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Additive effects of green tea and coffee on all-cause mortality in patients with type 2 diabetes mellitus: the Fukuoka Diabetes Registry

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ABSTRACT

Introduction The impact of consuming green tea or coffee on mortality in patients with diabetes is controversial. We prospectively investigated the impact of each beverage and their combination on mortality among Japanese patients with type 2 diabetes.

Research design and methods In all, 4923 patients (2790 men, 2133 women) with type 2 diabetes (mean age, 66 years) were followed prospectively (median, 5.3 years; follow-up rate, 99.5%). We evaluated the amount of green tea and coffee consumed using self-administered questionnaires.

Results During the follow-up period, 309 participants died. The consumption of green tea, coffee, and a combination of the beverages was associated with reduced all-cause mortality. Multivariable-adjusted hazard ratios (95% CIs) for green tea were as follows: none 1.0 (referent); 0.85 (0.60–1.22) for ≤1 cup/day; 0.73 (0.51–1.03) for 2–3 cups/day; 0.60 (0.42–0.85) for ≥4 cups/day; and P for trend, 0.002. For coffee, they were: none 1.0 (referent); 0.88 (0.66–1.18) for <1 cup/day; 0.81 (0.58–1.13) for 1 cup/day; 0.59 (0.42–0.82) for ≥2 cups/day; P for trend, 0.002. With the combination they were 1.0 (referent) for no consumption of green tea and coffee; 0.49 (0.24–0.99) for 2–3 cups/day of green tea with ≥2 cups/day of coffee; 0.42 (0.20–0.88) for ≥4 cups/day of green tea with 1 cup/day of coffee; and 0.37 (0.18–0.77) for ≥4 cups/day of green tea with ≥2 cups/day of coffee.

Conclusions Higher consumption of green tea and coffee was associated with reduced all-cause mortality: their combined effect appeared to be additive in patients with type 2 diabetes.

Significance of this study

What is already known about this subject?

- Higher green tea or coffee consumption has been reported to confer health benefits, and reduce all-cause mortality in the general population, respectively.
- No studies have investigated the association between green tea consumption and mortality in diabetic patients, and few studies have examined the association between coffee consumption and mortality in diabetic patients, and the results are controversial.

What are the new findings?

- Higher consumption of green tea and coffee was associated with reduced all-cause mortality.
- The combined effect of green tea and coffee on mortality appeared to be additive in patients with type 2 diabetes.

How might these results change the focus of research or clinical practice?

- This study suggests that consuming green tea and coffee may have beneficial effects on the longevity of Japanese people with type 2 diabetes.

INTRODUCTION

Worldwide, the number of patients with diabetes is increasing in both developed and developing countries.[1] Diabetic patients are at increased risk for classical micro- and macrovascular diseases as well as nonclassical diseases, such as dementia, malignancy, and fragility fracture, which affect both quality of life and life expectancy.[2] Recent advances in therapeutics (such as sodium-glucose cotransporter 2 inhibitors, glucagon-like peptide-1 receptor agonists, and bariatric surgery) have been remarkable, however, lifestyle improvements are still regarded as the basic therapy.[3] Lifestyle management comprises physical activity, smoking cessation, and nutrition therapy (including both food and beverages).[3] However, epidemiological research on nonalcoholic beverages, such as green tea and coffee, has been scarce for diabetic patients.

Asian, especially East Asian, populations have a traditional habit of drinking green tea. Green tea derives from fresh leaves of *Camellia sinensis*, and it contains various chemicals, such as phenolic compounds, theanine,

and caffeine.[4] Through antioxidant, anti-inflammatory, or anti-bacterial properties,[4 5] higher green tea consumption has been reported to confer health benefits, including preventing such chronic diseases as diabetes mellitus,[4 6] and reduce mortality.[7 8] Hitherto, however, no studies have investigated the association between green tea consumption and mortality in diabetic patients.

