Green Tea Consumption and the Risk of Incident Dementia in Elderly Japanese: The Ohsaki Cohort 2006 Study

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Objective: *Biologic studies have shown that certain components of green tea may have protective effects on neurocognition. However, because of the lack of human epidemiologic studies, the impact of green tea consumption on the incidence of dementia has never been confirmed. The objective of this cohort study was to clarify the association between green tea consumption and incident dementia.* **Methods:** *In this 5.7-year prospective cohort study, using a questionnaire, information on daily green tea consumption and other lifestyle factors was collected from elderly Japanese individuals aged 65 years or more. Data on incident dementia were retrieved from the public Long-term Care Insurance Database.* **Results:** *Among 13,645 participants, the 5.7-year rate of incident dementia was 8.7%. More frequent green tea consumption was associated with a lower risk of incident dementia (hazard ratio for ≥5 cups/day versus <1 cup/day: 0.73; 95% confidence interval: 0.61–0.87). The lower risk of incident dementia was consistent even after selecting participants who did not have subjective memory complaints at the baseline.* **Conclusion:** *Green tea consumption is significantly associated with a lower risk of incident dementia.* (Am J Geriatr Psychiatry 2016; 24:881–889)

Key Words: Green tea, dementia, elderly, cohort study

INTRODUCTION

Tea is a beverage widely consumed around the world.[1] Because of the high rates of tea consumption by the global population, even small effects of this daily habit on an individual could have a large impact on public health. Tea is generally consumed in the form of green, oolong, or black tea, although all originate from the leaves of *Camellia sinensis*. In Japan and other Asian countries, green tea is a popular beverage, whereas black tea is popular in Western countries.

Among the various types of tea, green tea and the polyphenols it contains have been extensively studied in connection with the prevention of neurodegenerative diseases, notably Alzheimer disease.[2,3] Although

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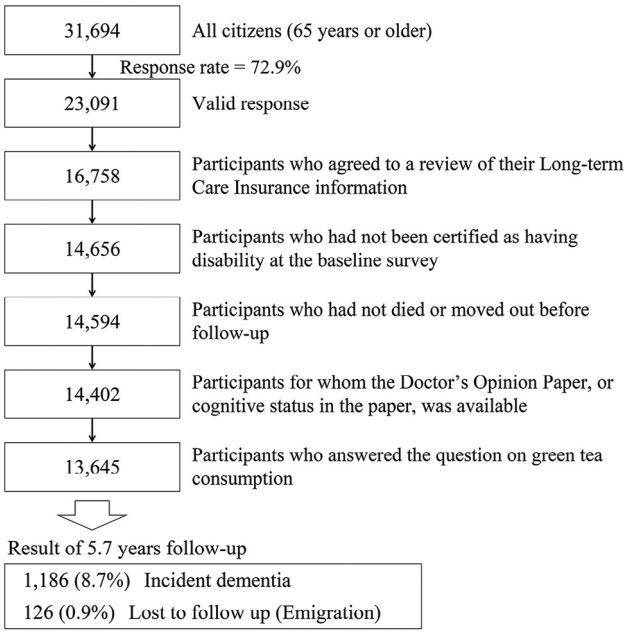
http://dx.doi.org/10.1016/j.jagp.2016.07.009

substantial evidence from in vitro and animal studies has indicated that green tea preparations exert neuroprotective activities, the possible preventive effect of green tea consumption against incident dementia in humans has remained unclear because of the paucity of epidemiologic studies. To date, only two prospective studies have been reported, and their results were not consistent: One study found that higher green tea consumption was associated with a lower risk of cognitive decline, whereas the other produced results that were not statistically significant.[4,5] In addition, both studies had a small sample size. Therefore, there is a need for a prospective study based on a larger sample. The aim of the present analysis was to clarify the association between green tea consumption and incident dementia.

FIGURE 1. Flowchart of study participants.



