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Green Tea Consumption and Mortality among Japanese Elderly People: The Prospective Shizuoka Elderly Cohort

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PURPOSE: To investigate the association between green tea consumption and mortality from all causes, cancer, and cardiovascular disease (CVD) among elderly people.
METHODS: In a population-based, prospective cohort study, a total of 14,001 elderly residents (aged 65–84 years), randomly chosen from all 74 municipalities in Shizuoka, Japan, completed questionnaires that included items about frequency of green tea consumption. They were followed for up to 6 years, from December 1999 to March 2006. Consequently, 12,251 subjects were analyzed to estimate the hazard ratios (HRs) for all-cause mortality, cancer, and CVD.
RESULTS: Among 64,002 person-years, 1,224 deaths were identified (follow-up rate, 71.6%). The multivariate HRs and 95% confidence intervals (CIs) for CVD mortality compared those who consumed seven or more cups per day with those who consumed less than one cup per day, were 0.24 (0.14–0.40), 0.30 (0.15–0.61), and 0.18 (0.08–0.40) for total participants, men, and women, respectively. Although green tea consumption was not inversely associated with cancer mortality, green tea consumption and colorectal cancer mortality were inversely associated with a moderate dose-response relationship.
CONCLUSIONS: Green tea consumption is associated with reduced mortality from all causes and CVD. This study also suggests that green tea could have protective effects against colorectal cancer.
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KEY WORDS: Aged, Cohort Studies, Japan, Prospective Studies, Tea.

INTRODUCTION

Green tea has been extensively studied for its potential preventive and therapeutic roles, especially for cardiovascular disease (CVD) and cancer (1, 2). In vitro and animal studies have provided strong evidence that tea polyphenols, including the catechins found predominantly in tea, may be sufficiently bioreactive to affect the pathogenesis of these chronic diseases (1–5). Epidemiological studies, however, have yielded inconsistent results concerning the associations between green tea and health, and thus, the effects of green tea remain unclear in humans (1, 2, 6–14).

In a recent cohort study in Miyagi, Japan (10), green tea consumption was shown to be associated with reduced all-cause mortality and CVD, but not with reduced mortality from cancer. One potential limitation of this study is the lack of a group which drank large amounts of green tea as the highest category only consumed five or more cups per day. This may have resulted in the moderate effects on reduced all-cause mortality and CVD as well as in the null association between green tea and cancer mortality (15). Furthermore, the associations were examined among subjects who were 40 to 79 years of age. However, these chronic diseases may have different etiology according to age, and these diseases are commonly observed among the elderly. Indeed, the possible benefits of green tea may be restricted to high intakes in high-risk populations (9, 16). Thus, it would be more appropriate to investigate the potential effects of green tea by targeting elderly people, who are expected to have consumed green tea for a longer period, since early childhood.

We therefore investigated the associations between green tea consumption and all-cause mortality and cancer, as well as CVD among the elderly in Shizuoka, which has the highest production of green tea leaves in Japan (17).

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Selected Abbreviations and Acronyms

CVD = cardiovascular disease
ICD = International Classification of Diseases
BMI = body mass index
HR = hazard ratio
CI = confidence interval

Furthermore, we examined the effects of green tea consumption on specific cancer mortalities.

METHODS

Participants

Individual data were extracted from the participants of the Shizuoka Elderly Cohort Study, an ongoing population-based, prospective cohort study in Shizuoka prefecture, an industrialized urban area in Japan. Shizuoka prefecture is located almost in the center of Japan and has an area of 7,780 km^2, a population of 3.8 million people, and 1.3 million households (18, 19). In December 1999, a total of 22,200 residents, who were stratified by both sex and age group (65 to 74; 75 to 84), were randomly chosen from all of the 74 municipalities in Shizuoka using random number lists. Then, the questionnaires were distributed to the subjects and returned from 14,001 residents (response rate: 63%). The self-administered questionnaire included the frequency of green tea consumption as well as age, sex, body weight, height, smoking habit, the frequency of alcohol consumption, past illness history (e.g., stroke, cancer, heart disease, hypertension, and diabetes), and other characteristics. The participants were followed up in December 2002 and March 2006 by using the same questionnaires. The 14,001 baseline respondents were defined as the Shizuoka cohort (Fig. 1).

