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Original Article

Protein source associated with risk of metabolic syndrome in adults with low and adequate protein intake: A prospective cohort study of middle-aged and older adults

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ABSTRACT

Objectives: Metabolic syndrome is associated with an increased risk of diabetes, cardiovascular disease, and all-cause mortality. Some evidence suggests that the cardiometabolic health benefits of protein intake may vary by the source (animal or plant); however, the evidence is inconsistent. This study aimed to assess the risk of developing metabolic syndrome according to the protein source.

Participants: Among a total of 3,310 participants aged 40 years or older in the Ansan and Ansung population based prospective cohort, 1,543 incident cases of metabolic syndrome were identified between 2007 and 2018.

Measurements: Dietary intake was assessed using a validated food frequency questionnaire. Cox proportional hazards models were used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) by quintile (Q), adjusting for demographics and health-related lifestyle factors.

Results: Higher intake of animal protein ($HR_{quintile5\ (Q5)\ vs\ quintile1\ (Q1)}$ [95% CIs]: 0.76 [0.59−0.96], P-trend ≤ 0.0307) and a higher relative intake of animal protein ($HR_{Q5\ vs.Q1}$: 0.78 [0.64−0.95], P-trend ≤ 0.0017) were associated with a significantly decreased risk of developing metabolic syndrome. In subgroup analyses, associations between the risk of metabolic syndrome and the relative intake of animal and plant protein differed according to whether the total protein intake was within the recommended nutrient intake (RNI). Specifically, significant associations were observed only among those with a total protein consumption below the RNI ($HR_{Q5vs\ Q1}$ [95% CIs]: 0.72 [0.56−0.93] for the relative intake of animal protein), but not among those consuming above the RNI. This association was more significant in women than in men.

Conclusion: A higher absolute and relative intake of animal protein were associated with a significantly decreased risk of metabolic syndrome, particularly among those who consumed less than the RNI of protein.

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1. Introduction

Metabolic syndrome, characterized by a constellation of metabolic abnormalities including abdominal obesity, hypertension, dyslipidemia, and glucose intolerance, is a significant public health challenge because of its strong association with an increased risk of diabetes, cardiovascular disease, and all-cause mortality [1,2]. Furthermore, the prevalence of metabolic syndrome has increased rapidly worldwide during the preceding decades [3,4]. In Korea, metabolic syndrome affects at least 23% of adults and 50% of older adults aged 65 years and older [5].

Diet is a well-known risk factors for metabolic syndrome [6]. In recent years, attention has focused on the potential benefit of high-protein diets for the prevention and management of metabolic syndrome owing to the

Abbreviations: BMI, body mass index; CI, confidence interval; FFQ, food frequency questionnaire; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; IRB, institutional review boards; KoGES, Korean Genome and Epidemiology Study; NCEP-ATP III, National Cholesterol Education Program Adult Treatment Panel III; Q, quintile; RNI, recommended nutrient intake; TG, triglyceride.

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involvement of protein in glucose and lipid metabolism [7–11]. However, epidemiologic evidence is inconsistent. Some studies have reported the inverse association between protein intake and risk of metabolic conditions, including weight reduction and maintenance [7], blood sugar levels [8], and lipoprotein profiles [9–11], whereas other prospective studies have shown variable results associated with high protein intake, including increased mortality [12], weight gain [13], and no effect on the risk of cardiovascular disease [14].

Previous studies on the health benefits and harms of a high-protein diet have had varying results. One possible reason could be differences in protein intake from different sources. Amino acid composition of protein varies depending on whether the protein originates from animal or plant sources [15]. Historically, animal proteins were considered more nutritious than plant proteins, which often have imbalanced amino acid profiles [16]. Previous research has shown that animal protein intake has beneficial effects of on some components of metabolic syndrome [17,18]. However, recent studies have increasingly demonstrated the benefits of plant protein [19,20]. For example, some cohort studies have reported that an increased intake of animal protein, but not plant protein, is associated with long-term weight gain [19,20]. Similarly, a comprehensive review of cohort studies and randomized controlled trials on the effects of dietary protein sources on metabolic condition concluded that plant protein, consumption may have a positive effect on the blood lipid profile [21] and overall health outcomes (especially cardiovascular outcomes) [22], compared with that of animal proteins. Notably, the associations often related to specific components of metabolic syndrome and most of the studies reviewed were cross-sectional studies.

To date, the association between protein intake, including plant and animal protein intake, and the risk of metabolic syndrome among Koreans has been examined primarily using cross-sectional studies [23–25]. Therefore, the aim of this study was to prospectively evaluate the potential benefits of protein intake on the risk of metabolic syndrome according to it source (plant or animal) using data from the Korean Genome and Epidemiology Study (KoGES). Specifically, we examined the association between the relative ratio of the protein source and the risk of metabolic syndrome. Additionally, we investigated whether this association varied based on the adherence to the recommended nutrient intake (RNI) for protein, given the potential effect of total protein intake on the risk of metabolic syndrome [26].

2. Methods

2.1. Study design and study participants

This large-scale prospective cohort study was conducted using data from the Ansan and Ansung cohort within the KoGES cohort [27]. Briefly, the Ansan and Ansung community-based cohort study was initiated in 2001 when 10,030 residents were recruited from an industrialized community in Ansan and a rural area in Ansung in Korea. The participants were followed up every 2 years. At baseline and biennial follow-ups, data were collected on sociodemographic characteristics, medical history, family history, and lifestyle behaviors through interviews using structured questionnaires and standardized protocols.

This analysis used Ansan and Ansung cohort data collected during follow-ups to the end 2018. Participants who met the following criteria were excluded: those who did not attend any follow-up visits (n = 2,806), had metabolic syndrome at baseline (n = 1,289), or did not provide data on covariates (n = 118). No participants were excluded owing to an implausible energy intake (<500 or >5000 kcal/day). After the exclusions, a total of 3,310 Korean adults (1,653 men and 1,657 women) were included in the final analysis (Fig. 1). The study was approved by the institutional review board of the Korea Disease Control and Prevention Agency (2018/No 2018-03-05-P-A). All participants provided written informed consent.

2.2. Dietary assessment

Dietary intake was assessed by trained staff using a validated 106 food-item, food frequency questionnaire (FFQ). The design and validation of the FFQ has been described in detail elsewhere [28]. The frequency of consumption was classified into nine categories: never or seldom, once a month, 2–3 times a month, 1–2 times a week, 3–4 times a week, 5–6 times a week, once a day, twice a day, and three times or more a day. The portion size of each food item was classified into three categories: small, medium, and large. The average daily intake of each nutrient was estimated by multiplying the reported frequency of each food item by its nutrient content per portion, using a food composition table developed by the Korean Nutrition Society [29], and then summing across all foods. For the analyses of protein sources, protein sources were classified into plant and animal categories. Plant protein sources included grains and grain products, potatoes and starches, legumes, vegetables, fruits, seaweed, nuts, and seeds. Animal protein sources included meat, fish, shellfish, processed and salted fish, eggs, milk, and dairy products (Supplementary Table S1) [25]. Plant and animal protein intakes were estimated by summing the protein intake from each source (the absolute amounts), and the percentage of protein from plant and animal sources relative to total protein intake was calculated by dividing the intake of each by the total protein intake (the relative amounts). The FFQ has been shown to have good validity in assessing protein intake, with a correlation coefficient of 0.43 for the correlation between total protein intake measured using the FFQ and 12-day dietary records [30]. To determine the criteria for low and high protein intake, the protein intake was divided into two groups based on whether it was within or below the Korean RNI specified in the 2020 Korean Dietary Reference Intake [31].

