

The Relationship between Green Tea and Total Caffeine Intake and Risk for Self-Reported Type 2 Diabetes among Japanese Adults

Hiroyasu Iso, MD; Chigusa Date, PhD; Kenji Wakai, MD; Mitsuru Fukui, PhD; Akiko Tamakoshi, MD; and the JACC Study Group*

Background: In western populations, coffee consumption is associated with a reduced risk for type 2 diabetes; however, the effect of green, black, and oolong teas is unclear.

Objective: To examine the relationship between consumption of these beverages and risk for diabetes.

Design: Retrospective cohort study.

Setting: 25 communities across Japan.

Participants: A total of 17 413 persons (6727 men and 10 686 women; 49% of the original study population) who were 40 to 65 years of age; had no history of type 2 diabetes, cardiovascular disease, or cancer at the baseline lifestyle survey; and completed the 5-year follow-up questionnaire. There was no difference in body mass index levels at baseline between respondents and non-respondents.

Measurements: Questionnaire on consumption of coffee; black, green, and oolong teas; and physician-diagnosed diabetes.

Results: During the 5-year follow-up, there were 444 self-reported new cases of diabetes in 231 men and 213 women (5-year event

rates, 3.4% and 2.0%, respectively). Consumption of green tea and coffee was inversely associated with risk for diabetes after adjustment for age, sex, body mass index, and other risk factors. Multivariable odds ratios for diabetes among participants who frequently drank green tea and coffee (≥ 6 cups of green tea per day and ≥ 3 cups of coffee per day) were 0.67 (95% CI, 0.47 to 0.94) and 0.58 (CI, 0.37 to 0.90), respectively, compared with those who drank less than 1 cup per week. No association was found between consumption of black or oolong teas and the risk for diabetes. Total caffeine intake from these beverages was associated with a 33% reduced risk for diabetes. These inverse associations were more pronounced in women and in overweight men.

Limitations: Diabetes was self-reported, no data were available on consumption of soda, and the follow-up rate was low.

Conclusions: Consumption of green tea, coffee, and total caffeine was associated with a reduced risk for type 2 diabetes.

Ann Intern Med. 2006;144:554-562.

www.annals.org

For author affiliations, see end of text.

*For members of the JACC Study Group, see the Appendix, available at www.annals.org.

The prevalence of type 2 diabetes has increased worldwide, particularly in Asian countries where it was previously low (1). In Japan, population-based studies have shown a 2-fold increase in the prevalence of diabetes during the past 2 decades, from 5% to 10% to 10% to 15% (2). Several cohort studies done in Europe and in the United States reported an association between coffee consumption, a major source of caffeine, and reduced risk for diabetes (3–7). Although these studies did not show any association between consumption of black tea and the risk for diabetes, they did not examine the effect of green or oolong teas, major sources of caffeine in Asian countries. Consumption of green tea is common in Japan; 80% of the population drinks green tea, and the average consumption per capita is 2 cups per day (8). We wanted to determine whether there is a relationship between consumption of green tea and the risk for type 2 diabetes and, if so, whether caffeine fully accounts for this relationship. To examine these questions, we analyzed data from a large cohort study of 19 487 middle-aged men and women in 25 communities across Japan. We also examined the effect of age, sex, body mass index (BMI), family history, smoking status, alcohol use, magnesium intake, and physical activity on the association between this mode of caffeine consumption and risk for diabetes.

METHODS

The Japan Collaborative Cohort Study for Evaluation of Cancer Risk (JACC Study) started between 1988 and 1990. A total of 110 792 individuals (46 465 men and 64 327 women) who were 40 to 79 years of age and living in 45 communities across Japan participated in municipal health screening examinations and completed self-administered questionnaires regarding lifestyle and medical history of cardiovascular disease and cancer (9). Informed consent was obtained before the completion of the questionnaire. Participants from 25 of the 45 communities completed 5-year follow-up surveys. Among 35 690 participants (15 177 men and 20 513 women) who were 40 to 65 years of age at baseline without a history of type 2 diabetes, stroke, coronary heart disease, or cancer, 17 413

See also:

Print

Editors' Notes 555
Summary for Patients I-28

Web-Only

Appendix
Conversion of tables into slides

individuals (49%; 6727 men and 10 686 women) completed the 5-year follow-up questionnaire and provided valid responses on tea or coffee consumption and history of type 2 diabetes. The data from these 17 413 individuals were used for the analyses. The mean age of the nonrespondents was 1 year younger for men (52.3 vs. 53.3 years of age) and did not differ for women (53.1 vs. 53.0 years of age) compared with the respondents. The mean BMI and the prevalence of a BMI of 25.0 kg/m² or greater did not differ between the respondents and nonrespondents. Mean BMI was 22.7 kg/m² versus 22.8 kg/m² for men and 22.8 kg/m² versus 22.9 kg/m² for women, respectively; the prevalence of overweight was 18% versus 19% for men and 21% versus 22% for women, respectively. The ethical committees at Nagoya University and the University of Tsukuba approved the study.

Assessment of Consumption of Tea and Coffee and Caffeine Intake

At baseline, consumption of tea and coffee was assessed by using a self-administered dietary questionnaire. Participants were asked to state their average consumption of green tea, black tea, oolong tea, and coffee during the previous year. They could select any of 4 frequency responses: “less than once a week,” “about 1 to 2 times a week,” “about 3 to 4 times a week,” and “almost every day.” Participants who selected the response of “almost every day” were also asked to state their average consumption of these beverages in number of cups per day. We classified the categories of consumption as less than 1 cup per week, 1 to 6 cups per week, 1 to 2 cups per day, 3 to 5 cups per day, and 6 or more cups per day. The highest 2 or 3 consumption categories were combined for coffee, black tea, and oolong tea because of the small number of participants in these categories. The consumption of decaffeinated coffee or tea was not recorded because these products were not commercially available in Japan in the early 1990s. The total intake of caffeine was calculated by adding the caffeine content from each specific beverage (1 cup

Context

Caffeine intake from coffee has been associated with a lower incidence of diabetes. Researchers have not studied the relationship of green tea, a popular beverage in Japan, where the incidence of diabetes is increasing rapidly.

