Original Article

Effect modification of green tea on the association between rice intake and the risk of diabetes mellitus: a prospective study in Japanese men and women

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Background and Objectives: Recent observational studies have suggested a positive association of white rice and protective associations of green tea and coffee with the risk of diabetes. However, none have examined the interaction between these dietary factors on the risk of diabetes. We prospectively investigated the effect modification of green tea and coffee on the association between rice and incident diabetes in elderly Japanese men and women. **Methods and Study Design:** Among subjects who participated in the baseline survey (2004–2007), 11717 (91 %) subjects responded to the follow-up survey (2010–2012). By using multiple logistic regression analysis, ORs of incident diabetes were calculated according to categories of cereal food, green tea, and coffee intakes, examining also the effect modification of green tea and coffee. **Results:** 464 new cases of diabetes were identified. Women, but not men, showed a positive association of rice intake (trend p=0.008) and an inverse association of green tea intake (trend p=0.02) with incident diabetes. Coffee showed no association with incident diabetes either in men or women. In the analysis stratified by green tea intake, the association between rice and diabetes disappeared among women with an intake of ≥7 cups/d of green tea (interaction p=0.08). **Conclusions:** Rice intake was associated with an increased risk of diabetes only in women, and women with a higher intake of green tea had a lower risk of diabetes. A high intake of green tea may be protective against increased risk of diabetes with a higher intake of rice in women.

Key Words: rice, green tea, diabetes mellitus, effect modification, cohort study

INTRODUCTION

The prevalence of type 2 diabetes mellitus (DM) has increased rapidly worldwide,[1] with the prevalence of DM in Japan having doubled during the past twodecades.[2] Changes in lifestyle toward an excessive intake of energy and insufficient energy expenditure have been ascribed to the increase.[2] Effects of specific foods on the development of DM have been a matter of interest. Recent data suggest an increased risk of type 2 DM associated with rice consumption[3] and a decreased risk with coffee and possibly green tea consumption.[4,5] A higher intake of white rice was associated with an increased risk of DM in Japan[6] and China.[7] Green tea is one of the most commonly consumed beverages in Japan, and is shown to have the most significant benefits on human health among all types of tea.[8] A meta-analysis of 9 cohort studies showed a significant reduction of DM risk in subjects consuming ≥4 cups/d of green tea compared with those who drank fewer or none.[9] A recent meta-analysis of 17 randomized controlled trials showed decreased fasting glucose and glycated hemoglobin (HbA_{1c}) concentrations following ingestion of green tea extracts.[10] Coffee consumption has consistently been shown to be associated with a decreased risk of DM.[4,5] Caffeine, chlorogenic acids, and the antioxidant activity of polyphenols have

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been implicated in improving the glucose homeostasis.[11]

Despite much interest in rice, green tea, and coffee, the interaction between rice and green tea and coffee on the risk of type 2 DM has not been examined. In the present study, we prospectively examined the associations of rice, green tea, and coffee with the incidence of DM and the effect modification of green tea and coffee on the association between the intake of rice and incident DM in a Japanese population-based cohort study.

MATERIALS AND METHODS

Study subjects

The Kyushu University Fukuoka Cohort Study is a population-based prospective cohort study, whose baseline survey was performed during the period between February 2004 and August 2007. The cohort consisted of men and women living in Higashi-ku (East Ward) in Fukuoka, aged 49 to 76 years at baseline. The study was approved by the Ethics Committee of the Kyushu University Faculty of Medical Sciences (No. 481). A total of 12,948 persons (5,817 men and 7,131 women) participated in the baseline survey. The participation rate was 24%. All subjects, who were informed of details of the baseline and follow-up surveys, provided written informed consent before participating in the study. The follow-up survey was conducted between February 2010 and December 2012, with an average interval of 5.3 years. Of the participants in the baseline survey, 11,717 (91%) responded to the follow-up survey.

Of the subjects who responded to the follow-up survey, a total of 2,123 subjects were excluded for the following diseases and conditions at baseline: DM (n=1,037), coronary artery disease (n=450), stroke (n=231), cancer (n=401),chronic liver disease or aspartate aminotransferase (AST) or alanine aminotransferase (ALT) greater than 3-fold of the upper limit of the normal range, i.e., >120 U/L (n=252), creatinine greater than 3.0 mg/dL or chronic renal failure (n=33), and alcohol addiction (n=2). The remaining 9594 persons were eligible in the present study. However, 993 subjects were excluded for unknown status of DM (n=987) at the follow-up survey and missing information on the covariates (n=6). In addition, we excluded 174 subjects who were in the top or bottom 1.0% of total energy intake. A total of 8,427 subjects (3,397 men and 5,030 women) remained in the analysis.

Baseline survey

Details of the baseline survey were described previously.[12] Each participant completed a self-administered questionnaire, inquiring about the smoking habits and alcohol intake, physical activity, dietary intake, diseases under current or previous treatment, use of drugs, and others. Blood pressure measurement, anthropometric measurements (height in cm and body weight in kg), and venous blood drawing were done for each participant.

