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The consumption of fish cooked by different methods was related to the risk of hyperuricemia in Japanese adults: A 3-year follow-up study

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Abstract *Background and aims:* Fish consumption is a recognized risk factor for elevated serum uric acid (UA) levels, hyperuricemia, and gout. However, the relationship between the consumption of fish cooked by different methods and the risk of hyperuricemia is unclear. Therefore, we aimed to investigate the relationship between the consumption of fish cooked by different methods and the risk of hyperuricemia in Japanese adults.
Methods and results: A 3-year follow-up study was conducted with 424 Japanese adults aged 29–74 years. Fish consumption was assessed using a validated self-administered dietary history questionnaire, and hyperuricemia was defined as serum UA $\geq$7 mg/dL in men and $\geq$6 mg/dL in women or the use of any anti-gout treatment. During the 3-year follow-up period, we documented 30 newly diagnosed cases of hyperuricemia. After adjusting for potential confounders, multivariate logistic regressions analysis revealed a significant positive relationship between the risk of hyperuricemia and raw (sashimi and sushi) or roasted fish consumption, but not boiled or fried fish consumption. The odds ratios (95% CI) for hyperuricemia with increasing raw fish consumption were 1.00 (reference), 2.51 (0.85, 7.39), and 3.46 (1.07, 11.14) (P for trend: 0.036). Similarly, the odds ratios (95% CI) with increasing roasted fish consumption were 1.00 (reference), 3.00 (0.75, 11.89), and 5.17 (1.30, 20.62) (P for trend: 0.018).
Conclusion: This 3-year follow-up study showed that the consumption of raw or roasted fish, but not boiled or fried fish, was related with a higher risk of hyperuricemia in Japanese adults.

Introduction

Habitual fish consumption has long been recognized as a healthy dietary pattern; fish is rich in the omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid [1], and consumption of these fatty acids can reduce the risk of coronary heart disease [2], type 2 diabetes [3], hypertension [4], and mortality [5]. Nationwide population surveys conducted in the U.S. reported that the average daily seafood (fish and shellfish) intake was about 22.6 g [6]. Compared with Western populations, Asian populations have a higher mean daily consumption of seafood, e.g., 41.1 g among Koreans [7] and 56–97 g among the Japanese [8]. In addition, findings from studies conducted in the U.S.

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and Europe support the specific dietary recommendation that twice-weekly consumption of fish (about 60 g/d) is associated with a reduced risk of coronary heart disease [9,10]. However, in recent years, epidemiological study showed that long-term fish consumption could cause early asymptomatic hyperuricemia and increasing the risk of gout [11] owing to the purine content of fish, which could cause uric acid (UA) to be overproduced in the kidneys [12] and subsequently increased the risk of hyperuricemia. The association between fish consumption and the risk of hyperuricemia has been well documented. To date, studies regarding the negative effect of fish consumption on hyperuricemia have primarily focused on simply investigating the association between fish consumption, as a whole, and the risk of hyperuricemia; in a cross-sectional study of 3978 men aged 40–74 years, greater fish consumption increased UA levels and the risk of hyperuricemia [13]. A recent case-crossover study that investigated the relationship between the intake of purine-rich foods and the risk of recurrent gout attacks among 633 patients with gout suggested that acute intake of foods with a high purine content result in an almost 5-fold increase in the risk of recurrent gout attacks. The authors proposed that future studies should investigate the possible association between the consumption of fish cooked by different methods and the risk of hyperuricemia, because the bioavailability of purine varies with the style of cooking or processing [14]. These findings indicated that the consumption of fish cooked by different methods could potentially affect UA levels. Therefore, we designed a 3-year follow-up study aiming to investigate the relationship between the consumption of fish cooked by different methods (raw fish [sashimi and sushi], roasted fish, boiled fish, and fried fish) and the risk of hyperuricemia in Japanese adults.