We excluded participants without green tea consumption frequency data (n = 365); thus 13,636 subjects were eligible. Among these participants, 1,302 were lost to follow-up between 1999 and 2002, and 2,567 were lost between 2002 and 2006. Consequently, 8,460 survivors and 1,307 decedents were identified in March 2006. In the analyses, we excluded those who were lost to follow-up by December 2002 (n = 1,302), and those whose date of death was not available (n = 83). Those who were lost to follow-up between December 2002 and March 2006 were treated as censored at 3 years and included in the analyses. Consequently, a total of 12,251 subjects were analyzed in the present study.

Data Assessment

The frequency of green tea consumption during the past month was determined from the questionnaires at baseline

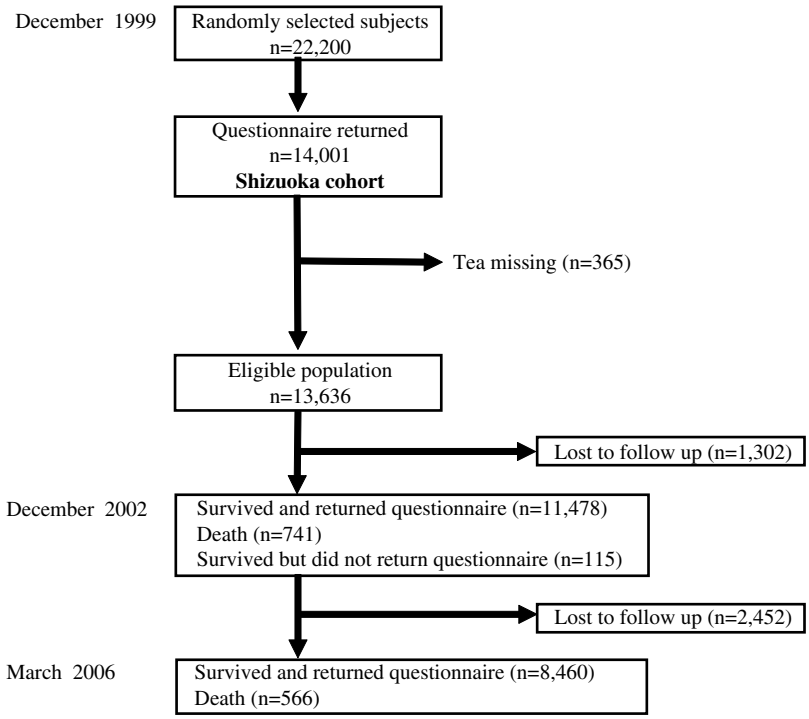

FIGURE 1. Flow diagram of participants in the Shizuoka Elderly Cohort study. Since we could not obtain the vital status of those who were lost to follow-up between 1999 and 2002, they were excluded from the analysis.

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from four predetermined categories: less than one cup per day, and one to three, four to six, and seven or more cups per day. Within the study region, the volume of a typical cup of green tea is 60 to 90 mL.

Identification of the causes of death of the deceased subjects was accomplished by record linkage of the cohort database with the National Vital Statistics Database from the Ministry of Health, Labour and Welfare of Japan, by matching birthday, sex, and residential area. The underlying causes of death were coded according to the *International Classification of Disease, Tenth Revision* (*ICD-10*). The numbers of deaths from all causes, cancer (*ICD-10* codes: C00–C97), CVD (*ICD-10* codes: I00–I99), gastric cancer (*ICD-10* code: C16), lung cancer (*ICD-10* codes: C33–C34), and colorectal cancer (*ICD-10* codes: C18–C21) were determined. Approval for this study was obtained from the Institutional Review Board of Okayama Graduate School of Medicine, Dentistry and Pharmaceutical Sciences on July 24, 2007 (No. 172).

We considered the following variables as potential confounders a priori: sex, age (continuous variable) at baseline, smoking status (never-, former-, and current smoker), habitual alcohol consumption (none or rarely, one to three times/week, four to six times/week, or everyday), body mass index (BMI), and the frequency of physical activity for more than 30 minutes (none, one to two times/week, three to four times/week, or five or more times/week). BMI was calculated as body weight in kilograms divided by height in square meters, and it was split into three parts (<20.5; 20.5–23.1; >23.1) to create dummy variables.