The average numbers of cigarettes smoked per day were ascertained for past and current smokers. Current alcohol drinkers reported frequencies and amounts of consumption of 5 different alcoholic beverages on average in the past year. The total ethanol intake per day was calculated on the basis of beverage-specific ethanol concentrations. As for physical activity over the past year, the amount in time per day was ascertained for four types of work-related physical activities (standing, bicycling, walking, and strenuous labor), and frequencies per week and hours per occasion were reported for three types of leisure-time physical activities (light, moderate, and heavy). The intensity of each physical activity was converted to a metabolic equivalent (MET) value[13] and was multiplied by time in hours spent on the activity. Thereby, physical activity was expressed as MET-h per day (work-related) or per week (leisure-time). Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared.

Dietary assessment was carried out by a 60-item food frequency questionnaire (FFQ), a modified version of the 47-item FFQ developed and validated by Tokudome et al.[14-16] The present FFQ added 6 items of non-alcoholic beverages and 8 items of specific foods and dishes, and deleted a single question on alcohol amount that was substituted with the above-mentioned question on 5-items of alcoholic beverage. Details of the dietary assessment were described previously.[12] For items other than staple foods (rice, bread, and noodles), consumption frequency was ascertained by choosing 1 of 8 options from almost nil to ≥3 times/d. Regarding the 3 staple foods, consumption frequencies (6 options from almost nil to daily) and amounts per occasion were ascertained for breakfast, lunch, and supper separately. Additionally, the size of bowl was chosen from among 3 options (small, medium, and large). The intake of green tea and coffee was assessed by a question with eight options (almost nil, 1–2 cups/w, 3–4 cups/w, 5–6 cups/w, 1–3 cups/d, 4–6 cups/d, and ≥10 cups/d). The volume of one cup of green tea and coffee was estimated to be equal to 150 mL. Typical portion sizes of foods were determined in accordance with those used by Tokudome et al.[16] Total energy and nutrient intakes were estimated with reference to the Food Composition Tables in Japan.[17]

HbA_{1c} was measured for all participants and assayed by using a latex agglutination turbidimetry at an external laboratory (SRL, Hachiohji, Japan). AST, ALT, and creatinine were measured at an external laboratory (SRL) or records of this information were used if the measurements had been made in the past year.

Follow-up survey

The follow-up survey was conducted by mail with a self-administered questionnaire. Height (cm) and body weight (kg) were also self-reported. The questionnaire was almost the same as the one used in the baseline survey except for the assessment of diseases. Current and previous treatments regarding a selected number of diseases including DM were ascertained. Missing or inconsistent answers were confirmed via telephone by research staff (nurse, dietician, or physician). Venous blood drawing was carried out at one of the 28 collaborating hospitals and clinics in Higashi-ku, Fukuoka. Whole blood and serum aliquots were sent to an external laboratory (SRL). HbA_{1c}were measured by the same method as employed in the baseline survey.

Determination of type 2 diabetes

HbA_{1c} was measured according to the method of the Japan Diabetes Society (JDS) in the baseline and follow-up survey. The value was converted to the National Glycohemoglobin Standardization Program (NGSP) equivalent value (%) using the formula: HbA_{1c} (%) = 1.02×HbA_{1c} (JDS) + 0.25 (%).[18] DM was defined as HbA_{1c} (NGSP) ≥6.5% and/or if the subjects were under medication for diabetes. Cases of DM newly identified in the follow-up survey were regarded as incident cases.

Statistical analyses

Intake (gram) of rice, bread, noodles, and cereals were adjusted to an energy intake of 2000 kcal/d for men and 1800 kcal/d for women by using the regression residual method. The intakes were transformed to a natural-logarithm scale, and a value of 1 g/d was assigned when the intake was 0 g/d. We used the sex-specific quintiles of the energy-adjusted food and nutrient intakes as cut offs. The intake of green tea was divided into 4 categories (<1, 1–3, 4–6, or ≥7 cups/d for green tea), and coffee intake was divided into 3 categories (almost never, <1, ≥1 cup/d); few subjects reported coffee intake of ≥4 cups/d. The confounding variables considered were age (continuous variable), BMI (<22.5, 22.5 to 24.9, or ≥25.0 kg/m^2), smoking (never, past, and current smoking with a consumption of <20 or ≥20 cigarettes/d), alcohol intake (never, past, and current drinking with an intake of <30, 30 to 59 or ≥60 mL of alcohol/d in men and <10, 10 to 19 or ≥20 mL of alcohol/d in women), physical activity (sex-specific quartiles of MET-h/d for work-related activity and MET-h/w for leisure time activity), and family history of DM. The trend of the association between rice intake (ordinal variable) and the confounding variables mentioned above, total energy intake (kcal/d), and intakes of cereals and carbohydrates (g/d) were examined by using the Mantel–Haenszel test for categorical variables and linear regression analysis for continuous variables.