2.3. Definition of metabolic syndrome

Metabolic syndrome was ascertained based on the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria [32,33]. Participants were required to satisfy at least three of the following five components to be classified as having metabolic syndrome: (1) a waist circumference of 90 cm or more in men or 80 cm in women; (2) a blood pressure of 130/85 mmHg or more, or taking antihypertensive medicine; (3) a triglyceride (TG) level or 150 mg/dL or more; (4) a high-density lipoprotein cholesterol (HDL-C) level of less than 40 mg/dL in men or 50 mg/dL in women; and (5) or a fasting glucose level of 100 mg/dL or more or taking an antidiabetic drug.

Anthropometric and blood tests were performed by trained staff using standardized protocols. Height and weight were measured using a stadiometer and scale, respectively. Waist circumference was measured at the midpoint between the ribs and iliac crest. Body mass index (BMI) was calculated as weight (kg) divided by height(m) squared. Blood pressure was measured twice in the arm using a standard mercury sphygmomanometer (Baumanometer, Baum Co., USA) with the participant was seated after having rested for at least 5 min. The average of the two the two systolic and diastolic blood pressure readings were used for the analysis. Blood samples were collected from each participant at baseline and every 2 years of follow-up after an 8-h fast, and serum concentrations of TG, HDL-C, and fasting glucose were analyzed using enzymatic methods (ADVIA 1650, Siemens, USA).

2.4. Other covariates

An interviewer administered structured questionnaire was used to obtain information on demographic (age and sex) and lifestyle variables of participants. Based on responses to the questionnaire, smoking status was grouped into “never-smokers” for those who had never smoked cigarettes or smoked less than 100 cigarettes in their lifetime, “former-smokers” for those who smoked 100 cigarettes or more in their lifetime but were not current smokers, and “current-smokers” for those who had

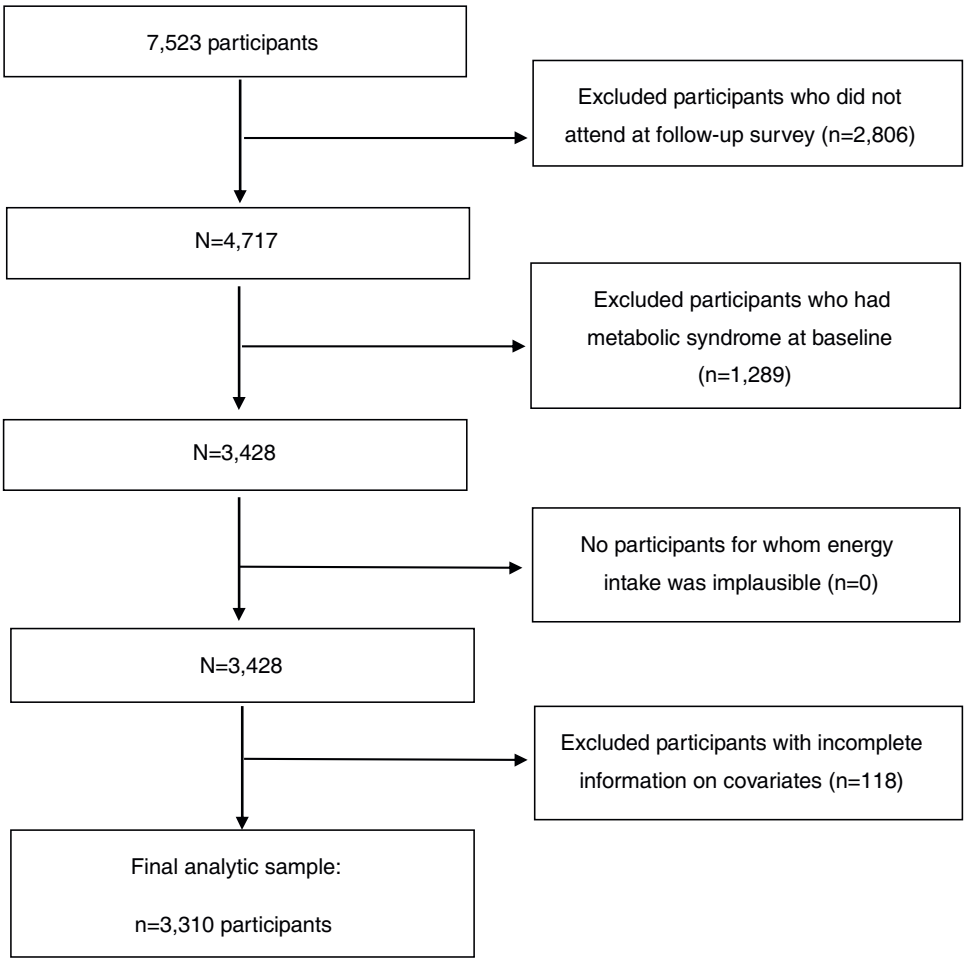


Fig. 1. Flow diagram of the study participants.

smoked 100 cigarettes or more in lifetime and were current smokers. Alcohol consumption status was classified as "never-drinker" for those who had never consumed any types of alcoholic beverages in their lifetime, "former-drinker" for those who had consumed alcoholic beverages in their lifetime but were not current drinkers, and "current-drinker" for those who had consumed alcoholic beverages more than once per month during the past year. For physical activity, participants who answered "yes" to the question "Do you exercise regularly enough to sweat? (yes/no)" were asked a follow-up question about average frequency and duration of activity per week.

2.5. Statistical analysis

The baseline characteristics of the study participants were presented as means ± standard deviations for continuous variables and numbers (percentages, %) for categorical variables. Differences in population characteristics were tested using chi-square tests for categorical variables and independent samples t-tests for continuous variables. The number of person-years of follow-up was calculated from the date of the baseline assessment to the date of metabolic syndrome diagnosis or the end of follow-up, whichever occurred first. Cox proportional hazards regression was used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) by quintile (Q) of protein intake, including absolute and relative intake of plant and animal protein, for risk of metabolic syndrome overall and stratified by sex, using Q1 as the reference category. Unadjusted and adjusted estimates were calculated. Model 1 was unadjusted; Model 2 was adjusted for age (years, continuous) and sex; and Model 3 was further adjusted for smoking status (never smoker, former smoker, or current smoker), alcohol consumption (never drinker, former drinker, or current drinker), regular physical activity (yes or no), and total energy intake (kcal/day, continuous). In addition, Model 3 was adjusted for total protein intake (g/day, continuous) in the analyses of plant protein and animal protein intake. Tests for linear trend were conducted by including the median values for each quintile of protein intake as a continuous variable in the model. The Wald test of the product between the protein intake and each stratification factor was used to test for effect modification. All data analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA). Statistical significance was set at a P value less than 0.05.

3. Results

During a mean of 8.6 years of follow-up (28319 person-years), 1,543 (46.6%) participants (709 men [42.9%] and 834 women [50.3%]) developed metabolic syndrome. At baseline, the mean age of study population were 54.3 years and the mean total protein intake was 57.1 g/day, of which 69.7% was from plant protein sources and 31.6% was from animal protein sources (Table 1). Of the participants 62.5% reporting never smoking, 45.0% reported never drinking alcohol and 39.3% reported exercising regularly. Several characteristics, including smoking status and alcohol consumption differed significantly by sex. In addition, men consumed more energy (kcal/d), carbohydrate, protein, plant protein, animal protein, and fat than women (all $P < 0.001$). Similarly, the relative intake of animal protein was higher in men than in women ($P = 0.0054$), although plant protein intake did not differ significantly by sex.