Contributions

The authors estimated the intake of caffeine-containing beverages in a community-based survey in Japan and measured the 5-year incidence of diabetes. Greater intake of green tea or coffee was associated with a reduced incidence of diabetes. The effect of green tea was largely observed in women, was dose-related, and reflected caffeine intake.

Implications

Higher intake of caffeine, whether from coffee or green tea, is associated with a lower incidence of diabetes.

—The Editors

for coffee or tea) and multiplying it by the participant’s weight proportional to the frequency of caffeine use. We estimated the size of the cup for each beverage from a validation study (10) and the caffeine content per 100 mL of each beverage from the Japan Food Tables (11). The estimated caffeine content was 153 mg per cup (170 mL) of coffee, 30 mg per cup (200 mL) of green tea, 51 mg per cup (170 mL) of black tea, and 38 mg per cup (190 mL) of oolong tea. The mean caffeine intake was 229 mg/d for men and 215 mg/d for women. Relative proportions of caffeine intake by beverage were 46% from green tea, 44% to 47% from coffee, 3% from black tea, and 4% to 5% from oolong tea.

For reproducibility, the Spearman correlation coefficients between the 2 questionnaires, administered 1 year apart for 85 participants (8 men and 77 women), were 0.79 for green tea, 0.87 for coffee, 0.77 for black tea, and 0.56 for oolong tea (10). The validity of the data was

Table 1. Baseline Characteristics of Study Participants

Variable	Men	Women
Participants, <i>n</i>	6727	10 686
Mean age (SD), <i>y</i>	53.3 (7.6)	53.1 (7.4)
Family history of diabetes, %	9.1	8.9
Current smoker, %	53.6	4.0
Mean alcohol intake (SD), <i>g/d</i>	26.1 (24.2)	1.8 (6.6)
Mean magnesium intake (SD), <i>mg/d</i>	235 (68)	230 (60)
Mean body mass index (SD), <i>kg/m</i> ²	22.7 (2.6)	22.8 (2.9)
Walking >0.5 h/d, %	54.1	55.3
Sports participation ≥5 h/wk, %	29.4	21.7
Consumption of ≥1 cup of green tea per day, %	53.3	53.1
Consumption of ≥1 cup of coffee per day, %	46.3	47.1
Consumption of ≥1 cup of black tea per day, %	1.6	2.3
Consumption of ≥1 cup of oolong tea per day, %	5.0	8.9

Table 2. Age-Adjusted Baseline Characteristics according to Consumption of Green Tea, Coffee, Black Tea, and Oolong Tea*

Variable	Men								
	Participants, n	Age, y	Family History of Diabetes, %	Current Smoker, %	Alcohol Intake, %	Magnesium Intake, mg/d	BMI, kg/m ²	Walking, >0.5 h/d, %	Sports Participation, ≥5 h/wk, %
Green tea									
<1 cup/wk	703	52.8	8.3	52.0	26.0	210	22.7	56.0	25.4
1–6 cups/wk	706	51.5	8.6	49.8	28.6	226	22.9	57.8	27.7
1–2 cups/d	1057	52.1	9.5	53.5	27.0	220	22.6	49.6	30.1
3–5 cups/d	2683	53.5	9.3	54.2	25.9	233	22.8	52.3	31.3
≥6 cups/d	1578	54.9	9.2	54.9	24.8	265	22.7	57.7	28.2
<i>P</i> value for trend		<0.001	0.66	0.052	0.076	<0.001	0.84	0.114	0.53
Coffee									
<1 cup/wk	1865	55.1	8.4	46.8	30.0	233	22.6	60.2	26.9
1–6 cups/wk	1305	53.3	9.1	45.0	26.1	233	22.6	56.2	30.1
1–2 cups/d	1970	52.5	10.3	57.6	34.9	231	22.8	50.8	30.9
≥3 cups/d	763	50.2	8.6	74.3	20.2	247	22.7	49.9	28.6
<i>P</i> value for trend		<0.001	0.73	<0.001	<0.001	<0.001	0.42	<0.001	0.60
Black tea									
<1 cup/wk	5856	53.3	9.0	54.5	26.6	234	22.7	54.9	28.6
1–6 cups/wk	548	52.5	11.0	46.5	22.7	245	22.9	47.0	36.4
≥1 cup/d	105	52.1	9.2	42.7	19.9	225	22.5	45.4	28.9
<i>P</i> value for trend		0.002	0.28	<0.001	<0.001	0.22	0.49	<0.001	0.009
Oolong tea									
<1 cup/wk	5565	53.4	9.0	53.6	26.4	235	22.6	55.4	28.1
1–6 cups/d	533	51.8	11.3	52.6	25.2	238	23.4	46.2	37.9
≥1 cup/d	322	53.1	8.2	50.1	23.4	234	23.6	44.9	35.2
<i>P</i> value for trend		0.123	0.82	0.179	0.122	0.97	<0.001	<0.001	0.002

* BMI = body mass index.

confirmed for the 85 participants by comparing the data from the questionnaire with those from four 3-day dietary records collected approximately 3 to 4 months apart (10). The mean frequency of consumption of green tea was 25.4 cups per week according to the questionnaire and 30.1 cups per week according to four 1-week dietary records (Spearman correlation coefficient, 0.47). The respective mean frequencies were 8.0 cups and 7.1 cups per week with a correlation coefficient of 0.79 for coffee, 1.4 cups and 1.6 cups per week with a correlation coefficient of 0.70 for black tea, and 1.8 cups and 1.2 cups per week with a correlation coefficient of 0.55 for oolong tea. When we restricted the data to the 77 women, the results were essentially the same.