Multiple logistic regression analysis was used to calculate adjusted ORs and 95% CIs for incident DM according to the quintiles of energy-adjusted intakes of food and carbohydrate, and the categories of green tea intake, with the lowest category as referent. The trend of the association was assessed by assigning the ordinal values 0 to 4 to the quintile categories of food and nutrient intake, values 0 to 3 to the green tea categories, and values of 0 to 2 to the coffee categories. Effect modification of green tea or coffee intake on the association between rice intake and incident DM was evaluated by using a likelihood ratio test comparing a multivariate-logistic regression model including 3 product terms of rice intake (ordinal variable) and green tea intake (3 indication variables) or and coffee intake (2 indication variables) with a model without them. Two-sided *p* values <0.05 were regarded as significant. All analyses were performed using Statistical Analysis System (SAS) version 9.2 (SAS Institute, Cary, NC).

RESULTS

The characteristics of the subjects according to the quintiles of rice intake are shown in Table 1. Both men and women with a higher intake of rice were less likely to be alcohol drinkers and to be physically active in their leisure time. Higher intakes of rice were related to lower BMI in men, while women with higher intakes of rice had higher BMI. Men with a higher intake of rice were younger and more likely to be engaged in strenuous work. Women with higher rice intakes were less likely to be smokers. Both men and women with a higher intake of rice showed higher intakes of cereals and carbohydrates. In the present study subjects, rice, bread, and noodles accounted for 57.7%, 7.0%, and 5.9%, respectively, of total carbohydrate intake in men and 47.3%, 8.1%, and 6.1%, respectively, in women. Percentages of energy intake from rice, bread, and noodles were 43.2%, 6.5%, and 4.7%, respectively, in men and 39.8%, 8.3%, and 5.4%, respectively, in women. Both men and women with a higher intake of rice showed a higher intake of green tea and a lower intake of coffee.

During the follow-up of an average of 5.3 years, 464 incident cases of DM were identified (235 for men and 229 for women). Table 2 shows adjusted ORs and 95% CIs of incident DM associated with intakes of cereal foods and carbohydrates in men and women. In men, intake of cereals and rice showed no association with the incidence of DM. In women, intakes of cereals and rice were significantly and positively associated with the incidence of DM; adjusted ORs and 95% CIs of incident DM for the lowest to the highest quintiles of the energy-adjusted intake of rice were 1.00 (referent), 1.42 (0.87–2.32), 1.90 (1.19–3.02), 1.43 (0.88–2.34),and 2.02 (1.27–3.22) (trend *p*=0.008), and those of cereals were 1.00 (referent), 1.33 (0.84–2.11), 1.17 (0.72–1.89), 1.65 (1.05–2.57), and 1.53 (0.97–2.41) (trend *p*=0.04). A higher intake of bread was associated with a significantly lower incidence of DM in both men and women; adjusted ORs and 95% CIs of incident DM for the lowest through to the highest quintiles of the energy-adjusted intake of bread were 1.00 (referent), 1.07 (0.73–1.58), 0.82 (0.54–1.24), 0.75 (0.49–1.15), and 0.57 (0.36–0.90) for men (trend *p*=0.004), and 1.00 (referent), 0.98 (0.66–1.46), 0.84 (0.56–1.26), 0.77 (0.50–1.17), and 0.66 (0.42–1.03)for women (trend *p*=0.03). Intake of noodles and carbohydrates showed no association with the incidence of DM in either men or women.

Adjusted ORs and 95% CIs of incident DM according to intake of green tea and coffee are shown in Table 3 and Table 4.While the intake of green tea showed no association with the incidence of DM in men, a higher intake of green tea was associated with a significantly lower risk of incident DM in women; adjusted ORs and 95% CIs of incident DM for the lowest through the highest categories of green tea intake were 1.00 (referent), 0.75 (0.50–1.13), 0.53(0.35–0.82), and 0.63 (0.40–0.99) in women (trend *p*=0.02). With regard to coffee intake, no association with the incidence of DM was observed either in men or women.

In the analysis stratified by green tea intake (Table 5), a significant positive association between rice intake and incident DM was observed limitedly in men, with an intake of 4–6 cups/d (trend *p*=0.03), but the interaction was far from being statistically significant. In women, increased risk of DM associated with a higher intake of rice was observed in subgroups with intakes of <1, 1–3, and 4–6 cups/d (trend *p*=0.02, 0.02, and 0.07, respectively), but not in the category of ≥7 cups/d (trend *p*=0.63), showing a nearly significant interaction (*p*=0.08). On the other

