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Purine-rich foods, protein intake, and the prevalence of hyperuricemia: The Shanghai Men's Health Study

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Abstract

Background and Aims—Diet may play an important role in the development of hyperuricemia and gout. However, the association between dietary factors and hyperuricemia remains unclear, and few studies have investigated direct links between food intake and hyperuricemia. The aim of this study was to investigate associations between high purine-content foods and protein intake with the prevalence of hyperuricemia by using data from a cross-sectional study of 3,978 men aged 40–74 yrs living in Shanghai, China.

Keywords

hyperuricemia; Uric acid; purine; diet

INTRODUCTION

Hyperuricemia has been associated with incident insulin resistance (1) and is highly prevalent among individuals with metabolic syndrome (2–4). A positive association between plasma uric acid and the incidence of type 2 diabetes has been found in some (5–7) but not all studies (8). Thus, identification of factors associated with the occurrence of hyperuricemia should help in the prevention of type 2 diabetes. Serum uric acid levels are likely to reflect current dietary habits (9). Uric acid is the end product of purine metabolism, and thus, eating foods rich in purines contributes to total uric acid levels (10). A high-protein diet typically contains large quantities of purines. However, such diets may have an uricosuric effect (i.e., increase excretion of uric acid in urine), resulting in lower serum acid levels (11,12). Although it has been postulated that diet plays an important role in the development of hyperuricemia and gout, data directly linking food intake with hyperuricemia is limited. Meat and seafood have been associated with higher uric acid levels in some studies (13,14), while dairy intake has been found to decrease plasma uric acid levels (15–17). No associations between total protein intake and uric acid (13,18) have been reported.

The association between dietary factors and hyperuricemia remains unclear (13,18). Using data collected in the Shanghai Men's Health Study (SMHS), a population-based study of middle-aged men living in urban Shanghai, China, we evaluated associations between the

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intake of protein and purine-rich foods and the prevalence of hyperuricemia among men who had provided fasting blood samples at baseline.

METHODS

The Shanghai Men's Health Study

The Shanghai Men's Health Study (SMHS) is a population-based cohort study of 61,504 Chinese men who were between 40 and 74 years of age and free of cancer at enrollment and who lived in urban Shanghai, China. Recruitment for the SMHS was initiated in April 2002 and completed in June 2006. A total of 83,058 eligible male residents of eight communities in urban Shanghai were invited to participate by trained interviewers. A total of 61,504 men with no prior history of cancer were enrolled in the study (response rate: 74.0%). Reasons for non-participation were refusal (21.1%), out of area during enrollment (3.1%), and other miscellaneous reasons, including poor health and hearing problems (1.8%). The study protocols were approved by the Institutional Review Boards of all participating institutes, and all participants provided written, informed consent. Through an interview, information was collected on demographic characteristics, disease history, and lifestyle factors, including dietary intake and physical activity. Participants were measured for weight and waist and hip circumferences according to a standard protocol. Participants were asked to provide biological samples, including a blood or cheek cell sample and a spot urine sample. In a sub-cohort of 3,978 participants who had no history of diabetes at baseline and who had provide a fasting blood sample, we measured levels of disease-related biomarkers. This sub-cohort forms the basis of the current study.

Uric Acid Measurement

At the time of the interview, a 10 ml blood sample was drawn into an EDTA vacutainer tube. The samples were kept in a portable Styrofoam box with ice packs (0–4 °C) and were processed within 6 hours. All samples were stored at –70°C immediately after processing. One set of samples was shipped to the US on dry ice and is being stored at Vanderbilt University. Among participants who donated a blood sample at baseline (n=46,169), 12.5% reported having had their last meal at least 8 hours prior to the blood draw. In this study, we included the first 3,978 participants who were free of diabetes at baseline and had provided a fasting blood sample. Levels of uric acid were measured by using the ACE® Uric acid reagent on ACE® Clinical Chemistry System (Alfa Wassermann, Inc, West Caldwell, NJ) following the manufacturer's protocol. Uric acid in plasma was oxidized by the uricase method. Hyperuricemia was defined as >7.0 mg/dl (19–21).