Methods

Study population

We analyzed data from the Oroshisho longitudinal study for the period August 2008–August 2011. Detailed information on this study was provided previously [15]. Our population consisted of individuals aged 29–74 years working at the Sendai Oroshisho Center, which includes more than 120 small and medium size organizations in Sendai, Northern Japan. The annual health examination was attended by 1170 participants at baseline, who completed a self-administered questionnaire and dietary history questionnaires; this provided information about demographics, anthropometrics, lifestyle factors, and dietary factors; on that occasion, blood samples were taken. Then, participants were excluded for the following reasons: n = 7, failure to provide written informed consent for analysis of their data; n = 306, missing data for the UA assessment (n = 234) or other variables (n = 72); n = 186, existing hyperuricemia (n = 176) or gout (n = 10) at baseline; and n = 247, missing hyperuricemia assessment data for 2011. Therefore, the follow-up study included 424 participants (336 men, 88 women). All research procedures in the current study adhered to the Declaration of Helsinki protocols [16]. The protocol for the study was approved by the institutional review board of the Tohoku University Graduate School of Medicine.

Assessment of dietary intake

The brief self-administered dietary history questionnaire (BDHQ), which includes questions on 75 principal food items [17], was administered at baseline to assess the usual consumption of “raw fish”, “roasted fish”, “boiled fish”, and “fried fish” during the preceding month. Subjects answered this question with a number ranging from 1 (≥2 times/day) to 7 (0 times/day). We grouped the subjects into three categories based on frequency of fish consumption for each of the different cooking methods: low (<1 time/week), middle (1 time/week), and high (≥2 times/week). Daily dietary intakes of total energy, total alcohol, total meat, other seafood, total bean products, and total dairy were calculated using an ad hoc computer program for the BDHQ, which was based primarily on the fifth edition of the Japanese food composition table. The reproducibility and validity of the BDHQ have been described in detail elsewhere [17].

Measurement of serum uric acid and diagnosis of hyperuricemia

Serum UA was measured enzymatically using a Pureauto SUA kit (Sekisui Medical Co., Ltd., Tokyo, Japan); at baseline, the lower limit of detection was 0.2 mg/dl. Hyperuricemia was diagnosed as serum UA levels ≥7 mg/dl in men and ≥6 mg/dl in women or use of any anti-gout treatment [18].

Determination of relevant covariates

Anthropometric variables (height, body weight) were measured using standard protocols. Body mass index (BMI) was calculated as weight (kg)/height^2 (m^2). Blood samples were drawn from the antecubital vein in the morning following an overnight fast while subjects were seated. Blood pressure (BP) was measured from the upper left arm using an automatic device (Yamasu 605P; Kenzmedico, Saitama, Japan) after participants rested for 5 min while seated. Hypertension was diagnosed as a systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg [19]. The fasting blood glucose (FBG) concentration was determined using enzymatic methods with appropriate kits (Sekisui Medical Co., Ltd., Tokyo, Japan). Diabetes was defined as an FBG level ≥ 126 mg/dl according to the American Diabetes Association diagnostic criteria [20]. Use of anti-hypertensive and lipid-lowering agents (yes or no) was assessed via a self-administered questionnaire.

Demographic variables and lifestyle factors including sex, age, education (college and above or not), occupation (deskwork or not), living alone (yes or no), and smoking status (never, former, or current) were also assessed via a self-administered questionnaire. Physical activity (PA) was assessed using the International Physical Activity Questionnaire [21]. The total weekly PA was calculated using metabolic equivalents [METs] × h/week and divided into three categories: 0, 0.1–22.9, and ≥23 METs h week^{-1} [22].

Statistical analysis

All continuous and categorical variables are presented as the mean (95% confidence interval [CI]) and percentages, respectively; continuous variables that were not normally distributed were log-transformed prior to multivariate statistical analyses. Differences in the baseline variables between the categories of raw or roasted fish consumption frequency were examined using ANCOVA for continuous variables and multiple logistic regression analysis for proportional variables, after adjustment for sex(categorical variable) and age(continuous variable).