Table 1. Characteristics of subjects according to quintiles (Q) of rice intake

Variable	Men				Women			
	Q1 (*n*=679)	Q3 (*n*=679)	Q5 (*n*=679)	Trend *p**	Q1 (*n*=1006)	Q3 (*n*=1006)	Q5 (*n*=1006)	Trend *p**
Age (y), mean (SD)	63.0 (6.9)	62.2 (6.9)	61.9 (6.3)	0.006*	61.2 (6.7)	61.7 (6.7)	61.8 (6.6)	0.07
Current smoking (%)	30.8	27.4	31.1	0.52	8.0	4.8	5.0	0.04*
Current alcohol intake (%)	86.3	74.4	58.2	<0.0001*	40.1	26.1	16.5	<0.0001*
BMI (kg/m^2), mean (SD)	23.6 (2.7)	23.6 (2.6)	23.3 (2.8)	0.03*	22.3 (2.9)	22.4 (2.9)	22.7 (3.3)	0.005*
Physical activity, median (IQR)								
Work-related (MET-h/d)	6 (2-12)	6 (2-14)	8 (2-19)	<0.0001*	10 (6-17)	11 (6-18)	10 (6-18)	0.11
Leisure-time (MET-h/w)	8 (2-18)	6 (2-17)	5 (1-13)	<0.0001*	8 (2-17)	6 (2-16)	5 (0-11)	<0.0001*
Parental diabetes mellitus (%)	10.3	10.9	9.1	0.72	14.7	14.2	14.4	0.69
Total energy (kcal/d), median (IQR)	1583(1383-1807)	1525 (1359-1767)	1533 (1296-1874)	0.22	1341 (1169-1549)	1422 (1200-1576)	1328 (1168-1490)	0.008*
Food/nutrient intake, median (IQR)†								
Rice (g/d)	217 (175-252)	399 (381-417)	616 (574-685)	<0.0001*	175 (140-198)	320 (304-335)	490 (456-536)	<0.0001*
Cereals (g/d)	383 (321-450)	492 (452-542)	670 (616-744)	<0.0001*	326 (274-387)	419 (386-458)	528 (491-574)	<0.0001*
Carbohydrates(g/d)	218 (191-244)	258 (238-275)	307 (290-325)	<0.0001*	225 (206-242)	250 (238-261)	279 (265-291)	<0.0001*
Green tea intake								
<1 cup/day (%)	26.1	19.8	18.3	<0.0001*	28.5	18.8	15.9	<0.0001*
1-3 cups/day (%)	20.5	19.7	18.7		24.4	18.4	18.5	
4-6 cups/day (%)	17.6	21.0	21.3		15.6	22.4	19.8	
≥7 cups/day (%)	13.1	19.0	24.7		15.5	19.4	25.0	
Coffee intake								
Almost never (%)	15.6	22.0	25.2	<0.0001*	11.4	16.5	32.4	<0.0001*
<1 cup/day (%)	16.8	21.0	21.9		13.9	21.4	24.2	
≥1 cup/day (%)	22.8	18.9	17.5		25.1	20.3	14.8	

*Based on linear regression analysis for continuous variables and the Mantel–Haenszel chi-square test for categorical variables, with ordinal scores assigned to the quintile categories.Values of MET-h were log-transformed in the regression analysis.

†Intakes were energy-adjusted to 2000 kcal/day for men, and 1800 kcal/day for women.

Table 2. Adjusted ORs (95% CIs) of incident diabetes mellitus according to quintile categories of the energy-adjusted intakes of foods/nutrients in men and women

	Quintiles of energy-adjusted intakes of foods/nutrients[†]					Trend p^*
	Q1 (low)	Q2	Q3	Q4	Q5 (high)	
Men						
Cereals						
Median (IQR), g/d	363 (320-390)	448 (430-463)	509 (492-526)	580 (557-602)	688 (650-751)	
No. (%)[‡]	35/679 (5.2)	57/680 (8.4)	52/679 (7.7)	43/680 (6.3)	48/679 (7.1)	
Adjusted OR (95% CI)[§]	1.00 (referent)	1.69 (1.08-2.64)	1.55 (0.98-2.46)	1.26 (0.78-2.05)	1.42 (0.87-2.33)	0.61
Rice						
Median (IQR), g/d	217 (175-252)	324 (303-345)	399 (381-417)	483 (462-508)	616 (574-685)	
No. (%)[‡]	44/679 (6.5)	49/680 (7.2)	47/679 (6.9)	42/680 (6.2)	53/679 (7.8)	
Adjusted OR (95% CI)[§]	1.00 (referent)	1.12 (0.73-1.71)	1.07 (0.69-1.65)	0.95 (0.61-1.49)	1.24 (0.80-1.93)	0.59
Bread						
Median (IQR), g/d	1 (1-1)	12 (12-12)	30 (24-36)	59 (58-59)	84 (65-119)	
No. (%)[‡]	54/679 (8.0)	59/680 (8.7)	46/679 (6.8)	43/680 (6.3)	33/679 (4.9)	
Adjusted OR (95% CI)[§]	1.00 (referent)	1.07 (0.73-1.58)	0.82 (0.54-1.24)	0.75 (0.49-1.15)	0.57 (0.36-0.90)	0.004*
Noodles						
Median (IQR), g/d	1 (1-19)	39 (23-40)	46 (43-61)	96 (81-103)	160 (132-198)	
No. (%)[‡]	56/679 (8.3)	47/680 (6.9)	40/679 (5.9)	49/680 (7.2)	43/679 (6.3)	
Adjusted OR (95% CI)[§]	1.00 (referent)	0.83 (0.55-1.25)	0.69 (0.45-1.05)	0.85 (0.57-1.28)	0.74 (0.48-1.12)	0.20
Carbohydrates						
Median (IQR), g/d	201 (185-215)	238 (231-244)	261(255-266)	283 (277-289)	313 (304-327)	
No. (%)[‡]	36/679 (5.3)	62/680 (9.1)	47/679 (6.9)	42/680 (6.2)	48/679 (7.1)	
Adjusted OR (95% CI)[§]	1.00 (referent)	1.94 (1.23-3.08)	1.47 (0.87-2.46)	1.25 (0.72-2.18)	1.46 (0.84-2.56)	0.91

