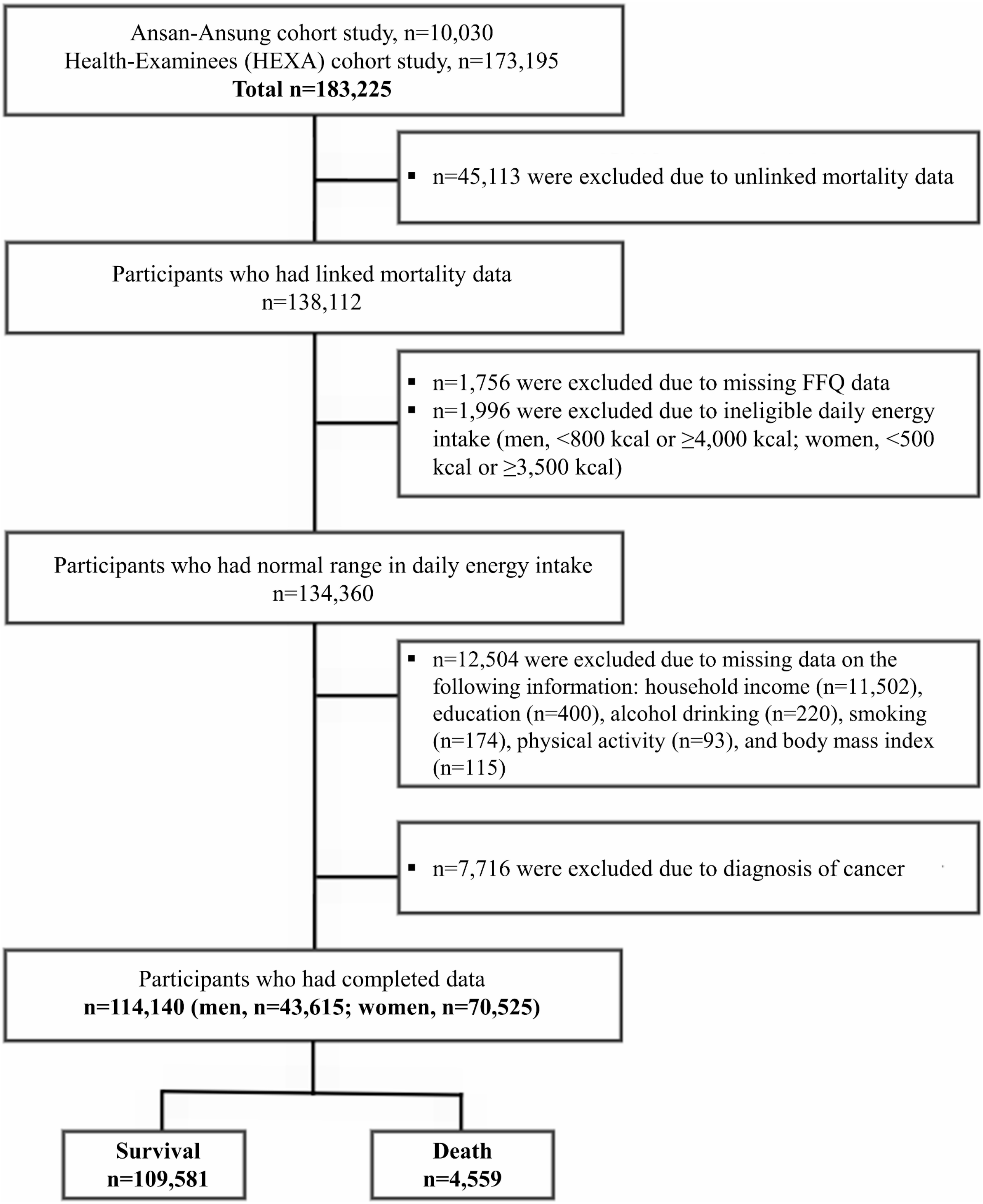

Fig. 1 Flowchart of participant selection

consumption. Categorical and continuous variables for the general characteristics of participants according to nut consumption were compared using the chi-squared test (χ^2 test) and analysis of variance (ANOVA). Energy and nutrient intake according to nut consumption is presented as means and standard errors after adjusting for energy, except for the percentage of energy from macronutrients, and differences were compared using a generalized linear regression model. A multivariable Cox proportional hazard regression analysis was performed to determine the HRs and 95% CIs for mortality according to nut consumption. To assess the association between nut consumption and mortality, this study applied four models adjusted for different potential confounders. Model 1 was unadjusted. Model 2 was adjusted for sex, age (continuous), and BMI (continuous). Model 3 was further adjusted for household income, education, alcohol drinking, smoking, physical activity, and energy intake (continuous). Model 4 was additionally adjusted for a history of disease. Stratified sub-analyses of the association between nut consumption and all-cause mortality were performed according to age group, sex, BMI, alcohol drinking, smoking, physical activity, and history of diseases. For stratified analysis, age group was categorized into 'under 60' and '60 or older'. Alcohol drinking and smoking status were categorized into 'ever' (combining past and current) and 'never'. The history of disease was classified as 'yes' if diabetes, CVD, hypertension, or metabolic syndrome was present. HRs, 95% CIs, and p for interaction for all-cause mortality in the comparison with the highest frequency of nut consumption by a stratified covariate are presented. Statistical significance was defined as a two-sided p-value of less than 0.05.

