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The Japan Public Health Center-Based Study Cohort

Yoshihiro Kokubo, MD, PhD, FAHA; Hiroyasu Iso, MD, PhD; Isao Saito, MD, PhD; Kazumasa Yamagishi, MD, PhD; Hiroshi Yatsuya, MD, PhD; Junko Ishihara, PhD; Manami Inoue, MD, PhD; Shoichiro Tsugane, MD, PhD

Background and Purpose—Few prospective studies have examined the impact of both green tea and coffee consumption on strokes. We investigated the association of the combination of those consumption with stroke incidence in a general population.

Methods—We studied 82 369 Japanese (aged 45–74 years; without cardiovascular disease [CVD] or cancer in 1995 and 1998 for Cohort I and II, respectively) who received 13 years of mean follow-up through the end of 2007. Green tea and coffee consumption was assessed by self-administered food frequency questionnaire at baseline.

Results—In the 1 066 718 person-years of follow-up, we documented the incidence of strokes (n=3425) and coronary heart disease (n=910). Compared with seldom drinking green tea, the multivariable-adjusted hazard ratios (95% confidence intervals) of all strokes were 0.86 (0.78–0.95) and 0.80 (0.73–0.89) in green tea 2 to 3 and ≥4 cups/d, respectively. Higher green tea consumption was associated with inverse risks of CVD and strokes subtypes. Compared with seldom drinking coffee, the multivariable-adjusted hazard ratios (95% confidence intervals) of all strokes were 0.89 (0.80–0.99), 0.80 (0.72–0.90), and 0.81 (0.72–0.91) for coffee 3 to 6 times/week and 1 and ≥2 times/day, respectively. Coffee consumption was associated with an inverse risk of CVD and cerebral infarction. Higher green tea or coffee consumption reduced the risks of CVD and stroke subtypes (especially in intracerebral hemorrhage, *P* for interaction between green tea and coffee=0.04). None of the significant association was observed in coronary heart disease.

Conclusions—Higher green tea and coffee consumption were inversely associated with risk of CVD and stroke in general population. **(*Stroke*. 2013;44:1369-1374.)**

Key Words: coffee ■ cohort study ■ coronary heart disease ■ green tea ■ stroke

Tea is one of the world's most popular beverages. Among the various kinds of teas, green tea has been extensively studied for its antioxidant activities and potential for reducing lifestyle-related diseases.[1,2] However, the evidence of cohort study is limited. Prospective cohort studies have shown that green tea consumption is associated with reductions in all-cause and cardiovascular disease (CVD) mortalities.[3,4] Only 1 has examined the inverse association between green tea consumption and incident of stroke.[5]

Furthermore, coffee, which is also the most popular beverage in the world, has recently come into the limelight because of its association with reduced diabetes mellitus[6] and cancer.[7] However, prospective studies on the association between coffee and stroke[8,9] have been inconsistent. These inconsistencies may be partly because of the different end points, types of participants, and small sample sizes. However, no large prospective study has examined the associations of green tea and coffee consumption with the incidence of stroke simultaneously. We examined the hypothesis that both green tea and coffee consumption would be independently preventative for stroke in the Japanese general population.

Subjects and Methods

Study Design and Samples

This is an ongoing cohort study focusing on CVD and cancer.[10] The study design was described in detail elsewhere.[11] Briefly, the age

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From the Department of Preventive Cardiology, National Cerebral and Cardiovascular Center, Osaka, Japan (Y.K.); Department of Public Health, Graduate School of Medicine, Osaka University, Osaka, Japan (H.I.); Program for Nursing and Health Services, Ehime University Graduate School of Medicine, Toon, Japan (I.S.); Department of Public Health Medicine, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan (K.Y.); Department of Public Health, School of Medicine, Fujita Health University, Nagoya, Japan (H.Y.); Epidemiology and Prevention Division, Research Center for Cancer Prevention and Screening, National Cancer Center, Tokyo, Japan (J.I., M.I., S.T.); Department of Health and Human Security, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan (M.I.); and Department of Nutrition, Sagami Women's University, Kanagawa, Japan (J.I.).