[†]Intakes were energy-adjusted to 2000 kcal/day in men and 1800 kcal/day in women.
[‡]Numbers of incident cases of diabetes mellitus (numerator) and non-diabetic subjects at the baseline (denominator). In parentheses are proportions of incident cases of diabetes mellitus.
[§]Adjusted for age (years, continuous variable), BMI (<22.5, 22.5 to 24.9, and ≥25.0 kg/m^2), smoking (life-long nonsmoker, past smoker, or current smoker with a consumption of <20 or ≥20 cigarettes/day), alcohol consumption (life-long nondrinker, past drinker, and current drinking with an intake of <30, 30 to 59, or ≥60 mL of alcohol/day for men, <10, 10 to 19, or ≥ 20 mL of alcohol/day for women), work-related and leisure-time physical activities (sex-specific quartiles of MET-h/d and MET-h/w, respectively), and parental diabetes mellitus.
[*]Ordinal values of 0–4 were assigned to quintile categories of energy-adjusted intake of food and nutrients to assess the trend of an association.

Table 2. Adjusted ORs (95% CIs) of incident diabetes mellitus according to quintile categories of the energy-adjusted intakes of foods/nutrients in men and women (cont.)

	Quintiles of energy-adjusted intakes of foods/nutrients†					Trend p*
	Q1 (low)	Q2	Q3	Q4	Q5 (high)	
Women						
Cereals						
Median (IQR), g/d	308 (269-333)	382 (369-394)	430 (418-441)	477 (466-490)	548 (524-586)	
No. (%)‡	34/1006 (3.4)	45/1006 (4.5)	38/1006 (3.8)	57/1006 (5.7)	55/1006 (5.5)	
Adjusted OR (95% CI) §	1.00 (referent)	1.33 (0.84-2.11)	1.17 (0.72-1.89)	1.65 (1.05-2.57)	1.53 (0.97-2.41)	0.04*
Rice						
Median (IQR), g/d	175 (140-198)	259 (242-274)	320 (304-335)	386 (368-404)	490 (456-536)	
No. (%)‡	29/1006 (2.9)	40/1006 (4.0)	56/1006 (5.6)	42/1006 (4.2)	62/1006 (6.2)	
Adjusted OR (95% CI) §	1.00 (referent)	1.42 (0.87-2.32)	1.90 (1.19-3.02)	1.43 (0.88-2.34)	2.02 (1.27-3.22)	0.008*
Bread						
Median (IQR), g/d	6 (1-12)	20 (13-25)	39 (32-46)	63 (61-64)	79 (71-99)	
No. (%)‡	55/1006 (5.5)	54/1006 (5.4)	46/1006 (4.6)	40/1006 (4.0)	34/1006 (3.4)	
Adjusted OR (95% CI) §	1.00 (referent)	0.98 (0.66-1.46)	0.84 (0.56-1.26)	0.77 (0.50-1.17)	0.66 (0.42-1.03)	0.03*
Noodles						
Median (IQR), g/d	2 (1-21)	38 (26-43)	53 (49-59)	89 (75-101)	151 (129-188)	
No. (%)‡	40/1006 (4.0)	50/1006 (5.0)	46/1006 (4.6)	44/1006 (4.4)	49/1006 (4.9)	
Adjusted OR (95% CI) §	1.00 (referent)	1.32 (0.86-2.03)	1.22 (0.79-1.90)	1.15 (0.74-1.80)	1.33 (0.86-2.06)	0.38
Carbohydrates						
Median (IQR), g/d	215 (200-223)	239 (234-242)	252 (249-255)	265 (262-270)	285 (280-295)	
No. (%)‡	44/1006 (4.4)	32/1006 (3.2)	44/1006 (4.4)	52/1006 (5.2)	57/1006 (5.7)	
Adjusted OR (95% CI) §	1.00 (referent)	0.66 (0.41-1.07)	0.87 (0.55-1.37)	1.00 (0.64-1.55)	1.04 (0.67-1.61)	0.29

