Associations between Green Tea Consumption and Coffee Consumption and the Prevalence of Coronary Artery Disease

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Summary Green tea and coffee contain various bioactive compounds (e.g., polyphenols), and their consumption has been proposed to decrease the risk of cardiovascular diseases. Here, we investigated the associations between the consumption of green tea and that of coffee and the prevalence of coronary artery disease (CAD) in Japanese patients. The study group was 612 patients who underwent coronary angiography at Tokyo Medical Center between July 2008 and February 2017. CAD was confirmed in 388 of the patients: one-vessel disease (1-VD, $n=166$); two-vessel disease (2-VD, $n=112$); three-vessel disease (3-VD, $n=110$). Myocardial infarction (MI) was found in 138 patients. After adjustment for well-known atherosclerotic risk factors and other dietary habits, greater green tea consumption was significantly inversely associated with CAD prevalence (p for trend=0.044), and the patients who drank >3 cups/d had a lower prevalence of CAD compared to those who drank <1 cup/d (odds ratio [OR]: 0.54, 95% CI: 0.30–0.98). Greater green tea consumption (>3 cups/d) was also associated with a decreased prevalence of 3-VD (OR: 0.49, 95% CI: 0.24–0.98, p -trend=0.047) and MI (OR: 0.51, 95% CI: 0.27–0.97, p -trend=0.037). In contrast, coffee consumption was not associated with CAD or MI. In subgroup analyses, the inverse association between green tea consumption and CAD or MI was found in the high intake groups of vegetables or fruits but not in the low intake groups of vegetables or fruits. These results suggest a beneficial effect of green tea consumption, especially with a diet rich in vegetables and fruits, against coronary atherosclerosis in Japanese.

Key Words green tea, coffee, coronary artery disease, myocardial infarction, atherosclerosis, observational study

Cardiovascular disease (CVD) is a major health problem and a major cause of death worldwide. Epidemiological studies have demonstrated that polyphenol-enriched diets may have beneficial effects on the prevention of CVD (1–3). The activity provided by polyphenol-enriched diets might be associated not only with antioxidant properties, but also with additional mechanisms including anti-inflammatory, anti-hypertensive, vasculoprotective, and lipid-lowering properties (4).

Green tea and coffee are popular beverages in Japan and were confirmed to be major sources of dietary polyphenol (5–10). A Japan Public Health Center-based prospective study demonstrated that coffee consumption and green tea consumption were inversely associated with risk of stroke, but not the risk of coronary

heart disease (CHD) (11). Other Japanese cohort studies reported that green tea consumption (12) and coffee consumption (13) were associated with reduced mortality due to all-causes and CVD. In addition, green tea consumption was reported to be inversely associated with angiographically confirmed coronary artery disease (CAD) (significant coronary stenosis) in two Japanese cross-sectional studies (14, 15), although our previous research found an inverse association between green tea intake and myocardial infarction (MI), but not with CAD (16, 17). The frequency of green tea and coffee consumption could be influenced by each other, and also related with subject's dietary patterns. A recent study that examined 13-y trends in dietary patterns using data from the National Health and Nutrition Survey, Japan 2003–2015 suggested the continuous Westernization of the Japanese diet (18). Therefore, it is necessary to examine and confirm the relationship between green tea and coffee consumption and the prevalence of

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Table 1. Clinical characteristics of the patients with and without CAD.

	CAD(-) (n=224)	<i>p</i> CAD(-) vs. CAD(+)	CAD(+)				<i>p</i> MI(+) vs. CAD(-)
			Overall (n=388)	MI(-) (n=250)	<i>p</i> MI(-) vs. MI(+)	MI(+) (n=138)	
Age (y)	65±12	0.011	68±11	69±10	<0.001	65±12	0.721
BMI (kg/m ²)	24±12	0.581	24±4	24±4	0.851	24±5	0.696
Gender (male)	141 (63%)	<0.001	304 (78%)	194 (78%)	0.629	110 (80%)	0.001
Hypertension	140 (63%)	0.002	289 (74%)	194 (78%)	0.058	95 (69%)	0.220
SBP (mmHg)	131±21	0.511	133±26	132±23	0.291	135±32	0.268
Diabetes mellitus	31 (14%)	<0.001	135 (35%)	95 (38%)	0.074	40 (29%)	<0.001
Hyperlipidemia	91 (41%)	<0.001	222 (57%)	149 (60%)	0.202	73 (53%)	0.023
Statin	57 (25%)	<0.001	155 (40%)	113 (45%)	0.004	42 (30%)	0.301
LDL-C (mg/dL)	112±29	0.022	118±34	115±33	0.015	124±35	0.001
HDL-C (mg/dL)	58±15	<0.001	49±12	51±13	<0.001	46±11	<0.001
Smoking	69 (31%)	0.007	162 (42%)	107 (43%)	0.573	55 (40%)	0.078

