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Coffee Consumption and Mortality Due to All Causes, Cardiovascular Disease, and Cancer in Japanese Women[1,2]

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Abstract

Coffee contains various compounds that have recently been reported to exert beneficial health effects. However, the conclusion of its relation with mortality has not yet been reached. In this study, we aimed to investigate the associations between coffee consumption and all-cause and cause-specific mortality in Japan. We included 37,742 participants (18,287 men and 19,455 women) aged 40–64 y without a history of cancer, myocardial infarction, or stroke at baseline in our analysis, based on the Miyagi Cohort Study initiated in 1990. The outcomes were mortality due to all causes, cardiovascular disease (CVD), and cancer. During the 10.3 y of follow-up, 2454 participants died, including 426 due to CVD and 724 due to cancer. In women, the multivariate hazard ratios (HR) (95% CI) for all-cause mortality in participants who drank coffee never, occasionally, 1–2 cups (150–300 mL)/d, and ≥3 cups/d were 1.00, 0.88 (0.73–1.06), 0.82 (0.66–1.02), and 0.75 (0.53–1.05), respectively (*P*-trend = 0.04). For CVD mortality in women, the multivariate HR (95% CI) were 1.00, 0.56 (0.36–0.86), 0.48 (0.29–0.80), and 0.45 (0.20–1.03), respectively (*P*-trend = 0.006). Of the specific CVD diseases, there was a strong inverse association between coffee consumption and mortality due to coronary heart disease (CHD) in women (*P*-trend = 0.02) but not in men. Death due to cancer was not associated with coffee consumption in either men or women, except for colorectal cancer in women. Our results suggest that coffee may have favorable effects on morality due to all causes and to CVD, especially CHD, in women. J. Nutr. 140: 1007–1013, 2010.

Introduction

Coffee is one of the most popular beverages consumed worldwide. This beverage contains substances such as caffeine and polyphenols (1), which were reported to exert antioxidant effects in vitro (2,3). In support of this report, an epidemiologic study suggested that coffee consumption may inhibit inflammation, resulting in reduction of the risk of inflammatory diseases and cardiovascular diseases (CVD)[6] (4). Thus, coffee is now acknowledged to be a healthy beverage, although the exact beneficial effect is still unknown.

Many previous investigations have examined the relationship between coffee consumption and mortality due to cancer and CVD (4–14). Associations with cancer have not been shown consistently (4–8). On the other hand, the association between coffee consumption and CVD mortality has been inconclusive (4,6–14). Some concluded that the risk increases as more coffee is consumed (6,9,10), whereas others found no significant association (7,11–13) or a U-shaped association (4,14). Lopez-Garcia et al. (8) recently reported a modest inverse association between coffee and CVD mortality based on a large cohort study of over 130,000 American men and women. We think our study is meaningful in that we investigated in Japan, where coffee consumption and other factors related to lifestyle, genetics, and disease structure differ from those in western countries and where there has rarely been a large cohort study conducted.

Methods

Study population. This study was based on a prospective cohort study conducted in Miyagi Prefecture, Japan. A previous report has described the details of this study (15). In brief, between June and August 1990, we delivered a self-administered questionnaire on various health habits to all residents aged 40–64 y (n = 51,921) in 14 municipalities of Miyagi

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[6] Abbreviations used: CHD, coronary heart disease; CVD, cardiovascular disease; HR, hazard ratio.
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TABLE 1 Baseline characteristics of men according to coffee consumption[1]