METHODS

Study Cohort

The design of the Ohsaki Cohort 2006 Study has been described in detail elsewhere.[6] In brief, the study subjects for the baseline survey comprised all older citizen residents in Ohsaki City, Miyagi Prefecture, northeastern Japan, on December 1, 2006: 31,694 men and women aged 65 years or older. The survey included questions about recent average consumption of tea (green tea, oolong tea, black tea) and 35 food items, as well as history of disease, blood pressure, education level, smoking, alcohol drinking, body weight, height, psychological distress score, time spent walking per day, social support, participation in community activities, motor function score, and cognitive function score.

The baseline survey was conducted between December 1 and December 15, 2006, and the follow-up survey was conducted between April 1, 2007 and November 30, 2012. A questionnaire was distributed by the heads of individual administrative districts and then collected by mail. Figure 1 shows the flowchart for study participation. For this analysis, 23,091 individuals who provided valid responses formed the study cohort. We excluded 6,333 individuals who did not provide written consent for review of their Long-term Care Insurance (LTCI) information, 2,102 persons who had already been certified as having a disability by the LTCI before the starting date of follow-up (March 30, 2007), 62 persons who had died or moved before the starting date of follow-up, 188 persons for whom the Doctor's Opinion Paper had been unavailable, 4 persons for whom the cognitive status entry on the Doctor's Opinion Paper had been left blank, and 757 persons who missed answering the questions on green tea consumption. Thus, 13,645 responses were analyzed for the purpose of this study.

Tea and Other Food Consumption

We asked about the consumption of tea and other food items using a food-frequency questionnaire (FFQ). The frequency of beverage consumption (green tea, oolong tea, black tea, coffee) was categorized as never, occasionally, or 1–2, 3–4, or 5 cups/day. Within the study region the volume of a typical cup of green tea is 100 mL.

We conducted a validation study of the FFQ in which 113 respondents provided four 3-day food records within 1 year and subsequently responded to the questionnaire; these data were used to develop a method for calculating food and nutrient intake from the FFQ. The Spearman rank correlation coefficient between green tea consumption according to the questionnaire

and that according to the food records was 0.71 for men and 0.53 for women; the correlation between consumption measured by the two questionnaires administered 1 year apart was 0.63 for men and 0.64 for women.[7]

The Spearman rank coefficient for the correlation between consumption of other beverages consumption according to the FFQ and that according to the food records for black tea was 0.25 among men and 0.32 among women, that for Chinese tea was 0.20 among men and 0.03 among women, and that for coffee was 0.07 among men and 0.27 among women.[7] For other covariates, the volume of consumption for green and yellow vegetables and fruit was calculated based on a previous study.[7] The Spearman rank correlation coefficient for records of green and yellow vegetable consumption was 0.54 among men and 0.44 among women and that for fruit was 0.76 among men and 0.70 among women. For energy intake, the Spearman rank correlation coefficient between the value calculated using the FFQ and the food records was 0.55 among men and 0.36 among women.

Covariates

Body mass index was calculated as the self-reported body weight (in kilograms) divided by the square of the self-reported body height (in meters). The K6 was used as an indicator of psychological distress.[8,9] Using six questions, respondents were asked about their mental status over the last month. Total point scores ranged from 0 to 24. As the optimal cut-off point for mental illness in the validation study, we classified individuals with scores ≥ 13 as having psychological distress.[9]

The degree of social support available to each individual was assessed by a social support questionnaire consisting of 5 questions, each requiring a "yes" or "no" answer:[10] Do you have someone (1) with whom you can talk when you are in trouble, (2) whom you can consult when you do not feel well, (3) who can help you with your daily housework, (4) who can take you to a hospital when you feel ill, and (5) who can take care of you if you become bedridden? This questionnaire was available only in Japanese. A validation study reported that the persons who responded "yes" had a higher average score on the Lubben Social Network Scale for each of these items.[11] We also assessed participation in community activities. We asked about how often each respondent participated in the following activities: neighborhood associations; sports, exercise, or hobbies; volunteering for activities related to nonprofit organizations; and any other type of social gatherings. The frequency of these activities was assessed as never, a few times each year, monthly, 2–3 times a month, once a week, 2–3 times a week, and 4 times a week.