Data represent the mean±SD or the number (%) of patients.

Table 2. Consumptions of green tea, coffee and foods in patients with and without CAD.

	CAD(-) (n=224)	<i>p</i> CAD(-) vs. CAD(+)	CAD(+)				<i>p</i> MI(+) vs. CAD(-)
			Overall (n=388)	MI(-) (n=250)	<i>p</i> MI(-) vs. MI(+)	MI(+) (n=138)	
Green tea (cups/d)							
<1	39 (17%)	0.086	92 (24%)	53 (21%)	0.237	39 (28%)	0.021
1-3	122 (55%)		211 (54%)	138 (55%)		73 (53%)	
>3	63 (28%)		85 (22%)	59 (24%)		26 (19%)	
Coffee (cups/d)							
<1	82 (37%)	0.502	124 (32%)	84 (34%)	0.058	40 (29%)	0.163
1-3	125 (56%)		233 (60%)	152 (61%)		81 (59%)	
>3	17 (8%)		31 (8%)	14 (6%)		17 (12%)	
Alcohol (glasses/wk)							
<1	104 (46%)	0.200	201 (52%)	124 (50%)	0.242	77 (56%)	0.083
≥1	120 (54%)		187 (48%)	126 (50%)		61 (44%)	
Fish (times/wk)							
<3	71 (32%)	0.435	143 (37%)	90 (36%)	0.431	53 (38%)	0.313
3-4	122 (54%)		195 (50%)	131 (52%)		64 (46%)	
>4	31 (14%)		50 (13%)	29 (12%)		21 (15%)	
Soybean products (times/wk)							
<3	62 (28%)	0.118	139 (36%)	88 (35%)	0.942	51 (37%)	0.181
3-4	93 (42%)		143 (37%)	93 (37%)		50 (36%)	
>4	69 (31%)		106 (27%)	69 (28%)		37 (27%)	
Vegetables (times/wk)							
<3	29 (13%)	0.005	85 (22%)	52 (21%)	0.457	33 (24%)	0.004
3-4	70 (31%)		132 (34%)	82 (33%)		50 (36%)	
>4	125 (56%)		171 (44%)	116 (46%)		55 (40%)	
Fruits (times/wk)							
<3	47 (21%)	0.006	125 (32%)	77 (31%)	0.614	48 (35%)	0.007
3-4	55 (25%)		96 (25%)	61 (24%)		35 (25%)	
>4	122 (54%)		167 (43%)	112 (45%)		55 (40%)	

Data represent the number (%) of patients.

Table 3. Clinical characteristics of the patients according to their green tea or coffee consumption.