	Coffee consumption,[2] *cup/d*				
	Never	Occasionally	1 or 2	≥3	*P*-value[3]
Participants, *n*	3123	6383	5716	3065	
Age, *y*	53.4 ± 0.1	52.4 ± 0.1	49.7 ± 0.1	47.7 ± 0.1	<0.0001
Years of education, %					
≤15	47.4	42.2	35.0	30.7	
16–18	41.2	44.1	48.2	50.6	
≥19	11.3	13.6	16.8	18.7	<0.0001
BMI, %					
<18.5 kg/m	2.2	1.8	1.9	2.1	
18.5–24.9 kg/m^2	67.3	70.3	71.6	72.3	
≥25 kg/m^2	30.5	27.9	26.5	25.6	0.0004
Walking duration, %					
<30 min/d	30.9	29.3	32.4	34.9	
30 min–1 h/d	21.1	24.2	25.2	25.1	
>1 h/d	48.0	46.5	42.4	40.0	<0.0001
History of hypertension, %					
Yes	23.9	19.7	13.8	10.5	
No	76.1	80.3	86.2	89.5	<0.0001
History of diabetes mellitus, %					
Yes	7.6	5.3	3.9	3.5	
No	92.4	94.7	96.1	96.5	<0.0001
Smoking status, %					
Never	24.6	22.9	17.6	10.5	
Former	23.8	22.2	18.1	13.2	
Current, <20 cigarettes/d	17.0	16.4	15.1	10.7	
Current, ≥20 cigarettes/d	34.6	38.5	49.2	65.6	<0.0001
Alcohol drinking, %					
Never	13.3	14.5	16.0	21.1	
Former	7.9	6.0	5.6	6.8	
Current, <22.8 g/d	20.7	26.0	27.1	26.3	
Current, ≥22.8 g/d	58.1	53.5	51.3	45.8	<0.0001
Total energy intake,[4] *kJ/d*	8206 ± 44.4	8365 ± 31.0	8215 ± 32.0	8487 ± 43.3	<0.0001
Rice, %					
<3 bowls	24.2	23.3	26.9	28.2	
3 bowls	32.0	29.1	29.3	30.7	
4 bowls	13.1	14.4	16.0	16.2	
>4 bowls	30.7	33.2	27.8	24.9	<0.0001
Miso soup, %					
Not everyday	12.9	11.7	14.1	17.0	
Everyday	87.1	88.3	85.9	83.0	<0.0001
Total meat,[5] *g*	16.4 ± 0.3	17.3 ± 0.2	18.3 ± 0.2	20.8 ± 0.3	<0.0001
Total fish,[6] *g*	117.7 ± 1.7	120.8 ± 1.2	120.8 ± 1.2	113.9 ± 1.7	0.03
Dairy products,[7] *g*	59.6 ± 0.6	56.2 ± 0.4	53.6 ± 0.4	53.2 ± 0.6	<0.0001
Total vegetables,[8] *g*	53.2 ± 0.7	51.1 ± 0.4	48.6 ± 0.4	49.1 ± 0.6	<0.0001
Total fruits,[9] *g*	65.8 ± 1.0	65.9 ± 0.7	66.2 ± 0.7	67.1 ± 1.0	0.77
Green tea, %					
Never	18.1	8.7	10.2	10.7	
Occasionally	15.7	20.0	19.7	23.2	
1–2 cups/d	21.0	20.8	29.0	26.1	
≥3 cups/d	45.2	50.5	41.1	40.0	<0.0001
Oolong tea, %					
Never	79.0	63.0	63.2	61.9	
Occasionally	14.4	31.2	29.0	28.8	
≥1 cup/d	6.7	5.8	7.8	9.3	<0.0001
Black tea, %					
Never	87.6	55.7	53.5	53.9	
Occasionally	11.1	42.2	43.0	41.7	
≥1 cup/d	1.3	2.1	3.5	4.4	<0.0001

[1] Values are means ± SEM or percentages.
[2] 1 cup = 150 mL.
[3] *P*-values calculated by ANOVA or χ^2 test.
[4] Upper and lower energy intake of 0.5% excluded.
[5] The maximum intake of beef, pork, and chicken.
[6] The maximum intake of milk, yogurt, and cheese.
[7] The maximum intake of fresh fish and boiled fish paste.
[8] The maximum intake of spinach, carrot, tomato, and cabbage.
[9] The maximum intake of orange and other fruits.

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Prefecture. Of these participants, 47,605 were confirmed as eligible (response rate: 91.7%; 22,836 men and 24,769 women). The study protocol was approved by the institutional review board of the Tohoku University School of Medicine. We considered the return of self-administered questionnaires signed by the participants to imply their consent to participate in the study.

