CLINICAL AND POPULATION SCIENCES



Green Tea and Coffee Consumption and All-Cause Mortality Among Persons With and Without Stroke or Myocardial Infarction

Masayuki Teramoto, MD; Isao Muraki, MD, PhD; Kazumasa Yamagishi[©], MD, PhD; Akiko Tamakoshi, MD, PhD; Hiroyasu Iso[®], MD, PhD, MPH

BACKGROUND AND PURPOSE: The effect of green tea and coffee consumption on mortality among cardiovascular diseases survivors is unknown. We examined the association between green tea and coffee consumption and mortality among persons with and without stroke or myocardial infarction (MI).

METHODS: In the Japan Collaborative Cohort Study, 46213 participants (478 stroke survivors, 1214 MI survivors, and 44521 persons without a history of stroke or MI), aged 40 to 79 years at baseline (1988–1990), completed a lifestyle, diet, and medical history questionnaire and were followed up regarding mortality until 2009. The Cox proportional hazard model was used to calculate the multivariable hazard ratios with 95% CIs of all-cause mortality after adjusting for potential confounding factors.

RESULTS: During the 18.5-year median follow-up period, 9253 cases were documented. Green tea consumption was inversely associated with all-cause mortality among stroke or MI survivors; the multivariable hazard ratios (95% CIs) for stroke survivors were 0.73 (0.42–1.27) for 1 to 6 cups/wk, 0.65 (0.36–1.15) for 1 to 2 cups/d, 0.56 (0.34–0.92) for 3 to 4 cups/d, 0.52 (0.31–0.86) for 5 to 6 cups/d, and 0.38 (0.20–0.71) for \geq 7 cups/d, compared with nondrinkers. A similar inverse association was observed for MI survivors, but not evident for those without a history of stroke or MI. Coffee consumption was inversely associated with all-cause mortality in persons without a history of stroke or MI; the multivariable hazard ratios (95% CIs) were 0.86 (0.82–0.91) for 1 to 6 cups/wk, 0.86 (0.80–0.92) for 1 cup/d, and 0.82 (0.77–0.89) for \geq 2 cups/d, compared with nondrinkers. The corresponding hazard ratios (95% CIs) for MI survivors were 0.69 (0.53–0.91), 0.78 (0.55–1.10), and 0.61 (0.41–0.90). No such association was observed for stroke survivors.

CONCLUSIONS: Green tea consumption can be beneficial in improving the prognosis for stroke or MI survivors, whereas coffee consumption can also be so for persons without a history of stroke or MI as well as MI survivors.

Key Words: coffee ■ cohort study ■ diet ■ green tea ■ myocardial infarction ■ prognosis ■ stroke

reen tea is one of the most commonly consumed beverages in Asia and has been extensively studied for its protective effect on chronic diseases, including cardiovascular diseases (CVD).^{1,2} Mineharu et al¹ previously showed that those who consumed 3 to 5 cups/d of green tea had a 41% lower CVD mortality

compared with nondrinkers of green tea in the general Japanese population. These beneficial effects of green tea consumption have also been reported in a recent meta-analysis.²

Moreover, coffee is a popular beverage worldwide and has been examined for its potential to reduce mortalities

Correspondence to: Hiroyasu Iso, MD, PhD, MPH, Public Health, Department of Social Medicine, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita, Osaka 565–0871, Japan. Email iso@pbhel.med.osaka-u.ac.jp

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Nonstandard Abbreviations and Acronyms

CVD JACC

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cardiovascular disease

Japan Collaborative Cohort Study for

Evaluation of Cancer Risk myocardial infarction

in the general population.^{1,3-5} Meta-analyses have concluded that moderate coffee consumption was associated with a lower risk of all-cause and CVD mortality in the general population.^{4,5}

Among myocardial infarction (MI) survivors, the consumption of caffeinated tea, which included both black and green teas, was associated with reduced CVD mortality,⁶ but the consumption of caffeinated coffee was not associated with the risk of cardiovascular events⁷ or all-cause mortality.⁸ This suggests that the consumption of tea and coffee may have different impacts on the prognosis of patients with CVD. To the best of our knowledge, no data are available on the association between green tea intake and subsequent mortality among MI survivors. No previous studies have examined the associations of green tea and coffee consumption among stroke survivors.

With an aging population and improvement in the case fatality rate of stroke or MI, scientific evidence focusing on the lifestyles of stroke or MI survivors has been garnering interest. Therefore, the objective of the present study was to examine and compare the association of green tea and coffee consumption in relation to all-cause mortality among persons with and without a history of stroke or MI, using the data of a large long-term cohort study of Japanese men and women.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Population

The JACC study (Japan Collaborative Cohort Study for Evaluation of Cancer Risk) is a large nationwide community-based prospective study that started between 1988 and 1990 and enrolled 110585 individuals (46395 men and 64190 women) aged 40 to 79 years, living in 45 communities across Japan. The methodology of the JACC study has been described elsewhere. 10 Briefly, a total of 110585 participants were asked to complete self-administered questionnaires, including demographic characteristics, medical history, lifestyle, and diet. According to self-reported history of stroke and MI, we classified participants into 3 groups: history of stroke, history of MI, and no history of stroke or MI.