In the analyses of absolute protein intake (Table 2), a higher animal protein intake was associated with a significantly lower risk of developing metabolic syndrome. The multivariable-adjusted HR comparing the

Table 1
Baseline characteristics of study participants.

	Total	Men	Women	*P* value[1)]
N	3,310 (100.0)[2)]	1,653 (49.9)	1,657 (50.1)	
Age (years)	54.3 ± 8.2[2)]	55.0 ± 8.3	53.7 ± 8.0	<0.0001
Smoking status				
Never-smokers	2,069 (62.5)	448 (27.1)	1,621 (97.8)	<0.0001
Former-smokers	638 (19.3)	628 (38.0)	10 (0.6)	
Current-smokers	603 (18.2)	577 (34.9)	26 (1.6)	
Alcoholic drinking status				
Never-drinker	1,489 (45.0)	335 (20.3)	1,154 (69.6)	<0.0001
Former-drinker	149 (4.5)	126 (7.6)	23 (1.4)	
Current-drinker	1,672 (50.5)	1,192 (72.1)	480 (29.0)	
Regular physical activity				
No	2,008 (60.7)	969 (58.6)	1,039 (62.7)	0.0162
Yes	1,302 (39.3)	684 (41.4)	618 (37.3)	
Body mass index (kg/m^2)	23.8 ± 2.8	23.5 ± 2.6	24.0 ± 3.0	<0.0001
Waist circumference (cm)	81.5 ± 7.9	82.7 ± 6.7	80.3 ± 8.9	<0.0001
Hip circumference (cm)	91.1 ± 5.0	90.9 ± 4.8	91.3 ± 5.1	0.0404
Systolic blood pressure (mmHg)	116.3 ± 14.2	113.8 ± 14.0	109.4 ± 14.1	<0.0001
Diastolic blood pressure (mmHg)	75.1 ± 9.5	77.3 ± 9.4	72.9 ± 9.0	<0.0001
Fasting blood glucose (mg/dL)	88.4 ± 8.0	90.4 ± 8.1	86.5 ± 7.3	<0.0001
Insulin (μIU/□)	6.9 ± 2.9	6.6 ± 2.7	7.2 ± 3.1	<0.0001
Total Cholesterol (mg/dL)	189.8 ± 33.3	186.7 ± 32.8	192.8 ± 33.5	<0.0001
Triglycerides (mg/dL)	110.2 ± 59.7	123.0 ± 70.7	97.5 ± 42.7	<0.0001
HDL-cholesterol (mg/dL)	46.6 ± 10.3	44.7 ± 10.0	48.5 ± 10.2	<0.0001
Daily dietary intake				
Total daily energy intake (kcal/d)	1,850.1 ± 528.0	1,960.2 ± 530.6	1,740.3 ± 502.2	<0.0001
Carbohydrate (g/d)	338.9 ± 91.0	354.8 ± 90.9	323.0 ± 88.4	<0.0001
Total protein (g/d)	57.1 ± 21.3	60.3 ± 21.2	53.9 ± 21.0	<0.0001
Plant protein (g/d)	38.3 ± 11.0	40.2 ± 11.0	36.3 ± 10.7	<0.0001
Relative of plant protein from protein (%)	69.7 ± 13.1	69.3 ± 13.0	70.1 ± 13.1	0.0685
Animal protein (g/d)	19.5 ± 14.2	20.9 ± 14.2	18.1 ± 14.1	<0.0001
Relative of animal protein from protein (%)	31.6 ± 12.9	32.2 ± 12.6	30.9 ± 13.1	0.0054
Fat (g/d)	26.8 ± 15.7	29.9 ± 16.4	23.7 ± 14.4	<0.0001

[1)] The *P* values were calculated using the chi-squared test for categorical variables or t-test for continuous variables when comparing baseline characteristics between men and women.
[2)] Data are presented as means ± standard deviation (SD) or numbers (%).

Table 2
Unadjusted and adjusted[1)]-hazard ratios and 95% confidence intervals of metabolic syndrome by quintiles of protein, plant protein and animal protein intakes in the Korean Genome and Epidemiology Study (Ansan-Ansung).

	Q1 (lowest)	Q2	Q3	Q4	Q5 (highest)	*P* for trend[2)]
Total protein intake						
Cases/person-years	344/5303	311/5690	296/5685	306/5787	286/5834	
Median intake (g/d)	35.0	45.4	54.5	65.1	83.2	
Model 1	1.00	0.85 (0.73–1.00)	0.81 (0.70–0.95)	0.83 (0.71–0.97)	0.77 (0.66–0.90)	0.0020
Model 2	1.00	0.88 (0.75–1.02)	0.87 (0.75–1.02)	0.89 (0.76–1.04)	0.87 (0.74–1.02)	0.1644
Model 3	1.00	0.90 (0.77–1.06)	0.89 (0.74–1.06)	0.91 (0.74–1.11)	0.89 (0.68–1.15)	0.4892
Plant protein intake						
Cases/person-years	315/5503	328/5651	309/5613	292/5758	299/5794	
Median intake (g/d)	25.7	32.3	37.0	42.3	52.6	
Model 1	1.00	1.02 (0.87–1.19)	0.97 (0.83–1.13)	0.90 (0.77–1.05)	0.91 (0.78–1.07)	0.1106
Model 2	1.00	1.05 (0.90–1.23)	1.01 (0.87–1.19)	0.97 (0.83–1.14)	1.02 (0.86–1.19)	0.8657
Model 3	1.00	1.10 (0.94–1.30)	1.09 (0.91–1.31)	1.09 (0.89–1.34)	1.21 (0.93–1.56)	0.2143
Animal protein intake						
Cases/person-years	362/5219	305/5621	294/5859	288/5804	294/5816	
Median intake (g/d)	5.8	11.4	16.6	23.5	36.0	
Model 1	1.00	0.79 (0.68–0.92)	0.74 (0.63–0.86)	0.73 (0.63–0.85)	0.74 (0.64–0.87)	0.0008
Model 2	1.00	0.83 (0.71–0.97)	0.79 (0.68–0.93)	0.79 (0.68–0.93)	0.83 (0.71–0.98)	0.0629
Model 3	1.00	0.83 (0.71–0.97)	0.78 (0.66–0.92)	0.76 (0.63–0.91)	0.76 (0.59–0.96)	0.0307

Abbreviations, Q: quintile.
[1)] Model 1 was unadjusted; Model 2 was adjusted for age (years, continuous) and sex (man or woman); and Model 3 was adjusted for age, sex, smoking status (never smoker, former smoker, or current smoker), alcohol consumption status (never drinker, former drinker, or current drinker), regular physical activity (yes or no), and total energy intake (kcal/day, continuous). In addition, in the analyses of plant protein and animal protein intake, Model 3 was adjusted for total protein intake (g/day, continuous).
[2)] The P value for trend was calculated by including the median quintile values of the total protein, plant protein, or animal protein intake as a continuous term in the model.

highest vs. the lowest Q (Q5 vs. Q1) of animal protein intake was 0.76 (95% CI: 0.59–0.96; P for trend = 0.0307). Total protein intake and plant protein intake were not significantly associated with the risk of developing metabolic syndrome. Furthermore, an analysis of the risk of metabolic syndrome based on protein intake per kilogram of body weight revealed that a higher protein intake was associated with a significantly lower risk of developing metabolic syndrome. This association remained consistent in the analyses of plant and animal protein intake per kilogram of body weight (data not shown).