Dietary Factors

Usual dietary intake was assessed by using a validated food frequency questionnaire (FFQ) (22). A total of 81 food items were included in the FFQ used in the SMHS. For each food item or food group, participants were asked how frequently (daily, weekly, monthly, yearly, or never) they consumed the food or food groups, which was followed by a question on the amount consumed in liang per unit of time (1 liang = 50 g). The reproducibility and validity of the FFQ was assessed in a random sample of 195 participants who completed one FFQ at baseline, 12 24-hour dietary recalls (24-HDR) (once/month for 12 consecutive months) and a second FFQ at the end of the study. The validity of the FFQ was evaluated by comparing nutrient and food group intake levels from the second FFQ and the multiple 24-HDR (22). Correlation coefficients ranged from 0.38 to 0.64 for macronutrients 0.33 to 0.58 for micronutrients, and from 0.35 to 0.72 for food groups. Correlation coefficients for protein red meat, poultry, fish, soy foods, and vegetables were 0.49, 0.45, 0.35, 0.49, 0.54, and 0.42, respectively. The reliability of the FFQ was assessed by comparing the intake levels from the two FFQs. Correlation coefficients were 0.39–0.53 for macronutrients, 0.38–0.52 for

micronutrients, and 0.39–0.64 for food groups. Correlation coefficients for protein, red meat, poultry, fish, soy foods, and vegetables were 0.47, 0.40, 0.48, 0.41, 0.50 and 0.43, respectively (22).

The Chinese Food Composition Tables (23) were used to estimate intake of nutrients and total energy (kcal/day). We estimated total protein, protein from animal sources, and protein from plant sources. For protein intake, we further applied the residual method to adjust for variation due to total energy intake (12).

The average daily intake of individual food items (g/day) was combined to compute the following food groups: total meat (poultry and red meat), seafood (fish and shellfish), purine-rich vegetables (beans, peas, spinach, cauliflower, mushrooms), and soy foods (soy beans, soy bean sprouts, bean curd [tofu], fried bean curd, vegetarian chicken, and bean curd cake). Because soy milk is a beverage, we analyzed soy milk separately from other soy products.

Confounding factors

We collected information on potential confounding factors in the association between dietary factors and the prevalence of hyperuricemia, including smoking, physical activity, alcohol intake, anthropometric measurements, and other factors, such as sociodemographics and disease history.

Physical activity measurement—A detailed assessment of physical activity was obtained using a validated physical activity questionnaire (PAQ) (24). The questionnaire evaluated regular exercise and sports participation during the 5 years preceding the interview and included daily activities, such as walking, stair climbing, cycling, household activities, and the daily commuting journey to/from work. Summary energy expenditure values (metabolic equivalent task [MET]-hr/day) for these activities were estimated using a compendium of physical activity values (25). We calculated total non-occupational physical activity (total METs) by combining all types of physical activity.

Smoking status—Never smokers were defined as participants who had never smoked at least one cigarette per day for more than 6 months. Ex-smokers were defined as participants that had smoked at least one cigarette per day for more than 6 months, but were not currently smoking. Current smokers were asked how many cigarettes they smoked per day. Participants were then classified according to their current smoking status into three categories: never smokers (n=728; 18.25%), ex-smokers (n=243; 6.09%), and current smokers (n=3,017; 75.65%).

Alcohol Intake—We asked each participant whether he had ever drunk alcoholic beverages at least once a week for six months or more. If the answer was yes, he was asked to provide the usual amount of consumption of rice wine, grape wine, beer, or liquor separately. Participants who had given up drinking were coded as ex-drinkers (n=149). One drink was defined as 360 g of beer (12.6 g of ethanol), 103 g of grape wine (12.3 g of ethanol), 30 g of liquor (12.9 g of ethanol), or 103 g of rice wine (12.3 g of ethanol) (26). Participants were then classified into 5 categories according to their alcohol intake level: non drinkers (n=2,340; 60.95%), occasional drinkers (less than 0.5 units/day; n=65; 1.69%), light drinkers (0.5–0.99 units per day; n=178; 4.64%), moderate drinkers (1.0–2.99 units per day; n=743; 19.43%), and heavy drinkers (more than 3 units per day; n=510; 13.28%). Because occasional drinkers were a small group, we combined them with light drinkers.