Consumption of fish cooked by different methods and hyperuricemia were used as the independent and dependent variables. Multivariate logistic regression analyses were conducted to examine the relationship between the consumption of fish cooked by different methods and the risk of hyperuricemia with adjustment for sex (categorical variable), age (continuous variable), and BMI (continuous variable) (model 1). For model 2, all of the above variables were used, in addition to hypertension (categorical variable: yes or no), diabetes (categorical variable: yes or no), education level (categorical variable: college and above or not), occupation (categorical variable: desk work or not), living alone (categorical variable: yes or no), smoking status (categorical variable: never, former, or current), PA (categorical variable: 0, 0.1–22.9, and ≧23 METs h week^{-1}), and total energy (continuous variable), total alcohol (continuous variable), total meat (continuous variable), other seafood (continuous variable), total bean product (continuous variable), and total dairy (continuous variable) intakes. For model 3, all variables in models 1 and 2 in addition to the use of anti-hypertensive and lipid-lowering agents (categorical variable: yes or no). P values for linear trends were calculated using the categories for fish consumption frequency. $P < 0.05$ was considered significant in all two-sided tests. All statistical analyses were performed using IBM SPSS Statistics 20.0 software (IBM SPSS Inc., Chicago, IL, USA).

Results

Table 1 shows the sex- and age-adjusted baseline characteristics according to the categories of raw or roasted fish consumption frequency. Raw or roasted fish was consumed ≥1 time/week (≥15.6 g/day and ≥16.0 g/day, respectively) by 60.8% and 77.4% of the participants, respectively.

For the participants who reported eating raw fish, a higher consumption frequency was associated with male sex and older age (P for trend: 0.001 and <0.001, respectively). The mean intakes of total energy, total alcohol, total meat, and other seafood were significantly higher with increasing consumption frequency (P for trend: <0.001, <0.001, 0.001, and <0.001, respectively). There were no significant differences in the other baseline characteristics between the categories.

Participants with a higher reported frequency of roasted fish consumption were generally older, worked at a desk, and had higher mean intakes of total energy, total meat, other seafood, and total bean products (P for trend: <0.001, 0.045, <0.001, 0.003, <0.001, and <0.001, respectively). There were no significant differences in the other baseline characteristics between the categories.

In this study, we analyzed the associations between the consumption of fish cooked by different methods and serum UA levels during the 3-year follow-up period after adjustment for potential confounders. Serum UA levels differed significantly among the categories of raw or roasted fish consumption frequency. For raw fish, the geometric means (95% CIs) for the low, middle, and high groups were 5.3 (5.1–5.4), 5.3 (5.1–5.5), and 5.6 (5.4–5.7), respectively (P for trend: 0.026). For roasted fish, the geometric means (95% CIs) for the low, middle, and high groups were 5.1 (4.9–5.3), 5.3 (5.2–5.5), and 5.5 (5.4–5.7), respectively (P for trend: 0.004) (Fig. 1).

The incidence rate of hyperuricemia was 7.1% (30/424) during the 3-year follow-up period. Table 2 shows the adjusted relationship between the consumption of fish cooked by different methods, and risk of hyperuricemia. A significant relationship between the frequency of raw fish consumption and the risk of hyperuricemia was present in the multivariate logistic regression models. The ORs (95% CIs) for hyperuricemia in the low, middle, and high groups for raw fish in model 3 were 1.00 (reference), 2.51 (0.85–7.39), and 3.46 (1.07–11.14), respectively (P for trend: 0.036). We also observed a multivariate-adjusted significant association between the frequency of roasted fish consumption and the risk of hyperuricemia. The ORs (95% CIs) for hyperuricemia in the low, middle, and high groups for roasted fish in model 3 were 1.00 (reference), 3.00 (0.75–11.89), and 5.17 (1.30–20.62), respectively (P for trend: 0.018). Hyperuricemia was not associated with the consumption of fish cooked by the other methods.

Discussion

This population-based follow-up study examined the relationship between the consumption of fish cooked by different methods and the risk of hyperuricemia. Increased consumption of raw or roasted fish resulted in a 3–5-fold increased risk of hyperuricemia. In contrast, the consumption of fish cooked by other methods was not associated with a risk of hyperuricemia. Our novel findings suggest that only increased consumption of raw or roasted fish might be a potential risk factor for the development of hyperuricemia.