The Kihon Checklist was developed by the Ministry of Health, Labour, and Welfare of Japan to predict functional decline in community-dwelling elderly. With regard to the motor function score in the Kihon Checklist, respondents were asked about their current motor function status by using five binary questions, yielding total point scores ranging from 0 to 5. As the optimal cut-off point for functional decline suggested in the validation study, we classified individuals with scores < 3 as having better motor function.[12] With regard to the Cognitive function score in the Kihon Checklist, respondents were asked about their current subjective memory complaints by using three binary questions yielding total point scores ranging from 0 to 3. The validity of the Cognitive function score in the Kihon Checklist had been confirmed in a previous study using the Clinical Dementia Rating as a gold standard.[13]

Follow-Up (Incident Dementia)

The primary outcome was incident dementia, defined as disabling dementia according to the criteria of the LTCI system used in Japan.[14] The LTCI is a mandatory form of national social insurance to assist daily activity in the disabled elderly.[15–17] Everyone aged 40 years and older pays premiums, and everyone aged 65 years and older is eligible for formal caregiving services under a uniform standard of disability certification. The procedure for disability certification comprises two parts: assessment of the degree of functional disability using a questionnaire developed by the Ministry of Health, Labour, and Welfare and reference to the Doctor's Opinion Paper prepared by the attending physician.[18] The Doctor's Opinion Paper is a standard form used for assessing patients' chronic medical conditions and functions of daily life.

Disabling dementia was defined as incident functional disability with dementia according to the LTCI system, whereby the dementia exceeded rank I (rank ≥ II) on the Dementia Scale (Degree of Independence in Daily Living for Elderly with Dementia), as

entered on the Doctor's Opinion Paper. The Dementia Scale is classified into six ranks: 0, I–IV, and M. Rank M means that an individual has severe dementia-related behavioral disturbance that requires medical intervention, and a rank exceeding I is typically used as an outcome measure of incident dementia because individuals who have mild or moderate dementia are classified as rank II.[14,19–21] A previous study has shown that the Dementia Scale is well correlated with the Mini-Mental State Exam score (Spearman rank correlation coefficient: –0.736).[22] Additionally, another study has also suggested that the Dementia Scale well reflects dementia as classified by the Clinical Dementia Rating.[21]

We obtained a dataset that included information on LTCI certification, death, or emigration from Ohsaki City based on an agreement. All data were transferred from the Ohsaki City Government under an agreement related to Epidemiologic Research and Privacy Protection.

Ethical Issues

We considered the return of completed questionnaires to imply consent to participate in the study involving the baseline survey data and subsequent follow-up of death and emigration. We also confirmed information regarding LTCI certification status after obtaining written consent along with the questionnaires returned from the subjects at the time of the baseline survey. The Ethics Committee of Tohoku University Graduate School of Medicine (Sendai, Japan) reviewed and approved the study protocol.

Statistical Analysis

We counted the person-years of follow-up for each subject from April 1, 2007 until the date of incident dementia, date of emigration from Ohsaki City, date of death, incident functional disability without dementia, or the end of the study period (November 30, 2012), whichever occurred first. In our analysis, deaths without LTCI certification were treated as censored.