For the present analysis, we excluded those who had incomplete responses for coffee consumption frequency (n = 8029, 3639 men and 4390 women), as well as those who reported extreme daily levels of energy consumption (n = 463; sex-specific cutoffs for upper 0.5%: 15.30 MJ/d for men and 9.79 MJ/d for women, and for the lower 0.5%: 2.32 MJ/d for men and 1.21 MJ/d for women). We then excluded participants who, at the time of the baseline survey, had cancer (n = 1113, 427 men and 686 women), myocardial infarction (n = 608, 361 men and 247 women), or stroke (n = 389, 253 men and 136 women), because those with such a history might have changed their diet or lifestyle after they had been diagnosed. With these exclusions, 37,742 participants (18,287 men and 19,455 women) remained eligible for our analysis.

Exposure data. Baseline data of each participant were collected by a questionnaire. It consisted of items inquiring about the frequency of recent average consumption of 4 beverages (coffee, green tea, oolong tea, and black tea) and 36 kinds of food, as well as items regarding the consumption of alcohol and tobacco, medical history, level of education, body weight, height, and time spent walking per day. As for the frequency of coffee consumption, we asked the participants to select from the following 5 categories: never, occasionally, 1–2 cups/d, 3–4 cups/d, and ≥5 cups/d. The method used to brew the coffee was not asked. The volume of a typical cup of coffee was 150 mL. The reproducibility and validity of coffee consumption among the participants have been reported previously (16,17). Spearman's coefficient for the correlation between consumption assessed by the FFQ and 4 3-d diet records was 0.70, and the correlation between consumption measured by the 2 questionnaires over 1 y was 0.72 (16).

Follow-up. The end points were all-cause mortality and cause-specific mortality. To follow-up the participants for mortality and migration, we established a Follow-up Committee (18). The Committee consisted of the Miyagi Cancer Society, the Community Health Divisions of all 14 municipalities, the Department of Health and Welfare of Miyagi Prefectural Government, and the Division of Epidemiology, Tohoku University Graduate School of Medicine. The Committee periodically reviewed the Residential Registration Record of each municipality.

With this review, we identified participants who had either died or emigrated during the follow-up period. We discontinued follow-up with those who had emigrated from the study area, because the Committee could not review the Residential Registration Record from outside the study area. During the follow-up period, 1994 participants (955 men and 1039 women, 5.2% of the total participants) were lost to follow-up. For identified decedents, we further investigated cause of death by reviewing the death certificates of the participants at Public Health Centers in the study area. Cause of death was defined[7] according to the *International Classification of Diseases*, 9th rev. (19) and 10th rev. (20).

Statistical analysis. From June 1, 1990, to March 31, 2001, we prospectively counted the number of person-years of follow-up for each participant from the beginning of follow-up until the date of death, the date of emigration from the study districts, or the end of follow-up, whichever occurred first.

For mortality due to all causes, CVD, cancer, and other causes, we combined the upper 2 categories of coffee consumption into the single category of ≥3 cups/d because of the small number of participants and cases in each category. As for cause-specific mortality, we combined the upper 3 categories of coffee consumption into the single category ≥1 cup/d.

Mortality was obtained by dividing the number of deaths by the number of person-years in each coffee consumption category. Cox proportional hazards regression analysis was used, both in men and women, to calculate the hazard ratios (HR) and 95% CI for each mortality according to coffee consumption categories and to adjust for potentially confounding variables, using the SAS statistical software package version 9.1 (SAS Institute). The lowest category of coffee consumption (participants who had never drunk coffee) was considered as the reference category. The P-values for analysis of linear trends were also calculated by scoring the categories, from 1 for the lowest category to 4 for the highest, entering the number as a continuous term in the regression model. For all models, the proportional hazards assumptions were tested and met through the addition of time-dependent covariates to the models.