Results

Cumulative hazard graph

A cumulative hazard graph was used to estimate the cumulative incidence risks of all-cause, CVD, and cancer mortality across the different nut consumption groups (Fig. 2). The 20-year cumulative incidence risks of all-cause, CVD, and cancer mortality were higher among non-consumers than among nut consumers. Based on the log-rank test results, there were significant differences in the cumulative hazard graphs for all-cause ($p<0.001$) and CVD mortality ($p=0.004$), whereas the difference was not significant for cancer mortality ($p=0.649$).

Baseline characteristics according to nut consumption

The baseline characteristics of the participants according to nut consumption are presented in Table 1. The average age of the participants was 52.8 years, with 38.2% men and 61.8% women. As nut consumption increased, the prevalence of obesity decreased, and household income and education levels increased ($p<0.001$). In addition, the rates of current alcohol drinking and smoking were lower, and the percentage of participants who engaged in physical activity was higher ($p<0.001$). Individuals who did not consume nuts had a higher prevalence of hypertension and metabolic syndrome ($p<0.001$) compared to those who frequently consumed nuts, whereas no significant differences were observed in the prevalence of diabetes or CVD according to nut consumption.

Energy and nutrient intake according to nut consumption

Energy and nutrient intake according to nut consumption are shown in Table 2. With an increase in nut consumption, there was a significant increase in energy intake (p for trend <0.001). The intake of all nutrients listed, including carbohydrate, protein, fat, dietary fiber, vitamins A, B_1, B_2, C, E, calcium, phosphorus, iron, potassium, and sodium significantly increased with

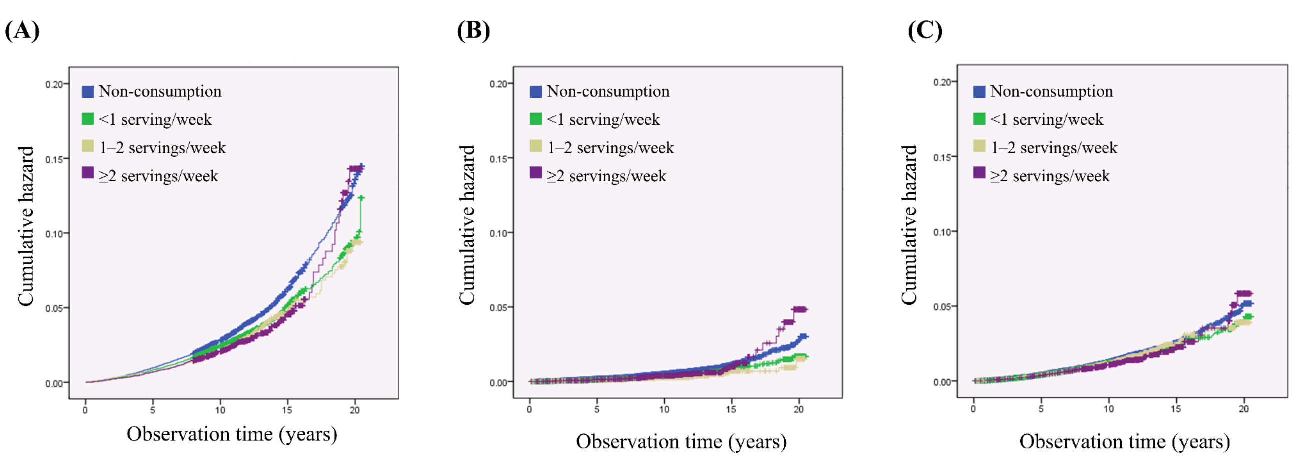

Fig. 2 Cumulative hazard graph of mortality associated with nut consumption. Cumulative hazard incidences of all-cause mortality (**A**), cardiovascular disease mortality (**B**), and cancer mortality (**C**)