†Intakes were energy-adjusted to 2000 kcal/day in men and 1800 kcal/day in women.
‡Numbers of incident cases of diabetes mellitus (numerator) and non-diabetic subjects at the baseline (denominator). In parentheses are proportions of incident cases of diabetes mellitus.
§Adjusted for age (years, continuous variable), BMI (<22.5, 22.5 to 24.9, and ≥25.0 kg/m^2), smoking (life-long nonsmoker, past smoker, or current smoker with a consumption of <20 or ≥20 cigarettes/day), alcohol consumption (life-long nondrinker, past drinker, and current drinking with an intake of <30, 30 to 59, or ≥60 mL of alcohol/day for men, <10, 10 to 19, or ≥ 20 mL of alcohol/day for women), work-related and leisure-time physical activities (sex-specific quartiles of MET-h/d and MET-h/w, respectively), and parental diabetes mellitus.
*Ordinal values of 0–4 were assigned to quintile categories of energy-adjusted intake of food and nutrients to assess the trend of an association.

Table 3. Adjusted ORs (95% CIs) of incident diabetes mellitus according to the intake of green tea in men and women

	Intake of green tea				Trend p*
	<1 cup/day	1-3 cups/day	4-6 cups/day	≥7 cups/day	
Men					
No. of subjects	677	1428	903	389	
No. of cases (%)†	53 (7.8)	91 (6.4)	59 (6.5)	32 (8.2)	
Adjusted OR (95% CI)‡	1.00 (referent)	0.81 (0.57-1.16)	0.86 (0.58-1.27)	1.07 (0.67-1.71)	0.85
Women					
No. of subjects	622	1623	1691	1094	
No. of cases (%)†	38 (6.1)	76 (4.7)	64 (3.8)	51 (4.7)	
Adjusted OR (95% CI)‡	1.00 (referent)	0.75 (0.50-1.13)	0.53 (0.35-0.82)	0.63 (0.40-0.99)	0.02*

†In parentheses are proportions of incident cases of diabetes mellitus.
‡Adjusted for age (years, continuous variable), BMI (<22.5, 22.5 to 24.9, and ≥25.0 kg/m^2), smoking (life-long nonsmoker, past smoker, or current smoker with a consumption of <20 or ≥20 cigarettes/day), alcohol consumption (life-long nondrinker, past drinker, and current drinking with an intake of <30, 30 to 59, or ≥60 mL of alcohol/day for men, <10, 10 to 19, or ≥ 20mL of alcohol/day for women), work-related and leisure-time physical activities (sex-specific quartiles of MET-h/d and MET-h/w, respectively), and parental diabetes mellitus.
*Ordinal values of 0–3 were assigned to intakes of green tea to assess the trend of an association.

Table 4. Adjusted ORs (95% CIs) of incident diabetes mellitus according to the intake of coffee in men and women

	Intake of coffee			Trend p*
	Almost never	<1 cup/day	≥1 cup/day	
Men				
No. of subjects	572	915	1910	
No. of cases (%)†	37 (6.5)	66 (7.2)	132 (6.9)	
Adjusted OR (95% CI)‡	1.00 (referent)	1.09 (0.71-1.65)	0.97 (0.66-1.65)	0.74
Women				
No. of subjects	762	1353	2915	
No. of cases (%)†	45 (5.9)	59 (4.4)	132 (4.5)	
Adjusted OR (95% CI)‡	1.00 (referent)	0.71 (0.48-1.07)	0.76 (0.53-1.09)	0.24

†In parentheses are proportions of incident cases of diabetes mellitus.
‡Adjusted for age (years, continuous variable), BMI (<22.5, 22.5 to 24.9, and ≥25.0 kg/m^2), smoking (life-long nonsmoker, past smoker, or current smoker with a consumption of <20 or ≥20 cigarettes/day), alcohol consumption (life-long nondrinker, past drinker, and current drinking with an intake of <30, 30 to 59, or ≥60 mL of alcohol/day for men, <10, 10 to 19, or ≥ 20 mL of alcohol/day for women), work-related and leisure-time physical activities (sex-specific quartiles of MET-h/d and MET-h/w, respectively), and parental diabetes mellitus.
*Ordinal values of 0–2 were assigned to intakes of coffee to assess the trend of an association.

hand, coffee intake did not modify the association between rice intake and DM at all (interaction p=0.80in men and p=0.69in women, respectively, data not shown).

DISCUSSION

The present finding that the risk of DM was increased with a higher intake of rice is consistent with previous observations.[6,7] A previous study in Japan reported that a higher intake of rice was associated with an increased risk of type 2 DM in women, but not in men.[6]An earlier study of Chinese women also reported a positive association between rice consumption and type 2 DM.[7] Higher glycemic index (GI) and glycemic load (GL) of white rice has been implicated as one of the potential mechanisms of the association between rice and risk of DM.[3] Postprandial hyperglycemia is a risk factor for DM[19] possibly due to enhanced oxidative stress and inflammation.[20-22] The sex difference in the association between rice intake and the risk of DM was suggested in a meta-analysis,[3]in which the pooled relative risk of DM associated with increased consumption of rice was1.46 (95% CI 1.16 to 1.83) in women and 1.08 (95% CI 0.87 to 1.34) in men. Given that inflammation seems to be of more importance in women in the pathogenesis of DM,[23] women exposed to higher postprandial glycemia due to increased intake of white rice may have a greater risk of deterioration in glucose tolerance, compared with men with similar exposure.