Assessment of Diabetes Cases

Participants who reported having diabetes newly diagnosed by physicians on the 5-year follow-up questionnaire were considered to have incident diabetes. To examine the validity of self-reporting of diabetes, we compared self-report data with laboratory findings and treatment status in a sample of 1230 men and 1837 women. We considered elevated glucose concentrations (fasting serum glucose concentration ≥7.8 mmol/L [≥140 mg/dL] or a randomly

measured concentration of ≥11.1 mmol/L [≥200 mg/dL]) or treatment with oral hypoglycemic agents or insulin to indicate new cases of diabetes. Recent criteria from the American Diabetes Association (12) were not used because the cases in our study were diagnosed before 1995. The sensitivity of self-reporting was 70% for men and 75% for women; the specificity was 95% for men and 98% for women.

Statistical Analysis

To examine potential confounding variables reported from previous studies (3–7), we presented baseline characteristics according to the frequency of consumption for each beverage. Tests for trends were conducted by using the median values of confounding variables in each category of beverage; the linear regression model was used for continuous variables, and the logistic regression model was used for categorical variables.

The odds ratios for incident type 2 diabetes were calculated in each category of beverage consumption and in each quartile of caffeine intake; less than 1 cup per week or the lowest quartile was used as the reference category. We estimated age, sex, and BMI-adjusted odds ratios and multivariable odds ratios using the logistic regression model, adjusting for age (in years), sex, sex-specific quintiles of

Table 2—Continued

Women								
Participants, n	Age, y	Family History of Diabetes, %	Current Smoker, %	Alcohol Intake, %	Magnesium Intake, mg/d	BMI, kg/m ²	Walking, >0.5 h/d, %	Sports Participation ≥5 h/wk, %
1327	52.8	9.3	4.1	2.3	208	22.8	59.3	16.4
1172	51.8	9.8	4.4	2.0	221	22.9	53.6	21.9
1565	52.0	10.7	4.4	1.9	219	22.8	55.3	23.8
4365	53.5	8.5	3.5	1.8	231	22.8	54.1	22.2
2257	54.1	7.6	4.7	1.6	252	23.0	56.4	22.5
	<0.001	0.007	0.63	0.008	<0.001	0.34	0.81	0.017
2931	55.2	8.0	2.1	1.6	224	23.0	59.7	19.2
1978	53.2	8.2	2.8	1.4	228	22.8	58.1	21.7
3585	52.0	10.0	4.5	2.3	229	22.8	53.7	22.1
794	49.6	11.5	13.3	2.5	242	22.8	50.6	21.5
	<0.001	<0.001	<0.001	<0.001	<0.001	0.94	<0.001	0.90
8887	53.2	8.4	4.2	1.9	229	22.9	56.3	20.6
1246	52.2	10.8	3.0	1.5	236	22.5	50.8	27.4
243	52.2	17.1	4.6	2.2	218	22.2	46.4	26.7
	<0.001	<0.001	0.26	0.31	0.90	<0.001	<0.001	<0.001
8133	53.2	8.8	3.3	1.7	229	22.7	56.7	20.1
1083	51.9	9.4	5.7	2.3	236	23.2	50.0	29.2
904	51.9	9.8	7.5	2.7	227	23.6	49.9	25.3
	<0.001	0.32	<0.001	<0.001	0.48	<0.001	<0.001	<0.001

BMI (weight in kilograms divided by the square of height in meters), parental history of diabetes (yes or no), smoking status (never, former, or current [1 to 19, 20 to 29, or ≥30 cigarettes/d]), alcohol intake (never, former, or current [1 to 22, 23 to 45, 46 to 68, or ≥69 g/d]), sex-specific quintiles of magnesium intake, hours of walking (<0.5, 0.5, 0.6 to 0.9, and ≥1.0 h/d), and hours of participation in sports (<1, 1 to 2, 3 to 4, and ≥5 h/wk). Sex-specific quintiles of BMI and magnesium intake were used because of different distributions between the sexes. We adjusted for magnesium intake because previous cohort studies indicated an inverse association between magnesium intake and risk for diabetes (13, 14). We conducted a test for trend by treating median values of each category of beverage or caffeine intake as continuous variables.

We examined the association between caffeine intake and the risk for diabetes stratified by age group (40 to 54 years and 55 to 65 years), sex, family history of diabetes (yes or no), current smoking status (yes or no), current alcohol intake (yes or no), magnesium intake (below and above the sex-specific median), BMI (<25.0 kg/m² and ≥25.0 kg/m²), hours of walking (<0.5 and ≥0.5 h/d), and hours of participation in sports (<5 and ≥5 h/wk). The interactions with these stratified variables were tested by using cross-product terms of caffeine intake and the

stratified variables. All analyses were conducted by using the SAS statistical package, version 8.2 (SAS Institute Inc., Cary, North Carolina). *P* values for statistical tests were 2-tailed, and 95% CIs were estimated.

Role of the Funding Source

The funding source had no role in the design, analysis, or interpretation of the study or in the decision to submit the manuscript for publication.

RESULTS

Table 1 shows the participants' baseline characteristics. Their mean age was 53 years, and their mean BMI was 22.7 kg/m² to 22.8 kg/m² for both men and women. Frequency of daily consumption was approximately 53% for green tea, 46% to 47% for coffee, 2% for black tea, and 5% to 9% for oolong tea. During the 5-year follow-up, 444 incident cases of type 2 diabetes were identified in 231 men and 213 women. The 5-year incidence rates were 3.4% and 2.0%, respectively.

Higher consumption of green tea was positively associated with age and magnesium intake for men and women and was inversely associated with alcohol intake for men and women and with family history of diabetes for women.