Table 1 Baseline participant characteristics according to nut consumption

		Nut consumption				Total	*p*-value
		Non-consumption	**< 1 serving/week**	**1–2 servings/week**	**≥ 2 servings/week**		
n (%)		49,966 (43.8)	44,667 (39.1)	9,766 (8.6)	9,741 (8.5)	114,140 (100.0)	
Age (years)		52.81 ± 0.04	52.53 ± 0.04	53.01 ± 0.08	53.78 ± 0.08	52.80 ± 0.02	< 0.001
Body mass index (kg/m^2)		24.05 ± 0.01	23.92 ± 0.14	23.85 ± 2.83	23.72 ± 0.03	23.95 ± 0.01	< 0.001
Sex	Men	19,397 (38.8)	17,644 (39.5)	3,577 (36.6)	2,997 (30.8)	43,615 (38.2)	< 0.001
	Women	30,569 (61.2)	27,023 (60.5)	6,189 (63.4)	6,744 (69.2)	70,525 (61.8)	
Body mass index	< 23 kg/m^2	18,788 (37.6)	17,438 (39.0)	3,920 (40.1)	4,100 (42.1)	42,211 (38.7)	< 0.001
	23–25 kg/m^2	13,748 (27.5)	12,564 (28.1)	2,683 (27.5)	2,681 (27.5)	31,676 (27.8)	
	≥ 25 kg/m^2	17,430 (34.9)	14,665 (32.8)	3,163 (32.4)	2,960 (30.4)	38,218 (33.5)	
Household income	< KRW 2,000,000	19,376 (38.8)	12,967 (29.0)	2,499 (25.6)	2,473 (25.4)	37,315 (32.7)	< 0.001
	KRW 2,000,000–4,000,000	20,285 (40.6)	19,385 (43.4)	4,438 (45.5)	4,157 (42.7)	48,265 (42.3)	
	≥ KRW 4,000,000	10,305 (20.6)	12,315 (27.6)	2,829 (29.0)	3,111 (31.9)	28,560 (25.0)	
Education	≤ Middle school	19,205 (38.4)	12,138 (27.2)	2,312 (23.7)	2,104 (21.6)	35,759 (31.3)	< 0.001
	≤ High school	19,745 (39.5)	19,055 (42.7)	4259 (43.6)	4,320 (44.3)	47,379 (41.5)	
	≥ College	11,016 (22.0)	13,474 (30.2)	319 (32.7)	3,317 (34.1)	31,002 (27.2)	
Alcohol drinking	No	24,470 (49.0)	21,045 (47.1)	4,697 (48.1)	5,134 (52.7)	55,346 (48.5)	< 0.001
	Past	1,910 (3.8)	1,607 (3.6)	336 (3.4)	368 (3.8)	4,221 (3.7)	
	Current	23,586 (47.2)	22,015 (49.3)	4,733 (48.5)	4,239 (43.5)	54,573 (47.8)	
Smoking	No	34,270 (68.6)	31,004 (69.4)	6,961 (71.3)	7,366 (75.6)	79,601 (69.7)	< 0.001
	Past	7,693 (15.4)	7,555 (16.9)	1,603 (16.4)	1,491 (15.3)	18,342 (16.1)	
	Current	8,003 (16.0)	6,108 (13.7)	1,202 (12.3)	884 (9.1)	16,197 (14.2)	
Physical activity	No	24,398 (48.8)	19,639 (44.0)	3,806 (39.0)	3,371 (34.6)	51,214 (44.9)	< 0.001
	Yes	25,568 (51.2)	25,028 (56.0)	5,960 (61.0)	6,370 (65.4)	62,926 (55.1)	
History of disease	Diabetes	4,966 (9.9)	4,259 (9.5)	946 (9.7)	932 (9.6)	11,103 (9.7)	0.193
	Cardiovascular disease	1,757 (3.5)	1,474 (3.3)	323 (3.3)	361 (3.7)	3,915 (3.4)	0.107
	Hypertension	14,930 (29.9)	12,426 (27.8)	2,687 (27.5)	2,718 (27.9)	32,761 (28.7)	< 0.001
	Metabolic syndrome	11,966 (23.9)	9,391 (21.0)	2,022 (20.7)	1,863 (19.1)	25,242 (22.1)	< 0.001

One serving of nuts is 15 g. Values are presented as numbers (%) or means ± standard errors. *p*-values were calculated using the chi-square test for categorical variables and analysis of variance for continuous variables