Statistical Analysis

For each study subject, person-years were counted from the baseline to the date of death, the date of censorship, or the end of the follow-up, whichever occurred first. Dummy variables were created for green tea consumption categories, and the lowest category (i.e., less than one cup per day) was used as a reference. Then, the age- and sex-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) of all causes and cause-specific mortality according to green tea consumption categories were estimated using the Cox proportional hazards model. Multivariate HRs were also estimated by including all the relevant confounders into the models. We conducted these analyses after stratifying on sex. To examine further the relationship of green tea consumption and cancer mortality, Cox proportional hazards regression analyses were conducted according to the specific cancer mortality. The analysis of linear trends was conducted by assigning the midrange scores of consumption categories (20), and HRs for an increased consumption of a cup of green tea were estimated. Regarding the uppermost, open-end category, the lower bound plus the width of the second-highest category was assigned (20). Furthermore, trend estimation analyses excluding the participants with the lowest category were also conducted to examine whether it is acceptable to use those who rarely consumed green tea as the reference (21).

To examine the possible effect-measure modifications, we performed a stratified analysis by smoking status (never/former vs. current). We also performed a stratified analysis for mortality from all causes, cancer, and CVD by dividing the follow-up period into the first and the second 3 years of follow-up. Furthermore, we also repeated all the analyses after excluding those who had died in the first 2 years of follow-up.

To enhance the precision of the estimates, we also conducted the analyses by using the participants who consumed one to three cups per day as the referent category. Furthermore, all the analyses were repeated after the data from the lower two categories were collapsed into the single category of three or less cups per day.

The Cox proportional hazards assumption was examined by visual inspection of log-log plots, with no violations detected. A p value of less than 0.05 (two-sided test) was considered statistically significant. SPSS 15.0 J (SPSS Inc., Chicago, IL) was used in the analysis.

RESULTS

The baseline characteristics of all the eligible subjects ($N = 13{,}636$) are shown according to the follow-up status in Table 1. The mean age of the participants was 74.3 years, 49.3% were women, and approximately 70% had never smoked. The proportions of subjects drinking less than one, one to three, four to six, and seven or more cups of green tea per day were 2.8%, 25.2%, 48.1%, and 23.9%, respectively. The deceased tended to be slightly older and were more likely to be men, smokers, and had sedentary life styles. Those who were lost to follow-up tended to consume alcohol slightly less and, compared with survivors, were more likely to be smokers and had a sedentary life style.

Table 2 shows the baseline characteristics of the analyzed subjects according to the green tea consumption categories. Those who consumed less than one cup per day tended to be men, smokers, and had a sedentary lifestyle.

Over the 6 years of follow-up, among 64,002 accrued person-years, a total of 1,224 deaths were identified with the information of the date of death (400 from cancer, and 405 from CVD). The follow-up rate was 71.6% with a mean follow-up of 5.2 years. Table 3 shows the association between green tea consumption and mortality from all causes, cancer, and CVD for the total participants and each sex. Green tea consumption and mortality from all causes and CVD were inversely associated. Regarding all-cause

TABLE 1. Baseline characteristics of all participants according to follow-up status, Shizuoka, Japan, 1999 to 2006