Table 3. Odds Ratios for Type 2 Diabetes Mellitus according to Consumption of Green Tea, Coffee, Black Tea, and Oolong Tea*

Variable	Total				Men			
	At Risk for Diabetes, n	Cases of Diabetes, n	Age- and BMI-Adjusted Odds Ratios (95% CI)	Multivariable Odds Ratios† (95% CI)	At Risk for Diabetes, n	Cases of Diabetes, n	Age- and BMI-Adjusted Odds Ratios (95% CI)	Multivariable Odds Ratios† (95% CI)
Green tea								
<1 cup/wk	2030	64	1.00	1.00	703	25	1.00	1.00
1–6 cups/wk	1878	39	0.64 (0.43–0.96)	0.66 (0.44–0.99)	706	12	0.47 (0.24–0.95)	0.48 (0.24–0.98)
1–2 cups/d	2622	61	0.73 (0.51–1.04)	0.72 (0.50–1.03)	1057	31	0.86 (0.50–1.47)	0.82 (0.47–1.41)
3–5 cups/d	7048	192	0.81 (0.60–1.08)	0.82 (0.61–1.11)	2683	110	1.12 (0.72–1.75)	1.12 (0.71–1.76)
≥6 cups/d	3835	88	0.63 (0.45–0.88)	0.67 (0.47–0.94)	1578	53	0.87 (0.54–1.42)	0.91 (0.55–1.52)
P value for trend			0.083	0.189			0.56	0.39
Coffee								
<1 cup/wk	4796	142	1.00	1.00	1865	73	1.00	1.00
1–6 cups/wk	3283	73	0.81 (0.61–1.08)	0.82 (0.61–1.10)	1305	35	0.72 (0.47–1.08)	0.71 (0.46–1.07)
1–2 cups/d	5555	144	0.99 (0.78–1.26)	0.93 (0.73–1.19)	1970	76	1.05 (0.75–1.47)	0.96 (0.68–1.36)
≥3 cups/d	1557	26	0.63 (0.41–0.97)	0.58 (0.37–0.90)	763	16	0.61 (0.35–1.06)	0.54 (0.30–0.97)
P value for trend			0.092	0.027			0.190	0.096
Black tea								
<1 cup/wk	14 743	381	1.00	1.00	5856	197	1.00	1.00
1–6 cups/wk	1794	34	0.81 (0.57–1.16)	0.83 (0.58–1.20)	548	20	1.08 (0.68–1.73)	1.12 (0.69–1.81)
≥1 cup/d	348	13	1.72 (0.97–3.05)	1.62 (0.91–2.88)	105	5	1.50 (0.60–3.75)	1.43 (0.56–3.64)
P value for trend			0.62	0.62			0.42	0.42
Oolong tea								
<1 cup/wk	13 698	345	1.00	1.00	5565	183	1.00	1.00
1–6 cups/wk	1616	39	0.94 (0.67–1.33)	0.98 (0.69–1.38)	533	21	1.14 (0.72–1.82)	1.14 (0.71–1.85)
≥1 cup/d	1226	35	1.10 (0.77–1.58)	1.08 (0.75–1.55)	322	16	1.33 (0.78–2.26)	1.41 (0.82–2.43)
P value for trend			0.62	0.70			0.27	0.20

* BMI = body mass index.

† Adjusted further for family history of diabetes mellitus, smoking status, alcohol intake, magnesium intake, hours of walking, hours of exercise, and consumption of other beverages.

Consumption of green tea was not consistently related to smoking, BMI, or physical activity (Table 2). Similar associations were observed for consumption of coffee, black tea, and oolong tea. Exceptions to this trend included a positive association between coffee and smoking; a positive association between coffee and black tea and a family history of diabetes for women; inverse associations between

coffee, black tea, and, for women, oolong tea and increasing age; inverse associations between black tea and BMI and, for women, smoking; a positive association between oolong tea and BMI; and no association between black tea and oolong tea and magnesium intake.

After adjustment for age and BMI, consumption of green tea was associated with a lower risk for type 2 diabe-

Table 4. Odds Ratios for Type 2 Diabetes Mellitus according to Quintiles of Caffeine Intake*

Caffeine Intake	Total				Men			
	Median Caffeine Intake, mg/d	At Risk for Diabetes, n	Cases of Diabetes, n	Multivariable Odds Ratios† (95% CI)	Median Caffeine Intake, mg/d	At Risk for Diabetes, n	Cases of Diabetes, n	Multivariable Odds Ratios† (95% CI)
Quintile 1	57	2754	75	1.00	57	1057	31	1.00
Quintile 2	137	3255	93	1.00 (0.73–1.37)	137	1344	49	1.23 (0.77–1.95)
Quintile 3	199	4254	111	0.98 (0.73–1.33)	203	1610	57	1.22 (0.77–1.91)
Quintile 4	273	3485	100	1.00 (0.74–1.37)	274	1344	60	1.47 (0.94–2.31)
Quintile 5	416	3665	65	0.67 (0.47–0.95)	480	1372	34	0.85 (0.51–1.42)
P value for trend				0.018				0.37

* Ranges of caffeine intake among men were <97 mg/d for quintile 1, 97 to 158 mg/d for quintile 2, 159 to 256 mg/d for quintile 3, 257 to 304 mg/d for quintile 4, and ≥305 mg/d for quintile 5. The respective ranges for women were <97, 97 to 153, 154 to 240, 241 to 281, and ≥282 mg/d.

† Adjusted further for family history of diabetes mellitus, smoking status, alcohol intake, hours of walking, and hours of exercise.