From 110 585 cohort participants, we excluded 3423 participants (1423 men and 2000 women) living in 2 communities because the questions on the frequency of green tea or

coffee consumption were not included in the questionnaire (Figure I in the Data Supplement). We also excluded 17 243 daily green tea or coffee drinkers (7636 men and 9607 women) living in 12 communities because the questions on the number of cups of green tea and coffee consumed per day were not included in the questionnaire. Subsequently, we excluded 12299 participants (4855 men and 7444 women) owing to missing information on history of stroke or MI. Furthermore, 962 participants (287 men and 675 women) who reported a history of cancer and 120 participants (73 men and 47 women) who reported both a history of stroke and MI were excluded. Finally, we excluded 30325 participants (13519 men and 16806 women) owing to missing or inappropriate responses to green tea and coffee consumption. A total of 46213 participants (18602 men and 27611 women) were included in the analyses.

Before completing the questionnaire, the participants or community representatives provided informed consent to be involved in this epidemiological study, according to the guidelines of the Council for International Organizations of Medical Sciences. Informed individual consent was obtained from each participant in 36 of the 45 study areas (written consent in 35 areas and oral consent in 1 area). In the remaining 9 areas, group consent was obtained from each area leader. This study protocol was approved by the Ethics Committees of Nagoya University and Osaka University.

Assessment of Green Tea and Coffee Consumption

We asked participants about their frequency and amount of green tea and coffee consumed using the following choices: almost every day, 3 to 4 cups per week, 1 to 2 cups per week, 1 to 2 cups per month, and almost never. For those who answered, almost every day, we further asked questions on the number of cups consumed per day. According to their responses to these 2 questions, we classified their response into 6 levels for green tea consumption (occasionally or none, 1-6 cups/wk, 1-2, 3-4, 5-6, and ≥ 7 cups/d) and into 4 levels for coffee consumption (occasionally or none, 1-6 cups/wk, 1, and ≥2 cups/d). The type of coffee, such as decaffeinated or caffeinated, was not asked because decaffeinated coffee was not common, and most participants consumed instant or drip brewed coffee during the baseline survey period in Japan. The volume of a typical cup of green tea and coffee was ≈100 and 150 mL, respectively. The validation study of the food frequency questionnaire used in this cohort was conducted during the 1-year follow-up period, indicating a relatively higher correlation coefficient of green tea (Spearman correlation coefficient: 0.62) and coffee (Spearman correlation coefficient: 0.86).11

Assessment of Confounding Variables

Other information on demographic and lifestyle factors was derived from a self-administered questionnaire at baseline: age, sex, height, weight, past medical history (such as diabetes and hypertension), smoking and alcohol drinking status, exercise and walking habits, mental status, educational level, occupation, and eating habits. Body mass index was calculated as body weight (kg) divided by the square of height (m²).

Table 1. Age-Adjusted Baseline Characteristics of Participants According to Green Tea Consumption

	Green tea consumption							
	None	1-6 cups/wk	1-2 cups/d	3-4 cups/d	5-6 cups/d	≥7 cups/d	P for tren	
History of stroke							_	
No. of participants	55	62	63	140	107	51		
Age, y	64.3	63.9	64.4	64.2	64.5	63.2	0.59	
Sex, % of men	45.5	72.6	69.8	62.1	59.8	58.8	0.83	
Body mass index, kg/m²	22.4	23.1	22.6	23.0	23.2	22.6	0.67	
History of hypertension, %	60.0	56.5	61.9	56.8	59.1	56.9	0.81	
History of diabetes, %	18.2	17.7	7.9	12.9	7.5	5.9	0.02	
Current smoker, %	15.7	27.1	27.1	27.3	16.8	27.7	0.82	
Current drinker, %	24.0	30.4	39.7	45.3	39.6	31.0	0.40	
High mental stress, %	25.7	25.0	16.1	20.9	11.0	11.9	0.02	
College or higher education, %	12.8	16.2	14.3	15.1	7.3	8.5	0.18	
Unemployed, %	68.0	56.9	54.8	52.2	53.5	40.8	0.02	
Walking ≥30 min/d, %	57.8	70.7	59.7	53.7	53.1	53.3	0.17	
Exercise ≥1 h/wk, %	30.4	26.7	30.0	34.4	34.0	17.4	0.48	
Vegetable intake, times/wk	10.2	14.9	13.3	14.5	15.0	15.9	0.009	
Fish intake, times/wk	4.3	5.2	6.2	5.6	5.8	6.7	0.02	
Fruits intake, times/wk	4.5	5.1	5.8	6.3	6.6	5.9	0.04	
Soybeans intake, times/wk	3.9	4.5	4.5	4.7	5.5	5.2	0.01	
History of MI								
No. of participants	159	170	162	336	263	124		
Age, y	63.9	62.5	62.6	64.5	62.9	64.3	0.26	
Sex, % of men	32.1	35.9	46.3	44.6	36.9	50.0	0.02	
Body mass index, kg/m²	23.2	23.3	23.1	23.2	23.0	23.1	0.64	
History of hypertension, %	56.0	50.9	50.0	48.8	52.9	43.9	0.12	
History of diabetes, %	14.9	9.0	6.3	14.6	13.1	13.8	0.29	
Current smoker, %	21.1	19.5	20.4	17.8	19.2	36.3	0.006	
Current drinker, %	25.5	34.3	43.0	39.4	34.8	43.2	0.04	
High mental stress, %	22.8	31.0	20.5	19.2	30.0	17.9	0.42	
College or higher education, %	10.6	11.1	16.0	16.6	13.2	16.4	0.20	
Unemployed, %	39.9	27.1	35.7	38.8	30.3	36.6	0.43	
Walking ≥30 min/d, %	56.2	55.5	59.4	59.6	51.6	50.0	0.18	
Exercise ≥1 h/wk, %	29.5	26.5	28.6	29.4	27.6	32.4	0.58	
Vegetable intake, times/wk	13.8	14.2	13.7	13.4	15.6	14.6	0.14	
Fish intake, times/wk	4.7	5.3	5.9	5.4	6.1	6.4	<0.001	
Fruits intake, times/wk	5.8	6.7	7.6	7.7	7.6	7.3	0.01	
Soybeans intake, times/wk	4.5	5.0	4.5	4.4	5.0	5.1	0.11	
No history of stroke or MI		1 272		1	1 -11	1		
No. of participants	4623	6235	5727	10809	11094	6033		
Age, y	57.0	55.6	55.3	56.9	57.1	57.4	<0.001	
Sex, % of men	36.3	38.8	43.1	37.8	40.1	45.0	<0.001	
Body mass index, kg/m²	22.9	23.0	22.6	22.7	22.9	22.9	0.45	
History of hypertension, %	19.9	18.1	17.5	18.8	18.9	17.7	<0.001	
History of diabetes, %	5.9	4.9	4.2	4.3	4.1	3.9	<0.001	
Current smoker, %	22.1	23.1	26.9	23.0	24.5	29.0	<0.001	
Current smoker, % Current drinker, %	33.8	42.1	45.3	39.6	39.5	41.2	0.004	
Carrent unilker, 70	21.8	21.1	22.8	20.4	19.0	17.9	<0.004	