Anthropometric Measurements—Anthropometric measurements of weight, height, and waist and hip circumferences were taken twice, according to a standard protocol. If the difference between the first two measurements was larger than 1 cm for circumferences or 1 kg for weight, a third measurement was taken. The average of the two closest measurements was applied in the present study. From these measurements, the following variables were created: BMI, weight in kg divided by the square of height in meters and WHR, waist circumference divided by hip circumference.

Other Confounding Factors—Socio-demographic factors such as age, level of education (none, elementary school, middle/high school, college), income in yuan/year (<500, 500–999, 1000–1999, >1999), occupation (professional, clerical, manual labor), use of anti-hypertensive medication (yes/no), hypertension (blood pressure ≥85/130 mm Hg and/or taking anti-hypertensive medication), and cardiovascular disease (CVD) at baseline (yes/no) were included in the analyses as potential confounders.

Statistical analysis

Associations between protein intake and food groups with hyperuricemia were investigated by using unconditional logistic regression analysis. The analyses were adjusted for age, kcal/day, BMI, WHR, income level, education, occupation, smoking, physical activity, alcohol intake, pre-existing CVD, hypertension, and use of anti-hypertensive medication. Tests for linear trend were performed by entering the dietary categorical variables as continuous parameters in the models. All analyses were performed using SAS (version 9.1), and all tests of statistical significance were based on two-sided probability.

RESULTS

The mean and median for uric acid in the population are 6.36 and 6.10 mg/dl, respectively. The prevalence of hyperuricemia (uric acid >7mg/dl) in this middle-aged, male population was 25.0% (Table 1). The median uric acid value for the hyperuricemia group was 8.3 mg/dl (Interquartile range 7.4–8.7) and that for the group with no hyperuricemia was 5.7mg/dl (Interquartile range 5.2–6.3). Participants with hyperuricemia were more likely to have higher BMI and WHR and to drink alcohol, but were less likely to smoke compared with those without hyperuricemia. They were also more likely to have a college education and a professional job. The prevalence of hyperuricemia was also related to the prevalence of hypertension and the use of anti-hypertensive medication. Participants with hyperuricemia had higher intake of seafood and lower daily caloric intake. Table 2 presents associations between hyperuricemia and protein intake. No association between total protein and hyperuricemia was observed. Protein from animal sources was significantly associated with prevalence of hyperuricemia. The ORs for quintiles of protein from animal sources were 1.00, 1.31, 1.23, 1.27, and 1.44; P for trend: 0.02 in analysis adjusted for age, kcal/day, WHR, BMI, physical activity, alcohol consumption, smoking, education level, income level, occupation, pre-existing CVD, hypertension, and use of anti-hypertensive medication. However, when the analysis was further adjusted for protein from vegetable sources, the association was attenuated and no longer statistically significant. We observed an inverse association between protein from plant sources and hyperuricemia, but the association was not independent of animal protein intake.

Seafood intake (fish and shellfish combined) was associated with higher prevalence of hyperuricemia (Table 3). The multivariate adjusted ORs for hyperuricemia across quintiles of total seafood intake were 1.00, 1.49, 1.35, 1.34, and 1.56 (p for trend: 0.01). We further adjusted the analysis by plant-origin protein and found similar results. Associations between fish and shellfish intake and hyperuricemia were attenuated after adjustment for plant protein intake. Although we observed a modest positive trend of marginal significance

between red meat intake and hyperuricemia, the association was no longer significant when plant-origin protein was included in the analysis. No associations between total meat or poultry intake and hyperuricemia were observed.