We used the multiple adjusted Cox proportional hazards model to calculate the hazard ratios (HRs) and 95% confidence intervals (CIs) for incident dementia according green tea consumption. Dummy variables were created for the groups of green tea consumption, and respondents who consumed less than 1 cup/day (lowest) were defined as a reference category. To test for linear trends, the green tea consumption categories were entered as a continuous term (score varying from <1 cup/day to ≥5 cups/day: 1, 2, 3, or 4) in the corresponding Cox model. Multivariate models were adjusted for the following variables. Model 1 was sex- and age-adjusted (65–69, 70–74, 75–79, 80–84, or 85 years). To examine whether the association between green tea consumption and dementia was attributable to a healthy physical status or other lifestyle factors known to be modifiable risk factors,[23,24] Model 2 was further adjusted for history of disease (stroke, myocardial infarction, hypertension [individuals with a self-measured systolic blood pressure ≥ 140 mm Hg or a diastolic blood pressure ≥ 90 mm Hg were also defined as hypertensive], diabetes, arthritis, osteoporosis and fracture: yes or no), education level (age at last school graduation: < 16, 16–18, ≥19 years, or missing), smoking (never, former, current, or missing), alcohol drinking (never, former, current, or missing), body mass index (in kg/m^2; <18.5, 18.5–24.9, ≥25.0, or missing), psychological distress score (<13, ≥13, or missing), time spent walking (<30 min/day, 30 min to 1 h/day, ≥1 h/day, or missing), social support (whether a subject perceived that he or she had support for all five categories), participation in community activities (whether a subject participated in any of four categories), motor function score (<3, ≥3, or missing), consumption volume of specific foods (green and yellow vegetables and fruit [sex-specific tertile categories, or missing]), coffee consumption (<1, 1–2, 3–4, or ≥5 cups a day or missing), and energy intake (sex-specific decile categories, or missing). Interaction between green tea consumption and sex was tested by addition of cross-product terms to the multivariate model.

We also conducted sensitivity analyses that selected only individuals who had no subjective memory complaints assumed as better cognitive function at the baseline. In this sensitivity analysis, "Cognitive function score in the Kihon Checklist = 0 points" was defined as better cognitive function.

We also analyzed the consumption of oolong tea and black tea as independent variables. In the analyses for oolong tea or black tea as a main exposure, persons with missing data were excluded (11,097 for oolong tea and 11,183 for black tea).

All data were analyzed using SAS version 9.4 (SAS Inc., Cary, NC). All statistical tests described here were two-sided, and differences at $p < 0.05$ were accepted as significant.

RESULTS

Subject Characteristics

The study subjects comprised 6,030 men (44.2%) and 7,615 women (55.8%), with a mean (standard deviation) age of 73.8 (5.9) years. During the 5.7-year study period, only 126 individuals were lost to follow-up because they moved away from the study area; thus, the follow-up rate was 99.1%. From the resulting 67,551 person-years, incident dementia was determined in 1,186 persons (8.7%).

Table 1 compares the characteristics of participants according to the green tea consumption groups. Subjects who consumed larger amounts of green tea were less likely to be men, to suffer from psychological distress, to have less than 16 years of education, to be current smokers, to be current alcohol drinkers, and to have a history of stroke or myocardial infarction. Subjects who consumed larger amounts of green tea were

TABLE 1. Baseline Characteristics According to the Green Tea Consumption Groups (N = 13,645)