(Continued)

Table 1. Continued

	Green tea consumption							
	None	1-6 cups/wk	1-2 cups/d	3-4 cups/d	5-6 cups/d	≥7 cups/d	P for trend	
College or higher education, %	9.6	11.6	14.2	13.2	12.2	11.9	0.008	
Unemployed, %	22.2	17.7	15.6	18.9	17.7	17.0	<0.001	
Walking ≥30 min/d, %	45.4	48.8	49.6	47.6	46.8	41.9	<0.001	
Exercise ≥1 h/wk, %	20.9	24.7	27.4	26.7	26.8	25.3	<0.001	
Vegetable intake, times/wk	13.6	13.7	13.8	14.0	14.6	15.3	<0.001	
Fish intake, times/wk	6.3	6.5	6.4	6.4	6.7	7.0	<0.001	
Fruits intake, times/wk	6.3	6.0	6.8	7.0	7.1	7.1	<0.001	
Soybeans intake, times/wk	4.6	4.7	4.7	4.7	5.0	5.0	<0.001	

Data are mean for continuous variables and percentages for categorical variables. MI indicates myocardial infarction.

Mortality Surveillance

To obtain the cause of death, a systematic review of death certificates was conducted in each area. Mortality data were sent centrally to the Ministry of Health and Welfare through the local public health center, and the underlying cause of death was coded for the National Vital Statistics according to the *International Classification of Diseases, Tenth Revision.* In 35 areas, the end of the follow-up was the end of 1999 in 4 areas, the end of 2003 in 4 areas, the end of 2008 in 4 areas, and the end of 2009 in the rest of the areas. The end point of death in this study was all causes. The date of moving from the community was verified using population-registration documents. When participants moved out, we treated them as censored cases.

Statistical Analysis

Person years of follow-up were calculated as the duration from the date of the baseline questionnaire to the date of death, emigration from the community, or the end of follow-up, whichever occurred first. Age-adjusted mean values and proportions of having cardiovascular risk factors were calculated by using the ANCOVA for means and logistic regression for proportion. Hazard ratios with 95% CIs of all-cause mortality were calculated using the Cox proportional hazards regression models according to green tea and coffee consumption. We adjusted for age (continuous), sex (women or men), history of hypertension (yes or no), history of diabetes (yes or no), body mass index (sex-specific quintile), smoking status (never, ex-smoker, current smoker of 1-19, or current smoker of ≥20 cigarettes per day), alcohol consumption (never drinker, ex-drinker, current drinker of 0.1-45.9, or ≥46.0 g ethanol per day), hours of exercise (almost never, 1-4 hours, or ≥5 hours per week), hours of walking (almost never, 0.5 hours, or >0.5 hours per day), perceived mental stress (low, moderate, or high), educational level (≤18 or ≥19 years of age upon completion of education), employment status (unemployed or employed), frequency of consuming vegetables, fish, and fruits, soybean intakes (quintile), and green tea or coffee consumption.

For secondary analyses, we conducted sex-specific analysis and cause-stratified analysis by CVD and cancer. To account for potential bias due to reverse causality, we performed sensitivity analyses by excluding all participants who died during the first 5 years of follow-up. SAS version 9.4 (SAS, Inc, Cary, NC) was used for all statistical analyses. This study followed

the Strengthening the Reporting of Observational Studies in Epidemiology statements.¹²

RESULTS

Age-adjusted baseline characteristics of the participants were presented according to green tea consumption in Table 1. Persons with more frequent green tea consumption were more likely to eat fish, fruits, and soybeans regardless of a history of stroke or MI. Among persons without a history of stroke or MI, frequent green tea consumption was associated with a lower prevalence of diabetes.