We considered the following variables to be potential confounders: age at baseline, years of education, BMI, time spent walking per day, history of hypertension and diabetes mellitus, smoking status, alcohol consumption, daily total energy consumption, and daily consumption of rice, miso soup, total meat, total dairy products, total fish, total vegetables, total fruits, green tea, oolong tea, and black tea. Interactions between coffee consumption and confounders were tested through the addition of cross-product terms to the multivariate model. All reported P-values are 2-tailed and differences of $P < 0.05$ were considered significant.

Results

Both men (**Table 1**) and women (**Table 2**) who consumed more coffee were more likely to be younger, to be in the normal BMI range, to have a higher level of education, to smoke, to have higher energy consumption, and to consume more total meat and fruit, and black tea, but were less likely to consume miso (soybean paste) soup and dairy products.

During the 10.3 y of follow-up, a total of 390,929 person-years accrued. Among these person-years, the total number of cases of death was 2454 (men, 1647; women, 807), including 426 cases of CVD death (men, 284; women, 142) and 724 cases of cancer death (men, 470; women, 254).

We found an inverse association between coffee consumption and all-cause mortality in women but not in men (**Table 3**). In women, the multivariate HR (95% CI) for all-cause mortality in participants who drank coffee never, occasionally, 1–2 cups/d, and ≥3 cups/d were 1.00, 0.88 (0.73–1.06), 0.82 (0.66–1.02), and 0.75 (0.53–1.05), respectively (P-trend = 0.04). There was a strong inverse association between coffee consumption and CVD mortality risk in women but not in men (Table 3). The multivariate HR (95% CI) for CVD mortality in women who drank coffee never, occasionally, 1–2 cups/d, and ≥3 cups/d were 1.00, 0.56 (0.36–0.86), 0.48 (0.29–0.80), and 0.45 (0.20–1.03), respectively (P-trend = 0.006). In contrast, death due to cancer was not associated with coffee consumption in either men or women.

We further analyzed the association between coffee consumption and specific CVD and cancer mortality (**Table 4**). We found in this analysis that women who consumed ≥1 cups of coffee/d had a 70% lower risk of death due to coronary heart disease (CHD) compared with women who never consumed coffee. Coffee consumption and death due to stroke were not associated in either men or women. For colorectal cancer specifically, higher coffee intake was associated with reduced risk of death in women. Mortality due to other specific cancers was not associated with coffee consumption. We found no interactions between coffee consumption and confounders.

Discussion

We prospectively studied the relationship between coffee consumption and all-cause and cause-specific mortality in a large

[7] Definition of diseases according to the *International Classification of Diseases*, 9th rev.codes (10th rev. codes): CVD, 390-459 (I00-I99); CHD, 410-414 (I20-I25); stroke, 430-438 (I60-I69); cancer, 140-239 (C00-C97); gastric cancer, 151 (C16); lung cancer, 162 (C34); colorectal cancer, 153-154 (C18-C21); breast cancer, 174 (C50).

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TABLE 2 Baseline characteristics of women according to coffee consumption[1]