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Correspondence to Yoshihiro Kokubo, MD, PhD, FACC, FAHA, FESC, Department of Preventive Cardiology, National Cerebral and Cardiovascular Center, 5-7-1, Fujishiro-dai, Suita, Osaka, 565-8565 Japan. E-mail ykokubo@hsp.ncvc.go.jp

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distributions at the time of entry were 40 to 59 for Cohort I (started in 1990) and 40 to 69 for Cohort II (started in 1993). Participants were identified using the population registry in each city or town without overlap (65 803 men and 67 520 women).

Baseline Data Collection

We assessed the dietary habits using a food-frequency questionnaire in 1995 and 1998 for Cohorts I and II, respectively. The questionnaires were returned by 47 400 men (72%) and 53 538 women (79%). We estimated the dietary intake of each individual based on a 138-food-item questionnaire, which was previously validated for estimating various nutrients and food groups.[12] The questionnaire also collected data on demographics, lifestyle factors, height, weight, smoking, alcohol consumption, and physical activity. Cohort members were excluded from the analyses, if they reported CVD or cancer in the questionnaires (n=5061), lost to follow-up and moved out of the area before the baseline survey (n=1327), or incompletely answered the food-frequency questionnaire (n=12 572). After applying these exclusions, 38 029 men and 43 949 women in total were included in the analyses. This study was approved by the institutional review board of the National Cancer Center, Tokyo. Each participant provided informed consent on completion of the baseline questionnaire, which described the study purposes and follow-up.

The frequency response choices for each food item were as follows: never; 1 to 3 times/month; 1 to 2, 3 to 4, and 5 to 6 times/week; 1, 2 to 3, 4 to 6, and ≥7 times/day. A standard portion was shown for each food item. The relative portion sizes were as follows: small (≈50% smaller than the standard), standard, and large (≈50% larger than the standard) size.[13] Daily intakes of individual nutrients were calculated using the food composition table developed for each questionnaire based on the fifth revised edition of the Standard Tables of Food Composition in Japan.[14]

Green tea and coffee consumption were obtained from the frequencies and amount of each beverage consumed using the choice of 0, 1 to 2, 3 to 4, and 5 to 6 times/week, and almost daily (further divided into 1, 2–3, 4–6, 7–9, and ≥10 cups/day). For the present analysis, we further grouped these categories based on their distribution among the subjects: green tea consumption for 0, 1 to 2, 3 to 6 times/week, 1, 2 to 3, and ≥4 cups/day; and coffee consumption for 0, 1 to 2, 3 to 6 times/week, 1 and ≥2 cups/day. The rank correlation coefficients for green tea and coffee consumption between the questionnaire and dietary record data were 0.37 and 0.59 for men and 0.43 and 0.51 for women, respectively.[15] We did not collect the type of coffee (decaffeinated or caffeinated), because decaffeinated coffee is not commonly consumed in Japan.

Confirmation of Stroke and Coronary Heart Disease

In the 9 Public Health Center areas, totally 54 major hospitals were capable of computed tomopgraphy (CT) scanning and/or magnetic resonance imaging.[10] Medical records were reviewed by hospital workers, physicians, or researchers who were blinded to the baseline data. Incidences of CVD were registered during the follow-up period. To complete surveillance for fatal CVD, we also conducted a systematic search for death certificates. We obtained information on the underlying cause of death by checking against death certificate files with permission to confirm mortality from CVD according to the International Classification of Death, 10th Revision: I00-I99. All cases of CVD based on death certificates only had been registered as death certificates only cases.

Strokes were confirmed according to the National Survey of Stroke criteria. These criteria require the rapid onset of a constellation of neurological deficits lasting at least 24 hours (or until death). For each stroke subtype (cerebral infarction [CI; thrombotic or embolic stroke], intracerebral hemorrhage [ICH], and subarachnoid hemorrhage), a definite diagnosis was established based on the examination of CT scans, magnetic resonance imaging, or autopsy findings.[16] Coronary heart disease (CHD) indicated in the medical records was confirmed according to the criteria of the MONICA project, which requires chest pain, electrocardiographic evidence, cardiac enzyme abnormalities, and autopsy findings.[17] In the absence of diagnosis of myocardial infarction, deaths that occurred within 1 hour from onset of event were regarded as sudden cardiac deaths. In this study, CVD was defined as stroke or CHD.