In the analyses of the relative intake of plant and animal protein, expressed as the plant and animal protein intake as a percentage of the total protein intake (Table 3), a higher relative intake of plant protein was associated with a significantly increased risk of developing metabolic syndrome (multivariable-adjusted HR $_{\text{quintile5 (Q5) vs. quintile1 (Q1)}}$ [95% CIs]: 1.28 [1.06−1.56]; *P* for trend = 0.0017), whereas a higher relative intake of animal protein was associated with a significantly decreased risk of developing metabolic syndrome (multivariable-adjusted HR $_{\text{Q5vs.Q1}}$ [95% CIs]: 0.78 [0.64−0.95]; *P* for trend = 0.0017). These results were consistent among women (multivariable-adjusted HR $_{\text{Q5vs.Q1}}$: 1.31 [1.01 −1.71] for the relative intake of plant protein and 0.76 [0.59−0.99] for the relative intake of animal protein; both *P* for trend = 0.0120), but among not among men. Neither the relative plant protein intake nor the relative animal protein intake were significantly associated with the risk of developing metabolic syndrome among men.

In stratified analyses, different associations were observed according to whether protein intake was below or above the RNI of total protein (Table 4). Among those with below the RNI of protein, a higher relative intake of animal protein was associated with a reduced risk of metabolic syndrome (multivariable-adjusted HR $_{\text{Q5vs.Q1}}$ [95% CI]: 0.72 [0.56–0.93]; *P* for trend = 0.0037). However, a higher relative intake of animal protein was not associated with a reduced risk of metabolic syndrome among those who consumed total protein above the RNI. Similarly, in analyses stratified by the RNI among women, in those with below the RNI of protein intake, a higher relative intake of animal protein was associated with a decreased risk of metabolic syndrome (multivariable-adjusted HR $_{\text{Q5vs.Q1}}$ [95% CIs]: 0.62 [0.42−0.92]; *P* for trend = 0.0179) were only evident among those consuming below the RNI, but not among those consuming above the RNI. In contrast, in men the relative intake of animal protein was not associated with risk of metabolic syndrome, regardless of the protein intake relative to the RNI. No significant effect modification was detected by other factors including age, smoking status, alcohol

Table 3
Unadjusted and adjusted[1)]-hazard ratios and 95% confidence intervals of metabolic syndrome by quintiles of the relative intake of plant and animal protein in the Korean Genome and Epidemiology Study (Ansan-Ansung).

	Q1 (lowest)	Q2	Q3	Q4	Q5 (highest)	*P* for trend[2)]
All population (N = 3,310)						
Relative of plant protein intakes, %						
Cases/person-years	295/5805	281/5862	292/5829	323/5468	352/5355	
Relative of Median intake (%)	52.5	62.2	68.8	75.9	85.6	
Model 1	1.00	0.95 (0.80−1.11)	0.99 (0.84−1.16)	1.15 (0.98−1.35)	1.27 (1.09−1.49)	0.0001
Model 2	1.00	0.94 (0.80−1.11)	0.97 (0.83−1.14)	1.11 (0.94−1.30)	1.18 (1.01−1.39)	0.0067
Model 3	1.00	0.98 (0.82−1.16)	1.04 (0.87−1.25)	1.19 (0.99−1.43)	1.28 (1.06−1.56)	0.0017
Relative of animal protein intakes, %						
Cases/person-years	352/5355	323/5468	292/5829	281/5862	295/5805	
Relative of Median intake (%)	14.4	24.1	31.2	37.8	47.5	
Model 1	1.00	0.90 (0.78−1.05)	0.77 (0.66−0.90)	0.74 (0.64−0.87)	0.79 (0.67−0.92)	0.0001
Model 2	1.00	0.93 (0.80−1.09)	0.82 (0.70−0.96)	0.79 (0.68−0.93)	0.85 (0.72−0.99)	0.0067
Model 3	1.00	0.93 (0.80−1.08)	0.81 (0.69−0.96)	0.76 (0.64−0.91)	0.78 (0.64−0.95)	0.0017
Men (N = 1,653)						
Relative of plant protein intakes, %						
Cases/person-years	141/2945	133/2930	137/2933	151/2767	147/2840	
Relative of Median intake (%)	52.0	61.8	75.1	84.5	85.6	
Model 1	1.00	0.95 (0.75−1.20)	0.97 (0.77−1.23)	1.13 (0.90−1.42)	1.08 (0.85−1.36)	0.2619
Model 2	1.00	0.95 (0.75−1.21)	0.98 (0.77−1.23)	1.13 (0.90−1.43)	1.08 (0.86−1.43)	0.2441
Model 3	1.00	1.01 (0.79−1.30)	1.07 (0.82−1.39)	1.28 (0.97−1.68)	1.24 (0.92−1.66)	0.0673
Relative of animal protein intakes, %						
Cases/ person-years	147/2840	151/2767	137/2933	1332930	141/2945	
Relative of Median intake (%)	15.5	24.9	31.6	38.2	48.0	
Model 1	1.00	1.05 (0.84–1.32)	0.91 (0.72−1.14)	0.88 (0.70−1.12)	0.93 (0.74−1.17)	0.2619
Model 2	1.00	0.95 (0.75−1.21)	0.98 (0.77−1.23)	1.13 (0.90−1.43)	1.08 (0.86−1.37)	0.2441
Model 3	1.00	1.03 (0.82−1.30)	0.87 (0.68−1.11)	0.82 (0.63−1.07)	0.81 (0.60−1.09)	0.0673
Women (N = 1,657)						
Relative of plant protein intakes, %						
Cases/person-years	155/2840	148/2945	155/2886	174/2731	202/2502	
Relative of Median intake (%)	52.9	62.6	69.6	76.3	86.5	
Model 1	1.00	0.93 (0.74−1.16)	0.99 (0.79−1.23)	1.16 (0.93−1.44)	1.44 (1.17−1.78)	<0.0001
Model 2	1.00	0.92 (0.73−1.15)	0.96 (0.77−1.20)	1.07 (0.86−1.33)	1.24 (1.00−1.53)	0.0172
Model 3	1.00	0.94 (0.74−1.18)	1.01 (0.79−1.29)	1.12 (0.87−1.43)	1.31 (1.01−1.71)	0.0120
Relative of animal protein intake, %						
Cases/person-years	202/2502	174/2731	155/2886	148/2945	155/2840	
Relative of Median intake (%)	13.5	23.7	30.4	37.4	47.1	
Model 1	1.00	0.80 (0.66−0.98)	0.68 (0.56−0.84)	0.64 (0.52−0.79)	0.69 (0.56−0.85)	<0.0001
Model 2	1.00	0.86 (0.70−1.06)	0.78 (0.63−0.96)	0.74 (0.60−0.92)	0.81 (0.65−1.00)	0.0172
Model 3	1.00	0.85 (0.69−1.05)	0.77 (0.62−0.96)	0.71 (0.57−0.90)	0.76 (0.59−0.99)	0.0120

Abbreviations, Q: quintile.

[1)] Model 1 was unadjusted; Model 2 was adjusted for age (years, continuous) and sex (man or woman); and Model 3 was adjusted for age, sex, smoking status (never smoker, former smoker, or current smoker), alcohol consumption status (never drinker, former drinker, or current drinker), regular physical activity (yes or no), and total energy intake (kcal/day, continuous). In addition, in the analyses of plant protein and animal protein intake, Model 3 was adjusted for total protein intake (g/day, continuous).