Bread intake was associated with a decreased risk of DM in both men and women. Bread consumed in Japan is mostly white bread, and there is a substantial difference in the GI between white rice and white bread; GI is 70 for white rice and 48 for white bread.[24] The GL of bread was much smaller than that of rice in the present study population because bread consumption was rather low. Median GLs in the highest quintile of bread intake were 9 in both men and women, while the corresponding values for the highest quintile of rice intake were 25 in men and 20 in women. Bread consumption was negatively correlated with rice consumption (Spearman's r=−0.36 in men and r=−0.48 in women), and thus the negative association between bread and DM may have been a reciprocal phenomenon. When rice and bread were included in the logistic regression model as covariates, the decreasing trend in the risk of DM according to intake of bread remained in men, while the trend became non-significant in women; adjusted ORs (95% CI) according to quintile categories of bread in men were: Q1 1.00 (referent), Q2 1.07 (0.73–1.58), Q3 0.80 (0.52–1.22), Q4 0.72 (0.45–1.13), and Q5 0.54 (0.33–0.88) (p for trend=0.004); those in women were:Q1 1.00 (referent), Q2 1.02 (0.68–1.51), Q3

Table 5. Adjusted ORs (95% CIs)[†] of incident diabetes mellitus according to quintile categories of the energy-adjusted intake of rice by the intake of green tea in men and women

Green tea (cups/d)	No.[§]	Quintiles of energy-adjusted intake of rice[‡]					Trend p[*]	Interaction p[**]
		Q1 (low)	Q2	Q3	Q4	Q5 (high)		
Men								
<1	53/677	1.00 (referent)	1.18 (0.49-2.84)	1.28 (0.54-3.03)	0.78 (0.27-2.22)	1.09 (0.43-2.77)	0.94	0.50
1-3	91/1428	1.00 (referent)	1.14 (0.60-2.18)	0.81 (0.41-1.62)	0.71 (0.35-1.44)	0.91 (0.45-1.82)	0.39	
4-6	59/903	1.00 (referent)	1.64 (0.59-4.58)	1.76 (0.65-4.76)	2.40 (0.90-6.43)	2.82 (1.03-7.71)	0.03[*]	
≥7	32/389	1.00 (referent)	0.77 (0.21-2.87)	0.78 (0.21-2.96)	0.65 (0.18-2.41)	1.05 (0.28-3.85)	0.96	
Women								
<1	38/622	1.00 (referent)	1.05 (0.30-3.70)	1.63 (0.50-5.30)	2.48 (0.81-7.58)	2.76 (0.91-8.36)	0.02[*]	0.08
1-3	76/1623	1.00 (referent)	1.91 (0.80-4.54)	2.40 (1.04-5.54)	1.90 (0.80-4.54)	2.86 (1.27-6.46)	0.02[*]	
4-6	64/1691	1.00 (referent)	1.64 (0.49-5.48)	4.49 (1.52-13.32)	2.11 (0.64-6.97)	3.18 (1.01-9.97)	0.07	
≥7	51/1094	1.00 (referent)	1.23 (0.50-3.00)	0.53 (0.18-1.52)	0.73 (0.28-1.89)	0.97 (0.40-2.34)	0.63	

[†]Adjusted for age (years, continuous variable), BMI (< 22.5, 22.5 to 24.9, and ≥25.0 kg/m^2), smoking (life-long nonsmoker, past smoker, or current smoker with a consumption of < 20 or ≥ 20 cigarettes/day), alcohol consumption (life-long nondrinker, past drinker, and current drinking with an intake of < 30, 30 to 59, or ≥ 60 mL of alcohol/day for men, < 10, 10 to 19, or ≥ 20 mL of alcohol/day for women), work-related and leisure-time physical activities (sex-specific quartiles of MET-h/d and MET-h/w, respectively), and parental diabetes mellitus.
[‡]Intakes were energy-adjusted to 2000 kcal/day for men and 1800 kcal/day for women.
[§]Numbers of incident cases of diabetes mellitus (numerator) and non-diabetic subjects at the baseline (denominator).
[*]Ordinal values of 0–4 were assigned to quintile categories of energy-adjusted intake of rice to assess the trend of an association.
[**]Interaction was examined by likelihood ratio test.

0.91 (0.59–1.41), Q4 0.87 (0.55–1.39), and Q5 0.79 (0.48–1.29) (p for trend=0.29) (data not shown).The inverse association between bread intake and the risk of DM may be attributed at least partly to the lower GL of bread in men, but it seems to be more difficult to distinguish the opposite effects of rice and bread on the risk of DM in women.