Statistical Analysis

For each subject, we calculated person-years of follow-up from the baseline to whichever of the following came first: the first end point, death, emigration, or December 31, 2007. Changes in residential status were identified through the residential registry in each area. Subjects who moved from their original residence (2% of the total participants) were censored at that time.

The Cox proportional hazards ratios and 95% confidence intervals were fitted to the categorized consumption (the reference group is the never consumption of green tea or coffee), after adjusting for age, sex, and other potential confounding factors: smoking status (never, ex-smoker, or current smoker of 1–19 or ≥20 cigarettes/day); alcohol intake (nondrinkers, occasional drinkers [1–3 days/month], weekly ethanol intake of 1–149, 150–299, 300–449, or ≥450 g/week); body mass index (in quintiles); history of diabetes mellitus (yes/no); medication use for hypertension or hypercholesterolemia (yes/no); quintiles of energy-adjusted dietary intakes of fruits, vegetables, and fish; leisure time spent engaged in exercise (<1, 1 to 3 days/month, or ≥1 day/week); public health center; and coffee or green tea consumption. Trend tests were conducted by assignment for green tea and coffee consumption to test the significance of these variables. Green tea and coffee consumption interactions were also analyzed (see the Statistical Analysis in the online-only Data Supplement). All statistical analyses were conducted using the SAS statistical package (version 8.2, SAS Institute Inc, Cary, NC).

Results

Table 1 shows the baseline characteristics according to green tea and coffee consumption categories. Higher frequencies of green tea consumption tended to have a higher prevalence of exercise. Higher frequencies of coffee consumption tended to be younger, had a higher prevalence of smoking and exercise, and had a lower prevalence of antihypertensive drug users and history of diabetes mellitus.

During a follow-up period (13-year of average), we documented 3425 strokes (1964 CI, 1001 ICH, and 460 subarachnoid hemorrhages) and 910 CHD events (489 definite myocardial infarctions and 28 sudden cardiac deaths). In total, 4335 CVD events were documented.

We observed inverse associations between green tea consumption and the incidences of CVD, strokes, and its subtypes (Table 2). Age- and sex-adjusted hazard ratios of CI for green tea consumption of 2 to 3 and ≥4 cups/day were inversely significant. After further adjustment, the significance was inversely associated with CI for green tea consumption of ≥4 cups/day.

We observed an inverse association between coffee consumption and the incidences of CVD, all strokes, and CI (Table 3). We observed inverse associations between coffee consumption (≥3 times/week) and the incidences of ICH by age- and sex-adjusted. However, after further adjustment, the association was attenuated.

The Figure shows the multivariable hazard ratios of CVD and stroke subtypes, according to combination of green tea and coffee consumption frequencies. Compared with seldom drinking green tea or coffee, higher green tea (≥2 times/day) or coffee (≥1 time/day) consumption reduced the risks of CVD, all strokes, CI, and ICH (In particular, *P* for interaction between green tea and coffee consumption was 0.04 in ICH.) The results were similar among men and women (data not shown). No significant association was observed in CHD (data not shown).

Table 1. Baseline Characteristic Variables in a Cohort Subjects According to Green Tea and Coffee Consumption

	Green Tea						Coffee				
	(Times/Week)			(Cups/d)			(Times/Week)			(Cups/d)	
	0	1–2	3–6	1	2–3	≥4	0	1–2	3–6	1	≥2
Number of subjects	17606	8497	7490	8103	17426	23247	19841	18762	13364	15128	15019
Age at baseline, y	54.1	52.7	52.7	53.1	53.8	55.4	56.6	55.2	53.5	53.2	50.4
Sex, % of men	47.3	47.6	50.3	48.9	47.5	42.3	42.2	45.0	51.7	44.3	51.3
Body mass index, kg/m^2	23.8	23.7	23.8	23.6	23.5	23.4	23.5	23.8	23.7	23.6	23.5
Current smoker, %	24.6	25.4	26.3	25.8	24.6	23.4	16.9	20.2	26.7	25.0	37.2
Current drinker, %	39.8	44.1	49.0	45.6	44.9	40.7	37.3	41.6	47.5	42.8	47.6
Sports at leisure time 1>time/week, %	17.2	18.7	20.5	20.0	20.0	21.7	18.8	21.0	21.0	21.4	22.5
Antihypertensive drug users, %	20.1	16.8	17.6	18.1	19.0	20.0	25.2	22.1	17.0	17.0	11.0
Antilipidemic drug users, %	4.5	4.6	5.0	4.7	5.4	5.5	5.9	5.7	4.4	4.7	3.0
History of diabetes mellitus, %	5.1	5.1	5.0	4.9	5.0	5.0	7.1	4.8	4.1	3.9	3.5
coffee >1 time/d	38	39	36	41	39	27	–	–	–	–	–
Green tea >1 time/d, %	–	–	–	–	–	–	60	63	57	59	54