Associations between purine-rich vegetables and soy foods with hyperuricemia are presented in Table 4. The ORs for quintiles of purine-rich vegetables were 1.00, 0.99, 0.94, 1.11, and 1.07 (p for trend: 0.31) in a fully-adjusted analysis, including adjustment for protein from animal sources. The ORs for quintiles of soy food intake were 1.00, 0.92, 0.86, 0.85, and 0.80 (p for trend: 0.07). Intake of soy products (bean curd/tofu, fried bean curd, vegetarian chicken, and bean curd cake) was associated with lower risk of hyperuricemia, while the association of unprocessed soy beans and hyperuricemia failed to reach significance. We also found that intake of soy milk was inversely associated with hyperuricemia.

DISCUSSION

In this study of 3,978 middle-aged men living in Shanghai, we found that intake of protein from animal sources and seafood was associated with higher prevalence of hyperuricemia, while soy products appeared to decrease hyperuricemia risk. No association between total protein intake and hyperuricemia was observed. The associations of animal protein intake and plant protein intake with hyperuricemia were not independent of each other.

Other studies have reported no association of protein intake (either total protein intake or intake from plant or animal sources) with serum uric acid (13,18). High protein diets typically contain large quantities of purines and, while such diets might be associated with enhanced purine production, they also frequently increase urinary urate excretion and thus reduce serum uric acid levels (12). In a large prospective study of US men, those in the highest quintile of vegetable protein intake had a 27% lower risk of developing gout compared with those in the lowest quintile (15).

Both meat intake and seafood intake have been associated with hyperuricemia in three recent studies. In one study conducted in 5 coastal cities in China, hyperuricemia was associated with higher consumption of meat (OR: 1.26, 95%CI: 1.10–1.33, $P < 0.05$), fish (OR: 1.28, 95%CI: 1.16–1.19, $P < 0.051$), and shellfish (OR: 1.34, 95%CI: 1.20–1.27, $P < 0.01$) (14). However, that study did not adjust for confounders, which could be a problem, as the authors reported both higher prevalences of hyperuricemia and higher consumption of meat and seafood in urban and more economically-developed areas. A study conducted in Taiwan found no association of meat, seafood, or other dietary factors with hyperuricemia (18). A US study of 14,809 participants from the Third National Health and Nutrition Examination Survey (NHANES-III) reported that serum uric acid levels increased with increasing intake of meat and seafood (13). The OR for the upper versus the lower quintile for intake of meat was 1.41 (95%CI: 1.07–1.86) and for intake of seafood was 1.51 (95%CI: 1.17–1.95). Other studies looking at associations between diet and hyperuricemia have been small, were not population-based, or have not properly adjusted for confounders (27,28). Meat and seafood have been associated with higher risk of gout in the Health Professionals Follow-Up Study (15).

We did not find an association between intake of purine-rich vegetables and the prevalence of hyperuricemia. To our knowledge, other studies have not reported associations between intake of high-purine content vegetables and hyperuricemia. Two recent studies indicated that eating purine-rich vegetables, including peas, lentils, and beans, was not associated with increased risk of gout (15,29).

Because soy foods are a good source of protein and could contribute to the amount of purine intake in Shanghai, we investigated associations between total soy food intake and hyperuricemia in this population. It has been suggested that soy products cause gout in Asian populations (30). However, we found an inverse association between soy food intake (soy beans and soy products) and prevalence of hyperuricemia that approached significance. When we investigated soy foods separated in two mutually exclusive groups (unprocessed soy beans and soy products), the association between soy beans and hyperuricemia failed to reach significance, while the association of soy products (bean curd/tofu, fried bean curd, vegetarian chicken, and bean curd cake) was inversely associated with prevalence of hyperuricemia. We found that soy milk intake was inversely associated with the prevalence of hyperuricemia.

No other studies have reported associations between soy food intake and hyperuricemia. A study conducted in Taiwan compared blood levels of uric acid between vegetarians (who usually consume soy products as a protein source) with non-vegetarians and found lower uric acid levels in vegetarians (31). A clinical study conducted in Japan examined the effect of tofu (bean curd) consumption on uric acid metabolism. Ingestion of tofu increased plasma concentrations of uric acid, as well as uric acid clearance and urinary excretion of uric acid. However, the increase in plasma concentrations of uric acid was fairly small (30).