A protective association of green tea intake with the risk of DM was also limited to women in the present study. The reason for the sex differences in the association between green tea intake and the incidence of DM is unclear. Only a limited number of prospective studies have assessed the association with green tea in men and women separately. A previous observational study in Japan showed a significant inverse association between green tea intake and incident DM only in women.[25] Another Japanese study reported that intake of green tea was unrelated to the risk of DM in both men and women.[26]

It is notable that the increasing trend of incident DM with higher intake of rice was nullified among women with the highest intake of green tea in the present study. There was a suggestive effect modification of green tea on the association between rice and DM in women. The OR of DM did not increase with increasing rice consumption in women with the highest consumption of green tea (≥7 cups/d) while the positive association was observed in women consuming a lower amount of green tea. No such effect modification was observed in men. Seemingly differential associations between rice and DM according to levels of green tea intake in women may be ascribed to chance, but deserve further investigation. Women with the highest intake of green tea (≥7 cups/d), compared with those with a lower green tea intake (<7 cups/d), showed significantly higher intakes of rice, cereals, and carbohydrates and a significantly lower intake of coffee. The lowest and the highest quintiles of rice intake accounted for 16% and 25%, respectively, of women with the highest intake of green tea, and 21% and 19%, respectively, of those with a lower green tea intake. Women with a higher intake of rice or foods with a lot of carbohydrates may be likely to benefit from green tea in relation to the development of DM. Percentages of women classified into the lowest to the highest category of coffee intake (almost never, <1 cup/d, and ≥1 cup/d) were 24%, 35%, and 41%, respectively, for those with the highest intake of green tea, and 13%, 25%, and 62%, respectively, for those with a lower intake of green tea. Considering that the lack of inverse association between coffee intake and the risk of DM in the present study population, the finding that the loss of association between rice intake and the risk of DM solely among women consuming rather less coffee may be understandable. Green tea possibly attenuated the risk associated with higher intake of rice by an inhibitory effect on the postprandial increase of blood glucose levels. A crossover-designed study showed that ingestion of green tea decreased carbohydrate absorption by 25% after a meal containing white rice in healthy humans.[27] It was also demonstrated that green tea extract (GTE) decreased blood glucose[28] or increased insulin sensitivity[29] in an oral glucose tolerance test. In animal studies, GTE increased insulin-stimulated glucose uptake and expression of glucose transporter 4 in adipocytes isolated from rats.[30,31] Furthermore, epigallocatechin gallate, a potent component of GTE, attenuated the increase in blood glucose level after oral administration of corn starch, the effect being attributed partly to the inhibition of α-amylase.[32]

The lack of an inverse association between coffee intake and the incidence of DM may be due to relatively low consumption of coffee in the present study; subjects reporting 4-6 cups/d of coffee intake were 9.8% and 7.8% in men and women, respectively, and those reporting ≥7 cups/d were only 1.9% in men and 0.9% in women. Although a prospective study in Japan showed an inverse association related to higher intake of coffee in both men and women in spite of a low consumption of coffee of the study population; ≥5 cups/d of coffee intake were 3.5% and 1.9% in men and women,[33] most of the studies observed a protective association with coffee among subjects with much higher intake of coffee. The summary relative risks (95% CIs) were 0.65 (0.54-0.78) for intakes of ≥6 or ≥7 cups/d and 0.72 (0.62-0.83) for the second highest (4-6 cups/d) category compared with the lowest category in a meta-analysis of 9 cohort studies.[4]Coffee intake was inversely correlated with green tea intake in the present study (Spearman's r=−0.13 in men and r=−0.20 in women), which was likely to be independent of the lack of an inverse association between coffee intake and the risk of DM.; in the multiple logistic regression analysis including green tea intake as a covariate, the trend of association between coffee intake and risk of DM remained non-significant either in men or women (p for trend=0.88 in men and p=0.16 in women, respectively).

Advantages of the present study were a large size of the study population, a high response to the follow-up survey (91%), determination of DM by HbA_{1c} which was uniformly measured, sex-specific analysis, and consideration of potential confounders. We should note several limitations, however. The low participation rate at the baseline survey (24%) was a concern. Selection bias would be possible if participation had been influenced by both potential risk factors for developing DM and the intake of food considered in the present study. The second problem was that dietary intake was assessed only once and thus may not have reflected the long-term intake of foods. Third, the type of rice consumed was not ascertained in the current study population. Although the consumption of whole-grain including brown rice, in contrast to white rice, has been shown to reduce the risk of DM,[34] brown or unrefined rice is not typically consumed in Japan.

In conclusion, rice consumption was associated with an increased risk of DM in women, but not in men. Likewise, women, but not men, with a higher consumption of green tea had a lower risk of DM. A high consumption of green tea may be protective against an increased risk of DM with a higher intake of rice.

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AUTHOR DISCLOSURES

The authors have no conflicts of interest.

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