Discussion

In this study, higher green tea and coffee consumption were found to be inversely associated with the incidences of CVD and stroke subtypes. In addition, higher green tea or coffee consumption reduced the risks of CVD, strokes, and its subtypes. To the best of our knowledge, this is the first study on the association between the combination of these 2 popular beverages and the incidences of CVD and stroke subtypes, especially in ICH independently.

Green tea consumption has been shown to reduce the risk of mortality because of all-cause and CVD.[3] Compared with green tea <1 cup/day, ≥5 cups/day had 15% and 26%

Table 2. Age and Multivariable-Adjusted Hazard Ratios of Cardiovascular Disease and its Subtypes According to Green Tea Consumption

	Green Tea Consumption						
	None	1–2 Times/Week	3–6 Times/Week	1 Cup/d	2–3 Cups/d	≥4 Cups/d	*P* for Trend
Person-years	228788	108408	95222	105019	226579	302703	
Cardiovascular disease							
Number of cases	1070	434	372	436	839	1184	
Age-adjusted HRs	1	0.95 (0.85–1.06)	0.91 (0.81–1.02)	0.93 (0.83–1.03)	0.81 (0.74–0.88)	0.78 (0.72–0.84)	<0.001
Multivariable-adjusted HRs	1	0.94 (0.84–1.05)	0.93 (0.82–1.05)	0.94 (0.84–1.05)	0.85 (0.78–0.93)	0.84 (0.77–0.92)	<0.001
All strokes							
Number of cases	848	361	289	346	672	909	
Age-adjusted HRs	1	0.99 (0.88–1.12)	0.90 (0.79–1.02)	0.94 (0.83–1.06)	0.81 (0.74–0.90)	0.75 (0.69–0.82)	<0.001
Multivariable-adjusted HRs	1	0.97 (0.86–1.10)	0.91 (0.80–1.05)	0.94 (0.83–1.07)	0.86 (0.78–0.95)	0.80 (0.73–0.89)	<0.001
Cerebral infarction							
Number of cases	471	196	165	202	385	545	
Age-adjusted HRs	1	1.00 (0.85–1.17)	0.94 (0.79–1.12)	1.00 (0.86–1.18)	0.84 (0.74–0.95)	0.80 (0.71–0.89)	<0.001
Multivariable-adjusted HRs	1	0.98 (0.83–1.16)	0.99 (0.83–1.19)	1.02 (0.86–1.20)	0.88 (0.77–1.01)	0.86 (0.76–0.98)	0.009
Intracerebral hemorrhage							
Number of cases	287	116	89	96	191	222	
Age-adjusted HRs	1	0.92 (0.74–1.13)	0.79 (0.63–1.00)	0.75 (0.60–0.94)	0.68 (0.57–0.81)	0.56 (0.47–0.66)	<0.001
Multivariable-adjusted HRs	1	0.92 (0.74–1.14)	0.81 (0.63–1.03)	0.78 (0.62–0.99)	0.77 (0.63–0.92)	0.65 (0.54–0.78)	<0.001
Coronary heart disease							
Number of cases	222	73	83	90	167	275	
Age-adjusted HRs	1	0.77 (0.60–1.00)	0.95 (0.74–1.21)	0.89 (0.70–1.13)	0.77 (0.64–0.93)	0.89 (0.75–1.04)	0.423
Multivariable-adjusted HRs	1	0.80 (0.61–1.04)	0.99 (0.76–1.29)	0.91 (0.70–1.18)	0.82 (0.67–1.02)	0.99 (0.83–1.20)	0.859

HRs indicates hazard ratios.