Table 2 shows the age-adjusted baseline characteristics of the participants according to coffee consumption. Persons with more frequent coffee consumption were more likely to be younger, current smokers, current drinkers, and less unemployed, regardless of a history of stroke or MI. Among MI survivors, coffee consumption was associated with a lower intake of vegetables and soybeans. In addition, among persons without a history of stroke or MI, frequent coffee consumption was associated with a lower prevalence of hypertension and diabetes, higher mental stress, higher educational level, less intake of fish, and more frequent walking.

Risk of All-Cause Mortality According to Green Tea Consumption

During the 18.5 years of median follow-up, a total of 9253 deaths were documented. In age- and sex-adjusted analyses, green tea consumption was associated with lower risks of all-cause mortality among persons with and without a history of stroke or MI (Table 3). After further adjustment for potential confounding factors, the association was attenuated among persons without a history of stroke or MI, while the association remained among persons with a history of stroke or MI. The multivariable hazard ratios of all-cause mortality among persons with a history of stroke were 0.73 (95% CI, 0.42–1.27) for 1 to 6 cups/wk, 0.65 (95% CI, 0.36–1.15) for 1 to 2

 Table 2.
 Age-Adjusted Baseline Characteristics of Participants According to Coffee Consumption

	Coffee cons				
	None	1-6 cups/wk	1 cup/d	≥2 cups/d	P for trend
History of stroke	'	-			
No. of participants	225	164	44	45	
Age, y	65.2	63.6	62.7	62.4	0.04
Sex, % of men	55.6	65.9	68.2	71.1	0.11
Body mass index, kg/m ²	23.1	22.8	22.4	22.9	0.73
History of hypertension, %	58.7	61.4	52.3	51.1	0.28
History of diabetes, %	13.3	10.4	9.1	8.9	0.53
Current smoker, %	17.5	24.7	27.5	46.5	<0.001
Current drinker, %	31.3	42.1	34.2	57.9	0.01
High mental stress, %	16.4	19.7	14.3	20.5	0.86
College or higher education, %	8.5	15.4	17.5	12.2	0.62
Unemployed, %	61.2	49.0	47.7	41.9	0.16
Walking ≥30 min/d, %	57.5	61.2	42.9	48.8	0.23
Exercise ≥1 h/wk, %	29.3	31.5	27.5	35.7	0.32
Vegetable intake, times/wk	14.0	14.3	14.7	14.2	0.92
Fish intake, times/wk	5.7	6.2	4.8	5.0	0.12
Fruits intake, times/wk	5.7	5.8	7.0	6.6	0.19
Soybeans intake, times/wk	4.9	4.6	4.7	5.0	0.77
History of MI					
No. of participants	392	373	226	223	
Age, y	65.1	63.3	63.7	61.1	<0.001
Sex, % of men	36.7	43.2	33.2	52.0	<0.001
Body mass index, kg/m ²	23.2	23.3	23.2	22.9	0.32
History of hypertension, %	57.1	47.7	52.5	42.0	0.006
History of diabetes, %	12.9	13.2	11.5	10.6	0.48
Current smoker, %	17.3	19.6	18.5	32.5	<0.001
Current drinker, %	28.3	34.2	42.1	50.5	<0.001
High mental stress, %	25.4	21.6	17.0	30.2	0.77
College or higher education, %	10.5	16.9	13.4	17.5	0.12
Unemployed, %	45.6	31.6	31.4	26.2	0.04
Walking ≥30 min/d, %	53.9	56.7	56.4	57.5	0.51
Exercise ≥1 h/wk, %	24.2	33.1	30.8	27.8	0.33
Vegetable intake, times/wk	15.1	14.7	14.0	12.3	<0.001
Fish intake, times/wk	5.8	6.2	5.0	5.2	0.02
Fruits intake, times/wk	6.3	7.5	8.0	7.7	0.003
Soybeans intake, times/wk	4.9	4.8	4.5	4.3	0.02
No history of stroke or MI					
No. of participants	13574	15102	6887	8958	
Age, y	59.8	56.4	56.2	52.6	<0.001
Sex, % of men	38.4	41.2	34.4	44.7	<0.001
Body mass index, kg/m²	22.9	22.9	22.8	22.6	<0.001
History of hypertension, %	24.1	18.1	17.3	11.8	<0.001
History of diabetes, %	5.7	4.1	3.9	3.3	<0.001
Current smoker, %	19.9	22.6	22.1	37.0	<0.001
Current drinker, %	35.2	40.8	41.1	46.6	<0.001
High mental stress, %	17.2	18.4	20.3	27.1	<0.001

(Continued)

Table 2. Continued

	Coffee con	Coffee consumption				
	None	1-6 cups/wk	1 cup/d	≥2 cups/d	P for trend	
College or higher education, %	9.4	12.4	13.1	15.9	<0.001	
Unemployed, %	25.7	16.1	17.4	10.8	0.01	
Walking ≥30 min/d, %	44.7	45.9	48.4	49.7	<0.001	
Exercise ≥1 h/wk, %	24.7	27.3	25.5	25.3	<0.001	
Vegetable intake, times/wk	14.9	14.2	14.1	13.2	<0.001	
Fish intake, times/wk	6.8	6.7	6.4	6.2	<0.001	
Fruits intake, times/wk	6.6	6.7	7.4	7.0	<0.001	
Soybeans intake, times/wk	5.0	4.9	4.8	4.6	<0.001	

MI indicates myocardial infarction.

cups/d, 0.56 (95% CI, 0.34–0.92) for 3 to 4 cups/d, 0.52 (95% CI, 0.31–0.86) for 5 to 6 cups/d, and 0.38 (95% CI, 0.20–0.71) for ≥7 cups/d (*P* for trend=0.002) compared with nondrinkers. A similar inverse association was observed among persons with a history of MI. These inverse associations were similarly observed between men and women among persons with a history of stroke but were observed only among men with a history of MI (Table I in the Data Supplement). The reduced all-cause mortality among persons with a history of stroke or MI was primarily due to CVD mortality (Table II in the Data Supplement). In the sensitivity analyses, the exclusion of all participants who died during the first 5 years of follow-up (n=1439) did not change the results materially (Table III in the Data Supplement).