Table 3—Continued

Women			
At Risk for Diabetes, <i>n</i>	Cases of Diabetes, <i>n</i>	Age- and BMI-Adjusted Odds Ratios (95% CI)	Multivariable Odds Ratios† (95% CI)
1327	39	1.00	1.00
1172	27	0.77 (0.46–1.27)	0.79 (0.47–1.32)
1565	30	0.66 (0.41–1.07)	0.66 (0.40–1.08)
4365	82	0.60 (0.41–0.89)	0.61 (0.41–0.91)
2257	35	0.47 (0.29–0.74)	0.49 (0.30–0.79)
		0.002	0.005
2931	69	1.00	1.00
1978	38	0.92 (0.61–1.38)	0.95 (0.63–1.44)
3585	68	0.94 (0.66–1.32)	0.88 (0.61–1.25)
794	10	0.69 (0.35–1.36)	0.61 (0.30–1.22)
		0.31	0.107
8887	184	1.00	1.00
1246	14	0.61 (0.35–1.05)	0.61 (0.35–1.07)
243	8	1.86 (0.90–3.86)	1.75 (0.83–3.68)
		0.98	0.96
8133	162	1.00	1.00
1083	18	0.80 (0.49–1.30)	0.81 (0.49–1.34)
904	19	0.94 (0.58–1.53)	0.80 (0.49–1.32)
		0.76	0.37

tes for all participants (Table 3). Additional adjustment for physical activity, smoking status, family history of diabetes, and other risk factors did not appreciably alter the results. The multivariable odds ratio for diabetes among participants who frequently drank green tea (≥ 6 cups/d) was 0.67 (CI, 0.47 to 0.94) compared with those who drank less than 1 cup per week. The inverse association was pri-

Table 4—Continued

Women			
Median Caffeine Intake, mg/d	At Risk for Diabetes, <i>n</i>	Cases of Diabetes, <i>n</i>	Multivariable Odds Ratios† (95% CI)
57	1697	44	1.00
137	1911	44	0.86 (0.56–1.32)
196	2644	54	0.81 (0.54–1.22)
267	2141	40	0.67 (0.43–1.05)
399	2293	31	0.52 (0.32–0.84)
			0.004

marily observed for women ($P = 0.001$ for interaction with sex), with a strong dose–response relationship (odds ratios, 0.79 [CI, 0.47 to 1.32], 0.66 [CI, 0.40 to 1.08], 0.61 [CI, 0.41 to 0.91], and 0.49 [CI, 0.30 to 0.79] for the second to the highest quintiles of green tea consumption, respectively; $P = 0.005$ for trend). For interval validity, we examined the association between BMI and risk for diabetes and found a strong positive association: The multivariable odds ratios were 1.39 (CI, 0.90 to 2.14), 1.93 (CI, 1.28 to 2.91), 2.33 (CI, 1.56 to 3.49), and 4.77 (CI, 3.26 to 6.98) for the second to the highest quintiles of BMI compared with the lowest quintile ($P = 0.001$ for trend).

Consumption of coffee was also associated with a lower risk for type 2 diabetes for all participants. The multivariable odds ratio for diabetes among participants who frequently drank coffee (≥ 3 cups/d) was 0.58 (CI, 0.71 to 0.90) compared with those who drank less than 1 cup per week. The inverse association was similarly observed for men and women ($P = 0.87$ for interaction). Consumption of oolong tea or black tea was not associated with risk for diabetes for all participants or either sex.

Caffeine intake from green tea, coffee, black tea, and oolong tea was associated with a lower risk for type 2 diabetes for all participants (Table 4). The multivariable odds ratio for diabetes was 0.67 (CI, 0.47 to 0.95) among persons with the highest quintile of caffeine intake compared with those with the lowest quintile. The inverse association was primarily observed for women ($P = 0.105$ for interaction with sex), with a strong dose–response relationship (odds ratios, 0.86 [CI, 0.56 to 1.32], 0.81 [CI, 0.54 to 1.22], 0.67 [CI, 0.43 to 1.05], and 0.52 [CI, 0.32 to 0.84] for the second to the highest quintiles of caffeine consumption, respectively; $P = 0.004$ for trend).

We conducted stratified analyses to evaluate whether the association between caffeine consumption and type 2 diabetes varies according to age, family history of diabetes, smoking status, alcohol intake, magnesium intake, BMI, and physical activity. Effect modification was observed only for BMI (Table 5). The inverse association was primarily observed for participants with a BMI of 25.0 kg/m² or greater (corresponding to the highest quintile of BMI) but not for those with lower BMI. This effect modification was evident for men but not for women.

DISCUSSION

We found significant and inverse associations of green tea and coffee consumption with the risk for type 2 diabetes. When compared with participants who did not consume these beverages, those who consumed 6 or more cups of green tea per day and 3 or more cups of coffee per day had their risk for diabetes lowered by 33% and 42%, respectively. The highest quintile of caffeine intake (median, 416 mg/d) was also associated with a 33% reduced risk for diabetes compared with the lowest quintile (median, 57 mg/d). The inverse associations for green tea consumption

Table 5. Odds Ratios for Type 2 Diabetes Mellitus according to Quintiles of Caffeine Intake, Stratified by Body Mass Index*

Variable	Total Participants			Men			Women		
	At Risk, n	Cases of Diabetes, n	Multivariable Odds Ratio† (95% CI)	At Risk, n	Cases of Diabetes, n	Multivariable Odds Ratio† (95% CI)	At Risk, n	Cases of Diabetes, n	Multivariable Odds Ratio† (95% CI)
Caffeine intake in those with BMI <25.0 kg/m²									
Quintile 1	2135	44	1.00	854	19	1.00	1281	25	1.00
Quintile 2	2527	54	1.01 (0.68–1.52)	1069	30	1.24 (0.69–2.23)	1458	24	0.82 (0.46–1.44)
Quintile 3	3316	67	1.07 (0.72–1.57)	1273	39	1.46 (0.83–2.57)	2043	28	0.74 (0.43–1.28)
Quintile 4	2729	59	1.05 (0.71–1.57)	1075	42	1.72 (0.98–3.02)	1654	17	0.52 (0.28–0.98)
Quintile 5	2843	39	0.75 (0.48–1.18)	1073	25	1.14 (0.61–2.13)	1770	14	0.42 (0.21–0.83)
<i>P</i> value for trend			0.23			0.77			0.005
Caffeine intake in those with BMI ≥25 kg/m²									
Quintile 1	499	30	1.00	155	11	1.00	344	19	1.00
Quintile 2	606	37	0.96 (0.58–1.59)	228	18	1.08 (0.48–2.43)	378	19	0.90 (0.46–1.75)
Quintile 3	800	38	0.76 (0.46–1.25)	283	15	0.71 (0.31–1.64)	517	23	0.77 (0.41–1.47)
Quintile 4	654	39	0.88 (0.53–1.45)	225	17	0.93 (0.41–2.11)	429	22	0.82 (0.43–1.59)
Quintile 5	719	23	0.49 (0.27–0.87)	252	7	0.35 (0.13–0.96)	467	16	0.55 (0.27–1.13)
<i>P</i> value for trend			0.009			0.023			0.106
<i>P</i> value for interaction			0.167			0.029			0.29