Multivariable were adjusted for age; sex; smoking; alcohol; body mass index; history of diabetes mellitus; medication of antihypercholesterolemia and antihypertension; sports; dietary intake of fruits, vegetables, fish, and energy; public health centers; and coffee consumption.

Table 3. Age and Multivariable-Adjusted Hazard Ratios of Cardiovascular Disease and its Subtypes According to Coffee Consumption

	Coffee Consumption					
	None	1–2 Times/Week	3–6 Times/Week	1 Cup/d	≥2 Cups/d	*P* for Trend
Person-years	254 006	242 850	172 976	199 104	196 914	
Cardiovascular disease						
Number of cases	1282	1045	678	679	616	
Age-adjusted HRs	1	0.84 (0.78–0.91)	0.84 (0.77–0.92)	0.77 (0.71–0.85)	0.84 (0.76–0.92)	<0.001
Multivariable-adjusted HRs	1	0.93 (0.86–1.01)	0.89 (0.81–0.98)	0.84 (0.76–0.92)	0.89 (0.80–0.99)	0.004
All strokes						
Number of cases	1038	843	534	529	441	
Age-adjusted HRs	1	0.85 (0.78–0.92)	0.82 (0.74–0.91)	0.74 (0.67–0.82)	0.75 (0.67–0.84)	<0.001
Multivariable-adjusted HRs	1	0.94 (0.85–1.02)	0.89 (0.80–0.99)	0.80 (0.72–0.90)	0.81 (0.72–0.91)	<0.001
Cerebral infarction						
Number of cases	614	469	298	298	248	
Age-adjusted HRs	1	0.80 (0.71–0.90)	0.79 (0.69–0.90)	0.73 (0.64–0.84)	0.76 (0.66–0.88)	<0.001
Multivariable-adjusted HRs	1	0.87 (0.78–0.98)	0.83 (0.72–0.96)	0.78 (0.68–0.90)	0.80 (0.68–0.94)	0.001
Intracerebral hemorrhage						
Number of cases	293	264	149	161	130	
Age-adjusted HRs	1	0.91 (0.78–1.06)	0.76 (0.63–0.92)	0.76 (0.63–0.91)	0.69 (0.56–0.85)	0.001
Multivariable-adjusted HRs	1	1.04 (0.88–1.22)	0.86 (0.70–1.05)	0.83 (0.68–1.02)	0.82 (0.66–1.02)	0.015
Coronary heart disease						
Number of cases	244	202	144	150	175	
Age-adjusted HRs	1	0.82 (0.69–0.98)	0.92 (0.75–1.12)	0.89 (0.73–1.08)	1.21 (1.00–1.46)	0.031
Multivariable-adjusted HRs	1	0.91 (0.76–1.10)	0.92 (0.75–1.14)	0.99 (0.81–1.23)	1.21 (0.98–1.50)	0.081

HRs indicates hazard ratios.

Multivariable were adjusted for age; sex; smoking; alcohol; body mass index; history of diabetes mellitus; medication of antihypercholesterolemia and antihypertension; sports; dietary intake of fruits, vegetables, fish, and energy; public health centers; and green tea consumption.

reduced risk of all-cause and CVD mortality, respectively. Green tea consumption has also been associated with a reduced risk of incidence of all strokes, CI, and ICH.[5] There has been no prospective study showing evidence that green tea consumption is preventive of CHD, which is consistent with our study.

Green tea content catechins, especially (–)-epigallocatechin-3-gallate, exerts vascular-protective effects through multiple mechanisms, including antioxidative,[18] anti-inflammatory,[19] antiproliferative,[20] increasing the plasma antioxidant capacity,[21] and antithrombogenic effects.[22] Moderate consumers of green tea are less likely to develop hypertension.[23] However, a meta-analysis of randomized controlled trials has shown that green tea is not associated with blood pressure, partly because of small studies number (n=2).[24] Further studies are waited for.