Table 2 Energy and nutrient intake according to nut consumption

	Nut consumption				Total	*p*-value	*p* for trend
	Non-consumption	< 1 serving/week	1–2 servings/week	≥ 2 servings/week			
Energy (kcal/day)	1,675.1 ± 2.15	1,756.1 ± 2.29	1,898.5 ± 5.17	1,959.1 ± 5.64	1,750.1 ± 1.48	< 0.001	< 0.001
Carbohydrate (g/day)	301.5 ± 0.37	312.3 ± 0.39	328.2 ± 0.87	332.2 ± 0.95	310.6 ± 0.25	< 0.001	< 0.001
Protein (g/day)	55.6 ± 0.10	59.4 ± 0.10	67.3 ± 0.23	70.9 ± 0.26	59.4 ± 0.07	< 0.001	< 0.001
Fat (g/day)	25.2 ± 0.07	27.9 ± 0.07	33.8 ± 0.16	38.0 ± 0.18	28.1 ± 0.05	< 0.001	< 0.001
Dietary fiber (g/day)	5.39 ± 0.01	5.67 ± 0.01	6.46 ± 0.03	7.22 ± 0.03	5.75 ± 0.01	< 0.001	< 0.001
Vitamin A (RE/day)	437.8 ± 1.43	477.08 ± 1.49	562.03 ± 3.34	620.0 ± 3.89	479.4 ± 0.98	< 0.001	< 0.001
Vitamin B_1 (mg/day)	0.96 ± 0.00	1.01 ± 0.00	1.12 ± 0.00	1.17 ± 0.00	1.01 ± 0.00	< 0.001	< 0.001
Vitamin B_2 (mg/day)	0.84 ± 0.00	0.90 ± 0.00	1.04 ± 0.00	1.12 ± 0.00	0.90 ± 0.00	< 0.001	< 0.001
Vitamin C (mg/day)	97.0 ± 0.29	105.1 ± 0.30	121.3 ± 0.66	134.3 ± 0.75	105.4 ± 0.20	< 0.001	< 0.001
Vitamin E (mg/day)	7.17 ± 0.02	8.05 ± 0.02	9.68 ± 0.04	11.3 ± 0.05	8.08 ± 0.01	< 0.001	< 0.001
Calcium (mg/day)	399.0 ± 1.01	437.2 ± 1.09	515.9 ± 2.40	589.3 ± 2.83	440.2 ± 0.71	< 0.001	< 0.001
Phosphorus (mg/day)	837.3 ± 1.37	888.6 ± 1.46	1,006.5 ± 3.24	1,087.0 ± 3.67	893.1 ± 0.95	< 0.001	< 0.001
Iron (mg/day)	9.13 ± 0.02	9.96 ± 0.02	11.53 ± 0.05	12.6 ± 0.05	9.96 ± 0.01	< 0.001	< 0.001
Potassium (mg/day)	2,074.8 ± 4.15	2,221.3 ± 4.43	2,548.0 ± 9.57	2,808.6 ± 11.05	2,235.3 ± 2.88	< 0.001	< 0.001
Sodium (mg/day)	2,453.3 ± 6.23	2,468.6 ± 6.38	2,724.3 ± 13.39	2,807.9 ± 14.45	2,512.7 ± 4.08	< 0.001	< 0.001
Percentage of energy from macronutrient							
Carbohydrate (%kcal)	73.4 ± 0.03	72.3 ± 0.03	70.0 ± 0.07	68.3 ± 0.07	72.3 ± 0.02	< 0.001	< 0.001
Protein (%kcal)	13.3 ± 0.01	13.6 ± 0.01	14.2 ± 0.02	14.5 ± 0.02	13.6 ± 0.01	< 0.001	< 0.001
Fat (%kcal)	13.3 ± 0.02	14.1 ± 0.02	15.8 ± 0.05	17.3 ± 0.05	14.1 ± 0.02	< 0.001	< 0.001

One serving of nuts is 15 g. Values are presented as means ± standard errors. *p*-values were calculated using the analysis of variance. *p* for trends were calculated using a generalized linear regression model after adjustment for energy intake, except for energy and the percentage of energy from macronutrients

nut consumption after adjusting for energy intake (*p* for trends < 0.001). As nut consumption increased to 2 or more servings/week, the energy contribution from carbohydrate decreased, while the energy contribution from protein and fat increased (*p* for trends < 0.001).

Association between nut consumption and mortality

Table 3 shows the HRs and 95% CIs for all-cause, CVD, and cancer mortality according to nut consumption. A total of 4,559 deaths occurred during an average 12.28 years of follow-up. After fully adjusting for potential covariates (Model 4), an inverse association was observed between the highest nut consumption (2 or more servings/week) and the risk of all-cause mortality (HR = 0.877; 95% CI = 0.772–0.996; *p* for trend = 0.006). In the fully adjusted model (Model 4), nut consumption of less than 1 serving/week and 1–2 servings/week were significantly associated with lower CVD mortality (HR = 0.800; 95% CI = 0.681–0.939, and HR = 0.656; 95% CI = 0.469–0.918, respectively), considering that non-consumers were the reference (*p* for trend = 0.080). Although Model 2 showed a significantly decreasing trend in the association between nut consumption and cancer mortality, no significant association was observed between nut consumption and cancer mortality after fully adjusting for covariates.