	Green tea consumption (cups/d)				Coffee consumption (cups/d)			
	<1 (n=131)	1–3 (n=333)	>3 (n=148)	<i>p</i>	<1 (n=206)	1–3 (n=358)	>3 (n=48)	<i>p</i>
Age (y)	62±11	67±12	70±10	<0.001	70±11	66±11	59±10	<0.001
Gender (male)	108 (82%)	242 (73%)	95 (64%)	0.003	142 (69%)	260 (73%)	43 (90%)	0.015
Hypertension	88 (67%)	236 (71%)	105 (71%)	0.712	152 (74%)	244 (68%)	33 (69%)	0.364
Diabetes mellitus	39 (30%)	89 (27%)	38 (26%)	0.723	53 (26%)	94 (26%)	19 (40%)	0.128
Hyperlipidemia	63 (48%)	173 (52%)	77 (52%)	0.733	92 (45%)	191 (53%)	30 (63%)	0.036
Statin	40 (31%)	116 (35%)	56 (38%)	0.438	70 (34%)	125 (35%)	17 (35%)	0.968
LDL-C (mg/dL)	116±30	117±34	114±32	0.665	109±31	118±32	126±36	<0.001
HDL-C (mg/dL)	52±13	53±15	52±14	0.754	54±14	52±14	49±15	0.169
Smoking	60 (46%)	125 (38%)	46 (31%)	0.040	62 (30%)	143 (40%)	26 (54%)	0.003
CAD	92 (70%)	211 (63%)	85 (57%)	0.086	124 (60%)	233 (65%)	31 (65%)	0.502
Number of stenotic coronary vessels	1.3±1.1	1.2±1.1	1.1±1.1	0.130	1.1±1.1	1.2±1.1	1.3±1.2	0.646
1-VD	38 (29%)	93 (28%)	35 (24%)	0.536	51 (25%)	106 (30%)	9 (19%)	0.182
2-VD	24 (18%)	64 (19%)	24 (16%)	0.734	34 (17%)	66 (18%)	12 (25%)	0.389
3-VD	30 (23%)	54 (16%)	26 (18%)	0.238	39 (19%)	61 (17%)	10 (21%)	0.738
MI	39 (30%)	73 (22%)	26 (18%)	0.048	40 (19%)	81 (23%)	17 (35%)	0.058
Green tea (≥1 cup/d)					172 (83%)	280 (78%)	29 (60%)	0.002
Coffee (≥1 cup/d)	97 (74%)	223 (67%)	86 (58%)	0.018				
Alcohol (≥1 glass/wk)	78 (60%)	163 (49%)	66 (45%)	0.036	101 (49%)	180 (50%)	26 (54%)	0.812
Fish (≥3 time/wk)	70 (53%)	210 (63%)	118 (80%)	<0.001	146 (71%)	225 (63%)	27 (56%)	0.065
Soybean products (≥3 times/wk)	58 (44%)	226 (68%)	127 (86%)	<0.001	136 (66%)	246 (69%)	29 (60%)	0.472
Vegetables (≥3 times/wk)	95 (73%)	275 (83%)	128 (86%)	0.008	167 (81%)	296 (83%)	35 (73%)	0.262
Fruits (≥3 times/wk)	72 (55%)	244 (73%)	124 (84%)	<0.001	156 (76%)	259 (72%)	25 (52%)	0.004

Data represent the mean±SD or the number (%) of patients.

CAD including MI in recent Japanese populations. We thus conducted the present study to determine whether green tea consumption and coffee consumption are associated with CAD in Japanese patients who have undergone coronary angiography.

PATIENTS AND METHODS

The patient population. A total of 739 consecutive patients who underwent coronary angiography (CAG) for suspected CAD at Tokyo Medical Center during the period from July 2008 to February 2017 participated in this study, which was approved by the Institutional Ethics Committees of Tokyo Medical Center (approval no. R07-054/R15-056) and Ochanomizu University (approval no. 2016-1) and conformed to the Declaration of Helsinki. All of the patients gave their written informed consent prior to participating in the study. We excluded patients with a history of percutaneous coronary intervention or cardiac surgery. Of the 739 patients, 70 patients with missing data in lipid levels and 57 with missing data regarding the intakes of ana-

lyzed foods and beverages were excluded from the present study. As a result, 612 patients were included and analyzed in the present study.

Blood samples were taken several days before admission or on admission from patients undergoing elective coronary angiography. However, from patients undergoing emergent coronary angiography, such as patients with MI, blood samples were taken on admission or the next morning after admission. Serum lipid levels were measured by standard laboratory methods. Hyperlipidemia was defined as a low-density lipoprotein (LDL) cholesterol (LDL-C) level >140 mg/dL or being on medication for hyperlipidemia. Low HDL (high-density lipoprotein) cholesterol (HDL-C) was defined as an HDL-C level <40 mg/dL. Diabetes mellitus was defined as a fasting plasma glucose level ≥126 mg/dL or being on medication for diabetes mellitus. Hypertension was defined as blood pressures of ≥140/90 mmHg or being on medication for hypertension.

Coronary angiograms were recorded on a cineangiogram system (Philips Electronics Japan, Tokyo).