Baseline characteristics	Total subjects (N = 13,636)	Survivors (n = 8,460)	Decedents (n = 1,307)	Lost to follow-up: Censored during 2002–2006 (n = 2,567)	Lost to follow-up: Censored during 1999–2002 (n = 1,302)
Sex (%)					
Male	6,916 (50.7)	4,166 (49.2)	889 (68.0)	1,232 (48.0)	629 (48.3)
Female	6,720 (49.3)	4,294 (50.8)	418 (32.0)	1,335 (52.0)	673 (51.7)
Mean age, years (SD)	74.3 (5.4)	73.4 (5.3)	77.4 (5.0)	74.9 (5.5)	75.6 (5.4)
Mean BMI, kg/m^2 (SD)	21.8 (3.1)	22.1 (2.9)	20.8 (3.2)	21.7 (3.2)	21.6 (3.4)
Daily alcohol intake (%)					
None/rarely	9,069 (66.5)	5,468 (64.6)	897 (68.6)	1,808 (70.4)	896 (68.8)
1–3 times/wk	1,198 (8.8)	814 (9.6)	86 (6.6)	200 (7.8)	98 (7.5)
4–6 times/wk	692 (5.1)	475 (5.6)	52 (4.0)	118 (4.6)	47 (3.6)
Every day	2,420 (17.7)	1,561 (18.5)	249 (19.1)	396 (15.4)	214 (16.4)
Missing	257 (1.9)	142 (1.7)	23 (1.8)	45 (1.8)	47 (3.6)
Smoking status (%)					
Never	9,468 (69.4)	6,028 (71.3)	790 (60.4)	1,796 (70.0)	854 (65.6)
Former	1,581 (11.6)	967 (11.4)	210 (16.1)	275 (10.7)	129 (9.9)
Current	2,242 (16.4)	1,279 (15.1)	264 (20.2)	436 (17.0)	263 (20.2)
Missing	345 (2.5)	186 (2.2)	43 (3.3)	60 (2.3)	56 (4.3)
Physical activity (%)					
None	6,480 (47.5)	3,783 (44.7)	750 (57.4)	1,286 (50.1)	661 (50.8)
1–2 times/wk	2,392 (17.5)	1,587 (18.8)	173 (13.2)	431 (16.8)	201 (15.4)
3–4 times/wk	1,751 (12.8)	1,139 (13.5)	136 (10.4)	332 (12.9)	144 (11.1)
⩾ 5 times/wk	2,368 (17.4)	1,591 (18.8)	181 (13.8)	409 (15.9)	187 (14.4)
Missing	645 (4.7)	360 (4.3)	67 (5.1)	109 (4.2)	109 (8.4)
Green tea consumption (cups/day)					
< 1	376 (2.8)	170 (2.0)	66 (5.0)	89 (3.5)	51 (3.9)
1–3	3,432 (25.2)	1,899 (22.4)	404 (30.9)	712 (27.7)	417 (32.0)
4–6	6,563 (48.1)	4,202 (49.7)	589 (45.1)	1,207 (47.0)	565 (43.4)
⩾ 7	3,265 (23.9)	2,189 (25.9)	248 (19.0)	559 (21.8)	269 (20.7)

SD = standard deviation; BMI = body mass index.

mortality, 62 deaths were observed in 1,465 person-years (42.3 deaths per 1,000 person-years; 95% CI, 32.4–54.3) among those who consumed less than one cup per day, whereas 231 deaths were observed in 16,049 person-years (14.4 deaths per 1,000 person-years; 95% CI, 12.6–16.4) among those who consumed seven or more cups per day. Regarding CVD mortality, 25 deaths (17.1 deaths per 1,000 person-years; 95% CI, 11.0–25.2) and 51 deaths (3.2 deaths per 1,000 person-years; 95% CI, 2.4–4.2) were observed, respectively. Green tea consumption and mortality from cancer, however, were not inversely associated. Thirteen deaths from cancer (8.9 deaths per 1,000 person-years; 95% CI, 4.7–15.2) were observed among those who consumed less than one cup per day, whereas 106 deaths (6.6 deaths per 1,000 person-years; 95% CI, 5.4–8.0) were observed among those who consumed seven or more cups per day. After exclusion of the subjects with the lowest category, the HRs for trend analyses did not vary substantially (data not shown). When the lower two categories were collapsed, similar patterns were observed, and the precision of the estimates for cancer mortality among women was improved; the multivariate HRs and 95% CIs, compared with those subjects who consumed three or less cups per day, were 1.65 (0.89–3.06) for four to six cups per day, and 1.17 (0.55–2.46) for seven or more cups per day, respectively.

In the further analyses of specific cancer mortalities, the green tea consumption and colorectal cancer mortality (28 from colon, 15 from rectum) were inversely associated in the total participants, whereas no clear patterns were observed with gastric and lung cancer mortality (Table 4). When the lower two categories were collapsed, the inverse relationship between green tea and colorectal cancer mortality still remained; the multivariate HRs and 95% CIs, compared with those who consumed three or less cups per day, were 0.67 (0.30–1.49) for four to six cups per day, and 0.69 (0.27–1.79) for seven or more cups per day, respectively. Similar patterns were also observed when we restricted to colon cancer deaths.