The precise purine content of most foods is not well known, especially for cooked or processed foods (11). The purine content of tofu is lower than in unprocessed soy beans, since purines can be lost during processing (30). The purine content of foods can also be altered by storage and cooking (32), and the specific sources of dietary purines also affects urate level (33). Thus, it is difficult to assess the effect of a particular food or food group on serum uric acid levels.

The strengths of our study include the population-based design, which was representative of the middle-aged, male population of urban Shanghai; the extensive information on confounders; and the validated food frequency questionnaire we used to collect data on dietary intake. Uric acid levels were measured in a single lab to reduce inter-lab variation. The wide range of soy foods consumed in our study population facilitated the evaluation of the effect of usual soy food intake on hyperuricemia.

Our study has some limitations. One limitation is the cross-sectional design, which prevented us from making any causal inferences based on our results. In addition, the study participants of this sub-cohort study were younger than those in the entire SMHS cohort and were more likely to smoke, consume alcohol, have a professional job, have a higher level of education, and were less likely to exercise. Thus, results of this study may not represent the entire cohort. Unfortunately we do not have information on gout prevalence in this population. Thus, it is possible that participants with gout may have changed their diet.

In conclusion, consumption of animal protein and seafood were associated with higher prevalence of hyperuricemia, while consumption of soy products was associated with lower prevalence of hyperuricemia among middle-aged Chinese men. Our results add to the limited data on associations between dietary intake and hyperuricemia and suggest that modification of adverse dietary habits could be advantageous in the prevention of hyperuricemia.

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Table 1Characteristics of the study population by prevalence of hyperuricemia¹

	No hyperuricemia	Hyperuricemia	P value³
	N=2982	N=996	
Age (Median, IQR)	48.0(45,54)	49.0 (45,54)	0.19
Uric acid (Median, IQR)	5.71 (5.2,-6.3).	5.71 (5.2, 6.3).	<0.001
BMI (Mean, SD)	22.91±0.06	24.4±3.1	<0.001
WHR² (Mean, SD)	0.89±0.05	0.91±0.05	<0.001
Current smoker (%)	76.93	71.7	<0.01
Alcohol consumption (%)	35.49	44.1	<0.001
Exercise participation (%)	21.70	22.0	0.85
Education (%)			
None	3.42	2.5	<0.01
Elementary	38.27	37.7	
Up to high school	41.45	38.2	
College	16.86	21.6	
Income Level (%)			
<500	19.08	20.0	0.32
500–999	42.66	39.3	
1000–1999	29.02	30.5	
>1999	9.24	10.2	
Occupation (%)			0.03
Professional	19.57	22.3	
Clerical	22.56	24.5	
Manual labor	57.87	53.1	
Hypertension	44.50	60.9	<0.001
Use of hypertensive medication	10.26	23.1	<0.001
Pre-existing CVD²	3.89	4.9	0.15
Dietary Factors (Median, IQR)			
Kcal/day	1884.9 (1583.1,2233.3)	1831.1 (1529.9,2206.5)	0.01
Total protein intake (g/day)	76.3 (62.9,94.4)	76.5 (63.3,93.8)	0.75
Total meat intake (g/day)	74.0 (47.6,112.9)	76.5 (50.4,114.8)	0.09
Seafood intake (g/day)	39.9 (21.1,69.0)	44.3 (24.9,74.0)	<0.01
High-purine vegetable intake (g/day)	39.5 (24.8,63.7)	41.8 (25.5,66.3)	0.16
Soy food intake (g/day)	77.9(47.6,112.0)	77.7 (46.2,114.4)	0.85

¹Hyperuricemia was defined as uric acid level >7 mg/dl).²Abbreviations: WHR, waist-to-hip ratio; CVD, cardiovascular disease³P trend calculated by chi square test for the prevalences of population characteristics, by ANOVA test for BMI and WHR and by Kruskal Wallis test for age and dietary variables.