Table 4. Odd ratios (95% confidence interval) for the prevalence of CAD, 3-VD, and MI according to daily green tea consumption.

	Green tea consumption (cups/d)			<i>p</i> -trend
	<1 (<i>n</i> =131)	1–3 (<i>n</i> =333)	>3 (<i>n</i> =148)	
CAD				
Number of case	92	211	85	
OR (Model 1)	1	0.70 (0.44–1.09)	0.52 (0.31–0.88)	0.015
OR (Model 2)	1	0.66 (0.41–1.06)	0.48 (0.27–0.84)	0.010
OR (Model 3)	1	0.72 (0.44–1.18)	0.54 (0.30–0.98)	0.044
3-VD				
Number of case	30	54	26	
OR (Model 1)	1	0.55 (0.33–0.93)	0.54 (0.29–1.01)	0.062
OR (Model 2)	1	0.53 (0.31–0.91)	0.49 (0.25–0.93)	0.033
OR (Model 3)	1	0.55 (0.32–0.97)	0.49 (0.24–0.98)	0.047
MI				
Number of case	39	73	26	
OR (Model 1)	1	0.72 (0.46–1.15)	0.60 (0.33–1.07)	0.078
OR (Model 2)	1	0.67 (0.42–1.08)	0.52 (0.28–0.95)	0.031
OR (Model 3)	1	0.67 (0.41–1.09)	0.51 (0.27–0.97)	0.037

Model 1: adjusted for age and gender.

Model 2: adjusted for age, gender, hypertension, hyperlipidemia, statin use, low HDL-C (<40 mg/dL), diabetes, smoking and alcohol use (≥ 1 glass/wk).

Model 3: adjusted for intake of coffee (≥ 1 cup/d), fish, soybean products, vegetables, and fruits (≥ 3 times/wk) in addition to the same covariates in model 2.

CAD was defined as at least one coronary artery having >50% luminal diameter stenosis on an angiogram. The severity of CAD was represented as the number of >50% stenotic coronary vessels. Each MI was confirmed by the documentation of coronary artery stenosis plus either elevation of cardiac enzymes or diagnostic electrocardiogram changes. All angiograms were evaluated by a single cardiologist (Y.M.) who was blinded to the patients' clinical and laboratory data.

We obtained the patients' data on their green tea and coffee consumption by using a quantitative questionnaire that we modified slightly from that used in earlier research (16, 17). Briefly, the frequencies of green tea consumption and coffee consumption were classified into three categories (<1 cup/d, 1–3 cups/d, and >3 cups/d). We did not collect the type of coffee (decaffeinated or caffeinated), because decaffeinated coffee is not commonly consumed in Japan. The patients' intakes of fish, soybean products, vegetable, and fruits were also determined and classified into three categories (<3 times/wk, 3–4 times/wk, and >4 times/wk). Since fish intake was reported to be associated with a decreased risk of CAD in a middle-aged Japanese population (19), we also assessed fish intake whose data were not collected in our previous studies (16, 17).

Statistical analysis. Continuous variables are expressed as the mean $\pm$ SD, and categorical variables are expressed as the number and proportion (%). Differences among three groups were evaluated by an analysis of variance for parametric variables and by the χ^2 test for categorical variables.

We performed a multiple logistic regression analysis to determine the independent associations between green tea or coffee consumption and CAD or MI. The adjusted covariates were as follows: (1) age (continuous as 10-y groups) and gender (model 1), (2) age, gender, hypertension (yes/no), hyperlipidemia (yes/no), low-HDL-C (<40 mg/dL) (yes/no), statin use (yes/no), diabetes mellitus (yes/no), smoking (yes/no), and alcohol (yes/no) (model 2), (3) the covariates in model 2 plus the intake of green tea or coffee (≥ 1 cup/d), fish, soybean products, vegetables, and fruits (≥ 3 times/wk) (model 3). Categorical variables were converted to dummy variables and inserted into the multiple regression models. Tests for trends were assessed by using the ordinal categorical variables of 1, 2, and 3 for each category of consumption (green tea and coffee). All statistical analyses were conducted with the SPSS software package (IBM SPSS ver. 25, Japan). A *p*-value <0.05 was considered significant.