The association between coffee consumption and the risk of stroke has been controversial. No association between coffee consumption and fatal and nonfatal stroke has been found in healthy populations.[25,26] However, coffee consumption has been associated with an increased risk of CI in hypertensive men.[27] In a meta-analysis of prospective studies,[28] moderate consumption of coffee showed a weak inverse, but heavy coffee consumption (≥7 cups/day) was not significantly associated with stroke risk. Recently, in a cohort of Swedish women (coffee >1 cups/day), risk of stroke was reduced in CI, but not in ICH, compared with <1 cup/day.[8]

In recent meta-analyses, the association between coffee consumption and the risk of CHD still remains controversial.[29,30] Our study showed no significant association between coffee consumption and CHD. Coffee intake (≥2 cups/day) was positively associated with CHD in age-adjusted analysis. However, after further adjustment, including smoking, the positive association was disappeared, which was similar to a cohort study in United States.[31] The finding of the present study might suggest that the unfavorable effects of smoking overcome the beneficial effects of coffee consumption.

Coffee contains several biologically active substances, such as caffeine and diterpene, which were inconsistently associated with serum cholesterol and blood pressure levels, and decrease insulin sensitivity.[32–34] Coffee also contains chlorogenic acid and quinides, which may reduce body weight and blood glucose tolerance.[35] In a prospective study, higher coffee consumption may reduce the incidence of diabetes mellitus.[36] In our study, higher coffee consumption had a lower prevalence of diabetes mellitus. Elevated blood glucose is a risk of incident CI.[37] Therefore, coffee consumption may reduce the risk of CI by improving glucose levels.

Our study showed that combination of higher green tea and coffee consumptions contributed to the reduced risk of stroke as an interaction effect for each other. Protective effects may be related to weak but strength the different antioxidant and other biological contents in these 2 beverages, but the underlying combinational mechanism is still not clear.