The findings of the present study agree with those of several previous studies. In a cross-sectional study with 3978 men aged 40–74 years living in Shanghai, China, fish, shellfish, and total seafood intakes were significantly associated with a higher risk of hyperuricemia after

Table 1 Sex- and age-adjusted baseline characteristics according to frequency of raw or roasted fish consumption.

Participants (n = 424)	Low (n = 166)	Middle (n = 134)	High (n = 124)	P for trend[a]
Raw fish				
Mean intake, g/day	6.0	15.6	40.0	–
Sex (men), %	71.7	80.6	87.9	0.001
Age, years	46.5 (45.1–47.9)	47.0 (45.4–48.5)	50.6 (48.9–52.2)	<0.001
BMI, kg/m^2	23.0 (22.5–23.5)	22.8 (22.3–23.4)	23.1 (22.5–23.7)	0.597
Diabetes, %	4.2	7.5	8.9	0.561
Hypertension, %	20.5	23.1	23.4	0.498
Use of medications, %				
Anti-hypertensive	8.4	10.4	16.9	0.576
Lipid-lowering	3.0	3.7	4.8	0.898
Education (≥college), %	25.3	29.1	24.2	0.284
Occupation (desk work), %	62.7	64.9	66.9	0.192
Living alone (yes), %	6.6	6.0	4.0	0.569
Smoking status				
Current, %	42.8	41.8	46.8	0.928
Former, %	9.0	14.9	13.7	0.253
Alcohol intake, g/day	13.8 (10.3–17.3)	24.1 (20.2–27.9)	25.7 (21.6–29.8)	<0.001
PA, MET·h·week^{-1} (≥23)	31.3	36.6	38.7	0.500
Daily nutrient intake				
Total energy intake, kcal/day	1747.4 (1661.0–1833.7)	1881.1 (1785.9–1976.3)	2126.6 (2025.9–2227.4)	<0.001
Total meat intake, g/day	48.1 (41.6–54.6)	55.1 (48.0–62.3)	61.2 (53.6–68.8)	0.001
Other seafood intake, g/day	32.4 (27.2–37.7)	36.9 (31.1–42.6)	63.8 (57.6–69.9)	<0.001
Total bean product intake, g/day	62.6 (56.1–69.1)	66.0 (58.8–73.1)	70.0 (62.5–77.6)	0.185
Total dairy intake, g/day	105.5 (88.3–122.6)	93.7 (74.8–112.7)	99.3 (79.3–119.3)	0.851
Roasted fish	**Low (n = 96)**	**Middle (n = 148)**	**High (n = 180)**	**P for trend[a]**
Mean intake, g/day	5.8	16.0	43.0	–
Sex (men), %	76.0	77.7	82.2	0.305
Age, years	45.3 (43.5–47.1)	46.3 (44.9–47.8)	50.5 (49.1–51.8)	<0.001
BMI, kg/m^2	23.5 (22.9–24.2)	22.5 (22.0–23.0)	23.0 (22.6–23.5)	0.344
Diabetes, %	2.1	6.8	8.9	0.373
Hypertension, %	25.0	16.2	25.6	0.528
Use of medications, %				
Anti-hypertensive	8.3	6.1	17.8	0.295
Lipid-lowering	4.2	2.7	4.4	0.664
Education (≥college), %	26.0	30.4	22.8	0.165
Occupation (desk work), %	51.0	73.0	65.0	0.045
Living alone (yes), %	9.4	5.4	3.9	0.097
Smoking status				
Current, %	53.1	40.5	41.1	0.083
Former, %	11.5	13.5	11.7	0.937
Alcohol intake, g/day	19.3 (14.5–24.0)	20.4 (16.6–24.2)	21.3 (17.9–24.8)	0.491
PA, MET·h·week^{-1} (≥23)	29.2	33.1	40.0	0.268
Daily nutrient intake				
Total energy intake, kcal/day	1686.1 (1573.3–1798.9)	1812.3 (1721.9–1902.7)	2087.5 (2004.4–2170.6)	<0.001
Total meat intake, g/day	49.3 (40.8–57.9)	50.1 (43.3–56.9)	60.0 (53.8–66.3)	0.003
Other seafood intake, g/day	23.8 (16.9–30.8)	40.1 (34.5–45.7)	55.6 (50.4–60.7)	<0.001
Total bean product intake, g/day	53.6 (45.2–61.9)	60.9 (54.2–67.6)	76.5 (70.3–82.6)	<0.001
Total dairy intake, g/day	94.2 (71.7–116.7)	90.0 (72.0–108.0)	111.3 (94.7–127.8)	0.640