* Ranges of caffeine intake among men were <97 mg/d for quintile 1, 97 to 158 mg/d for quintile 2, 159 to 256 mg/d for quintile 3, 257 to 304 mg/d for quintile 4, and ≥305 mg/d for quintile 5. The respective ranges for women were <97, 97 to 153, 154 to 240, 241 to 281, and ≥282 mg/d. BMI = body mass index.

† Adjusted for age, sex, body mass index, family history of diabetes mellitus, smoking status, alcohol intake, magnesium intake, hours of walking, and hours of exercise.

and caffeine intake were primarily observed for women, although the inverse association for coffee consumption was observed in both sexes.

The inverse association with coffee consumption was consistent with recent epidemiologic studies of European men and women (3–5, 7) and U.S. nurses and health professionals (6). Persons who drank coffee frequently (≥7 cups/d) had a 29% to 52% reduced risk for diabetes compared with those who drank less coffee (≤2 cups/d or no cups/d) (3–7). To our knowledge, our study is the first to show the inverse association between consumption of green tea and the risk for diabetes among western and Asian populations and between coffee consumption and the risk for diabetes in Asian populations.

We think that these inverse associations were mostly due to the association between caffeine intake and the risk for diabetes because green tea and coffee are both major sources (approximately 45% for each) of caffeine in Japan. We did not find an association between the consumption of black tea or oolong tea and the risk for diabetes. The smaller variations in the consumption of these beverages may have contributed in part to the noted lack of association with diabetes.

The reason for nonsignificant associations of green tea and caffeine intake with the risk for diabetes among men is unclear. It is possible that men did not report the frequency of their green tea consumption with the same reliability as did women. However, only 8 men participated in our reliability and validity study; therefore, we were not able to examine sex-specific reliability and validity.

Another possibility is the confounding by consump-

tion of soda, such as cola, which is another potential source of caffeine. Our cross-sectional study for 1 of the surveyed communities indicated that the frequency of soda consumption among 1086 persons 40 to 65 years of age was inversely associated with the frequency of green tea consumption among men and was less evidently associated with green tea consumption among women; the Spearman correlation coefficients were -0.14 ($P = 0.009$) and -0.06 ($P = 0.100$), respectively. This result suggests that persons who frequently drink green tea probably would consume less soda and vice versa, which may mask the associations of green tea consumption and caffeine intake with the risk for diabetes, especially for men.

We found a statistically significant inverse association between caffeine intake and diabetes among men with a BMI of 25.0 kg/m² or greater but not among those with lower BMI. This effect modification by BMI was not found for women. The reason for the lack of effect modification among women is unknown, but a similar finding was reported in a previous U.S. study (6). Our finding suggests that a protective effect of green tea and caffeine intake is pronounced among men at high risk for diabetes.

Several epidemiologic studies showed that dietary intake of magnesium, which is abundant in coffee, is associated with a reduced risk for type 2 diabetes (13, 14). In our study, there was a tendency for magnesium intake to be inversely associated with the risk for diabetes; the multivariable odds ratio for the highest versus lowest quartiles of magnesium intake was 0.67 (CI, 0.48 to 0.95) for all participants ($P = 0.042$ for trend). Even after adjustment for

magnesium intake, the inverse association persisted between coffee consumption and the risk for diabetes.

The mechanisms responsible for the inverse association between caffeine intake and diabetes risk include increased basal energy expenditure (15), stimulation of fat oxidation and mobilization of glycogen in muscles (16), and stimulation of free fatty acid release (increased lipolysis) from peripheral tissues (15). The acute effect of decreased insulin sensitivity induced by caffeine (17) is known to be tolerated after several days of caffeine use (18). Besides these potential effects of caffeine, antioxidant substances, such as epigallocatechin gallate (19, 20) from green tea and phenol chlorogenic acid (21, 22) from coffee, may have beneficial effects on the risk for diabetes through their action on insulin resistance and glucose metabolism. In the present study, the inverse association between caffeine intake and the risk for diabetes was primarily observed in women and in overweight men. Again, this finding provides evidence for the beneficial effect of caffeine in persons with a higher risk for insulin resistance or diabetes.

Our study has limitations. First, we did not have data on other dietary sources of caffeine, such as soda. Again, soda consumption may confound the association between coffee consumption and caffeine intake and risk for diabetes, particularly among men. Second, 25% to 30% of participants who had diabetes did not report it. However, this underreporting is probably not associated with consumption of green tea or coffee; the potential bias due to underreporting may be small. Third, we followed 49% of the participants for ascertainment of incident diabetes. We do not believe that a potential follow-up bias would be large enough to affect our findings because there was no difference in mean BMI and prevalence of overweight, a major determinant of diabetes, between the participants who were followed and those who were not.