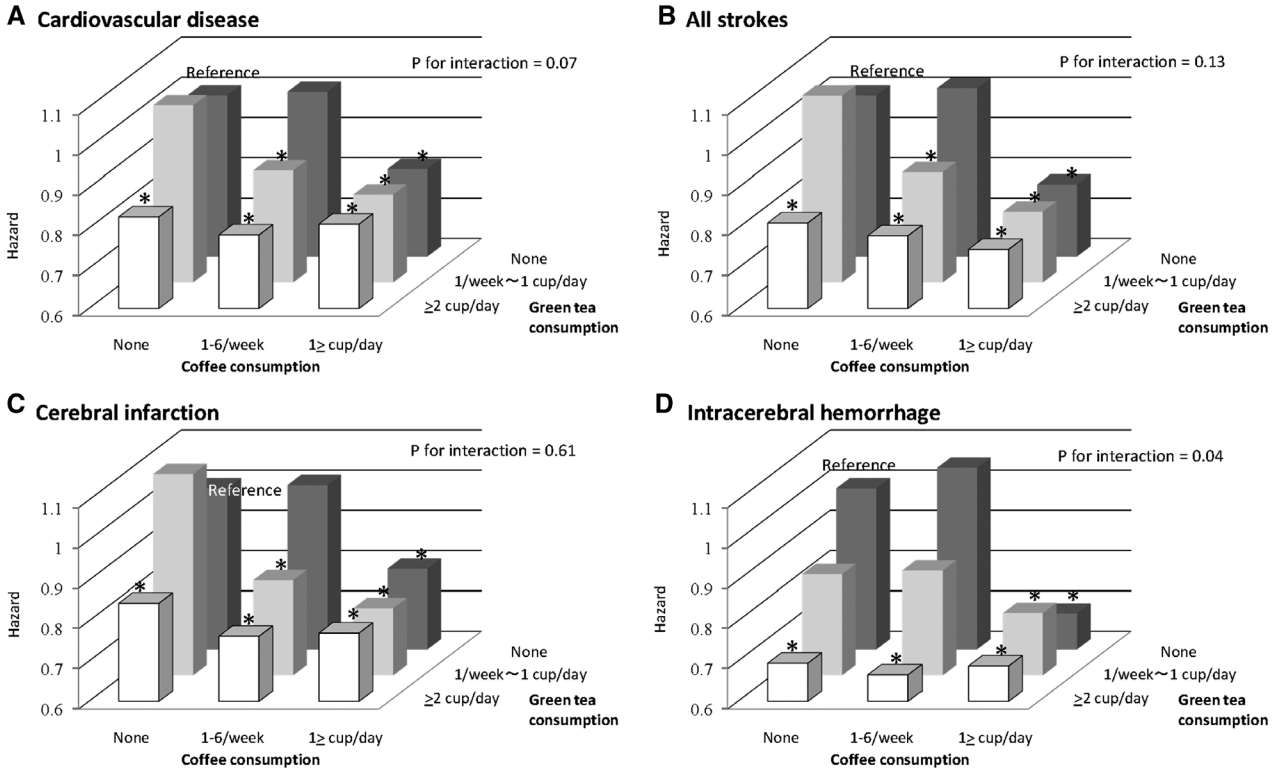

Figure. Multivariable-adjusted hazard ratios of cardiovascular disease (**A**), all strokes (**B**), cerebral infarction (**C**), and intracerebral hemorrhage (ICH; **D**) according to combination of green tea and coffee consumption frequencies. Data were expressed as multivariable-adjusted hazard ratios adjusted for age, sex, smoking, alcohol, body mass index, history of diabetes mellitus, medication for antihypercholesterolemia and antihypertension, sports, dietary intake of fruits, vegetables, fish, and energy, and public health centers. *indicates $P<0.05$ compared with seldom green tea or coffee (reference).

The present study has certain methodological strengths compared with previous investigations. First, we evaluated a large cohort enrolled from the Japanese general population, and the higher response rate to the questionnaire (>80%) and the smaller loss to follow-up (0.4%) were acceptable for study settings. Second, incidence is a more direct measure of CVD risk than death because treatment influences CVD death. Third, we estimated green tea and coffee consumption using a validated questionnaire.

Our study has several limitations. First, data regarding present illnesses, green tea, and coffee consumption were self-reported, raising the problem of potential misclassification. However, our self-reported data may be reasonably accurate because nationwide annual health screenings, conducted since 1992 in Japan, produced similar results. Our validation study showed relatively high validity.[38] Second, measurement errors concerning nutrient intake are inevitable when using a food-frequency questionnaire. Changes in green tea and coffee consumption during the follow-up period may also have caused misclassification. In the current study, the reproducibility of green tea and coffee consumption estimates suggests that any overestimates or underestimates are likely to cancel each other out and result in an accurate overall estimate. We have no decaffeinated coffee in our cohort study. The Japanese do not drink the decaffeinated coffee. In the previous article, similar associations were observed whether participants drank predominantly caffeinated or decaffeinated coffee.[39]

Conclusions

Higher green tea or coffee consumption was beneficial for reducing risks of CVD, all strokes, CI, and ICH, as a preventive medical point of view.

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Disclosures

None.

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The Impact of Green Tea and Coffee Consumption on the Reduced Risk of Stroke Incidence in Japanese Population: the Japan Public Health Center-Based (JPHC) Study Cohort

Yoshihiro Kokubo,MD,PhD,FAHA[1]; Hiroyasu Iso,MD PhD[2]; Isao Saito,MD,PhD[3]; Kazumasa Yamagishi,MD,PhD[4]; Hiroshi Yatsuya,MD,PhD[5]; Junko Ishihara,PhD[6,7]; Manami Inoue,MD,PhD[6]; and Shoichiro Tsugane,MD,PhD[6]

Supplemental Methods

Supplementary Statistical Analysis

Green tea and coffee consumption interactions were calculated with the following logistic regression model:

$$\text{logit } p = \beta_0 + \beta_{tea}X_{tea} + \beta_{cof}X_{cof} + \beta_{int}X_{tea}X_{cof},$$

where X_{tea} and X_{cof} are green tea and coffee consumption data (each of three categories: None, 1 time/week to 1 cup/day, and $\geq$2 cups/day for green tea; None, 1 to 6 times/week, and >1 cups/day for coffee consumption), respectively; β_0 is an intercept term; β_{tea} is the main effect due to green tea consumption; and β_{cof} is the main effect of coffee consumption. The coefficient β_{int} of the product $X_{tea}X_{cof}$ estimates green tea and coffee consumption interaction on the logit scale.