Association between nut consumption and all-cause mortality stratified by covariates

Nut consumption was found to have a significant inverse relationship with all-cause mortality in Table 3, further analyses stratified by covariates were conducted to determine the association between nut consumption and all-cause mortality according to health-related variables (Fig. 3). Significant differences in the association between nut consumption and all-cause mortality were observed according to age group, BMI status, and physical activity level. There was a significant interaction by age group in the association between nut consumption and all-cause mortality *p*. HR for all-cause mortality in the highest nut consumption group was lower among individuals ≥ 60 years than that among individuals < 60 years (HR = 0.867; 95% CI = 0.731–1.028; *p* for interaction = 0.027). When comparing the HR for all-cause mortality in the highest nut consumption group by BMI status, individuals with a BMI of 23–25 kg/m^2 had a lower HR than individuals with BMI < 23 kg/m^2 or BMI ≥ 25 kg/m^2 (HR = 0.626; 95% CI = 0.475–0.826; *p* for interaction = 0.015). For nut consumption of 2 or more servings per week, individuals who reported no physical activity exhibited a lower risk of all-cause mortality than that in those who regularly engaged physical activity (HR = 0.750; 95% CI = 0.601–0.936; *p* for interaction = 0.008).

Table 3 Risks of all-cause, cardiovascular disease, and cancer mortality according to nut consumption

	Nut consumption				Total	p for trend
	Non-consumption	< 1 serving/week	1–2 servings/week	≥ 2 servings/week		
Person-time (years), sum	632,384.80	543,684.00	113,715.20	111,312.70	1,401,096.70	
Person-time (years), mean ± SD	12.66 ± 2.87	12.17 ± 2.52	11.64 ± 2.52	11.43 ± 2.28	12.28 ± 2.69	
All-cause mortality						
Events	2,402	1,576	304	277	4,559	
Incidence per 1,000 person-years	3.80	2.90	2.67	2.49	3.25	
Model 1	1.000 (Ref)	0.810 (0.760–0.863)	0.773 (0.686–0.872)	0.743 (0.655–0.841)		< 0.001
Model 2	1.000 (Ref)	0.853 (0.800–0.909)	0.800 (0.710–0.902)	0.735 (0.649–0.833)		< 0.001
Model 3	1.000 (Ref)	0.928 (0.870–0.990)	0.912 (0.808–1.029)	0.882 (0.776–1.002)		0.008
Model 4	1.000 (Ref)	0.927 (0.869–0.989)	0.908 (0.805–1.026)	0.877 (0.772–0.996)		0.006
Cardiovascular disease mortality						
Events	449	239	38	55	781	
Incidence per 1,000 person-years	0.71	0.44	0.33	0.49	0.56	
Model 1	1.000 (Ref)	0.667 (0.570–0.780)	0.525 (0.377–0.732)	0.807 (0.609–1.069)		< 0.001
Model 2	1.000 (Ref)	0.717 (0.612–0.840)	0.554 (0.397–0.772)	0.801 (0.605–1.062)		< 0.001
Model 3	1.000 (Ref)	0.798 (0.680–0.937)	0.655 (0.468–0.916)	1.010 (0.757–1.348)		0.078
Model 4	1.000 (Ref)	0.800 (0.681–0.939)	0.656 (0.469–0.918)	1.009 (0.756–1.347)		0.080
Cancer mortality						
Events	1,028	763	163	138	2,092	
Incidence per 1,000 person-years	1.63	1.40	1.43	1.24	1.49	
Model 1	1.000 (Ref)	0.900 (0.819–0.988)	0.945 (0.801–1.115)	0.835 (0.699–0.998)		0.023
Model 2	1.000 (Ref)	0.942 (0.857–1.035)	0.972 (0.823–1.147)	0.827 (0.692–0.988)		0.046
Model 3	1.000 (Ref)	1.000 (0.909–1.100)	1.057 (0.894–1.251)	0.931 (0.776–1.118)		0.768
Model 4	1.000 (Ref)	0.997 (0.906–1.097)	1.052 (0.889–1.245)	0.931 (0.775–1.117)		0.710

One serving of nuts is 15 g. Values are presented as hazard ratios (95% confidence intervals) obtained from Cox proportional hazard regression analysis. Model 1: unadjusted; Model 2: adjusted for sex, age, and body mass index; Model 3: adjusted for Model 2 + household income (< 2 million won, 2–4 million won, ≥ 4 million won), education (≤ middle school, ≤ high school, ≥ college), alcohol drinking (never, past, or current drinker), smoking (never, past, or current smoker), physical activity (no or yes), and energy intake; Model 4: adjusted for Model 3 + history of diabetes, cardiovascular disease, hypertension, or metabolic syndrome

Discussion

This study investigated the association between nut consumption and all-cause and cause-specific mortality using data from two large Korean prospective cohort studies. The results showed that individuals who consumed more than 2 servings/week of nuts had a 12% lower risk of all-cause mortality than those who did not. Furthermore, for CVD mortality, individuals consuming 1–2 servings per week had a 34% lower risk than non-consumers after full adjustment for covariates. However, no significant association was observed between nut consumption and cancer mortality. Stratified analysis identified significant interactions in the association between nut consumption and all-cause mortality by age, BMI, and physical activity.