Risk of All-Cause Mortality According to Coffee Consumption

Coffee consumption was inversely associated with the risk of all-cause mortality among persons without a history of stroke or MI (Table 4). Additional adjustment for potential confounding factors did not change the inverse associations. The multivariable hazard ratios of all-cause mortality among persons without a history of stroke or MI were 0.86 (95% CI, 0.82-0.91) for 1 to 6 cups/wk, 0.86 (95% CI, 0.80–0.92) for 1 cup/d, and 0.82 (95% CI, 0.77-0.89) for ≥ 2 cups/d (P for trend ≤ 0.001) compared with nondrinkers. Among persons with a history of stroke, no significant association between coffee consumption and all-cause mortality was found. Among persons with a history of MI, coffee consumption was associated with a reduced risk of all-cause mortality. The reduced all-cause mortality among persons with a history of MI was observed between men and women (Table IV in the Data Supplement) and was primarily due to CVD mortality (Table V in the Data Supplement). In the sensitivity analyses, similar associations were observed among persons with a history of MI and without a history of stroke or MI when all participants who died during the first 5 years of follow-up were excluded (Table VI in the Data Supplement).

DISCUSSION

In this large prospective study of Japanese men and women aged 40 to 79 years with the median follow-up of 18.5 years, we observed that stroke survivors who consumed ≥7 cups/d of green tea had ≈60% lower risks of all-cause mortality than those who rarely consumed green tea, while such an association was not observed among persons without a history of stroke or MI. To the best of our knowledge, this is the first to find the associations of green tea consumption with all-cause mortality among stroke survivors. Our results suggest a beneficial effect of green tea consumption on patients' health outcomes after CVD events.

In addition, an inverse association of coffee consumption in relation to all-cause mortality was observed among persons without a history of stroke or MI and with a history of MI, but not among stroke survivors. Our findings on the suggestive inverse association between coffee consumption and the risk of all-cause mortality among MI survivors are consistent with findings from previous studies in Western countries. A cohort study of 1369 patients hospitalized with a confirmed first acute MI in Sweden showed that coffee consumption was associated with a lower risk of subsequent all-cause mortality after MI: the multivariable hazard ratios were 0.68 (95% CI, 0.45-1.02) for persons who consumed 1 to 3 cups/d, 0.56 (95% CI, 0.37-0.85) for 3 to 5 cups/d, 0.52 (95% CI, 0.34-0.83) for 5 to 7 cups/d, and 0.58 (95% CI, 0.34-0.98) for ≥ 7 cups/d, compared with those who consumed <1 cup.13 Another cohort study of 4365 Dutch MI patients, clinically diagnosed 10 years before study enrollment, showed a borderline inverse association between coffee consumption and the risk of allcause mortality among individuals who consumed ≥2 to 4 cups of coffee/d, compared with nondrinkers; the multivariable hazard ratio was 0.84 (95% CI, 0.71-1.00).14

A potential mechanism for the influence of green tea on cardiovascular health can be primarily attributed to the effect of (—)-epigallocatechin3-gallate, which is the most abundant polyphenol in green tea.¹⁵ Previous experimental research revealed the cardiovascular health

Table 3. Hazard Ratios (95% CIs) of All-Cause Mortality According to Green Tea Consumption

	Green te	Green tea consumption						
	None	1-6 cups/wk	1-2 cups/d	3-4 cups/d	5-6 cups/d	≥7 cups/d	P for trend	
History of stroke								
Person years	578	752	685	1676	1405	752		
No. of cases	34	41	29	60	47	21		
Mortality rate (per 1000 person years)	58.8	54.5	42.3	35.8	33.5	27.9		
Age- and sex-adjusted HR (95% CI)	Ref	0.84 (0.53-1.32)	0.64 (0.39-1.05)	0.53 (0.35-0.81)	0.43 (0.28-0.68)	0.36 (0.21-0.63)	<0.001	
Multivariable HR (95% CI)	Ref	0.73 (0.42-1.27)	0.65 (0.36-1.15)	0.56 (0.34-0.92)	0.52 (0.31-0.86)	0.38 (0.20-0.71)	0.002	
History of MI								
Person years	1820	2227	1912	3753	3313	1755		
No. of cases	59	49	43	93	71	40		
Mortality rate (per 1000 person years)	32.4	22.0	22.5	24.8	21.4	22.8		
Age- and sex-adjusted HR (95% CI)	Ref	0.64 (0.44-0.93)	0.58 (0.39-0.86)	0.66 (0.48-0.92)	0.65 (0.46-0.92)	0.48 (0.32-0.72)	0.02	
Multivariable HR (95% CI)	Ref	0.74 (0.49-1.12)	0.66 (0.43-1.01)	0.83 (0.58-1.19)	0.72 (0.49-1.05)	0.47 (0.30-0.72)	0.01	
No history of stroke or MI								
Person years	73555	102230	87 758	166783	177037	99923		
No. of cases	1023	1222	954	1986	2133	1348		
Mortality rate (per 1000 person years)	13.9	12.0	10.9	11.9	12.0	13.5		
Age- and sex-adjusted HR (95% CI)	Ref	0.92 (0.85-1.00)	0.89 (0.81-0.97)	0.89 (0.83-0.96)	0.87 (0.81-0.94)	0.87 (0.80-0.94)	0.002	
Multivariable HR (95% CI)	Ref	0.96 (0.88-1.05)	0.96 (0.88-1.05)	0.97 (0.90-1.05)	0.94 (0.87-1.02)	0.92 (0.85-1.01)	0.08	