[2)] The P value for trend was calculated by including the median quintile values of the relative intake of plant protein and animal protein as a continuous term in the model.

Table 4
Unadjusted and adjusted[1)] hazard ratios and 95% confidence intervals for the incidence of metabolic syndrome by quintiles of the relative of animal protein intake stratified by recommended nutrient intake of total protein in the Korean Genome and Epidemiology Study (Ansan-Ansung).

	Q1 (lowest)	Q2	Q3	Q4	Q5 (highest)	*P* for trend [2)]	*P* interaction[3)]
Total (N = 3,310)							
< RNI of protein (N = 1,990)							0.9865
Relative of animal protein intakes, %							
Cases/ person-years	225/3128	195/3323	178/3335	164/3546	172/3512		
Relative of Median intake (%)	12.2	20.4	27.2	33.7	43.4		
Model 1	1.00	0.83 (0.69–1.01)	0.75 (0.62–0.92)	0.66 (0.54–0.81)	0.70 (0.57–0.85)	<0.0001	
Model 2	1.00	0.87 (0.72–1.05)	0.80 (0.65–0.97)	0.73 (0.59–0.90)	0.78 (0.63–0.96)	0.0062	
Model 3	1.00	0.86 (0.71–1.05)	0.78 (0.64–0.96)	0.70 (0.56–0.88)	0.72 (0.56–0.93)	0.0037	
≥ RNI of protein (N = 1,320)							
Relative of animal protein intakes, %							
Cases/ person-years	137/2161	120/2343	109/2348	117/2362	126/2261		
Relative of Median intake (%)	22.0	30.5	36.6	42.7	51.5		
Model 1	1.00	0.82 (0.64–1.05)	0.74 (0.58–0.96)	0.79 (0.62–1.01)	0.88 (0.69–1.12)	0.3020	
Model 2	1.00	0.83 (0.65–1.06)	0.77 (0.60–0.99)	0.83 (0.65–1.06)	0.92 (0.72–1.17)	0.4943	
Model 3	1.00	0.83 (0.65–1.06)	0.75 (0.58–0.97)	0.80 (0.62–1.04)	0.84 (0.63–1.12)	0.1839	
Men (N = 1,653)							
< RNI of protein (N = 1,195)							0.8570
Relative of animal protein intakes, %							
Cases/ person-years	109/ 2057	99/2029	110/2041	97/2122	98/2130		
Relative of Median intake (%)	14.1	22.3	29.3	35.4	44.8		
Model 1	1.00	0.92 (0.70–1.21)	1.01 (0.78–1.32)	0.87 (0.66–1.14)	0.88 (0.67–1.15)	0.3068	
Model 2	1.00	0.92 (0.70–1.21)	1.02 (0.78–1.33)	0.87 (0.66–1.15)	0.88 (0.66–1.17)	0.3508	
Model 3	1.00	0.91 (0.69–1.20)	0.98 (0.74–1.30)	0.80 (0.59–1.09)	0.77 (0.54–1.11)	0.1403	
≥ RNI of protein (N = 458)							
Relative of animal protein intakes, %							
Cases/ person-years	44/766	37/825	36/810	33/878	46/757		
Relative of Median intake (%)	22.0	31.51	38.1	44.3	53.1		
Model 1	1.00	0.80 (0.52–1.24)	0.79 (0.51–1.23)	0.67 (0.43–1.05)	1.06 (0.70–1.60)	0.9412	
Model 2	1.00	0.78 (0.51–1.21)	0.76 (0.49–1.19)	0.65 (0.41–1.02)	1.02 (0.67–1.55)	0.8241	
Model 3	1.00	0.74 (0.47–1.15)	0.73 (0.46–1.15)	0.60 (0.37–0.97)	0.92 (0.56–1.51)	0.4562	
Women (N = 1,657)							
< RNI of protein (N = 795)							0.6795
Relative of animal protein intakes, %							
Cases/ person-years	109/1139	89/1284	79/1291	76/1342	68/1409		
Relative of Median intake (%)	9.3	17.5	24.0	30.4	41.0		
Model 1	1.00	0.75 (0.56–0.99)	0.66 (0.49–0.88)	0.62 (0.46–0.83)	0.53 (0.39–0.72)	<0.0001	
Model 2	1.00	0.81 (0.61–1.07)	0.70 (0.53–0.94)	0.69 (0.51–0.93)	0.60 (0.44–0.82)	0.0007	
Model 3	1.00	0.81 (0.60–1.09)	0.73 (0.53–1.01)	0.71 (0.51–1.00)	0.62 (0.42–0.92)	0.0179	
≥ RNI of protein (N = 862)							
Relative of animal protein intakes, %							
Cases/ person-years	88/1407	87/1520	70/1558	85/1468	83/1486		
Relative of Median intake (%)	22.0	30.2	35.6	41.7	50.7		
Model 1	1.00	0.92 (0.69–1.24)	0.73 (0.53–1.00)	0.93 (0.69–1.25)	0.90 (0.67–1.21)	0.5566	
Model 2	1.00	0.94 (0.70–1.26)	0.78 (0.57–1.06)	0.95 (0.71–1.28)	0.90 (0.67–1.22)	0.5709	
Model 3	1.00	0.95 (0.70–1.28)	0.78 (0.56–1.07)	0.94 (0.69–1.29)	0.84 (0.59–1.19)	0.3614	

Abbreviations, quintile.
[1)] Model 1 was unadjusted; Model 2 was adjusted for age (years, continuous) and sex (man or woman); and Model 3 was adjusted for age, sex, smoking status (never smoker, former smoker, or current smoker), alcohol consumption status (never drinker, former drinker, or current drinker), regular physical activity (yes or no), and total energy intake (kcal/day, continuous). In addition, in the analyses of plant protein and animal protein intake, Model 3 was adjusted for total protein intake (g/day, continuous).
[2)] The P value for trend was calculated by including the median quintile values of the intakes of the relative intake of plant and animal protein as a continuous term in the model.
[3)] The P value of the interaction between the incidence of metabolic syndrome and the RNI.

consumption status, and regular physical activity (Supplementary Table S2).

In sensitivity analyses, similar results were observed with additional adjustment for dietary intake of fat, vitamins and minerals, and exclusion of participants with metabolic syndrome diagnosed within 2 years of baseline (data not shown).

4. Discussion

In this study, the absolute and relative intake of animal protein were inversely associated with a lower risk of metabolic syndrome, which was more marked in women than in men. Furthermore, in women these associations were stronger among those who consumed less than the RNI of protein.

To date, four cross-sectional studies [17,18,25,34], two cohort studies [35,36] and one case-control study [37] have examined the association between sources of protein and risk of metabolic syndrome in several regions in Asia [17,18,25,34], Australia [35], North America [36], and Europe [37]. Our findings of an inverse association between animal protein intake and risk of metabolic syndrome are consistent with those of three of cross-sectional studies [17,18,34]. For example, a cross-sectional study of 7,585 Japanese adults found that higher animal protein intake, but not higher plant protein intake, was associated with a lower blood pressure [17]. Similarly, in a cross-sectional study of 2,241 Chinese women, a higher protein intake was associated with a significantly lower blood pressure [18]. In contrast, a cross-sectional study of middle-aged Korean men suggested that low animal protein intake might be beneficial in managing metabolic syndrome [25]. Moreover, in studies conducted in Western populations, animal protein intake has been associated with

adverse effects on other metabolic syndrome risk factors [35–37]. For example, in a cohort study conducted in Melbourne, Australia, higher plant protein consumption and lower animal protein consumption was associated with lower risk of metabolic syndrome [35]. Similarly, a cohort study with a 16-year follow-up period conducted in the United States found that a higher intake of plant protein was associated with a lower cardiovascular disease mortality [36]. Additionally, a Swedish study found that higher meat consumption was associated with higher cholesterol levels [37].