BMI = body mass index; PA = physical activity; MET = metabolic equivalent.
Continuous variables without a normal distribution were log-transformed and are expressed as the estimated geometric means (95% confidence intervals).
[a] Linear trends were assessed using ANCOVA for continuous variables and logistic regression analyses for categorical variables.

adjustment for a considerably large number of potential confounders [13]. Similarly, a cross-sectional study conducted in the Shandong Coastal Cities of Eastern China reported a significant association between the consumption of fish and shellfish and hyperuricemia; participants with hyperuricemia had a higher fish and shellfish intake

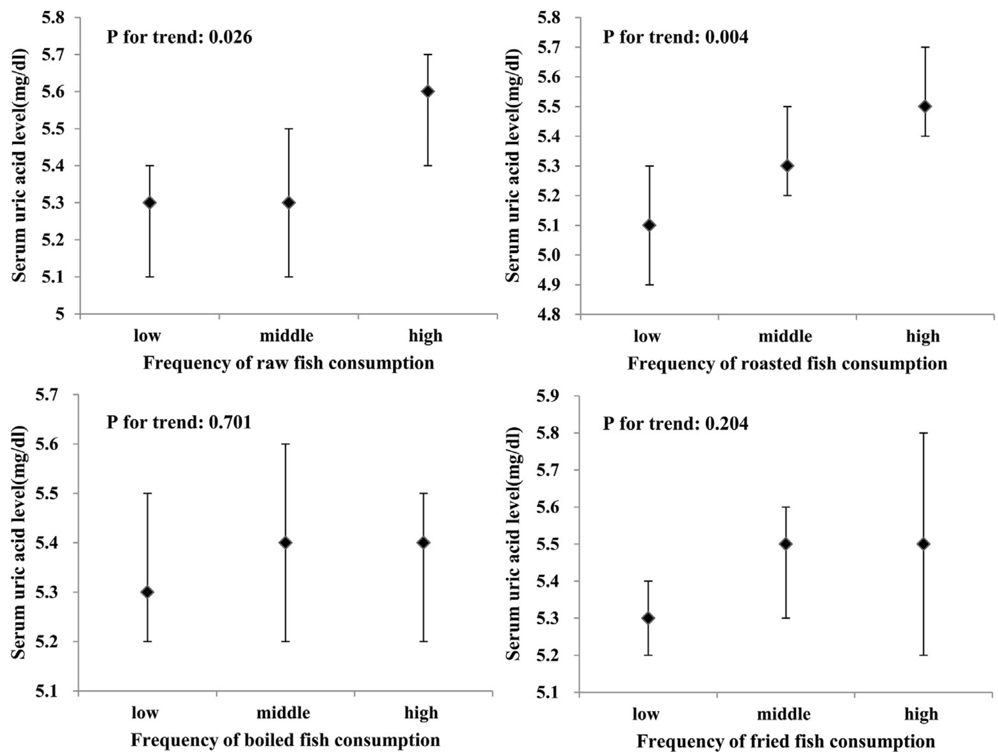

Figure 1 Associations between the consumption of fish cooked by different methods and serum uric acid (UA) levels during the 3-year follow-up. Adjusted for sex (categorical variable), age (continuous variable), body mass index (continuous variable), diabetes (categorical variable: yes or no), hypertension (categorical variable: yes or no), use of anti-hypertensive and lipid-lowering agents (categorical variable: yes or no), education level (categorical variable: college and above or not), occupation (categorical variable: desk work or not), living alone (categorical variable: yes or no), smoking status (categorical variable: never, former, and current), physical activity (categorical variable: 0, 0.1–22.9, and ≥23 METs h week^{-1}), and total energy (continuous variable), alcohol (continuous variable), total meat (continuous variable), other seafood (continuous variable), total bean product (continuous variable), and total dairy (continuous variable) intakes at baseline. Data are shown as geometric means (serum UA) and 95% confidence intervals.

than the participants without hyperuricemia [23]. These findings strongly suggest that greater consumption of fish is associated with the risk of hyperuricemia. Compare with those studies, our study was the first longitudinal study that investigated the relationship between the consumption of fish cooked by different methods and the risk of hyperuricemia in the general adult population aged 29–74 years.