Multivariable HR: adjusted for age, sex, coffee consumption, history of hypertension, history of diabetes, body mass index, smoking status, alcohol consumption, hours of exercise, hours of walking, perceived mental stress, educational level, regular employment, and dietary intakes of vegetable, fish, fruits, and soybeans. HR indicates hazard ratio

promoting effects of (—)-epigallocatechin3-gallate, such as alleviating atherosclerosis, ^{16,17} ameliorating ischemia/reperfusion injury, ^{18,19} enhancing endothelial function, ^{20,21} and attenuating inflammation. ^{22–24} Previous animal studies showed that (—)-epigallocatechin3-gallate exerted a neuro-protective effect against ischemic damage in the acute phase of ischemic stroke ^{25,26} and had a long-term effect of promoting neurogenesis after stroke, ²⁷ which suggests that green tea consumption can contribute, not only to an improvement in prognosis among stroke survivors but also to patients' functional recovery after stroke.

Moreover, caffeinated coffee consumption was associated with lower serum cholesterol levels,28 improved endothelial function (lowering E-selectin levels), and reduced inflammation (lowering C-reactive protein levels) in diabetic women.29 Coffee intake was also associated with higher plasma adiponectin concentrations in women with or without type 2 diabetes.30 The underlying mechanisms concerning the lack of an association between coffee consumption and mortality among stroke survivors are uncertain. One hypothesis is that daily coffee consumption might lead to an increment in blood pressure among stroke survivors. A previous meta-analysis reported that chronic caffeinated coffee consumption was associated with higher systolic and diastolic blood pressure levels,31 whereas green tea consumption was associated with lower blood pressure levels.32 Further studies are necessary to explore the mediating factors of the association between coffee consumption and mortality among stroke survivors.

The strength of the present study is the prospective study design minimizing recall bias of the exposure assessment and a large sample size of stroke and MI survivors. However, this study has several limitations.

First, because histories of stroke or MI and consumption of green tea or coffee were self-reported, false reporting can be a potential problem. Second, we did not have information on behavioral changes over time, although green tea and coffee consumption might have changed during the long follow-up period. Nondifferential misclassification could result in a potential underestimation of the association between green tea or coffee consumption and mortality outcome. Finally, since the present study is an observational study, the causality of the consumption of green tea and coffee in relation to protective cardiovascular health cannot be determined.

CONCLUSIONS

Green tea consumption was inversely associated with all-cause mortality, especially among stroke or MI survivors but not in persons without a history of stroke or MI. Coffee consumption was inversely associated with all-cause mortality among persons without a history of stroke or MI as well as with a history of MI. Our observational study suggests that green tea consumption can be

Table 4. Hazard Ratios (95% CIs) of All-Cause Mortality According to Coffee Consumption

	Coffee consumption				
	None	1-6 cups/wk	1 cup/d	≥2 cups/d	P for trend
History of stroke					
Person years	2703	2072	535	538	
No. of cases	116	82	14	20	
Mortality rate (per 1000 person years)	42.9	39.6	26.2	37.2	
Age- and sex-adjusted HR (95% CI)	Ref	1.01 (0.76-1.34)	0.71 (0.40-1.24)	1.18 (0.73–1.90)	0.87
Multivariable HR (95% CI)	Ref	1.31 (0.94-1.82)	0.81 (0.44-1.50)	1.52 (0.87-2.68)	0.32
History of MI					
Person years	5092	4864	2398	2427	
No. of cases	163	104	49	39	
Mortality rate (per 1000 person years)	32.0	21.4	20.4	16.1	
Age- and sex-adjusted HR (95% CI)	Ref	0.73 (0.57-0.93)	0.82 (0.59-1.13)	0.65 (0.45-0.92)	0.03
Multivariable HR (95% CI)	Ref	0.69 (0.53-0.91)	0.78 (0.55-1.10)	0.61 (0.41-0.90)	0.03
No history of stroke or MI					
Person years	215936	248 431	104707	138212	
No. of cases	3734	2832	1034	1066	
Mortality rate (per 1000 person years)	17.3	11.4	9.9	7.7	
Age- and sex-adjusted HR (95% CI)	Ref	0.82 (0.78-0.86)	0.83 (0.77-0.89)	0.84 (0.79-0.90)	<0.001
Multivariable HR (95% CI)	Ref	0.86 (0.82-0.91)	0.86 (0.80-0.92)	0.82 (0.77-0.89)	<0.001

Multivariable HR: adjusted for age, sex, green tea consumption, history of hypertension, history of diabetes, body mass index, smoking status, alcohol consumption, hours of exercise, hours of walking, perceived mental stress, educational level, regular employment, and dietary intakes of vegetable, fish, fruits, and soybeans. HR indicates hazard ratio.

beneficial for the secondary prevention of CVD, whereas coffee consumption can also be so for primary prevention. More research is needed to confirm the cardio- and neuro-protective effects of green tea and coffee among CVD survivors.