RESULTS

Among the 612 study patients, CAD was detected in 388 patients: one-vessel disease (1-VD, *n*=166), two-vessel disease (2-VD, *n*=112), and three-vessel disease (3-VD, *n*=110). Of the 388 patients with CAD, 138 (36%) had MI. Compared to 224 patients without CAD, 388 patients with CAD were significantly older, predominantly male, and had higher prevalence of hypertension, diabetes, smoking, hyperlipidemia, and statin use as well as higher LDL-C and lower HDL-C levels (Table 1). Moreover, we divided the 388 patients with CAD into

Table 5. Odd ratios (95% confidence interval) for the prevalence of CAD, 3-VD, and MI according to daily coffee consumption.

	Coffee consumption (cups/d)			<i>p</i> -trend
	<1 (<i>n</i> =206)	1–3 (<i>n</i> =358)	>3 (<i>n</i> =48)	
CAD				
Number of case	124	233	31	
OR (Model 1)	1	1.36 (0.94–1.97)	1.35 (0.68–2.69)	0.144
OR (Model 2)	1	1.20 (0.81–1.78)	0.87 (0.42–1.84)	0.748
OR (Model 3)	1	1.25 (0.84–1.86)	0.76 (0.35–1.64)	0.823
3-VD				
Number of case	39	61	10	
OR (Model 1)	1	1.04 (0.66–1.65)	1.67 (0.73–3.84)	0.391
OR (Model 2)	1	0.98 (0.61–1.57)	1.36 (0.57–3.22)	0.700
OR (Model 3)	1	0.97 (0.60–1.57)	1.18 (0.49–2.84)	0.867
MI				
Number of case	40	81	17	
OR (Model 1)	1	1.13 (0.73–1.74)	1.83 (0.90–3.73)	0.156
OR (Model 2)	1	1.03 (0.65–1.61)	1.55 (0.73–3.28)	0.402
OR (Model 3)	1	1.01 (0.64–1.59)	1.37 (0.64–2.94)	0.561

Model 1: adjusted for age and gender.

Model 2: adjusted for age, gender, hypertension, hyperlipidemia, statin use, low HDL-C (<40 mg/dL), diabetes, smoking and alcohol use (≥ 1 glass/wk).

Model 3: adjusted for intakes of green tea (≥ 1 cup/d), fish, soybean products, vegetables, and fruits (≥ 3 times/wk) in addition to the same covariates in model 2.

Table 6. Odd ratios (95% confidence interval) for the prevalence of CAD, 3-VD, and MI according to weekly vegetables or fruits consumption.

	Vegetables consumption (times/wk)			<i>p</i> -trend
	<3 (<i>n</i> =114)	3–4 (<i>n</i> =202)	>4 (<i>n</i> =296)	
CAD				
Number of case	85	132	171	
Multivariate adjusted OR	1	0.64 (0.36–1.14)	0.44 (0.24–0.81)	0.007
3-VD				
Number of case	20	40	50	
Multivariate adjusted OR	1	1.00 (0.52–1.91)	0.76 (0.38–1.52)	0.352
MI				
Number of case	33	50	55	
Multivariate adjusted OR	1	0.80 (0.46–1.41)	0.62 (0.34–1.13)	0.111

	Fruits consumption (times/wk)			<i>p</i> -trend
	<3 (<i>n</i> =172)	3–4 (<i>n</i> =151)	>4 (<i>n</i> =289)	
CAD				
Number of case	125	96	167	
Multivariate adjusted OR	1	0.79 (0.46–1.35)	0.51 (0.31–0.84)	0.005
3-VD				
Number of case	36	25	49	
Multivariate adjusted OR	1	0.66 (0.35–1.24)	0.55 (0.31–0.98)	0.046
MI				
Number of case	48	35	55	
Multivariate adjusted OR	1	0.87 (0.50–1.51)	0.67 (0.40–1.13)	0.123

Adjusted for age, gender, hypertension, hyperlipidemia, statin use, low HDL-C (<40 mg/dL), diabetes, smoking and alcohol use (≥ 1 glass/wk), intake of green tea and coffee (≥ 1 cup/d), fish, soybean products, and vegetables or fruits (≥ 3 times/wk).