The reason for the inconsistent associations between animal protein intake and the risk of metabolic syndrome is unclear. However, substantial differences exist in the protein composition and sources of food protein consumed among participants in the Western countries and this study. For example, in the studies conducted in the United States [36] and Australia [35] participants received 60–62% of their protein intake from animal sources, whereas participants in this study received 69.7% of their protein from plant sources and 31.6% from animal sources. Given that the red meat, processed meat, and other major sources of saturated fat, a risk factor for metabolic syndrome [38] contribute more to the animal protein consumption in Western countries than in the Korean population [39], the discrepancy in the results could be due to the effect of other nutrients in different animal protein sources [40], influenced by cultural differences in diet.

Another possible explanation for the observed differences in the results for the association between animal protein intake and the risk of metabolic syndrome, could be the interaction between animal protein intake and total protein intake. A recent study found that the amount of protein, rather than the protein source, had a stronger effect on cardiac metabolic health indicators, including blood glucose, serum insulin, and serum TG [41]. It underscores the adequacy of total protein on metabolic condition and greater contribution of animal protein addressing deficiencies in total protein over the plant protein. Indeed, supporting our speculation, when we conducted analyses stratified by protein intake according to the RNI in the present study, higher animal protein intake was associated with a reduced risk of metabolic syndrome among those who consumed less than the RNI. This finding is consistent with the results of previous studies with comparable total protein. For example, participants in the Chinese study, that found a lower risk of metabolic syndrome with higher animal protein intake, the total protein intake was relatively low, (51.7 g/d in men and 40.1 g/d in women) [18], which is approximately 60.3% of the total protein intake reported in Western countries [35]. In the cross-sectional study conducted in Korean [25] which did not find an in inverse association between protein intake and the risk of metabolic syndrome, the participants had a relatively high average protein intake of 87.6 g in men and 63.3 g in women, compared with was 60.3 g in men and 53.9 g in women in this study. In a study conducted in Iran, in which the participants consumed a diet composed primarily of carbohydrates, a higher frequency of consumption of total protein, animal protein, and vegetable protein was associated with a reduced risk of metabolic syndrome [34].

Plant protein consumption has certain beneficial properties in preventing metabolic stress, including being associated with a diet that is low in saturated fat and rich in fiber and phytochemicals, which have antioxidant properties [42]. However, animal proteins contain all the essential amino acids required by the body and are more efficient in supporting muscle growth and repair especially when total protein intake is insufficient [43,44]. Specifically, branched-chain amino acids, such as leucine, are crucial not only for muscle protein synthesis and maintaining lean body mass [45], but also for metabolic regulation [46], which increases insulin sensitivity and energy expenditure. Branched-chain amino acids are provided mainly by animal protein intake [47–49].

The results of the study showed that the association between the relative ratio of protein type and metabolic syndrome risk was more marked in women, than in men. Although the reason for this sex difference remains unclear, some hormones have sex-specific effects on glucose and lipid metabolism, which are associated with the development of metabolic syndrome [50,51]. Women might be more sensitive than men to the effects of diet on the development of metabolic. For example, a previous study showed that, a higher dietary protein/energy ratio was associated with a lower risk of obesity in older women but not in older men [52]. Alternatively, men have higher rates of drinking and smoking, which are risk factors for the development of metabolic syndrome. Despite our adjustment for smoking and alcohol consumption, some residual confounding may be present owing to these sex-related differences in lifestyle. Further studies are needed to investigate the mechanisms underlying the interaction between protein intake and sex in modifying the risk of metabolic syndrome.

This study has several limitations. First, the analyses relied on reported food item data listed in the FFQ, which might not have fully captured all the plant-based and animal-based foods consumed by the participants. Nonetheless, the FFQ is an established instrument for assessing usual intake of foods and nutrients, and has previously been validated by comparing the estimated protein intake with that estimated based on 12-day dietary records (correlation r: 0.43) [30]. Second, certain foods, such as pizza, hamburgers, jam, honey, butter, and margarine, could not be exclusively classified as plant- or animal-based food, posing challenges in classifying the type of protein consumption. Third, the analysis was based on baseline data, and we did not take into account changes in dietary behavior, food availability, or lifestyle habits during the follow-up period. Fourth, the study participants were recruited from a specific region (Ansan and Ansung) in Korea and were aged 40 years or older, limiting the generalizability of the results to the broader general Korean population. Finally, we cannot rule out the possibility of unmeasured or residual confounding.

Nevertheless, this study has several strengths. To our knowledge, it is the first large prospective cohort study to examine the risk of metabolic syndrome in relation to type of protein consumed in Korean adults. Owing to its large sample size, prospective design, and long-term follow-up the data are less susceptible to recall bias. In particular, we focused on the association of the relative intake animal and plant of protein with the risk of metabolic syndrome, rather than the absolute intake. This approach may provide the advantage of examining the effect of the protein source in the overall diet, instead of looking at absolute intake level of each source. Additionally, we were able to finely adjust for potential dietary and lifestyle confounders and performed explored stratified analyses to control for effect modification.

5. Conclusions

In summary, this study found that animal protein intake may be associated with a lower risk of metabolic syndrome in the Korean population. This association was stronger in participants with an animal protein consumption below the RNI. Additionally, compared with men, in women, a higher relative consumption of plant proteins was associated with a greater increase in the risk of metabolic syndrome, whereas consumption of animal protein was associated with a greater decrease in the risk. Plant and animal protein intake was not associated with a significantly increased risk of metabolic syndrome in men. The results of this study suggest that Korean adults, especially middle-aged and older women who rely heavily on plant protein, may be at risk of metabolic syndrome due to inadequate protein intake from animal sources; therefore, the importance of adequate protein intake from animal sources to reduce the risk of metabolic syndrome should be emphasized among those at risk of nutritional deficiency. Further a large prospective study of a representative sample of the Korean population, covering a wider age range, is required to validate our results.

CRediT authorship contribution statement

All authors contributed to the conceptualization and methodology; J. L.: investigation, data collection, formal analysis, writing – original draft,

and writing – review and editing; J.Y.L.: writing – review and editing and funding acquisition; Y.H. and K.N.: writing – review and editing; S.J.: writing – review and editing and formal analysis; Y.J.P.: writing – review and editing and supervision. All authors commented on previous versions of the manuscript and read and approved the final version of the manuscript.

Ethics standards

This study was conducted in accordance with the principles of the Declaration of Helsinki. This study was approved by the Korea Disease Control and Prevention Agency Institutional Review Board (approval date: March 22. 2018; approval number: 2018/No 2018-03-05-P-A). Informed consent was obtained from all participants prior to inclusion in the study.

Declaration of Generative AI and AI-assisted technologies in the writing process

The authors declare that they have not used generative AI (a type of artificial intelligence technology that can produce various types of content including text, imagery, audio and synthetic data) and AI-assisted technologies in the writing process.

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Declaration of competing interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jnha.2024.100393.