	Green Tea Consumption				
	<1 Cup/Day (N = 2,234)	1–2 Cups/Day (N = 3,059)	3–4 Cups/Day (N = 3,890)	≥5 Cups/Day (N = 4,462)	Significance[a]
Male sex, %	56.9	49.0	42.5	H = 36.0	$\chi^2_{(1)} = 297.97, p < 0.001$
Age,[b] years	73.5 ± 6.0	73.7 ± 6.0	73.8 ± 5.8	73.9 ± 5.7	$F_{(1,13641)} = 8.11, p = 0.004$
Body mass index, kg/m^2	23.7 ± 3.8	23.6 ± 3.4	23.6 ± 3.2	23.6 ± 3.2	$F_{(1,11818)} = 1.16, p = 0.282$
Psychological distress,[c] %	6.5	4.6	4.1	3.9	$\chi^2_{(1)} = 17.73, p < 0.001$
Education level < 16 years, %	34.7	30.9	26.2	27.8	$\chi^2_{(1)} = 36.89, p < 0.001$
Past history, %					
Stroke	4.1	3.3	2.4	2.0	$\chi^2_{(1)} = 28.21, p < 0.001$
Myocardial infarction	5.9	5.0	5.0	4.1	$\chi^2_{(1)} = 9.93, p = 0.002$
Hypertension	43.2	44.2	44.0	43.1	$\chi^2_{(1)} = 0.15, p = 0.696$
Diabetes	12.1	12.0	11.9	11.5	$\chi^2_{(1)} = 0.76, p = 0.382$
Arthritis	14.2	15.0	15.9	17.3	$\chi^2_{(1)} = 13.24, p < 0.001$
Osteoporosis	9.8	10.2	11.2	11.3	$\chi^2_{(1)} = 4.90, p = 0.027$
Fracture	16.0	16.7	15.8	15.0	$\chi^2_{(1)} = 2.48, p = 0.115$
Cancer	8.5	7.9	9.0	8.4	$\chi^2_{(1)} = 0.19, p = 0.666$
Current smoker, %	18.5	14.2	11.4	11.5	$\chi^2_{(1)} = 57.85, p < 0.001$
Current alcohol drinker, %	44.6	40.4	37.1	33.0	$\chi^2_{(1)} = 88.78, p < 0.001$
Social support, %					
To consult when you are in trouble	85.4	89.3	91.5	92.9	$\chi^2_{(1)} = 98.33, p < 0.001$
To consult when you are in poor physical condition	91.2	93.9	94.1	95.2	$\chi^2_{(1)} = 33.39, p < 0.001$
To help with your daily housework	82.8	85.1	86.3	86.9	$\chi^2_{(1)} = 20.34, p < 0.001$
To take you to a hospital	90.3	92.8	93.3	93.7	$\chi^2_{(1)} = 21.82, p < 0.001$
To take care of you	85.0	88.0	87.0	86.9	$\chi^2_{(1)} = 1.30, p = 0.255$
Participation in community activities, %					
Activities in neighborhood association	42.1	49.5	51.3	51.1	$\chi^2_{(1)} = 35.01, p < 0.001$
Sports or exercise	40.6	48.4	49.7	50.7	$\chi^2_{(1)} = 45.14, p < 0.001$
Volunteering	29.0	32.8	34.1	34.2	$\chi^2_{(1)} = 14.04, p < 0.001$
Social gathering	41.7	49.8	53.0	53.5	$\chi^2_{(1)} = 65.28, p < 0.001$
Time spent walking ≥1 hour/day, %	26.1	27.5	27.1	29.1	$\chi^2_{(1)} = 6.12, p = 0.013$
Better motor function,[d] %	77.2	77.2	79.7	80.4	$\chi^2_{(1)} = 14.24, p < 0.001$
Better cognitive function,[e] %	56.5	61.7	65.1	66.5	$\chi^2_{(1)} = 65.91, p < 0.001$
Intake, g/day					
Green and yellow vegetables	79.8 ± 46.1	89.7 ± 47.3	96.2 ± 45.9	105.4 ± 47.3	$F_{(1,11466)} = 401.88, p < 0.001$
Fruit	114.5 ± 89.5	132.4 ± 91.8	145.7 ± 90.7	160.6 ± 91.7	$F_{(1,11663)} = 359.21, p < 0.001$
Coffee consumption < 1 cup/day, %	49.6	39.8	47.9	55.1	$\chi^2_{(1)} = 62.31, p < 0.001$
Energy intake,[f] kcal/day	1359 ± 419	1406 ± 417	1447 ± 393	1496 ± 374	$F_{(1,6836)} = 99.33, p < 0.001$

Notes: [a]Probability values for trend were calculated by the Mantel-Haenszel χ^2 test for variables of proportion and by ANOVA (linear contrast) for continuous variables.
[b]Mean ± standard deviation for all such values.
[c]Kessler 6-item psychological distress scale score ≥ 13.
[d]Motor function score of the Kihon Checklist < 3.
[e]Cognitive function score of the Kihon Checklist = 0.
[f]Except energy intake from alcohol drinking.

more likely to have a better perception of support in all five social support categories, to show greater participation in the four community activity categories, to walk at least 1 hour/day, to have better motor function, to have better cognitive function, and to consume greater amounts of green and yellow vegetables, or fruits.

Green Tea Consumption and Incident Dementia

The association between green tea consumption and incident dementia is shown in Table 2, along with the HRs and associated 95% CIs. Even with the addition of some adjustment items, we found that green tea consumption was inversely associated with incident dementia. This inverse association did not differ significantly between the sexes (Wald χ^2 of interaction term: 0.01 [df = 1]; p-interaction = 0.929 in Model 2; table not shown).