	Coffee consumption,[2] *cup/d*				
	Never	Occasionally	1 or 2	≥3	*P*-value[3]
Participants, *n*	3577	7370	6512	1996	
Age, *y*	54.8 ± 0.1	52.9 ± 0.1	49.1 ± 0.1	46.9 ± 0.1	<0.0001
Years of education, %					
≤15	48.4	39.7	32.8	28.1	
16–18	41.2	47.6	51.9	54.2	
≥19	10.4	12.7	15.4	17.7	<0.0001
BMI, %					
<18.5 kg/m^2	3.0	2.2	2.8	3.3	
18.5–24.9 kg/m^2	63.1	64.7	69.8	73.8	
≥25 kg/m^2	33.9	33.1	27.5	23.0	<0.0001
Walking duration, %					
<30 min/d	28.5	27.6	32.8	35.0	
30 min–1 h/d	26.6	25.5	24.3	23.1	
>1 h/d	45.0	46.9	42.9	41.9	<0.0001
History of hypertension, %					
Yes	26.4	20.8	15.1	9.6	
No	73.6	79.2	84.9	90.4	<0.0001
History of diabetes mellitus, %					
Yes	5.7	2.6	1.8	0.9	
No	94.4	97.5	98.2	99.2	<0.0001
Smoking status, %					
Never	92.0	92.9	88.9	77.3	
Former	2.2	1.5	1.9	3.6	
Current, <20 cigarettes/d	3.9	4.3	6.8	11.6	
Current, ≥20 cigarettes/d	1.9	1.3	2.4	7.5	<0.0001
Alcohol drinking, %					
Never	78.8	73.7	65.2	56.5	
Former	3.6	3.4	3.7	5.1	
Current, <22.8 g/d	14.6	20.5	28.1	34.2	
Current, ≥22.8 g/d	3.0	2.4	3.0	4.2	<0.0001
Total energy intake,[4] *kJ/d*	5414 ± 23.1	5619 ± 16.0	5648 ± 16.7	5979 ± 32.1	<0.0001
Rice, %					
<3 bowls	26.6	25.7	34.5	40.9	
3 bowls	57.9	57.8	52.4	45.4	
4 bowls	7.9	8.8	7.5	9.0	
>4 bowls	7.6	7.7	5.6	4.7	<0.0001
Miso soup, %					
Not everyday	14.7	13.0	17.7	23.2	
Everyday	85.3	87.0	82.3	76.9	<0.0001
Total meat,[5] *g*	11.6 ± 0.2	12.8 ± 0.1	14.7 ± 0.1	15.9 ± 0.3	<0.0001
Total fish,[6] *g*	128.6 ± 1.7	138.2 ± 1.1	144.1 ± 1.2	138.6 ± 2.2	<0.0001
Dairy products,[7] *g*	51.2 ± 0.5	50.0 ± 0.3	48.5 ± 0.4	47.6 ± 0.6	<0.0001
Total vegetables,[8] *g*	70.4 ± 0.7	68.3 ± 0.5	68.4 ± 0.5	65.2 ± 0.8	<0.0001
Total fruits,[9] *g*	104.5 ± 1.1	105.5 ± 0.8	109.2 ± 0.8	107.0 ± 1.4	0.0007
Green tea, %					
Never	14.1	6.4	8.6	11.7	
Occasionally	16.9	18.8	23.0	26.8	
1–2 cups/d	18.2	21.1	29.2	26.6	
≥3 cups/d	50.7	53.7	39.2	34.9	<0.0001
Oolong tea, %					
Never	72.8	58.7	56.9	56.5	
Occasionally	17.1	30.9	30.9	30.3	
≥1 cup/d	10.1	10.4	12.2	13.3	<0.0001
Black tea, %					
Never	85.8	55.6	50.6	49.4	
Occasionally	12.7	42.6	45.4	45.7	
≥1 cup/d	1.4	1.8	4.0	4.9	<0.0001

[1] Values are means ± SEM or percentages.
[2] 1 cup = 150 mL.
[3] *P*-values calculated by ANOVA or χ^2 test.
[4] Upper and lower energy intake of 0.5% excluded.
[5] The maximum intake of beef, pork, and chicken.
[6] The maximum intake of milk, yogurt, and cheese.
[7] The maximum intake of fresh fish and boiled fish paste.
[8] The maximum intake of spinach, carrot, tomato, and cabbage.
[9] The maximum intake of orange and other fruits.

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TABLE 3 Cox proportional HR and their 95% CI for 10.3-y mortality from all-cause, CVD, and cancer according to coffee consumption in the Miyagi Cohort Study