Consistent with previous meta-analyses, this study showed that a higher weekly consumption of nuts was associated with a reduction in the risk of all-cause mortality. According to an umbrella review, an intake of 28 g/day of nuts compared with not consuming nuts was associated with a 22% risk reduction of all-cause mortality (relative risk [RR] = 0.78; 95% CI = 0.72–0.84) [29]. Aune et al. suggested that an increased intake of nuts to 20 g/day or more could have averted 4.4 million deaths in North and South America, Europe, Southeast Asia, and the Western Pacific [30]. In addition, the Prospective Urban and Rural Epidemiology (PURE) study found that higher nut intake (> 120 g/week vs. < 30 g/month) was associated with a lower risk of all-cause mortality (HR = 0.77; 95% CI = 0.69–0.87; p for trend < 0.0001) [31]. Although nut consumption in Asian populations is much lower than that in Western countries [32–34], frequent nut consumption has been consistently associated with all-cause mortality in Asian countries [35, 36].

Nut consumption is associated with improvements in markers related to CVD, such as triglycerides [37–39], total cholesterol [37–39], HDL-cholesterol [40], LDL-cholesterol [37–39], and blood pressure [39, 40]. Moreover, protective effects of nuts against the development of CVD have also been observed. According to the pooling analysis of three large US prospective cohort studies, individuals with a higher total nut consumption (≥ 0.5 servings/day) had a lower risk of CVD incidence (RR = 0.75; 95% CI = 0.67–0.84) that that non-consumers over a 4-year interval [41]. An umbrella review found that consuming 28 g of nuts daily, compared with not consuming nuts, was linked to a 21% reduction in CVD incidence (RR = 0.79; 95% CI = 0.70–0.89) [29]. The current study showed that the risk of CVD mortality