ARTICLE INFORMATION

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Affiliations

Public Health, Department of Social Medicine, Osaka University Graduate School of Medicine, Japan (M.T., I.M., H.I.). Department of Public Health Medicine, Faculty of Medicine, and Health Services Research and Development Center, University of Tsukuba, Japan (K.Y., H.I.). Department of Preventive Medicine, Hokkaido University Graduate School of Medicine, Sapporo, Japan (A.T.).

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Disclosures

None.

Supplemental Materials

Tables I-VI Figure I

REFERENCES

- Mineharu Y, Koizumi A, Wada Y, Iso H, Watanabe Y, Date C, Yamamoto A, Kikuchi S, Inaba Y, Toyoshima H, et al; JACC study Group. Coffee, green tea, black tea and oolong tea consumption and risk of mortality from cardiovascular disease in Japanese men and women. *J Epidemiol Community Health*. 2011;65:230–240. doi: 10.1136/jech.2009.097311
- Tang J, Zheng JS, Fang L, Jin Y, Cai W, Li D. Tea consumption and mortality of all cancers, CVD and all causes: a meta-analysis of eighteen prospective cohort studies. Br J Nutr. 2015;114:673–683. doi: 10.1017/S0007114515002329
- Freedman ND, Park Y, Abnet CC, Hollenbeck AR, Sinha R. Association of coffee drinking with total and cause-specific mortality. N Engl J Med. 2012;366:1891–1904. doi: 10.1056/NEJMoa1112010
- Ding M, Bhupathiraju SN, Satija A, van Dam RM, Hu FB. Long-term coffee consumption and risk of cardiovascular disease: a systematic review and a dose-response meta-analysis of prospective cohort studies. *Circulation*. 2014;129:643–659. doi: 10.1161/CIRCULATIONAHA.113.005925
- Kim Y, Je Y, Giovannucci E. Coffee consumption and all-cause and causespecific mortality: a meta-analysis by potential modifiers. Eur J Epidemiol. 2019;34:731–752. doi: 10.1007/s10654-019-00524-3
- Mukamal KJ, Maclure M, Muller JE, Sherwood JB, Mittleman MA. Tea consumption and mortality after acute myocardial infarction. *Circulation*. 2002;105:2476–2481. doi: 10.1161/01.cir.0000017201.88994.f7
- Silletta MG, Marfisi R, Levantesi G, Boccanelli A, Chieffo C, Franzosi M, Geraci E, Maggioni AP, Nicolosi G, Schweiger C, et al; GISSI-Prevenzione

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- Investigators. Coffee consumption and risk of cardiovascular events after acute myocardial infarction: results from the GISSI (Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico)-Prevenzione trial. *Circulation*. 2007;116:2944–2951. doi: 10.1161/CIRCULATIONAHA.107.712976
- Mukamal KJ, Maclure M, Muller JE, Sherwood JB, Mittleman MA. Caffeinated coffee consumption and mortality after acute myocardial infarction. *Am Heart J.* 2004;147:999–1004. doi: 10.1016/j.ahj.2003.12.038
- Feigin VL, Norrving B, Mensah GA. Global burden of stroke. Circ Res. 2017;120:439–448. doi: 10.1161/CIRCRESAHA.116.308413
- Tamakoshi A, Ozasa K, Fujino Y, Suzuki K, Sakata K, Mori M, Kikuchi S, Iso H, Sakauchi F, Motohashi Y, et al; JACC Study Group. Cohort profile of the Japan collaborative cohort study at final follow-up. *J Epidemiol*. 2013;23:227–232. doi: 10.2188/jea.je20120161
- Date C, Fukui M, Yamamoto A, Wakai K, Ozeki A, Motohashi Y, Adachi C, Okamoto, Kurosawa M, Tokudome Y, et al. Reproducibility and validity of a self-administered food frequency questionnaire used in the JACC study. J Epidemiol. 2005;1:S9–S23. doi: 10.2188/jea.15.S9.
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet.* 2007;370:1453–1457. doi: 10.1016/ S0140-6736(07)61602-X
- Mukamal KJ, Hallqvist J, Hammar N, Ljung R, Gémes K, Ahlbom A, Ahnve S, Janszky I. Coffee consumption and mortality after acute myocardial infarction: the Stockholm heart epidemiology program. *Am Heart J*. 2009;157:495–501. doi: 10.1016/j.ahj.2008.11.009
- van Dongen LH, Mölenberg FJ, Soedamah-Muthu SS, Kromhout D, Geleijnse JM. Coffee consumption after myocardial infarction and risk of cardiovascular mortality: a prospective analysis in the Alpha Omega Cohort. Am J Clin Nutr. 2017;106:1113–1120. doi: 10.3945/ajcn.117.153338
- Graham HN. Green tea composition, consumption, and polyphenol chemistry. Prev Med. 1992;21:334–350. doi: 10.1016/0091-7435(92)90041-f
- Yin J, Huang F, Yi Y, Yin L, Peng D. EGCG attenuates atherosclerosis through the Jagged-1/Notch pathway. Int J Mol Med. 2016;37:398–406. doi: 10.3892/ijmm.2015.2422
- 17. Wang W, Zhang ZZ, Wu Y, Wang RQ, Chen JW, Chen J, Zhang Y, Chen YJ, Geng M, Xu ZD, et al. (-)-Epigallocatechin-3-Gallate ameliorates atherosclerosis and modulates hepatic lipid metabolic gene expression in apolipoprotein E knockout mice: involvement of TTC39B. Front Pharmacol. 2018;9:195. doi: 10.3389/fphar.2018.00195
- Othman AI, Elkomy MM, El-Missiry MA, Dardor M. Epigallocatechin-3-gallate prevents cardiac apoptosis by modulating the intrinsic apoptotic pathway in isoproterenol-induced myocardial infarction. *Eur J Pharmacol*. 2017;794:27–36. doi: 10.1016/j.ejphar.2016.11.014
- Salameh A, Schuster R, Daehnert I, Seeger J, Dhein S. Epigallocatechin gallate reduces ischemia/reperfusion injury in isolated perfused rabbit hearts. Int J Mol Sci. 2018;19:628. doi: 10.3390/ijms19020628.
- Liu SM, Sun ZW, Chu P, Li HL, Ahsan A, Zhou ZR, Zhang ZH, Sun B, Wu JJ, Xi YL, et al. EGCG protects against homocysteine-induced human umbilical