	Coffee consumption,[1] *cup/d*				
	Never	Occasionally	1 or 2	≥3	*P*-trend
Men					
Person-years, *n*	31,959	65,962	58,813	31,422	
All-cause					
Deaths, *n*	365	629	443	210	
Age-adjusted HR (95% CI)	1.00 (referent)	0.89 (0.78–1.01)	0.87 (0.75–0.99)	0.92 (0.77–1.09)	0.19
Multivariate HR[2] (95% CI)	1.00 (referent)	0.96 (0.83–1.10)	0.91 (0.78–1.06)	0.89 (0.74–1.08)	0.16
CVD					
Deaths, *n*	64	117	68	35	
Age-adjusted HR (95% CI)	1.00 (referent)	0.94 (0.69–1.28)	0.76 (0.54–1.07)	0.87 (0.57–1.32)	0.20
Multivariate HR[2] (95% CI)	1.00 (referent)	1.09 (0.79–1.51)	0.85 (0.56–1.23)	0.88 (0.56–1.39)	0.28
Cancer					
Deaths, *n*	103	160	140	67	
Age-adjusted HR (95% CI)	1.00 (referent)	0.81 (0.63–1.04)	1.04 (0.80–1.34)	1.16 (0.85–1.59)	0.15
Multivariate HR[2] (95% CI)	1.00 (referent)	0.88 (0.67–1.14)	1.09 (0.83–1.44)	1.15 (0.82–1.62)	0.18
Other causes					
Deaths, *n*	198	352	235	108	
Age-adjusted HR (95% CI)	1.00 (referent)	0.91 (0.76–1.08)	0.82 (0.68–0.99)	0.82 (0.65–1.04)	0.04
Multivariate HR[2] (95% CI)	1.00 (referent)	0.96 (0.79–1.15)	0.84 (0.69–1.04)	0.79 (0.60–1.02)	0.03
Women					
Person-years, *n*	37,138	77,154	68,003	20,477	
All-cause					
Deaths, *n*	222	331	206	48	
Age-adjusted HR (95% CI)	1.00 (referent)	0.82 (0.69–0.97)	0.77 (0.63–0.93)	0.72 (0.52–0.99)	0.006
Multivariate HR[2] (95% CI)	1.00 (referent)	0.88 (0.73–1.06)	0.82 (0.66–1.02)	0.75 (0.53–1.05)	0.04
CVD					
Deaths, *n*	50	51	33	8	
Age-adjusted HR (95% CI)	1.00 (referent)	0.55 (0.37–0.82)	0.53 (0.34–0.84)	0.51 (0.23–1.09)	0.006
Multivariate HR[2] (95% CI)	1.00 (referent)	0.56 (0.36–0.86)	0.48 (0.29–0.80)	0.45 (0.20–1.03)	0.006
Cancer					
Deaths, *n*	73	110	52	19	
Age-adjusted HR (95% CI)	1.00 (referent)	0.83 (0.61–1.11)	0.59 (0.41–0.86)	0.87 (0.52–1.47)	0.04
Multivariate HR[2] (95% CI)	1.00 (referent)	0.87 (0.63–1.21)	0.63 (0.43–0.94)	0.95 (0.53–1.68)	0.13
Other causes					
Deaths, *n*	99	170	121	21	
Age-adjusted HR (95% CI)	1.00 (referent)	0.94 (0.73–1.20)	1.02 (0.77–1.34)	0.71 (0.44–1.16)	0.53
Multivariate HR[2] (95% CI)	1.00 (referent)	1.05 (0.81–1.38)	1.13 (0.84–1.53)	0.75 (0.45–1.26)	0.91

[1] 1 cup = 150 mL.

[2] Adjusted for age in years (continuous variable), sex (when calculating among total participants), past history of hypertension and diabetes (for each disease; yes, no), education level (≤15, 16–18, ≥19 y), BMI (<18.5, 18.5–24.9, ≥25 kg/m^2), walking time (<30 min/d, 30 min–1 h/d, >1 h/d), cigarette smoking (never, past, current smoker < 20 cigarettes/d, ≥20 cigarettes/d), consumption of alcohol (never, past, current drinker < 22.8 g/d, ≥22.8 g/d), green tea (never, occasionally, 1–2 cups/d, ≥3 cups/d), oolong tea (never, occasionally, ≥ 1cup/d), black tea (never, occasionally, ≥1 cup/d), intake of rice (<3, 3, 4, >4 bowls/d), miso soup (not everyday, everyday), total meat, total dairy products, total fish, total vegetables, total fruits (for each food; continuous variables), and energy (continuous variables).

population-based cohort. For all-cause mortality, we found that coffee intake was inversely associated with mortality in women but not in men. Similar to all-cause mortality, we observed a significant inverse association of coffee consumption with CVD mortality in women. Among types of CVD, we found that coffee consumption was significantly associated with a reduction of mortality due to CHD. The association between coffee consumption and cancer mortality, including specific cancer mortality, was null, except for the relationship with colorectal cancer mortality in women.