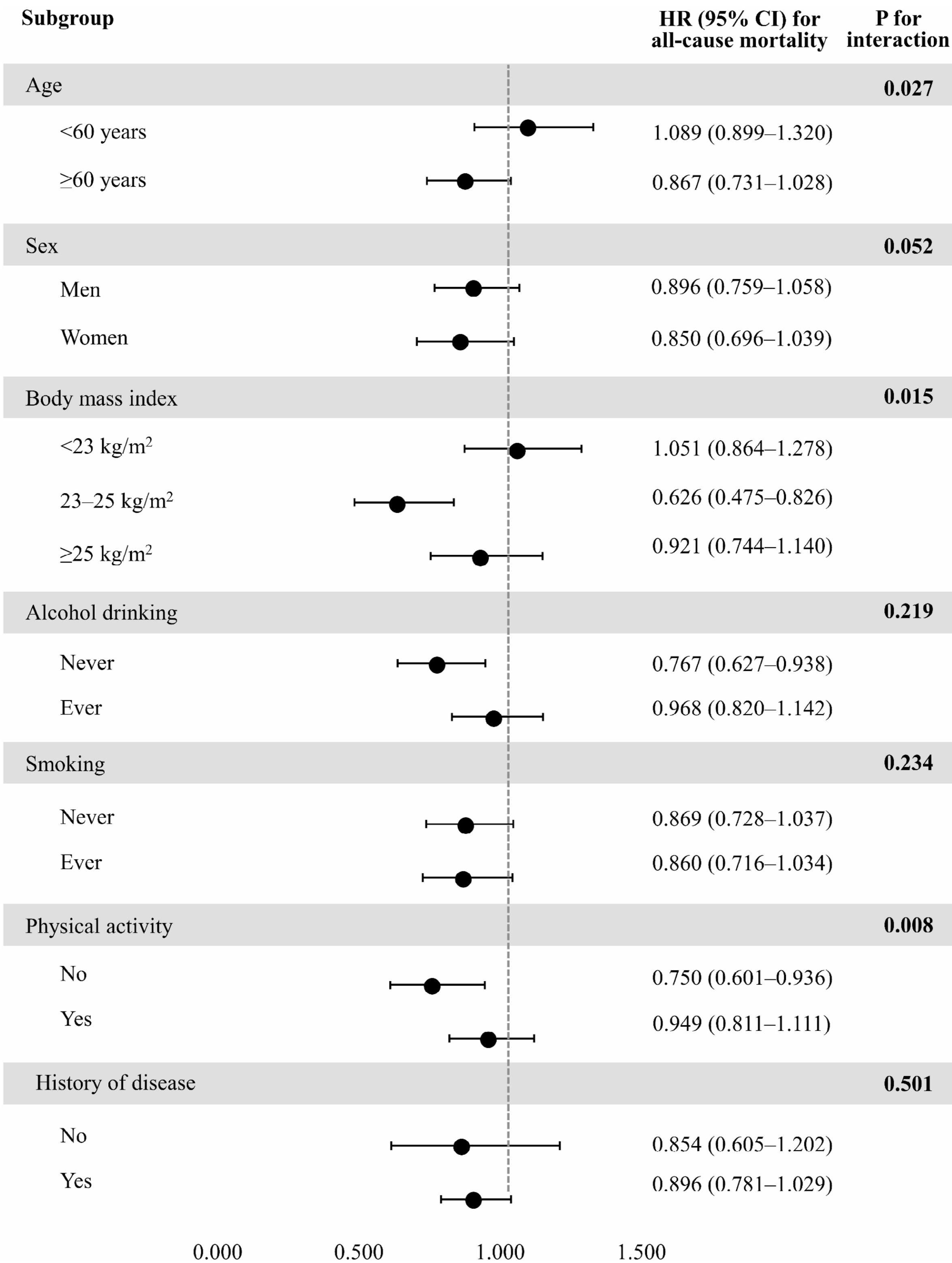

Fig. 3 The risk of all-cause mortality in the highest frequency of nut consumption stratified by covariates. Hazard ratio (HR) and 95% confidence interval (CI) for all-cause mortality and *p* for interaction were determined using Cox proportional hazard regression analysis after adjustment for sex, age, BMI, household income (< 2 million won, 2–4 million won, ≥ 4 million won), education (≤ middle school, ≤ high school, ≥ college), alcohol drinking (never, past, or current drinker), smoking (never, past, or current smoker), physical activity (no or yes), energy intake, and history of diabetes, cardiovascular disease, hypertension, or metabolic syndrome. The dots show HRs and the line ranges show 95% CIs. BMI, body mass index

decreased up to 1–2 servings/week of nut consumption, but there was no significant association observed at ≥2 servings/week. Although this study did not show a significant trend, consistent with previous research, frequent nut consumption was significantly associated with a decreased risk of CVD mortality. As heart and cerebrovascular diseases are the second and fourth leading causes of death in Korea, respectively, the findings of this study imply that frequent nut consumption in the daily diet of Koreans may be an effective strategy for CVD prevention and management.

The inverse association among nut consumption, all-cause mortality, and CVD mortality in this study may be explained by the fact that nuts are rich in polyunsaturated fatty acids, dietary fiber, and antioxidants. Polyunsaturated fatty acids have been shown to reduce triglycerides level, thereby reducing risk factors associated with CVD [42]. Dietary fiber increases bile excretion rates, thereby reducing serum total and LDL-cholesterol levels. Both soluble and insoluble dietary fibers can induce satiety and decrease energy intake, leading to weight control [43]. Furthermore, dietary fiber influences the gut microbiota; the fermentation of dietary fiber by these microbiota generates short-chain fatty acids as byproducts, which can lower blood pressure [44]. Antioxidants contained in nuts are known to reduce chronic inflammation and lower the risk of related diseases, thus aiding in the prevention and management of CVD [7, 31].

However, this study did not observe a relationship between nut consumption and cancer mortality, which is inconsistent with previous meta-analyses. According to an umbrella review, a nut intake of 28 g/day compared with not eating nuts was associated with an 11% risk reduction in cancer deaths (RR=0.89; 95% CI=0.83–0.94) [29]. According to the review, clinical trials assessing the impact of nut consumption on inflammatory outcomes reported changes in C-reactive protein, interleukins, tumor necrosis factor-alpha, cell adhesion molecules, and antioxidant defense system [29]. Similar to the current study findings, three large prospective cohort studies in the US reported no significant association between nut consumption and total cancer incidence [13]. These inconsistent findings cannot be fully explained. One possible explanation is that nut intake is differently associated with specific types of cancer. According to a systematic review, nut intake was associated with a decreased risk of developing colorectal, endometrial, and pancreatic cancers; however, no significant association was found with upper aerodigestive tract cancer, breast cancer, gastric cancer, hepatocellular carcinoma, ovarian cancer, prostate cancer, or stomach cancer [12]. Moreover, the current study excluded individuals diagnosed with cancer at baseline, as they have different dietary practices, suggesting that cancer mortality could also be related to cancer incidence.