Although we do not know the causal relationship between raw or roasted fish consumption and the risk of hyperuricemia, we explored the possible mechanisms. First, we hypothesized that different cooking methods may explain this relationship. In a previous study, purine content increased slightly during roasting because of moisture and fat loss from the tissues [24]. In contrast, the decreasing purine content is transformed into water or oil after boiling and frying [25,26]. In addition, dietary consumption of purine-rich sources might increase the risk of hyperuricemia [13,27]. Second, other dietary habits may mediate the observed association between raw or roasted fish consumption and the risk of hyperuricemia. In the present study, participants with greater consumption of raw or roasted fish were inclined to consume other purine-rich foods such as meat and other sea foods (Table 1); the relationship between raw or roasted fish consumption and the risk of hyperuricemia did not change even after adjustment for these purine-rich foods. Furthermore, in Japan, people eat raw fish with wasabi root paste and soy sauce. Interestingly, wasabi root paste has antimicrobial effects on food poisoning bacteria [28]. Wasabi root paste is a pungent spice that can enhance sympathetic nervous activity [29] and increase the renal absorption of UA [30,31]. Finally, another plausible explanation is that adipose tissue may play a role in the development of hyperuricemia. Animal experiments showed that adipose tissue in obese individuals is hypoxic, and local hypoxia in adipose tissue upregulated intracellular xanthine oxidoreductase activity and increased UA production in 3T3-L1 mature adipocytes [32]. Furthermore, lipogenesis and/or lipolysis are characterized by active fatty acid synthesis [33], and activation of the pentose phosphate pathway related to active synthesis of fatty acids may be associated with high xanthine oxidoreductase activity, resulting in the production and secretion of UA [32]. Unfortunately, we were unable to provide strong evidence for the relationship between body fat, visceral fat, and the risk of hyperuricemia. Therefore, further studies are required to confirm this relationship. In fact, adjustment for BMI did not change the significant relationship between the frequency of raw or roasted fish consumption and the risk of hyperuricemia. Therefore, we concluded that the significant relationship between raw or roasted fish

Table 2 Adjusted relationships between the consumption of fish cooked by different methods, and the risk of hyperuricemia during the 3-year follow-up period.

	Total sample (n = 424)	Participants with hyperuricemia (n = 30)	Mean intake, g/day	Model 1[a]	Model 2[b]	Model 3[c]
Raw fish						
Low	166	7	6.0	Reference	Reference	Reference
Middle	134	11	15.6	2.43 (0.87–6.77)[d]	2.50 (0.84–7.37)	2.51 (0.85–7.39)
High	124	12	40.0	2.79 (0.99–7.90)	3.52 (1.09–11.37)	3.46 (1.07–11.14)
P for trend[e]	–	–	–	0.053	0.034	0.036
Roasted fish						
Low	96	4	5.8	Reference	Reference	Reference
Middle	148	9	16.0	2.16 (0.60–7.79)	3.03 (0.76–12.11)	3.00 (0.75–11.89)
High	180	17	43.0	3.50 (1.04–11.75)	5.28 (1.32–21.15)	5.17 (1.30–20.62)
P for trend	–	–	–	0.034	0.016	0.018
Boiled fish						
Low	159	11	26.5	Reference	Reference	Reference
Middle	101	7	39.9	1.18 (0.43–3.26)	1.18 (0.41–3.43)	1.20 (0.41–3.50)
High	164	12	87.1	1.25 (0.51–3.06)	1.20 (0.44–3.26)	1.21 (0.45–3.28)
P for trend	–	–	–	0.627	0.717	0.707
Fried fish						
Low	255	14	27.3	Reference	Reference	Reference
Middle	129	14	42.9	2.06 (0.92–4.64)	2.17 (0.92–5.14)	2.20 (0.93–5.20)
High	40	2	61.7	0.97 (0.20–4.64)	0.92 (0.17–5.05)	0.94 (0.17–5.28)
P for trend	–	–	–	0.354	0.380	0.355

