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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 ≥7 mg/dL in men and ≥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.
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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 ($\geq$2 times/day) to 7 (0 times/day). We grouped the subjects into three categories based on frequency of fish consumption for each of the different cooking methods: low ($<$1 time/week), middle (1 time/week), and high ($\geq$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 $\geq$7 mg/dl in men and $\geq$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 $\geq$ 140 mm Hg or diastolic BP $\geq$ 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 $\geq$ 126 mg/dl according to the American Diabetes Association diagnostic criteria [20]. Use of antihypertensive 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

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