Table 2

Associations between hyperuricemia¹ and protein intake^{*}

	Median (g/day)	OR1	(95% CI)	P trend	OR2	(95% CI)	P trend
Total Protein							
Intake							
Quintile 1	59.7	1.00		0.11			
Quintile 2	67.7	1.07	0.82–1.33				
Quintile 3	71.9	1.27	0.99–1.64				
Quintile 4	79.7	1.22	0.95–1.57				
Quintile 5	95.4	1.20	0.93–1.54				
Animal Protein							
Intake							
Quintile 1	13.5	1.00		0.02	1.00		0.16
Quintile 2	20.9	1.31	1.01–1.69		1.29	0.99–1.66	
Quintile 3	26.0	1.23	0.94–1.59		1.19	0.91–1.55	
Quintile 4	32.6	1.27	0.99–1.64		1.22	0.94–1.59	
Quintile 5	46.3	1.44	1.12–1.85		1.32	0.99–1.76	
Plant protein							
Intake							
Quintile 1	22.7	1.00		0.02	1.00		0.45
Quintile 2	27.6	0.97	0.78–1.22		1.03	0.82–1.29	
Quintile 3	30.8	0.86	0.68–1.08		0.93	0.73–1.19	
Quintile 4	33.5	0.82	0.65–1.04		0.93	0.72–1.20	
Quintile 5	37.5	0.79	0.61–1.01		0.93	0.70–1.25	

* Energy adjusted.

OR1: Adjusted for age, kcal/day, WHR, BMI, physical activity, alcohol consumption, smoking, education level, income level, occupation, pre-existing CVD, hypertension, and use of anti-hypertensive medication.

OR2: Adjusted as above, plus additional adjustment of animal protein intake and plant protein analysis for animal protein intake.

¹Hyperuricemia was defined as uric acid level of >7mg/dl.

Table 3
Associations between hyperuricemia and high-purine content, animal-source food groups

	<u>Median (g/day)</u>	<u>OR1</u>	<u>(95% CI)</u>	<u>P trend</u>	<u>OR2</u>	<u>(95% CI)</u>	<u>P trend</u>
Total Meat Intake							
Quintile 1	30.5	1.00		0.20	1.00		0.65
Quintile 2	52.8	1.08	0.85–1.38		1.07	0.84–1.37	
Quintile 3	74.9	1.14	0.89–1.46		1.11	0.86–1.42	
Quintile 4	104.2	1.17	0.91–1.50		1.10	0.85–1.43	
Quintile 5	162.9	1.17	0.89–1.54		1.04	0.78–1.40	
Red Meat Intake							
Quintile 1	21.8	1.00		0.09	1.00		0.33
Quintile 2	42.3	0.97	0.76–1.24		0.96	0.75–1.23	
Quintile 3	60.1	1.23	0.97–1.57		1.21	0.95–1.54	
Quintile 4	84.0	1.00	0.78–1.29		0.96	0.74–1.24	
Quintile 5	132.0	1.29	0.99–1.69		1.19	0.89–1.58	
Poultry Intake							
Quintile 1	0.91	1.00		0.76	1.00		0.80
Quintile 2	5.5	1.00	0.79–1.28		1.01	0.79–1.28	
Quintile 3	10.9	0.98	0.77–1.25		0.97	0.76–1.24	
Quintile 4	20.7	1.04	0.82–1.33		1.01	0.79–1.29	
Quintile 5	41.6	1.02	0.79–1.31		0.96	0.74–1.24	
Total Seafood Intake							
Quintile 1	10.9	1.00		0.01	1.00		0.05
Quintile 2	26.0	1.49	1.16–1.91		1.47	1.15–1.89	
Quintile 3	41.0	1.35	1.05–1.73		1.32	1.03–1.70	
Quintile 4	63.0	1.34	1.04–1.73		1.30	1.01–1.68	
Quintile 5	117.5	1.56	1.20–2.02		1.46	1.11–1.92	
Fish Intake							
Quintile 1	6.7	1.00		0.05	1.00		0.17
Quintile 2	17.9	1.16	0.91–1.49		1.16	0.90–1.48	
Quintile 3	30.1	1.18	0.92–1.51		1.16	0.90–1.48	
Quintile 4	48.2	1.21	0.94–1.55		1.18	0.92–1.51	