To consider the possibility that cognitive function at the baseline might affect the association between green tea consumption and incident dementia, we also analyzed the association after selecting 8,416 participants who did not have subjective memory complaints (Cognitive function score of the Kihon Checklist: 0). However, the results for green tea consumption did not change substantially; the multivariate HRs (Model 2) were 1.00 (reference) for less than 1 cup/day, 0.99 (95% CI: 0.74–1.34) for 1–2 cups/day, 0.93 (95% CI: 0.70–1.24) for 3–4 cups/day, and 0.68 (95% CI: 0.50–0.92) for at least 5 cups/day (Wald $\chi^2 = 8.32$ [df = 1], p-trend = 0.004 in Model 2; table not shown).

To examine possible reverse causality for the association between green tea consumption and incident dementia, we also analyzed the association after excluding 347 participants who developed incident dementia in the first 2 years of follow-up, but the results for green tea consumption did not change substantially. The multivariate HRs (Model 2) were 1.00 (reference) for <1 cup/day, 1.03 (95% CI: 0.83–1.27) for 1–2 cups/day, 0.90 (95% CI: 0.73–1.11) for 3–4 cups/day, and 0.74 (95% CI: 0.59–0.91) for at least 5 cups/day (Wald $\chi^2 = 10.97$ [df = 1], p-trend < 0.001 in Model 2) (table not shown).

Consumption of Other Tea Types and Incident Dementia

The HRs for incident dementia according to the frequency of consumption of other tea types (oolong tea and black tea) are compared in Table 3. Although the HRs of the groups showing highest consumption of oolong tea and black tea tended to be lower than the reference group, especially in the age- and sex-adjusted models, no significant associations were observed in the multiple-adjusted models.

Sensitivity Analysis

We also conducted sensitivity analyses using consumption of green tea, oolong tea, and black tea in a simultaneous set as an independent variable to adjust for consumption of each tea type. In this analysis, persons for whom any data for any tea variable were

TABLE 2. Association Between Green Tea Consumption and Incident Dementia (N = 13,645)

	Sample Size	Events	HR (95% CI)[a]	
			Model 1[b]	Model 2[c]
Green tea				
<1 cup/day	2,234	222	1 (Reference)	1 (Reference)
1–2 cups/day	3,059	307	0.94 (0.79–1.11)	1.06 (0.89–1.27)
3–4 cups/day	3,890	334	0.74 (0.63–0.88)	0.88 (0.74–1.04)
≥5 cups/day	4,462	323	0.60 (0.51–0.72)	0.73 (0.61–0.87)
p-Trend[d]			<0.001 ($\chi^2_{[1]} = 43.71$)	<0.001 ($\chi^2_{[1]} = 18.60$)

Notes: [a]HRs (95% CIs) were estimated using Cox proportional hazards model.
[b]Model 1 was adjusted for age (65–69, 70–74, 75–79, 80–84, or 85 years) and sex.
[c]Model 2 was adjusted as for Model 1 plus history of disease (stroke, myocardial infarction, hypertension, diabetes, arthritis, osteoporosis, or fracture), education level, smoking, alcohol drinking, body mass index, psychological distress score, time spent walking, social support, participation in community activities, motor function score, consumption volume of specific foods (green and yellow vegetables and fruit), coffee consumption, and energy intake.
[d]Probability value for trend (Wald χ^2 value) was computed by entering the categories as a continuous term (score variable: 1, 2, 3, 4) in the Cox model.