The results of stratified analyses according to 3-year follow-up periods are shown in Table 5. The multivariate HRs for mortality from all causes and CVD tended to be further away from the null in the second 3-year follow-up. No substantial differences were observed in cancer mortality. When we stratified by smoking status, similar results were obtained among the never-/former-smokers (data not shown).

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TABLE 2. Baseline characteristics of all participants according to green tea consumption categories, Shizuoka, Japan, 1999 to 2006

	Green tea consumption, cups per day			
	<1 (*n* = 321)	1–3 (*n* = 2,981)	4–6 (*n* = 5,970)	⩾7 (*n* = 2,979)
Sex (%)				
Male	209 (65.1)	1,621 (54.4)	2,859 (47.9)	1,542 (51.8)
Female	112 (34.9)	1,360 (45.6)	3,111 (52.1)	1,437 (48.2)
Mean age, years (SD)	74.3 (5.6)	74.6 (5.5)	74.1 (5.4)	73.6 (5.3)
Mean BMI, kg/m^2 (SD)	21.5 (3.3)	21.8 (3.2)	21.9 (3.0)	21.9 (3.0)
Daily alcohol intake (%)				
None/rarely	222 (69.2)	1,946 (65.3)	3,983 (66.7)	1,960 (65.8)
1–3 times/wk	17 (5.3)	250 (8.4)	552 (9.2)	279 (9.4)
4–6 times/wk	16 (5.0)	149 (5.0)	314 (5.3)	160 (5.4)
Every day	64 (19.9)	573 (19.2)	1,019 (17.1)	538 (18.1)
Missing	2 (0.6)	63 (2.1)	102 (1.7)	42 (1.4)
Smoking status (%)				
Never	212 (66.0)	2,078 (69.7)	4,271 (71.5)	1,999 (67.1)
Former	39 (12.1)	347 (11.6)	697 (11.7)	359 (12.1)
Current	69 (21.5)	470 (15.8)	873 (14.6)	553 (18.6)
Missing	1 (0.3)	86 (2.9)	129 (2.2)	68 (2.3)
Physical activity (%)				
None	201 (62.6)	1,557 (52.2)	2,705 (45.3)	1,299 (43.6)
1–2 times/wk	36 (11.2)	485 (16.3)	1,125 (18.8)	541 (18.2)
3–4 times/wk	33 (10.3)	362 (12.1)	828 (13.9)	377 (12.7)
⩾ 5 times/wk	42 (13.1)	456 (15.3)	1,039 (17.4)	633 (21.2)
Missing	9 (2.8)	121 (4.1)	273 (4.6)	129 (4.3)

SD = standard deviation; BMI = body mass index.

When we used those who consumed one to three cups per day as the reference, the precision of the estimates moderately improved, and we reached the same conclusions (data not shown). When we excluded people who had died in the first 2 years of follow-up (140 from cancer, 167 from CVD) the results did not significantly change (data not shown).

DISCUSSION

The inverse associations between green tea and mortality were observed in an ongoing population-based, prospective cohort study among the elderly in Shizuoka prefecture, which has the highest production of green tea leaves in Japan (17). We found significant inverse associations between green tea consumption and mortality from all causes and CVD. Those who consumed seven or more cups per day, compared with those who consumed less than one cup per day, had a risk of all-cause and CVD mortality that was 55% lower and 75% lower, respectively. These inverse associations were observed in both sexes, and no substantial differences were observed. Although green tea consumption and mortality from cancer were not inversely associated, green tea consumption was associated with lower risk of colorectal cancer mortality with a moderate dose-response relationship.