[a] Model 1: Adjusted for sex (categorical variable), age (continuous variable), and body mass index (continuous variable) at baseline.
[b] Model 2: Adjusted for the variables in model 1 and hypertension (categorical variable: yes or no), diabetes (categorical variable: yes or no), education level (categorical variable: college and above or not), occupation (categorical variable: desk work or not), living alone (categorical variable: yes or no), smoking status (categorical variable: never, former, or current), physical activity (categorical variable: 0, 0.1–22.9, and $\geq$23 MET·h·week^{-1}), and total energy (continuous variable), alcohol (continuous variable), total meat (continuous variable), other seafood (continuous variable), total bean product (continuous variable), and total dairy (continuous variable) intakes at baseline.
[c] Model 3: Adjusted for the variables in model 2 and the use of anti-hypertensive and lipid-lowering agents (categorical variable: yes or no) at baseline.
[d] Adjusted data are expressed as odds ratio (95% confidence intervals).
[e] Linear trends were obtained using multivariate logistic regression analyses.

consumption and the risk of hyperuricemia was independent of BMI.

In addition to a purine-rich diet, previous studies have demonstrated positive and negative associations between hyperuricemia and various single food items. Positive associations between sugar-sweetened soft drink intake [34] and inverse associations between coffee [35] and dairy product [36] intake and the risk of hyperuricemia or gout have been demonstrated. A recent case-control study in Taiwan also indicated that the consumption of vegetables and fruit, which are rich in dietary fiber, folate, and vitamin C, could effectively inhibit the development of gout [37]. However, given the potential interactive and synergistic effects of the diverse and complex daily dietary activities, the effects of dietary patterns determined by multiple food items on UA and the risk of hyperuricemia have recently gained much attention. Mediterranean-style dietary pattern characterized by a high consumption of fruits and vegetables, legumes, olive oil, nuts, and whole grains; moderate consumption of fish, wine, dairy products, and poultry; and low consumption of red meat, sweet beverages, cream, and pastries [38] could play an important role against the risk of hyperuricemia. The studies indicated that a higher Mediterranean diet score was associated with 57% [39] and 70% [40] lower likelihoods of having hyperuricemia. In particular, a 5-year follow-up study suggested that higher Mediterranean diet score was associated with 73% higher likelihoods of hyperuricemia reversion [41]. Although all current results regarding the association between dietary intake and the risk of hyperuricemia or gout are widely based on epidemiologic studies and the mechanism underlying the effect of dietary intake on UA levels is uncertain, the primary purpose of these studies was to provide plausible dietary recommendations to prevent the development of hyperuricemia and gout, reinforcing the public health message for a rational dietary pattern. Future intervention studies to demonstrate the effect of a single food factor as well as dietary patterns on the excretion of UA and treatment or recurrence for gout should be conducted, because they are more likely to identify causal relationships. These studies will also provide evidence regarding appropriate and inappropriate dietary choices that can be used by physicians and patients with gout, as well as information about certain foods that could help lower the risk of recurrent gout attacks. The present study suggests that not only single food items and dietary patterns, but cooking style needs also to be taken into consideration for evidence-based dietary recommendation intended to reduce the risk of hyperuricemia.

Our study also had several potential limitations. First, despite the consideration of a number of demographic variables, stratified analyses for different demographic variables could not be performed owing to the small sample size. Second, because this study was a cross-sectional study, we could not establish a causal relationship between the frequency of raw or roasted fish consumption and the risk of hyperuricemia. Finally, the results may not be representative of the general population; therefore, further investigations with larger sample sizes are needed to confirm our findings.

In conclusion, this population-based 3-year follow-up study showed that the consumption of raw or roasted fish, but not boiled or fried fish, is related with a higher risk of hyperuricemia in Japanese adults. Therefore, raw or roasted fish may promote the development of hyperuricemia. Further interventional or experimental studies are required to confirm the causality of this relationship.

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