References

[1] Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. Diabetes Care 2005;28:1769–78, doi:http://dx.doi.org/10.2337/diacare.28.7.1769.
[2] Hayden MR. Overview and new insights into the metabolic syndrome: risk factors and emerging variables in the development of type 2 diabetes and cerebrocardiovascular disease. Medicina (Kaunas) 2023;59:561, doi:http://dx.doi.org/10.3390/medicina59030561.
[3] Saklayen MG. The global epidemic of the metabolic syndrome. Curr Hypertens Rep 2018;20:12, doi:http://dx.doi.org/10.1007/s11906-018-0812-z.
[4] Wu SH, Liu Z, Ho SC. Metabolic syndrome and all-cause mortality: a meta-analysis of prospective cohort studies. Eur J Epidemiol 2010;25:375–84, doi:http://dx.doi.org/10.1007/s10654-010-9459-z.
[5] Huh JH, Kang DR, Kim JY, Koh KK. Metabolic syndrome fact sheet 2021: executive report. Cardiometab Syndr J 2021;1:125–34, doi:http://dx.doi.org/10.51789/cmsj.2021.1.e15.
[6] Kim H-L, Chung J, Kim K-J, Kim H-J, Seo W-W, Jeon K-H, et al. Lifestyle modification in the management of metabolic syndrome: statement from Korean Society of CardioMetabolic Syndrome (KSCMS). Korean Circ J 2022;52:93–109, doi:http://dx.doi.org/10.4070/kcj.2021.0328.
[7] Leidy HJ, Clifton PM, Astrup A, Wycherley TP, Westerterp-Plantenga MS, Luscombe-Marsh ND, et al. The role of protein in weight loss and maintenance. Am J Clin Nutr 2015;101:1320S–9S, doi:http://dx.doi.org/10.3945/ajcn.114.084038.
[8] Gannon MC, Nuttall FQ, Saeed A, Jordan K, Hoover H. An increase in dietary protein improves the blood glucose response in persons with type 2 diabetes. Am J Clin Nutr 2003;78:734–41, doi:http://dx.doi.org/10.1093/ajcn/78.4.734.
[9] Pasiakos SM, Lieberman HR, Fulgoni [169_TD$DIFF]III VL. Higher-protein diets are associated with higher HDL cholesterol and lower BMI and waist circumference in US adults. J Nutr 2015;145:605–14, doi:http://dx.doi.org/10.3945/jn.114.205203.
[10] Rietman A, Schwarz J, Blokker BA, Siebelink E, Kok FJ, Afman LA, et al. Increasing protein intake modulates lipid metabolism in healthy young men and women consuming a high-fat hypercaloric diet. J Nutr 2014;144:1174–80, doi:http://dx.doi.org/10.3945/jn.114.191072.
[11] Campos-Nonato I, Hernandez L, Barquera S. Effect of a high-protein diet versus standard-protein diet on weight loss and biomarkers of metabolic syndrome: a randomized clinical trial. Obes Facts 2017;10:238–51, doi:http://dx.doi.org/10.1159/000471485.
[12] Trichopoulou A, Psaltopoulou T, Orfanos P, Hsieh CC, Trichopoulos D. Low-carbohydrate–high-protein diet and long-term survival in a general population cohort. Eur J Clin Nutr 2007;61:575–81, doi:http://dx.doi.org/10.1038/sj.ejcn.1602557.
[13] Bulló Bonet M, Basora Gallisà J, Hernandez-Alonso P, Fitó Colomer M, Estruch R, Salas Salvadó J. High dietary protein intake is associated with an increased body weight and total death risk. Clin Nutr 2016;35:496–506, doi:http://dx.doi.org/10.1016/j.clnu.2015.03.016.
[14] Mantzouranis E, Kakargia E, Kakargias F, Lazaros G, Tsioufis K. The impact of high protein diets on cardiovascular outcomes: a systematic review and meta-analysis of prospective cohort studies. Nutrients 2023;15:1372, doi:http://dx.doi.org/10.3390/nu15061372.
[15] Huang S, Wang LM, Sivendiran T, Bohrer BM. Review: amino acid concentration of high protein food products and an overview of the current methods used to determine protein quality. Crit Rev Food Sci Nutr 2018;58:2673–8, doi:http://dx.doi.org/10.1080/10408398.2017.1396202.
[16] Day L, Cakebread JA, Loveday SM. Food proteins from animals and plants: differences in the nutritional and functional properties. Trends Food Sci Technol 2022;119:428–42, doi:http://dx.doi.org/10.1016/j.tifs.2021.12.020.
[17] Umesawa M, Sato S, Imano H, Kitamura A, Shimamoto T, Yamagishi K, et al. Relations between protein intake and blood pressure in Japanese men and women: the Circulatory Risk in Communities Study (CIRCS). Am J Clin Nutr 2009;90:377–84, doi:http://dx.doi.org/10.3945/ajcn.2008.27109.
[18] Liu R, Dang S, Yan H, Wang D, Zhao Y, Li Q, et al. Association between dietary protein intake and the risk of hypertension: a cross-sectional study from rural western China. Hypertens Res 2013;36:972–9, doi:http://dx.doi.org/10.1038/hr.2013.71.
[19] Halkjær J, Olsen A, Overvad K, Jakobsen MU, Boeing H, Buijsse B, et al. Intake of total, animal and plant protein and subsequent changes in weight or waist circumference in European men and women: the Diogenes project. Int J Obes (Lond) 2011;35:1104–13, doi:http://dx.doi.org/10.1038/ijo.2010.254.
[20] Bujnowski D, Xun P, Daviglus ML, Van Horn L, He K, Stamler J. Longitudinal association between animal and vegetable protein intake and obesity among men in the United States: the Chicago Western Electric Study. J Am Diet Assoc 2011;111:1150–1155.e1, doi:http://dx.doi.org/10.1016/j.jada.2011.05.002.
[21] Li SS, Blanco Mejia S, Lytvyn L, Stewart SE, Viguiliouk E, Ha V, et al. Effect of plant protein on blood lipids: a systematic review and meta-analysis of randomized controlled trials. J Am Heart Assoc 2017;6:e006659, doi:http://dx.doi.org/10.1161/JAHA.117.006659.
[22] Ferrari L, Panaite S-A, Bertazzo A, Visioli F. Animal- and plant-based protein sources: a scoping review of human health outcomes and environmental impact. Nutrients 2022;14:5115, doi:http://dx.doi.org/10.3390/nu14235115.
[23] Park K-B, Park HA, Kang J-H, Kim K, Cho YG, Jang J. Animal and plant protein intake and body mass index and waist circumference in a Korean elderly population. Nutrients 2018;10:577, doi:http://dx.doi.org/10.3390/nu10050577.
[24] Ha K, Nam K, Song Y. A moderate-carbohydrate diet with plant protein is inversely associated with cardiovascular risk factors: the Korea National Health and Nutrition Examination survey 2013–2017. Nutr J 2020;19:84, doi:http://dx.doi.org/10.1186/s12937-020-00603-2.
[25] Chung S, Chung M-Y, Choi H-K, Park JH, Hwang J-T, Joung H. Animal protein intake is positively associated with metabolic syndrome risk factors in middle-aged Korean men. Nutrients 2020;12:3415, doi:http://dx.doi.org/10.3390/nu12113415.
[26] Lonnie M, Hooker E, Brunstrom JM, Corfe BM, Green MA, Watson AW, et al. Protein for life: review of optimal protein intake, sustainable dietary sources and the effect on appetite in ageing adults. Nutrients 2018;10:360, doi:http://dx.doi.org/10.3390/nu10030360.
[27] KoGES Group. Kim Y, Han B-G. Cohort profile: the Korean genome and epidemiology study (KoGES) consortium. Int J Epidemiol 201746:, doi:http://dx.doi.org/10.1093/ije/dyv316 e20-e.
[28] Ahn Y, Lee J-E, Paik H-Y, Lee H-K, Jo I. Development of a semi-quantitative food frequency questionnaire based on dietary data from the Korea National Health and Nutrition Examination Survey. Nutr Sci 2003;6:173–84.
[29] The Korean Nutrition Society. Food composition table. Recommended dietary allowances for Koreans. 7th ed. Seoul: The Korean Nutrition Society; 2000.
[30] Ahn Y, Kwon E, Shim JE, Park MK, Joo Y, Kimm K, et al. Validation and reproducibility of food frequency questionnaire for Korean genome epidemiologic study. Eur J Clin Nutr 2007;61:1435–41, doi:http://dx.doi.org/10.1038/sj.ejcn.1602657.
[31] Korean Nutrition Society. 2020 Dietary Reference Intakes for Koreans: Energy and Macronutrients. Sejong, Republic of Korea: Ministry of Health and Welfare; 2020.
[32] Howard WJ. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Yearbook Endocrinol 2006;2006:113–4, doi:http://dx.doi.org/10.1016/S0084-3741(08)70316-0.