While the findings that consumption of green tea is associated with lower risk of CVD mortality are consistent with past studies (10, 13, 14), the magnitude of the current associations are larger than the results of past studies in Japan. For example, Nakachi et al. (13) reported that those who consumed 10 or more cups per day, compared with those who consumed three or less cups per day, had a risk of CVD mortality that was 28% lower. And, in a recent study, Kuriyama et al. (10) reported that those who consumed five or more cups per day, compared with those who consumed less than one cup per day, had a risk of all-cause and CVD mortality that was 16% lower and 26% lower, respectively. The reason for larger differences in the present study may be the result of the participants' age. Whereas both studies included subjects older than 40 years, we restricted our subjects to those who were 65 to 84 years of age at baseline. Assuming that green tea consumption at the time of assessment is sufficiently representative of long-term, previous exposure to make a plausible link with the risk of mortality, the longer cumulative exposure to green tea may be responsible for the stronger effects of the present study. It is indeed likely that the current participants had consumed freshly brewed green tea for decades, even from their childhood, since family expenditure for tea leaves in the city of Shizuoka is highest in Japan (22). Another possible explanation is the differences in the amount of green tea leaves used to brew the drink and the frequency of renewing a tea batch in the urn (23).

To our knowledge, this is the first cohort study that shows the inverse association between green tea and colorectal cancer mortality (10, 13, 24–26). To date, only one cohort study among Chinese women reported that regular

TABLE 3. Hazard ratios for mortality from all causes, cancer, and cardiovascular disease by green tea consumption, Shizuoka, Japan, 1999 to 2006

	Green tea consumption, cups/day				
	<1	1–3	4–6	⩾7	Test for trend HR* (95% CI)
			Total participants		
Person-years	1,465	14,932	31,556	16,049	
All-cause mortality					
No. of deaths	62	370	561	231	
Age- and sex-adjusted HR (95% CI)	1.00	0.57 (0.44–0.75)	0.45 (0.34–0.58)	0.37 (0.28–0.49)	0.94 (0.92–0.96)
Multivariate HR† (95% CI)	1.00	0.63 (0.47–0.84)	0.50 (0.37–0.66)	0.42 (0.31–0.56)	0.94 (0.92–0.96)
Cancer mortality					
No. of deaths	13	85	196	106	
Age- and sex-adjusted HR (95% CI)	1.00	0.66 (0.37–1.19)	0.79 (0.45–1.39)	0.83 (0.47–1.47)	1.02 (0.99–1.05)
Multivariate HR† (95% CI)	1.00	0.63 (0.34–1.16)	0.76 (0.42–1.37)	0.82 (0.45–1.50)	1.02 (0.99–1.06)
Cardiovascular disease mortality					
No. of deaths	25	139	190	51	
Age- and sex-adjusted HR (95% CI)	1.00	0.52 (0.34–0.79)	0.36 (0.24–0.55)	0.20 (0.13–0.33)	0.88 (0.85–0.91)
Multivariate HR† (95% CI)	1.00	0.61 (0.39–0.98)	0.43 (0.27–0.67)	0.24 (0.14–0.40)	0.88 (0.84–0.92)
			Men		
Person-years	940	8,093	14,814	8,196	
All-cause mortality					
No. of deaths	45	244	369	175	
Age-adjusted HR (95% CI)	1.00	0.57 (0.41–0.78)	0.47 (0.35–0.64)	0.42 (0.30–0.58)	0.95 (0.93–0.97)
Multivariate HR† (95% CI)	1.00	0.63 (0.44–0.88)	0.53 (0.38–0.74)	0.48 (0.33–0.68)	0.96 (0.93–0.98)
Cancer mortality					
No. of deaths	11	69	135	89	
Age-adjusted HR (95% CI)	1.00	0.69 (0.37–1.31)	0.74 (0.40–1.37)	0.90 (0.48–1.68)	1.03 (0.99–1.07)
Multivariate HR† (95% CI)	1.00	0.61 (0.32–1.17)	0.69 (0.37–1.27)	0.82 (0.44–1.55)	1.03 (0.99–1.07)
Cardiovascular disease mortality					
No. of deaths	15	83	117	29	
Age-adjusted HR (95% CI)	1.00	0.56 (0.32–0.97)	0.44 (0.26–0.75)	0.21 (0.11–0.39)	0.88 (0.84–0.92)
Multivariate HR† (95% CI)	1.00	0.79 (0.42–1.50)	0.62 (0.33–1.16)	0.30 (0.15–0.61)	0.89 (0.84–0.94)
			Women		
Person-years	525	6,839	16,742	7,853	
All-cause mortality					
No. of deaths	17	126	192	56	
Age-adjusted HR (95% CI)	1.00	0.58 (0.35–0.97)	0.40 (0.24–0.66)	0.28 (0.16–0.47)	0.90 (0.87–0.94)
Multivariate HR† (95% CI)	1.00	0.70 (0.40–1.23)	0.47 (0.27–0.82)	0.32 (0.17–0.58)	0.90 (0.86–0.94)
Cancer mortality					
No. of deaths	2	16	61	17	
Age-adjusted HR (95% CI)	1.00	0.61 (0.14–2.67)	1.03 (0.25–4.20)	0.66 (0.15–2.88)	0.99 (0.92–1.06)
Multivariate HR† (95% CI)	1.00	1.14 (0.15–8.82)	1.85 (0.25–13.57)	1.31 (0.17–10.01)	1.00 (0.93–1.09)
Cardiovascular disease mortality					
No. of deaths	10	56	73	22	
Age-adjusted HR (95% CI)	1.00	0.45 (0.23–0.88)	0.27 (0.14–0.52)	0.19 (0.09–0.41)	0.88 (0.82–0.93)
Multivariate HR† (95% CI)	1.00	0.46 (0.23–0.91)	0.27 (0.13–0.53)	0.18 (0.08–0.40)	0.87 (0.81–0.93)