Table 7. Subgroup analyses by vegetables and fruits intake categories of odd ratios (95% confidence interval) for the prevalence of CAD and MI according to daily green tea consumption.

	Green tea consumption (cups/d)			p-trend	Green tea consumption (cups/d)			p-trend
	<1	1-3	>3		<1	1-3	>3	
High intake group of vegetables (>4 times/wk), n=296								
CAD								
Number of case	27/43	100/171	44/82					
Multivariate adjusted OR	1	0.59 (0.25-1.38)	0.42 (0.16-1.11)	0.084				
MI								
Number of case					14/43	31/171	10/82	
Multivariate adjusted OR	1				1	0.35 (0.14-0.87)	0.18 (0.06-0.56)	0.004
Low intake group of vegetables (≤4 times/wk), n=316								
CAD								
Number of case	65/88	111/162	41/66					
Multivariate adjusted OR	1	0.77 (0.41-1.47)	0.62 (0.28-1.40)	0.247				
MI								
Number of case					25/88	42/162	16/66	
Multivariate adjusted OR	1				1	0.86 (0.46-1.60)	0.87 (0.39-1.97)	0.705
High intake group of fruits (>4 times/wk), n=289								
CAD								
Number of case	29/38	95/171	43/80					
Multivariate adjusted OR	1	0.31 (0.12-0.80)	0.25 (0.09-0.72)	0.025				
MI								
Number of case					15/38	32/171	8/80	
Multivariate adjusted OR	1				1	0.29 (0.12-0.70)	0.10 (0.03-0.33)	<0.001
Low intake group of fruits (≤4 times/wk), n=323								
CAD								
Number of case	63/93	116/162	42/68					
Multivariate adjusted OR	1	1.22 (0.65-2.29)	0.85 (0.39-1.87)	0.767				
MI								
Number of case					24/93	41/162	18/68	
Multivariate adjusted OR	1				1	0.89 (0.47-1.67)	1.22 (0.54-2.74)	0.714
Adjusted for age, gender, hypertension, hyperlipidemia, statin use, low HDL-C (<40 mg/dL), diabetes, smoking, alcohol use (≥1 glass/wk), and intakes of coffee (≥1 cup/d), fish, soybean products, vegetables, and fruits (≥3 times/wk).								

Adjusted for age, gender, hypertension, hyperlipidemia, statin use, low HDL-C (<40 mg/dL), diabetes, smoking, alcohol use (≥1 glass/wk), and intakes of coffee (≥1 cup/d), fish, soybean products, vegetables, and fruits (≥3 times/wk).

2 groups of 250 CAD patients without MI and 138 with MI. Compared to CAD patients without MI, patients with MI were younger and had less statin use and higher LDL-C and lower HDL-C levels (Table 1).

The consumptions of green tea, coffee and foods in patients with and without CAD are shown in Table 2. There was no significant difference in the consumptions of green tea, coffee or alcohol between patients with and without CAD. Notably, the percentage of patients with <1 cup/d intake of green tea was higher in patients with MI than in those without CAD. Regarding the food intakes, the percentages of patients with <3 times/wk intakes of vegetables and fruits were higher in patients with CAD, especially in those with MI, than in those without CAD.

Table 3 provides clinical characteristics of patients according to green tea and coffee consumption. Patients with greater green tea consumption were older and had less male predominance, fewer smokers, a lower coffee intake and higher intakes of fish, soybeans, vegetables and fruits. Notably, patients with greater green tea consumption tended to have lower prevalence of CAD and had significantly lower prevalence of MI. In contrast, patients with greater coffee consumption were younger and had male predominance, more smokers and higher LDL-C levels. There was no significant difference in the prevalence of CAD or MI among the 3 groups of coffee consumption.