[33] Lee SY, Park HS, Kim DJ, Han JH, Kim SM, Cho GJ, et al. Appropriate waist circumference cutoff points for central obesity in Korean adults. Diabetes Res Clin Pract 2007;75:72–80, doi:http://dx.doi.org/10.1016/j.diabres.2006.04.013.
[34] Hajihashemi P, Hassannejad R, Haghighatdoost F, Mohammadifard N, Sadeghi M, Roohafza H, et al. The long-term association of different dietary protein sources with metabolic syndrome. Sci Rep 2021;11:19394, doi:http://dx.doi.org/10.1038/s41598-021-98688-0.
[35] Shang X, Scott D, Hodge A, English DR, Giles GG, Ebeling PR, et al. Dietary protein from different food sources, incident metabolic syndrome and changes in its components: an 11-year longitudinal study in healthy community-dwelling adults. Clin Nutr 2017;36:1540–8, doi:http://dx.doi.org/10.1016/j.clnu.2016.09.024.
[36] Huang J, Liao LM, Weinstein SJ, Sinha R, Graubard BI, Albanes D. Association between plant and animal protein intake and overall and cause-specific mortality. JAMA Intern Med 2020;180:1173–84, doi:http://dx.doi.org/10.1001/jamainternmed.2020.2790.
[37] Igl W, Kamal-Eldin A, Johansson A, Liebisch G, Gnewuch C, Schmitz G, et al. Animal source food intake and association with blood cholesterol, glycerophospholipids and sphingolipids in a northern Swedish population. Int J Circumpolar Health 2013;72:21162, doi:http://dx.doi.org/10.3402/ijch.v72i0.21162.
[38] Guo H, Ding J, Liang J, Zhang Y. Association of red meat and poultry consumption with the risk of metabolic syndrome: a meta-analysis of prospective cohort studies. Front Nutr 2021;8:410, doi:http://dx.doi.org/10.3389/fnut.2021.691848.
[39] Kim Y, Je Y. Meat consumption and risk of metabolic syndrome: results from the Korean population and a meta-analysis of observational studies. Nutrients 2018;10:390, doi:http://dx.doi.org/10.3390/nu10040390.
[40] Lee JE, McLerran DF, Rolland B, Chen Y, Grant EJ, Vedanthan R, et al. Meat intake and cause-specific mortality: a pooled analysis of Asian prospective cohort studies. Am J Clin Nutr 2013;98:1032–41, doi:http://dx.doi.org/10.3945/ajcn.113.062638.
[41] MacArthur MR, Mitchell SJ, Treviño-Villarreal JH, Grondin Y, Reynolds JS, Kip P, et al. Total protein, not amino acid composition, differs in plant-based versus omnivorous dietary patterns and determines metabolic health effects in mice. Cell Metab 2021;33:1808–1819.e2, doi:http://dx.doi.org/10.1016/j.cmet.2021.06.011.
[42] Li SS, Blanco Mejia S, Lytvyn L, Stewart SE, Viguiliouk E, Ha V, et al. Effect of plant protein on blood lipids: a systematic review and meta-analysis of randomized controlled trials. J Am Heart Assoc 2017;6(12):e006659, doi:http://dx.doi.org/10.1161/JAHA.117.006659.
[43] Reid-McCann RJ, Brennan SF, McKinley MC, McEvoy CT. The effect of animal versus plant protein on muscle mass, muscle strength, physical performance and sarcopenia in adults: protocol for a systematic review. Syst Rev 2022;11:64, doi:http://dx.doi.org/10.1186/s13643-022-01951-2.
[44] Hackney KJ, Trautman K, Johnson N, McGrath R, Stastny S. Protein and muscle health during aging: benefits and concerns related to animal-based protein. Anim Front Rev Mag Anim Agric 2019;9:12–7, doi:http://dx.doi.org/10.1093/af/vfz030.
[45] Wolfe Robert R. Branched-chain amino acids and muscle protein synthesis in humans: myth or reality? J Int Soc Sports Nutr 2017;14:1–7, doi:http://dx.doi.org/10.1186/s12970-017-0184-9.
[46] Vanweert F, Schrauwen P, Phielix E. Role of branched-chain amino acid metabolism in the pathogenesis of obesity and type 2 diabetes-related metabolic disturbances BCAA metabolism in type 2 diabetes. Nutr Diabetes 2022;12(1):35, doi:http://dx.doi.org/10.1038/s41387-022-00213-3.
[47] Cheung W, Keski-Rahkonen P, Assi N, Ferrari P, Freisling H, Rinaldi S, et al. A metabolomic study of biomarkers of meat and fish intake. Am J Clin Nutr 2017;105:600–8, doi:http://dx.doi.org/10.3945/ajcn.116.146639.
[48] Rousseau M, Guénard F, Garneau V, Allam-Ndoul B, Lemieux S, Pérusse L, et al. Associations between dietary protein sources, plasma BCAA and short-chain acylcarnitine levels in adults. Nutrients 2019;11(1):173, doi:http://dx.doi.org/10.3390/nu11010173.
[49] Im J, Park H, Park K. Higher intake of total dietary essential amino acids is associated with a lower prevalence of metabolic syndrome among Korean adults. Nutrients 2022;14(22):4771, doi:http://dx.doi.org/10.3390/nu14224771.
[50] Sugiyama MG, Agellon LB. Sex differences in lipid metabolism and metabolic disease risk. Biochem Cell Biol 2012;90:124–41, doi:http://dx.doi.org/10.1139/o11-067.
[51] Kautzky-Willer A, Handisurya A. Metabolic diseases and associated complications: sex and gender matter. Eur J Clin Invest 2009;39:631–48, doi:http://dx.doi.org/10.1111/j.1365-2362.2009.02161.x.
[52] Ferreira E, Hatta M, Laymon K, Ikeda I, Takeuchi M, Takeda Y, et al. Higher dietary protein/energy ratio is associated with a lower risk for obesity in older women with type 2 diabetes: cross-sectional analysis of Japanese patients with type 2 diabetes mellitus. Hum Nutr Metab 2024;36:200257, doi:http://dx.doi.org/10.1016/j.hnm.2024.200257.