HR = hazard ratio; CI = confidence interval.
*Hazard ratios for an increased consumption of a cup of green tea per day are shown.
†Smoking status, alcohol consumption, body mass index, and the frequency of physical activity were also adjusted for.

consumption of green tea may reduce risk of colorectal cancer incidence (27), and a recent review concluded that epidemiologic data are insufficient to conclude that green tea may protect against colorectal cancer (28). The inverse association in the current study, however, seems to be large enough to be explained by residual confounding. Indeed, a recent study in Japan found no association between Japanese dietary pattern (which is highly correlated with green tea consumption) and colorectal adenomas (29), indicating that the possible confounding due to "Japanese-style" diet is not a major concern. Besides, considering the inverse associations between green tea and all-cause and CVD mortality, which are consistent with past findings (10, 13, 14), it is unlikely that our finding regarding colorectal cancer is due to chance. Regarding gastric and lung cancer mortality, the precision of the estimated HRs were fairly lower than that of colorectal cancer, and the epidemiological studies have yielded inconsistent findings (1, 2, 6–10, 30). Although

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TABLE 4. Hazard ratios for mortality from specific cancers by green tea consumption among the total participants, Shizuoka, Japan, 1999 to 2006

	Green tea consumption, cups/day				
	<1	1–3	4–6	≥7	Test for trend HR* (95% CI)
Person-years	1,465	14,932	31,556	16,049	
Gastric cancer mortality					
No. of deaths	2	14	32	20	
Age- and sex-adjusted HR (95% CI)	1.00	0.72 (0.16–3.18)	0.86 (0.21–3.61)	1.04 (0.24–4.45)	1.04 (0.96–1.12)
Multivariate HR† (95% CI)	1.00	0.49 (0.11–2.28)	0.78 (0.19–3.30)	0.81 (0.18–3.54)	1.04 (0.95–1.13)
Lung cancer mortality					
No. of deaths	2	15	45	26	
Age- and sex-adjusted HR (95% CI)	1.00	0.82 (0.19–3.58)	1.30 (0.32–5.37)	1.40 (0.33–5.91)	1.05 (0.98–1.13)
Multivariate HR† (95% CI)	1.00	0.85 (0.19–3.74)	1.13 (0.27–4.68)	1.24 (0.29–5.25)	1.04 (0.97–1.12)
Colorectal cancer mortality					
No. of deaths	3	12	20	8	
Age- and sex-adjusted HR (95% CI)	1.00	0.38 (0.11–1.35)	0.32 (0.09–1.08)	0.26 (0.07–0.98)	0.93 (0.84–1.04)
Multivariate HR† (95% CI)	1.00	0.47 (0.10–2.18)	0.35 (0.08–1.55)	0.36 (0.07–1.74)	0.95 (0.84–1.08)

HR = hazard ratio; CI = confidence interval.
*Hazard ratios for an increased consumption of a cup of green tea per day are shown.
†Smoking status, alcohol consumption, body mass index, and the frequency of physical activity were also adjusted for.

the associations between green tea and overall cancer rates remains unclear, because it is possible that green tea has organ-specific benefits (1), our research needs to be replicated in further studies.