- vein endothelial cells apoptosis by modulating mitochondrial-dependent apoptotic signaling and Pl3K/Akt/eNOS signaling pathways. *Apoptosis*. 2017;22:672–680. doi: 10.1007/s10495-017-1360-8.
- Zhan XL, Yang XH, Gu YH, Guo LL, Jin HM. Epigallocatechin gallate protects against homocysteine-induced vascular smooth muscle cell proliferation. Mol Cell Biochem. 2018;439:131–140. doi: 10.1007/s11010-017-3142-6
- Oyama JI, Shiraki A, Nishikido T, Maeda T, Komoda H, Shimizu T, Makino N, Node K. EGCG, a green tea catechin, attenuates the progression of heart failure induced by the heart/muscle-specific deletion of MnSOD in mice. *J Cardiol.* 2017;69:417–427. doi: 10.1016/j.jicc.2016.05.019
- Zhao J, Liu J, Pang X, Zhang X, Wang S, Wu D. Epigallocatechin-3-gallate inhibits angiotensin II-induced C-reactive protein generation through interfering with the AT1-ROS-ERK1/2 signaling pathway in hepatocytes. *Naunyn Schmiedebergs Arch Pharmacol.* 2016;389:1225–1234. doi: 10.1007/s00210-016-1279-6
- 24. Wang TF, Xiang ZM, Wang Y, Li X, Fang CY, Song S, Li CL, Yu HS, Wang H, Yan L, et al. (—)-Epigallocatechin gallate targets Notch to attenuate the inflammatory response in the immediate early stage in human macrophages. *Front Immunol.* 2017;8:433. doi: 10.3389/fimmu.2017.00433.
- Yao C, Zhang J, Liu G, Chen F, Lin Y. Neuroprotection by (-)-epigallocatechin-3-gallate in a rat model of stroke is mediated through inhibition of endoplasmic reticulum stress. *Mol Med Rep.* 2014;9:69–76. doi: 10.3892/mmr.2013.1778
- Zhang F, Li N, Jiang L, Chen L, Huang M. Neuroprotective effects of (-)-epigallocatechin-3-gallate against focal cerebral ischemia/reperfusion injury in rats through attenuation of inflammation. *Neurochem Res.* 2015;40:1691– 1698. doi: 10.1007/s11064-015-1647-5
- Zhang JC, Xu H, Yuan Y, Chen JY, Zhang YJ, Lin Y, Yuan SY. Delayed treatment with green tea polyphenol EGCG promotes neurogenesis after ischemic stroke in adult mice. *Mol Neurobiol.* 2017;54:3652–3664. doi: 10.1007/s12035-016-9924-0
- 28. Jee SH, He J, Appel LJ, Whelton PK, Suh I, Klag MJ. Coffee consumption and serum lipids: a meta-analysis of randomized controlled clinical trials. *Am J Epidemiol.* 2001;153:353–362. doi: 10.1093/aje/153.4.353
- Lopez-Garcia E, van Dam RM, Qi L, Hu FB. Coffee consumption and markers of inflammation and endothelial dysfunction in healthy and diabetic women. Am J Clin Nutr. 2006;84:888–893. doi: 10.1093/ajcn/84.4.888
- Williams CJ, Fargnoli JL, Hwang JJ, van Dam RM, Blackburn GL, Hu FB, Mantzoros CS. Coffee consumption is associated with higher plasma adiponectin concentrations in women with or without type 2 diabetes: a prospective cohort study. *Diabetes Care*. 2008;31:504–507. doi: 10.2337/dc07-1952
- Jee SH, He J, Whelton PK, Suh I, Klag MJ. The effect of chronic coffee drinking on blood pressure: a meta-analysis of controlled clinical trials. *Hypertension*. 1999;33:647–652. doi: 10.1161/01.hyp.33.2.647
- Peng X, Zhou R, Wang B, Yu X, Yang X, Liu K, Mi M. Effect of green tea consumption on blood pressure: a meta-analysis of 13 randomized controlled trials. Sci Rep. 2014;4:6251. doi: 10.1038/srep06251