Coffee consumption is frequently associated with unhealthy behaviors, such as smoking and a sedentary lifestyle. In our study, it was associated with smoking and fewer hours walked per day. The confounding effects of these variables would probably bias the results toward a positive, not an inverse, association. In contrast, consumption of green tea is often associated with healthy behaviors, such as increased physical activity. In our study, these variables were statistically controlled, but we could not explain the residual confounding. Because consumption of green tea and coffee and physician-diagnosed diabetes were self-reported on the questionnaire, some misclassification of exposure and outcome was inevitable. However, such misclassification in cohort studies would have biased the results toward the null hypothesis.

In conclusion, the present cohort study showed an inverse association between green tea, coffee, and caffeine consumption and the risk for diabetes in women and in overweight men. Clinical trials are necessary to confirm the protective effect of green tea and coffee for type 2 diabetes.

From Osaka University and Osaka City University, Osaka, Japan; Nara Women's University, Nara, Japan; and Aichi Cancer Center and Nagoya University, Nagoya, Japan.

Acknowledgments: The authors thank Dr. Kunio Aoki, Professor Emeritus, Nagoya University School of Medicine and former chairman of the JACC Study Group; Dr. Haruo Sugano, former director of the Cancer Institute of the Japanese Foundation for Cancer Research, who greatly contributed to the initiation of the study; and Professor Aaron R. Folsom, University of Minnesota, for valuable scientific suggestions.

Grant Support: The JACC Study has been supported by Grants-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture of Japan (61010076, 62010074, 63010074, 1010068, 2151065, 3151064, 4151063, 5151069, 6279102, and 11181101).

Potential Financial Conflicts of Interest: None disclosed.

Requests for Single Reprints: Hiroyasu Iso, MD, Public Health, Department of Social and Environmental Health, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita-shi, Osaka 565-0871, Japan; e-mail, iso@pbhel.med.osaka-u.ac.jp.

Current author addresses and author contributions are available at www.annals.org.

References

- King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. *Diabetes Care*. 1998;21:1414-31. [PMID: 9727886]
- Ohmura T, Ueda K, Kiyohara Y, Kato I, Iwamoto H, Nakayama K, et al. Prevalence of type 2 (non-insulin-dependent) diabetes mellitus and impaired glucose tolerance in the Japanese general population: the Hisayama Study. *Diabetologia*. 1993;36:1198-203. [PMID: 8270136]
- van Dam RM, Feskens EJ. Coffee consumption and risk of type 2 diabetes mellitus. *Lancet*. 2002;360:1477-8. [PMID: 12433517]
- Rosengren A, Dotevall A, Wilhelmsen L, Thelle D, Johansson S. Coffee and incidence of diabetes in Swedish women: a prospective 18-year follow-up study. *J Intern Med*. 2004;255:89-95. [PMID: 14687243]
- Tuomilehto J, Hu G, Bidel S, Lindstrom J, Jousilahti P. Coffee consumption and risk of type 2 diabetes mellitus among middle-aged Finnish men and women. *JAMA*. 2004;291:1213-9. [PMID: 15010442]
- Salazar-Martinez E, Willett WC, Ascherio A, Manson JE, Leitzmann MF, Stampfer MJ, et al. Coffee consumption and risk for type 2 diabetes mellitus. *Ann Intern Med*. 2004;140:1-8. [PMID: 14706966]
- Carlsson S, Hammar N, Grill V, Kaprio J. Coffee consumption and risk of type 2 diabetes in Finnish twins [Letter]. *Int J Epidemiol*. 2004;33:616-7. [PMID: 15105411]
- Sasazuki S, Inoue M, Hanaoka T, Yamamoto S, Sobue T, Tsugane S. Green tea consumption and subsequent risk of gastric cancer by subsite: the JPHC Study. *Cancer Causes Control*. 2004;15:483-91. [PMID: 15286468]
- Ohno Y, Tamakoshi A, JACC Study Group. Japan collaborative cohort study for evaluation of cancer risk sponsored by Monbusho (JACC study). *J Epidemiol*. 2001;11:144-50. [PMID: 11512570]
- Date C, Fukui M, Yamamoto A, Wakai K, Ozeki A, Motohashi Y, et al. Reproducibility and validity of a self-administered food frequency questionnaire used in the JACC study. *J Epidemiol*. 2005;15 Suppl 1:S9-23. [PMID: 15881192]
- The Resource Council of the Science and Technology Agency of Japan. Standard Tables of Food Composition in Japan. 5th ed, revised. Tokyo: Printing Bureau, Ministry of Finance; 2000.
- The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*. 1997;20:1183-197. [PMID: 12502614]

13. Salmeron J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. *JAMA*. 1997;277:472-7. [PMID: 9020271]
14. Kao WH, Folsom AR, Nieto FJ, Mo JP, Watson RL, Brancati FL. Serum and dietary magnesium and the risk for type 2 diabetes mellitus: the Atherosclerosis Risk in Communities Study. *Arch Intern Med*. 1999;159:2151-9. [PMID: 10527292]
15. Astrup A, Toubro S, Cannon S, Hein P, Breum L, Madsen J. Caffeine: a double-blind, placebo-controlled study of its thermogenic, metabolic, and cardiovascular effects in healthy volunteers. *Am J Clin Nutr*. 1990;51:759-67. [PMID: 2333832]
16. Spriet LL, MacLean DA, Dyck DJ, Hultman E, Cederblad G, Graham TE. Caffeine ingestion and muscle metabolism during prolonged exercise in humans. *Am J Physiol*. 1992;262:891-8. [PMID: 1616022]
17. Keijzers GB, De Galan BE, Tack CJ, Smits P. Caffeine can decrease insulin sensitivity in humans. *Diabetes Care*. 2002;25:364-9. [PMID: 11815511]
18. Robertson D, Wade D, Workman R, Woosley RL, Oates JA. Tolerance to the humoral and hemodynamic effects of caffeine in man. *J Clin Invest*. 1981;67:1111-7. [PMID: 7009653]
19. Waltner-Law ME, Wang XL, Law BK, Hall RK, Nawano M, Granner DK. Epigallocatechin gallate, a constituent of green tea, represses hepatic glucose production. *J Biol Chem*. 2002;277:34933-40. [PMID: 12118006]
20. Song EK, Hur H, Han MK. Epigallocatechin gallate prevents autoimmune diabetes induced by multiple low doses of streptozotocin in mice. *Arch Pharm Res*. 2003;26:559-63. [PMID: 12934649]
21. Devasagayam TP, Kamat JP, Mohan H, Kesavan PC. Caffeine as an antioxidant: inhibition of lipid peroxidation induced by reactive oxygen species. *Biochim Biophys Acta*. 1996;1282:63-70. [PMID: 8679661]
22. Hemmerle H, Burger HJ, Below P, Schubert G, Rippel R, Schindler PW, et al. Chlorogenic acid and synthetic chlorogenic acid derivatives: novel inhibitors of hepatic glucose-6-phosphate translocase. *J Med Chem*. 1997;40:137-45. [PMID: 9003513]