In the stratified analyses on the follow-up periods, we found that the associations for all-cause and CVD mortality tended to be weaker in the first half period. If green tea consumption at the baseline had been altered by the preclinical disease status, the associations during the first half period are more likely to be influenced by residual confounding. Analyses of the second half period yielded larger impacts of green tea consumption, a finding that supports the protective effects of green tea on all-cause and CVD mortality, and that would not be expected if our findings were due to residual confounding.

Our study has several limitations. First, 28.4% of the participants were lost to follow-up and it is possible that the participants with less consumption of green tea were more likely to be lost to follow-up. Although the accurate reasons of lost to follow-up of individuals are unknown, given that those who were lost to follow-up tended to be smoking and have a more sedentary lifestyle compared with survivors, this may have resulted in an underestimate of the magnitude of the effects of green tea consumption. Second, green tea consumption was assessed by a single question in a self-administered questionnaire, which is yet to be validated. Since this may have resulted in non-differential misclassification, it is likely that the current findings are underestimated. Indeed, similar methods to assess green tea consumption have been employed in other studies in Japan, implying the reasonable validity of this assessment (10, 30–33). Third, detailed information about other food items and socioeconomic status is not available. Thus, the possibility of residual confounding cannot be ruled out. Nonetheless, BMI was

TABLE 5. Multivariate hazard ratios* for mortality from all causes, cancer, and cardiovascular disease by green tea consumption, stratified on follow-up periods, Shizuoka, Japan, 1999 to 2006

	Green tea consumption, cups/day				
	<1	1–3	4–6	≥7	Test for trend HR† (95% CI)
All-cause mortality					
HR for first 3 yr (95% CI)	1.00	0.97 (0.68–1.38)	0.83 (0.58–1.18)	0.74 (0.50–1.09)	0.97 (0.94–0.99)
HR for second 3 yr (95% CI)	1.00	0.69 (0.40–1.21)	0.69 (0.40–1.18)	0.56 (0.32–0.98)	0.97 (0.94–1.00)
Cancer mortality					
HR for first 3 yr (95% CI)	1.00	0.73 (0.34–1.57)	0.93 (0.44–1.97)	1.08 (0.50–2.36)	1.04 (0.99–1.09)
HR for second 3 yr (95% CI)	1.00	0.65 (0.23–1.86)	0.92 (0.34–2.53)	0.88 (0.32–2.48)	1.02 (0.97–1.08)
Cardiovascular disease mortality					
HR for first 3 yr (95% CI)	1.00	1.03 (0.60–1.76)	0.80 (0.47–1.39)	0.52 (0.27–1.00)	0.92 (0.88–0.97)
HR for second 3 yr (95% CI)	1.00	0.78 (0.28–2.20)	0.76 (0.28–2.09)	0.38 (0.13–1.14)	0.92 (0.86–0.98)

HR = hazard ratio; CI = hazard ratio.
*Smoking status, alcohol consumption, body mass index, and the frequency of physical activity were also adjusted for.
†Hazard ratios for an increased consumption of a cup of green tea per day are shown.

adjusted for to attenuate the possible confounding effect due to the overall dietary patterns of the subjects. Furthermore, the impact of green tea consumption on mortality did not change substantially when a variety of potential confounders were adjusted for in an earlier study among a Japanese cohort (10). These facts indicate that our findings are unlikely to be fully explained by residual confounding. Fourth, the number of cases for cancer mortality in the referent category (i.e., less than one cup per day) was comparatively small. This is expected to be achieved in future studies by continuing the follow-up assessments in this cohort.

In conclusion, the present study provides more evidence of the protective effects of green tea on all-cause and CVD mortality. The protective effects could have significant implications for public health. This study also suggests that green tea could have protective effects against colorectal cancer. Since higher cumulative exposure to green tea may produce these benefits, future studies with long-term follow-up assessments are warranted.

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