Tables 4 and 5 summarize the data regarding the associations between green tea or coffee consumption and CAD, 3-VD or MI obtained by multiple logistic regression analyses. The prevalence of CAD significantly decreased depending on green tea consumption even after the adjustment for age, gender, hypertension, hyperlipidemia, low HDL-C, statin use, diabetes, smoking, alcohol, and intakes of coffee, fish, soybean products, vegetables, and fruits (Table 4). The odds ratio (OR) for >3 cups/d intake of green tea compared to <1 cup/d was 0.54 (95% CI: 0.30-0.98, *p*-trend=0.044). The prevalence of 3-VD and MI also significantly decreased depending on green tea consumption. The ORs for >3 cups/d intake of green tea compared to <1 cup/d were 0.49 (95% CI: 0.24-0.98, *p*-trend=0.047) for 3-VD and 0.51 (95% CI: 0.27-0.97, *p*-trend=0.037) for MI, respectively. In contrast, coffee consumption was not associated with any prevalence of CAD, 3-VD or MI (Table 5). Table 6 summarizes the data regarding the associations between vegetables or fruits consumption and CAD, 3-VD or MI obtained by multiple logistic regression analyses. The prevalence of CAD significantly decreased depending on vegetables or fruits consumption.

To elucidate the effects of the intakes of vegetables and fruits on the association between green tea consumption and CAD or MI, we divided the 612 patients into 2 subgroups by the intakes of vegetables and fruits (Table 7). The prevalence of CAD significantly decreased depending on green tea consumption in the subgroup with fruits intake >4 times/wk but not in the subgroup with fruits intake ≤4 times/wk. The prevalence of MI also decreased depending on green tea consumption in

the subgroups with vegetables intake >4 times/wk and with fruits intake >4 times/wk but not in those with vegetables intake $\leq$ 4 times/wk or with fruit intake $\leq$ 4 times/wk.

DISCUSSION

The results of our analyses demonstrate that greater green tea consumption by Japanese adults was associated with decreased risks of CAD, especially 3-VD and MI, after adjustment for well-known atherosclerotic risk factors and other dietary habits. In contrast, there was no significant association between coffee consumption and CAD.

A few studies have investigated the relationship between green tea consumption and CAD. Sasazuki et al. reported an weak inverse association between green tea consumption and the prevalence of CAD in men ($n=302$), but not in women ($n=210$), who underwent coronary angiography at hospitals in Fukuoka City, Japan (14). Sano et al. stated that green tea consumption was associated with a lower incidence of CAD and that it was an independent factor for CAD in 203 patients who underwent coronary angiography at hospitals in Chiba Prefecture, Japan (15). Wang et al. reported that green tea consumption was inversely associated with the prevalence of CAD in Chinese male subjects (20). Our prior study of 725 patients who underwent coronary angiography in Saitama Prefecture found that green tea consumption was inversely associated with the prevalence of MI, but not with CAD (17). In the same line of the results of our prior study, our present study also demonstrated the inverse association between green tea consumption and MI.

In the Japanese population, the percentage of elderly people (≥ 65 y) is steadily increasing from 17% in 2000 to 23% in 2010 (<https://www.stat.go.jp/english/data/handbook/pdf/2019all.pdf>). Since the age of patients with MI is known to be younger than those with stable CAD (21), the incidence of MI is reported to decrease with an increase in elderly people from 2004 to 2011 in Kumamoto Prefecture (22). The incidence of MI in Iwate Prefecture also decreased with increased percentages of elderly people and statin use from 2006 to 2014 (23). In our prior study performed from 1999 to 2006 (17), the mean age of patients with CAD was 64 ± 11 y, and 43% of CAD patients had MI. However, probably reflecting trends in the age composition and the MI incidence in Japanese population, in our present study from 2008 to 2017, the age of CAD patients was older (68 ± 11 y), and the percentage of MI in CAD patients was lower (36%) than in our prior study. In spite of lower prevalence of MI, our present study confirmed the results of our prior study regarding that green tea consumption was inversely associated with MI. Moreover, our present study demonstrated that green tea consumption was inversely associated with CAD, especially 3-VD, as well as MI. These findings thus suggest that green tea consumption may play a protective role against not only the development of MI but also the progression of CAD in Japanese population.

It is noteworthy that the green tea drinkers in our patient population were more likely to consume traditional Japanese foods (i.e., fish and soybean products) and antioxidants-rich foods (i.e., vegetables and fruits), which are thought to be protective against CAD. In fact, the present study found that vegetables and fruits consumption was inversely associated with the prevalence of CAD. However, the prevalence of CAD and 3-VD as well as MI significantly decreased depending on green tea consumption even after the adjustment for these dietary factors. Interestingly, the inverse association between green tea consumption and CAD or MI was found in the high intake groups of vegetables or fruits but not in the low intake groups of vegetables or fruits. These findings thus suggest that green tea consumption may have synergistic effect on the protective role of vegetables and fruits against the development of CAD.