Our results for all-cause and cancer mortality were consistent with previous studies (4–8,11,12), but the results for CVD mortality among the previous studies have been highly variable (4,6–14). Greenland (21) found no association with CVD mortality through a meta-analysis of 14 cohort studies conducted until 1992. However, 2 studies (4,14) published after this meta-analysis provided new evidence for a U-shaped association with CVD mortality. These results suggest that moderate coffee consumption may reduce CVD mortality, thus supporting our present findings. Lopez-Garcia et al. (8) also found a modest inverse association, but their result differed from ours in that they discovered an inverse association in men also. We consider that this difference may have been due to the difference in the proportion of smoking status in men among the 2 studies. We think that smoking may affect mortality. In fact, Lopez-Garcia et al. (8) found no association for current smokers but an inverse association for nonsmokers. Similarly, in our stratified analyses for the smoking status in men, we found no

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TABLE 4 Cox proportional HR and their 95% CI for 10.3-y mortality from particular disease and cancer according to coffee consumption in the Miyagi Cohort Study

	Coffee consumption,[1] cup/d			
	Never	Occasionally	1	*P*-trend
Men				
CHD				
Deaths, *n*	21	28	32	
Multivariate HR[2] (95% CI)	1.00 (referent)	0.78 (0.42–1.43)	0.85 (0.46–1.60)	0.70
Stroke				
Deaths, *n*	21	53	44	
Multivariate HR[2] (95% CI)	1.00 (referent)	1.51 (0.89–2.57)	1.06 (0.60–1.87)	0.83
Subarachnoid hemorrhage				
Deaths, *n*	5	11	17	
Multivariate HR[2] (95% CI)	1.00 (referent)	1.16 (0.38–3.50)	1.32 (0.44–3.95)	0.60
Cerebral hemorrhage				
Deaths, *n*	7	23	12	
Multivariate HR[2] (95% CI)	1.00 (referent)	1.92 (0.79–4.65)	0.89 (0.32–2.43)	0.53
Cerebral infarction				
Deaths, *n*	9	17	13	
Multivariate HR[2] (95% CI)	1.00 (referent)	1.38 (0.58–3.24)	1.05 (0.42–2.67)	0.98
Gastric cancer				
Deaths, *n*	23	26	39	
Multivariate HR[2] (95% CI)	1.00 (referent)	0.69 (0.38–1.25)	0.97 (0.54–1.74)	0.89
Lung cancer				
Deaths, *n*	12	31	39	
Multivariate HR[2] (95% CI)	1.00 (referent)	1.45 (0.72–2.92)	1.72 (0.85–3.47)	0.14
Colorectal cancer				
Deaths, *n*	14	18	26	
Multivariate HR[2] (95% CI)	1.00 (referent)	0.51 (0.24–1.10)	0.67 (0.32–1.42)	0.52
Women				
CHD				
Deaths, *n*	12	10	8	
Multivariate HR[2] (95% CI)	1.00 (referent)	0.37 (0.15–0.94)	0.30 (0.10–0.85)	0.02
Stroke				
Deaths, *n*	21	28	24	
Multivariate HR[2] (95% CI)	1.00 (referent)	0.88 (0.47–1.62)	0.91 (0.46–1.81)	0.80
Subarachnoid hemorrhage				
Deaths, *n*	6	7	11	
Multivariate HR[2] (95% CI)	1.00 (referent)	0.59 (0.18–1.96)	1.24 (0.37–4.14)	0.54
Cerebral hemorrhage				
Deaths, *n*	8	9	10	
Multivariate HR[2] (95% CI)	1.00 (referent)	0.91 (0.32–2.59)	1.18 (0.39–3.58)	0.75
Cerebral infarction				
Deaths, *n*	6	11	3	
Multivariate HR[2] (95% CI)	1.00 (referent)	1.46 (0.49–4.39)	0.32 (0.06–1.59)	0.21
Gastric cancer				
Deaths, *n*	9	11	15	
Multivariate HR[2] (95% CI)	1.00 (referent)	0.62 (0.24–1.59)	0.71 (0.27–1.88)	0.58
Lung cancer				
Deaths, *n*	10	16	7	
Multivariate HR[2] (95% CI)	1.00 (referent)	0.96 (0.40–2.30)	0.38 (0.13–1.16)	0.08
Colorectal cancer				
Deaths, *n*	14	16	5	
Multivariate HR[2] (95% CI)	1.00 (referent)	0.74 (0.34–1.63)	0.26 (0.08–0.82)	0.02
Breast cancer				
Deaths, *n*	3	8	8	
Multivariate HR[2] (95% CI)	1.00 (referent)	1.66 (0.40–6.86)	1.54 (0.34–6.93)	0.65