	Median (g/day)	OR1	(95% CI)	P trend	OR2	(95% CI)	P trend
Quintile 5	95.4	1.31	1.02–1.70		1.23	0.94–1.60	
<u>Shellfish Intake</u>							
Quintile 1	0.80	1.00		0.02	1.00		0.05
Quintile 2	4.2	0.95	0.74–1.22		0.94	0.74–1.21	
Quintile 3	8.3	1.22	0.96–1.56		1.21	0.95–1.54	
Quintile 4	14.4	1.29	1.01–1.64		1.25	0.98–1.60	
Quintile 5	32.8	1.21	0.94–1.57		1.14	0.87–1.49	

OR1: Adjusted for age, kcal/day, WHR, BMI, physical activity, alcohol consumption, smoking, education level, income level, occupation, pre-existing CVD, hypertension, and use of anti-hypertensive medication.

OR2: Adjusted as above, plus additional adjustment for plant protein intake.

[†]Hyperuricemia was defined as uric acid level of >7 mg/dl.

Table 4
Associations between hyperuricemia^a and high-purine content, plant-source food groups

	OR1	(95% CI)	P trend	OR2	(95% CI)	P trend
Purine Vegetable						
Intake						
Quintile 1	1.00		0.12	1.00		0.31
Quintile 2	1.02	0.80–1.30		1.00	0.78–1.27	
Quintile 3	0.99	0.73–1.33		0.95	0.70–1.28	
Quintile 4	1.16	0.93–1.45		1.11	0.89–1.40	
Quintile 5	1.14	0.89–1.48		1.08	0.83–1.39	
Total Soy Food						
Intake						
Quintile 1	1.00		0.17	1.00		0.07
Quintile 2	0.93	0.73–1.18		0.90	0.71–1.15	
Quintile 3	0.73	0.57–0.93		0.70	0.55–0.89	
Quintile 4	0.93	0.73–1.19		0.89	0.69–1.14	
Quintile 5	0.82	0.63–1.05		0.77	0.59–0.99	
Soy Bean Intake						
Quintile 1	1.00		0.69	1.00		0.45
Quintile 2	1.00	0.79–1.27		0.99	0.45–1.26	
Quintile 3	0.88	0.69–1.12		0.85	0.67–1.09	
Quintile 4	0.99	0.78–1.26		0.96	0.76–1.22	
Quintile 5	0.95	0.74–1.22		0.91	0.71–1.17	
Soy Product Intake[*]						
Quintile 1	1.00		0.08	1.00		0.03
Quintile 2	0.92	0.72–1.17		0.90	0.71–1.15	
Quintile 3	0.87	0.69–1.11		0.84	0.66–1.06	
Quintile 4	0.85	0.66–1.10		0.81	0.63–1.05	
Quintile 5	0.80	0.62–1.03		0.76	0.59–0.99	
Soy Milk Intake						
Quintile 1	1.00		<0.01	1.00		<0.01

	<u>OR1</u>	<u>(95% CI)</u>	<i>P trend</i>	<u>OR2</u>	<u>(95% CI)</u>	<i>P trend</i>
Quintile 2	0.81	0.53–1.22		0.82	0.54–1.24	
Quintile 3	0.83	0.66–1.04		0.83	0.67–1.05	
Quintile 4	0.80	0.66–0.96		0.78	0.65–0.94	
Quintile 5	0.78	0.62–0.99		0.77	0.61–0.98	

OR1: Adjusted for age, kcal/day, WHR, BMI, physical activity, alcohol consumption, smoking, education level, income level, occupation, pre-existing CVD, hypertension and hypertension medication

OR2: Adjusted as above, plus additional adjustment for animal protein intake.

* Bean curd/tofu, fried bean curd, vegetarian chicken, and bean curd cake.

[†]Hyperuricemia was defined as uric acid level of >7 mg/dl.