This study analyzed the relationship between nut consumption and all-cause mortality stratified by health-related variables and significant interactions were observed in the subgroups stratified by age, BMI status, and physical activity. Our findings revealed that nut consumption had a greater impact on reducing mortality risk in populations over 60 years of age, suggesting that the nutritional value of nuts and their effect on preventing mortality may be particularly important in the elderly. For individuals with a BMI between 23 and 25 kg/m^2, a higher nut intake was associated with a more pronounced decrease in all-cause mortality risk. According to Bao et al., there was a stronger association between nut intake and mortality in overweight/obese participants than that in normal-weight participants (p for interaction=0.004) [45]. The large-cohort PURE study examined the association of nuts with mortality by BMI and found that the HR for mortality decreased progressively as BMI increased from less than 25 kg/m^2 (HR=0.89; 95% CI=0.79–1.01), to 25–30 kg/m^2 (HR=0.85; 95% CI=0.73–0.99), and 30 kg/m^2 or more (HR=0.79; 95% CI=0.61–0.98) [31]. Unlike these previous studies, our study found a reduced risk of mortality only in individuals with a BMI of 23–25 kg/m^2, with no significant reduction in the mortality risk in individuals with higher BMI (over 25 kg/m^2). While the reasons for this U-shaped relationship cannot be interpreted with certainty, several considerations should be explored. Firstly, the use of different BMI cut-offs may account for the inconsistent results. Notably, the World Health Organization standards classify a BMI of over 25 kg/m^2 as overweight and a BMI of over 30 kg/m^2 as obese, whereas Korean guidelines classify a BMI of 23–25 kg/m^2 as overweight and a BMI of over 25 kg/m^2 as obese [23]. Secondly, Koreans exhibit a different distribution of BMI values compared to individuals in Western countries. Using a threshold of 30 kg/m^2, the rates for men above this threshold were 26.7% in Canada, 27.0% in the UK, and 13.5% in France. In Korean adults, only 6.2% for men and 5.5% of women were above this threshold [46]. Additionally, given that mortality rates were lowest for individuals in the overweight range of 23–26 kg/m^2 [47, 48], the impact of nut consumption on mortality in individuals with a BMI of 23–25 kg/m^2 could have been more distinctly pronounced rather than in other ranges of BMI. This study also found that nut consumption significantly contributed to a reduction in mortality risk among individuals who did not engage in physical activity, although the interpretation of this result requires further investigation owing to insufficient evidence. The results from the subgroup analysis in this study underscore the need for further research on different populations to clarify the relationship between nut consumption and mortality risk and determine how nuts can provide health benefits based on specific demographic characteristics or lifestyle factors.

This study has some limitations. First, this study grouped peanuts, almonds, and pine nuts together instead of analyzing them individually and did not consider the association with mortality of other types of nuts. Second, the current study did not examine the salt content or preparation methods, such as roasting, of the nuts consumed by the participants. Third, although covariates that could affect nut consumption and mortality were adjusted for as much as possible, further covariates may exist. Despite these limitations, to the best of our knowledge, this is the first study to examine the relationship between nut consumption and all-cause and cause-specific mortality among Korean adults, with a large sample size and long-term follow-up period, providing important evidence for the long-term health benefits of nut intake among Asians.

Conclusions

This prospective cohort study revealed that frequent nut consumption is linearly associated with a reduced risk of all-cause mortality among Korean adults and shows a non-linear dose-response relationship with CVD mortality. However, no association was found with cancer mortality. Individuals who consumed more than 2 servings (30 g) of nuts weekly had a 12% lower risk of all-cause mortality than non-consumers. Additionally, individuals consuming 1–2 servings (15–30 g) of nuts per week exhibited a 34% lower risk of CVD mortality than non-consumers. These findings underscore the importance of including nuts in a balanced diet to improve the long-term health outcomes in this population. They also support the incorporation of nut consumption into dietary practices through the provision of nutrition education and dietary guidelines may be an effective strategy in reducing the risk of mortality, particularly from CVD, among Koreans. Future studies with detailed specifications of nut varieties and nut processing conditions are necessary to validate the results of this study. Furthermore, it may be necessary to examine whether the impact of nut consumption on mortality varies according to socioenvironmental factors and lifestyle patterns.

Abbreviations

NCD	Noncommunicable disease
CVD	Cardiovascular disease
BMI	Body mass index
HR	Hazard ratio
CI	Confidence interval
KoGES	Korean Genome and Epidemiology Study
HEXA	Health Examinees
FFQ	Food frequency questionnaire
ANOVA	Analysis of variance
RR	Relative risk
PURE	Prospective Urban and Rural Epidemiology

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Author contributions

JK and SS conceptualized and designed the study; HRS and SS conducted data analysis; HRS, JK and SS drafted the manuscript and revised the manuscript. All authors have reviewed and agreed to the published version of this manuscript.

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Data availability

The data supporting the findings of this study are available from the KoGES. Restrictions apply to the availability of these data, which were used under license for this study, and so are not publicly available. Data can be accessed [http://nih.go.kr/ko/main/contents.do?menuNo=300563] with KoGES's permission.

Declarations

Ethics approval and consent to participate

This study was conducted according to the guidelines of the Declaration of Helsinki. Ethical approval for the KoGES was obtained from the Institutional Review Boards of National Institute of Health under the Korean government and collaborators of the KoGES groups. All study participants provided written informed consent. Furthermore, the secondary data analysis of this study qualified for an exemption issued by the Institutional Review Board of Hannam University (2023-E-01-09-0625).

Consent for publication

All research participants provided consent for the use of de-identified data in scientific publications.

Competing interests

The authors declare no competing interests.

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