TABLE 3. Association Between Consumption of Other Tea Types and Incident Dementia

	Sample Size	Events	HR (95% CI)[a] Model 1[b]	HR (95% CI)[a] Model 2[c]
Oolong tea (Chinese tea)				
<1 cup/day	10,239	842	1 (Reference)	1 (Reference)
1–2 cups/day	491	25	0.67 (0.45–0.99)	0.69 (0.46–1.04)
3–4 cups/day	219	16	0.89 (0.54–1.45)	1.03 (0.62–1.72)
≥5 cups/day	148	9	0.69 (0.36–1.34)	0.68 (0.34–1.35)
p-Trend[d]			0.071 ($\chi^2_{[1]}$ = 3.26)	0.180 ($\chi^2_{[1]}$ = 1.80)
Black tea				
<1 cup/day	10,157	820	1 (Reference)	1 (Reference)
1–2 cups/day	772	63	1.05 (0.81–1.35)	1.05 (0.80–1.39)
3–4 cups/day	188	17	0.98 (0.61–1.59)	1.13 (0.68–1.87)
≥5 cups/day	66	5	0.83 (0.34–1.99)	0.71 (0.28–1.79)
p-Trend[d]			0.932 ($\chi^2_{[1]}$ = 0.01)	0.967 ($\chi^2_{[1]}$ = 0.002)

Notes: [a]HRs and 95% CIs were estimated using Cox proportional hazards model.
[b]Adjusted for Model 1 in Table 2.
[c]Adjusted for Model 2 in Table 2.
[d]Probability value for trend (Wald χ^2 value) was computed by entering the categories as a continuous term (score variable: 1, 2, 3, 4) in the Cox model.

missing were excluded. Even when the three tea variables (green tea, oolong tea, and black tea) were set as exposure variables at the same time, we also found that only green tea consumption was inversely associated with incident dementia (Table 4).

TABLE 4. Sensitivity Analysis of the Association Between Tea and Incident Dementia: Simultaneous Input of All Three Tea Variables (N = 10,642)

	HR (95% CI)[a] Model 1[b]	HR (95% CI)[a] Model 2[c]
Green tea		
<1 cup/day	1 (Reference)	1 (Reference)
1–2 cups/day	0.93 (0.76–1.14)	1.09 (0.89–1.34)
3–4 cups/day	0.69 (0.57–0.84)	0.84 (0.68–1.03)
≥5 cups/day	0.59 (0.48–0.72)	0.76 (0.61–0.93)
p-Trend[d]	<0.001 ($\chi^2_{[1]}$ = 36.58)	<0.001 ($\chi^2_{[1]}$ = 12.00)
Oolong tea (Chinese tea)		
<1 cup/day	1 (Reference)	1 (Reference)
1–2 cups/day	0.59 (0.37–0.92)	0.58 (0.36–0.93)
3–4 cups/day	0.97 (0.57–1.66)	1.16 (0.66–2.03)
≥5 cups/day	0.86 (0.41–1.79)	0.94 (0.43–2.06)
p-Trend[d]	0.213 ($\chi^2_{[1]}$ = 1.55)	0.401 ($\chi^2_{[1]}$ = 0.71)
Black tea		
<1 cup/day	1 (Reference)	1 (Reference)
1–2 cups/day	1.09 (0.81–1.47)	1.13 (0.83–1.55)
3–4 cups/day	0.98 (0.54–1.79)	1.04 (0.55–1.97)
≥5 cups/day	1.06 (0.35–3.20)	0.70 (0.21–2.37)
p-Trend[d]	0.759 ($\chi^2_{[1]}$ = 0.09)	0.762 ($\chi^2_{[1]}$ = 0.09)

Notes: [a]HRs and 95% CIs were estimated using Cox proportional hazards model.
[b]Adjusted for Model 1 in Table 2.
[c]Adjusted for Model 2 in Table 2.
[d]Probability value for trend (Wald χ^2 value) was computed by entering the categories as a continuous term (score variable: 1, 2, 3, 4) in the Cox model.

DISCUSSION

In this cohort study we investigated the association between green tea consumption and incident dementia. We found significant inverse associations between green tea consumption and incident dementia. The lower risk of incident dementia was consistent even after selecting participants who did not have subjective memory complaints, assumed to have better cognitive function at the baseline. Our study had a number of strengths: (1) it was a large cohort study of 13,645 persons, (2) it had a follow-up rate of almost 100%, (3) many confounding factors were taken into account, and (4) the study subjects lived in an area in which green tea is widely consumed.