A meta-analysis including two cohorts and three case-control studies revealed a significant 28% reduction in the risk of CAD with the highest green tea consumption, and it demonstrated that an increase in green tea consumption of 1 cup/d was associated with a 10% decrease in the risk of developing CAD (24). Green tea content catechins, especially (–)-epigallocatechin-3-gallate (EGCG), are known to exert anti-atherosclerotic effects through multiple mechanisms. We reported that the daily consumption of green tea decreased serum malondialdehyde-modified (MDA)-LDL concentrations in healthy male volunteers (25), and that an acute intake of green tea catechins prevented LDL oxidation via their accumulation in LDL particles in healthy volunteers (26). Green tea catechins also reported to reduce blood cholesterol levels (27) and suppress the postprandial increase in plasma triacylglycerol levels after a fat load (28). Experimental and clinical studies suggested that green tea catechins improved endothelial function (29), thereby providing an additional beneficial effect against CAD.

In contrast to green tea, our present analyses did not detect any association between coffee consumption and the risk of CAD. The results of previous studies on coffee consumption and CHD-related outcomes have been largely inconsistent. A meta-analysis by Wu et al. of 21 independent cohort studies showed that coffee consumption was not associated with an increased risk of CHD and that habitual moderate coffee drinking was associated with a lower risk of CHD in women (30). On the other hand, a recent meta-analysis of six cohorts and 11 case-control studies by Mo et al. indicated that the consumption of >3 cups of coffee per day was associated with a significantly increased risk of MI compared with <1 cup, but this positive association was found only in men (31). These two meta-analyses did not include Japanese studies; therefore, our present study provides evidence of no association between coffee consumption and the prevalence of CAD among Japanese population. Moreover, our present study showed that patients with greater coffee consumption significantly had lower intakes of green tea and fruits. The gender differences in the association between coffee consumption and CHD

risk may be partly explained by genders' smoking status and the related lifestyle habits. Many studies have indicated that smoking is associated with other unhealthy habits (e.g., physical inactivity and alcohol abuse) and also strongly related to coffee drinking (31). Although most of those studies as well as our present study had made adjustment for smoking, not all smoking-related unhealthy habits cannot be adjusted. Further studies are needed to evaluate the impact of a smoking habit on the association between coffee consumption and the risk of CHD.

Our study has several limitations. First, angiography was used to evaluate coronary atherosclerosis. Angiography cannot visualize plaques and shows only lumen characteristics. Second, of the 739 patients, 70 with missing data in lipid levels and 57 with missing data in the intakes of foods and beverages were excluded from the present study, as done in our prior studies (16, 17). This may have affected the results of our study. Third, for patients undergoing emergent angiography, like patients with MI, blood samples were taken on admission or the next morning after admission. Although blood cholesterol levels were believed to decrease soon after acute MI, a recent study reported that the changes in cholesterol levels after acute MI were much smaller than those noted in older studies (32). However, the day of blood sampling in patients with MI may have affected the results of our study. Fourth, our study's design was cross-sectional and thus could not establish causality, since it only showed some associations and led to some hypotheses. Finally, we studied only Japanese patients who underwent coronary angiography, and such individuals are generally considered to be a highly select population at high risk for CAD. Our results therefore may not be applicable to the general Japanese population or other ethnic populations.

In conclusion, our findings demonstrated that greater green tea consumption was inversely associated with the prevalence of CAD, especially 3-VD and MI, independent of atherosclerotic risk factors and other dietary habits in Japanese patients. Green tea consumption, especially with a diet rich in vegetables and fruits, may play a protective role against not only the development of MI but also the progression of CAD.

Authorship

Research conception and design: RO, KK and YM; data curation: MA and YI; experiments: YK, ES and CT; statistical analysis of the data: YK and YM; interpretation of the data: YK and YM; writing of the manuscript: YK and YM; project administration: YM.

Disclosure of state of COI

Our study has no conflict of interest to disclose.

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