[1] 1 cup = 150 mL.

[2] Adjusted for age in years (continuous variable), sex (when calculating among total participants), past history of hypertension and diabetes (for each disease; yes, no), education level (≤15, 16–18, ≥19 y), BMI (<18.5, 18.5–24.9, ≥25 kg/m^2), walking time (<30 min/d, 30 min–1 h/d, >1 h/d), cigarette smoking (never, past, current smoker < 20 cigarettes/d, ≥20 cigarettes/d), consumption of alcohol (never, past, current drinker <22.8 g/d, ≥22.8 g/d), green tea (never, occasionally, 1–2 cups/d, ≥3 cups/d), oolong tea (never, occasionally, ≥1 cup/d), black tea (never, occasionally, ≥1 cup/d), intake of rice (<3, 3, 4, >4 bowls/d), miso soup (not every day, everyday), total meat, total dairy products, total fish, total vegetables, total fruits (for each food; continuous variables), and energy (continuous variables).

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association among current male smokers (data not shown). The proportion of current male smokers in our study was considerably higher, which might have had stronger influence than in the study of Lopez-Garcia et al. (8) on the CVD mortality in men, resulting in a null association. Apart from that, we must take into account that there is a discrepancy in that we found no association also among nonsmokers (data not shown). However, we think this analysis for nonsmokers was insufficient, primarily due to the small number of events.

We hypothesize that the reduction of all-cause mortality in women results from the reduction of mortality due to CVD, especially CHD. Presumably, this reduction in mortality may be due to the antioxidants, such as caffeine (2) and polyphenols (3), or to the antiinflammatory activity of coffee, as suggested in a previous study (4). The reason for the discrepancy in the effect of coffee on all-cause and CVD mortality between men and women is unknown. One possibility is the adverse affect of the apparently higher smoking status among men.

Our study had certain limitations. First, the number of cases of specific diseases in the CVD and cancer groups was modest. Second, our questionnaire did not ask about coffee-drinking in detail: the method of preparation, the type of coffee beans, whether the coffee was decaffeinated, and the amount, if any, of milk and sugar added. Because it was reported that decaffeinated coffee consumption was associated with a small reduction in all-cause and CVD mortality (8), there is a possibility that coffee preparation may have an effect on health (1).

In conclusion, consumption of coffee may reduce mortality due to all causes and CVD, especially CHD, in women. Our results from Japan support the previous report of Lopez-Garcia (8), suggesting that the findings of these 2 studies are likely to be reproducible. If so, the effect of coffee on longevity may be considerable, in view of the fact that it is one of the most consumed beverages in the world.

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S.K. and I.T. composed the study conception and design; S.K., T.S., K.O-M., N.N., Y.N., Y.T., and I.T. acquired the data; K.S., M.A., S.K., T.S., K.O-M., N.N., Y.N., Y.T., and I.T. analyzed the data; K.S. wrote the manuscript; K.S., S.K., and I.T. revised the manuscript; I.T. obtained the funding; T.S., K.O-M., N.N., Y.N., and Y.T. gave administrative, technical, or material support; I.T. supervised the study. K.S. had primary responsibility for final content. All authors read and approved the final manuscript.

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