Because any individual who already has weaker cognitive function might not tend to consume green tea, we also considered the effects of reverse causality. However, even after excluding individuals who developed incident dementia in the first 2 years of follow-up, the HRs for each category were almost the same as those before exclusion, and the inverse association between green tea consumption and incident dementia persisted. These findings suggest that the present results are unlikely to be attributable to reverse causality.

In contrast to green tea, we observed nonsignificant associations between oolong tea and black tea and incident dementia, which were consistent with previous epidemiologic studies.[4,25] This discrepancy among beverages suggests that the effect of green tea might be attributable to a unique component of green tea. As compared with black tea and oolong tea, green tea contains a large amount of polyphenols such as green tea catechin (epigallocatechin gallate [ECGC]), which would be expected to exert a neuroprotective action through antioxidant activity, activation of protein kinase C, iron chelation, and so on.[2] The levels of ECGC were highest in green tea, followed in order by oolong tea and black tea.[26] Although green tea also contains a certain amount of caffeine, which is expected to have a protective role against dementia,[27] the levels of caffeine were highest in black tea, followed in order by oolong tea and green tea.[26] In the present study, the inverse association with incident dementia tended to be stronger for teas with a higher content of ECGC (i.e., green tea > oolong tea > black tea). Therefore, the present result is consistent with the interpretation that one of the active ingredients of green tea is ECGC. One randomized controlled trial based on 12 healthy young adults indicated that green tea extract had a beneficial effect on working memory processing as a component of cognitive function.[28] Another randomized controlled trial based on 91 older persons with pre-existing mild cognitive impairment indicated that a combination of green tea extract and L-theanine marginally improved the Rey Auditory Verbal Learning Test score.[29] Although these studies were not based on incident dementia as an outcome, these results also suggested a preventive effect of green tea against incident dementia. Further clinical trials are necessary to confirm this preventive effect of green tea extract.

This study had several limitations. First, we did not evaluate the causes of dementia, for example Alzheimer disease or vascular dementia. Thus, the mechanism responsible for dementia reduction by green tea consumption remained unidentified. Second, because we did not consider information about clinical diagnosis of dementia, some misclassification of incident dementia might have occurred. If there was much nondifferential misclassification, the results of the present study would have been underestimated.[30,31] Third, information on green tea consumption using the FFQ was obtained only at the baseline. Thus, the study subjects might have changed their consumption of green tea during the course of follow-up. Fourth, not all potential confounding factors were considered. In particular, it cannot be ruled out that residual confounding of dietary factors existed, because our FFQ data could not fully consider diet quality such as total antioxidant intake.[32,33] Motor and cognitive function at the baseline might also have been a residual confounding factor, because we used only self-reported data about these factors. Fifth, because not all candidates applied for LTCI certification, this study may not have been completely free from detection bias of the outcome measure. However, the significant inverse relationship persisted even when the Cox proportional hazards model was changed to competing-risks regression for considering the competing risk of death (p-trend <0.001 in Model 2; data not shown). The significant inverse relationship also persisted even when competing-risks regression was used for considering the competing risk of any other type of disability or death (p-trend = 0.002 in Model 2; data not shown). Therefore, it seems unlikely that the main result of this study was affected by detection bias.

In conclusion, this study has shown that green tea consumption is associated with a decreased risk of incident dementia in Japanese elderly individuals. This suggests that green tea consumption may have a preventive effect against dementia.

The authors thank Yoshiko Nakata, Yumi Tamura, Yukiko Asano, and Mami Takahashi for their technical assistance.

This study was supported by Health Sciences Research grants (nos. H24-Choju-Ippan-005) from the Ministry of Health, Labour and Welfare, Japan and a Grant-in-Aid for Young Scientists (B; 15K16201) from the Japan Society for the Promotion of Science. None of the funding organizations or sponsors was involved in the study design; in collection, analysis, or interpretation of data; in writing the report; and in making decision to submit the article for publication. The authors have no disclosures to report.

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