Supplementary contents

Additional Contributors to the Japan Public Health Center-based Prospective Study (JPHC Study, principal investigator: S. Tsugane) Group are: S. Tsugane, M. Inoue, T. Sobue, and T. Hanaoka, National Cancer Center, Tokyo; J. Ogata, S. Baba, T. Mannami, A. Okayama, and Y. Kokubo, National Cardiovascular Center, Osaka; K. Miyakawa, F. Saito, A. Koizumi, Y. Sano, I. Hashimoto, T. Ikuta and Y. Tanaba, Iwate Prefectural Ninohe Public Health Center, Iwate; Y. Miyajima, N. Suzuki, S. Nagasawa, Y. Furusugi, and N. Nagai, Akita Prefectural Yokote Public Health Center, Akita; H. Sanada, Y. Hatayama, F. Kobayashi, H. Uchino, Y. Shirai, T. Kondo, R. Sasaki, Y. Watanabe, Y. Miyagawa, Y. Kobayashi and M. Machida, Nagano Prefectural Saku Public Health Center, Nagano; Y. Kishimoto, E. Takara, T. Fukuyama, M. Kinjo, M. Irei, and H. Sakiyama, Okinawa Prefectural Chubu Public Health Center, Okinawa; K. Imoto, H. Yazawa, T. Seo, A. Seiko, F. Ito, F. Shoji and R. Saito, Katsushika Public Health Center, Tokyo; A. Murata, K. Minato, K. Motegi, T. Fujieda and S. Yamato, Ibaraki Prefectural Mito Public Health Center, Ibaraki; K. Matsui, T. Abe, M. Katagiri, and M. Suzuki, Niigata Prefectural Kashiwazaki and Nagaoka Public Health Center, Niigata; M. Doi, A. Terao, Y. Ishikawa, and T. Tagami, Kochi Prefectural Chuo-higashi Public Health Center, Kochi; H. Sueta, H. Doi, M. Urata, N. Okamoto, and F. Ide, Nagasaki Prefectural Kamigoto Public Health Center, Nagasaki; H. Sakiyama, N. Onga, H. Takaesu, and M. Uehara, Okinawa Prefectural Miyako Public Health Center, Okinawa; F. Horii, I. Asano, H. Yamaguchi, K. Aoki, S. Maruyama, M. Ichii, and M. Takano, Osaka Prefectural Suita Public Health Center, Osaka; Y. Tsubono, Tohoku University, Miyagi; K. Suzuki, Research Institute for Brain and Blood Vessels Akita, Akita; Y. Honda, K. Yamagishi, S. Sakurai and N. Tsuchiya, Tsukuba University, Ibaraki; M. Kabuto, National Institute for Environmental Studies, Ibaraki; M. Yamaguchi, Y. Matsumura, S. Sasaki, and S. Watanabe, National Institute of Health and Nutrition, Tokyo; M. Akabane, Tokyo University of Agriculture, Tokyo; T. Kadowaki, Tokyo University, Tokyo; M. Noda and T. Mizoue, International Medical Center of Japan, Tokyo; Y. Kawaguchi, Tokyo Medical and Dental University, Tokyo; Y. Takashima and Y. Yoshida, Kyorin University, Tokyo; K. Nakamura, Niigata University, Niigata; S. Matsushima and S. Natsukawa, Saku General Hospital, Nagano; H. Shimizu, Sakihae Institute, Gifu; H. Sugimura, Hamamatsu University, Shizuoka; S. Tominaga, Aichi Cancer Center Research Institute, Aichi; H. Iso, Osaka University, Osaka; M. Iida, W. Ajiki, and A. Ioka, Osaka Medical Center for Cancer and Cardiovascular Disease, Osaka; S. Sato, Chiba Prefectural Institute of Public Health, Chiba; E. Maruyama, Kobe University, Hyogo; M. Konishi, K. Okada, and I. Saito, Ehime University, Ehime; N. Yasuda, Kochi University, Kochi; S. Kono, Kyushu University, Fukuoka.