ANNALS VITAL STATISTICS

About 85 000 physicians subscribe to *Annals*, and millions of people access it through institutional libraries or the Web. In 2004, newspapers, magazines, and radio and television stations published or produced nearly 3000 stories based on *Annals* articles. Video news releases on articles aired on 1457 stations with viewing audiences of 113.9 million. Print publications with *Annals* news reached more than 265 million readers. Our impact factor for 2004 was 13.1, up from 12.43 in 2003.

Current Author Addresses: Dr. Iso: Public Health, Department of Social and Environmental Health, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita-shi, Osaka 565-0871, Japan.

Dr. Date: Nara Women's University, Kitauoyanishi-machi, Nara 630-8506, Japan.

Dr. Wakai: Aichi Cancer Center, 1-1 Kanokoden, Chikusan-ku, Nagoya 466-8681, Japan.

Dr. Fukui: Osaka City University, 1-4-3 Asahi-machi, Abeno-ku, Osaka 545-8585, Japan.

Dr. Tamakoshi: Nagoya University, 65 Tsurumai-cho, Showa-ku, Nagoya, Aichi 466-8550, Japan.

Author Contributions: Conception and design: H. Iso.

Analysis and interpretation of the data: H. Iso.

Drafting of the article: H. Iso.

Critical revision of the article for important intellectual content: H. Iso, C. Date, K. Wakai, M. Fukui, A. Tamakoshi.

Final approval of the article: H. Iso, C. Date, K. Wakai, M. Fukui, A. Tamakoshi.

Provision of study materials or patients: The JACC Study Group.

Statistical expertise: H. Iso, K. Wakai, M. Fukui.

APPENDIX

The present members of the JACC Study Group and their affiliations are as follows: Dr. Akiko Tamakoshi (*Chair*), Nagoya University Graduate School of Medicine; Dr. Mitsuru Mori, Sapporo Medical University School of Medicine; Dr. Yutaka Motohashi, Akita University School of Medicine; Dr. Ichiro Tsuji, Tohoku University Graduate School of Medicine; Dr. Yosikazu Nakamura, Jichi Medical School; Dr. Hiroyasu Iso, Institute of Community Medicine, University of Tsukuba; Dr. Haruo Mikami, Chiba Cancer Center; Dr. Shuji Hashimoto, Fujita Health University School of Medicine; Dr. Yutaka Inaba, Jun-tendo University School of Medicine; Dr. Yoshiharu Hoshiyama, Showa University School of Medicine; Dr. Hiroshi Suzuki, Niigata University School of Medicine; Dr. Hiroyuki Shimizu, Gifu University School of Medicine; Dr. Hideaki Toyoshima, Nagoya University Graduate School of Medicine; Dr. Shinkan Toku-

dome, Nagoya City University Graduate School of Medicine; Dr. Yoshinori Ito, Fujita Health University School of Health Sciences; Dr. Shogo Kikuchi, Aichi Medical University School of Medicine; Dr. Akio Koizumi, Graduate School of Medicine and Faculty of Medicine, Kyoto University; Dr. Takashi Kawamura, Kyoto University Center for Student Health; Dr. Yoshiyuki Watanabe, Kyoto Prefectural University of Medicine, Research Institute for Neurological Diseases and Geriatrics; Dr. Tsuneharu Miki, Kyoto Prefectural University of Medicine; Dr. Chigusa Date, Faculty of Human Environmental Sciences, Mukogawa Women's University; Dr. Kiyomi Sakata, Wakayama Medical University; Dr. Takayuki Nose, Tottori University Faculty of Medicine; Dr. Norihiko Hayakawa, Research Institute for Radiation Biology and Medicine, Hiroshima University; Dr. Taksumi Yoshimura, Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health, Japan; Dr. Katsuhiko Fukuda, Kurume University School of Medicine; Dr. Naoyuki Okamoto, Kanagawa Cancer Center; Dr. Hideo Shio, Shiga Medical Center; Dr. Yoshiyuki Ohno, Nagoya University Graduate School of Medicine; Dr. Tomoyuki Kitagawa, Cancer Institute of the Japanese Foundation for Cancer Research; Dr. Toshio Kuroki, Gifu University; and Dr. Kazuo Tajima, Aichi Cancer Center Research Institute.

The past investigators of the study group are listed in reference 22 except for the following members (affiliations listed are those where the investigators participated in the study): Dr. Takashi Shimamoto, Institute of Community Medicine, University of Tsukuba; Dr. Heizo Tanaka, Medical Research Institute, Tokyo Medical and Dental University; Dr. Shigeru Hisamichi, Tohoku University Graduate School of Medicine; Dr. Masahiro Nakao, Kyoto Prefectural University of Medicine; Dr. Takachiro Suzuki, Research Institute, Osaka Medical Center for Cancer and Cardiovascular Diseases; Dr. Tsutomu Hashimoto, Wakayama Medical University; and Dr. Teruo Ishibashi, Asama General Hospital.