Coffee is one of the most frequently consumed beverages worldwide. It contains numerous bioactive chemicals, including phenolic compounds and caffeine, that have been reported to impact health through various mechanisms, such as antioxidant, anti-inflammatory, and anti-mutagenic effects:[9 10] the result is a reduced risk of developing type 2 diabetes, dyslipidemia, or malignancy.[10] In contrast to these health-promoting effects, coffee also has harmful effects, such as increasing blood pressure[10] and the risk of myocardial infarction.[11] In the general population, there is growing evidence that coffee consumption is associated with reduced risk of all-cause and cause-specific mortality.[12–15] However, few epidemiological studies have examined this association in diabetic patients, and the results are controversial.[16–19] This discrepancy may be due to the presence of diabetic complications, including cardiovascular disease (CVD), which could be affected by caffeine consumption.[11] Further, most studies have been conducted only with developed country populations, which have higher risks of CVD than Asian ones.[20]

Recently, green tea has attracted considerable attention as a healthy beverage in developed countries.[21] Japan has the culinary culture of both its own traditional food with green tea and developed country food with coffee: this provides a unique opportunity to investigate the combined effect of green tea and coffee consumption on mortality. Accordingly, in the present study, we prospectively investigated the impact of green tea, coffee consumption, and their combination on all-cause and cause-specific mortality in Japanese patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS

Study participants

The Fukuoka Diabetes Registry is a multicenter prospective study (UMIN Clinical Trial Registry 000002627) designed to investigate the effect of modern treatments and lifestyles on the prognoses of patients with diabetes mellitus. The registry includes patients who regularly attended teaching hospitals certified by the Japan Diabetes Society or certified diabetes clinics in Fukuoka Prefecture, Japan.[22] In all, 5131 patients with diabetes mellitus aged 20 years or older were registered during regular visits between April 2008 and October 2010. The registry exclusion criteria were as follows: patients with drug-induced diabetes or those undergoing corticosteroid treatment; patients undergoing renal replacement therapy; patients with serious diseases other than diabetes, such as advanced malignancies and decompensated liver cirrhosis; and patients unable to visit diabetologists regularly. After excluding 208 participants with type 1 diabetes, we enrolled the remaining 4923 participants in this study. The study conformed with the principles of the Declaration of Helsinki and was approved by the Kyushu University Institutional Review Board (approval number 290). All participants provided their written informed consent to take part.

Clinical evaluation at registration as baseline

Information regarding diabetes duration from its diagnosis, smoking habits, alcohol intake, leisure-time physical activity (LTPA), sleep duration, depressive symptoms, and history of coronary heart disease (CHD), stroke, and cancer was obtained using a self-administered questionnaire. Smoking habits and alcohol intake were classified as either current or not. LTPA was estimated as metabolic equivalent-hours per week.[23] We assessed the presence of depressive symptoms using the Center for Epidemiologic Studies Depression Scale:[24] participants who scored 16 or more among 60 points were defined as having depressive symptoms.

Body weight and height were measured, and body mass index (BMI) was calculated. Blood pressure was measured in a sitting position: hypertension was defined as blood pressure ≥140/90 mmHg or current use of antihypertensive agents. Medical charts were reviewed for all medications, including insulin, oral hypoglycemic agent, antihypertensive drugs, antiplatelet drugs, and statins.

The dietary survey, including green tea and coffee consumption, was conducted using a self-administered brief diet history questionnaire (Gender Medical Research Inc., Tokyo) regarding the frequency of 58 food items and supplements. The validity of many nutrients has previously been studied in an adult Japanese population.[25] Green tea and coffee consumption was self-reported and assessed by answering the question "How often do you drink each beverage?" Participants were asked to select one among eight categories: none;<1 cup/week; 1 cup/week; 2–3 cups/week; 4–6 cups/week; 1 cup/day; 2–3 cups/day; and ≥4 cups/day. The amounts of green tea and coffee consumed differed: green tea, none 12%, ≤1 cup/day 23%, ≥2 cups/day 64%; and coffee, none 20%, ≤1 cup/day 46%, ≥2 cups/day 34%. Accordingly, we categorized the participants into the following four groups by beverage: green tea, none, ≤1 cup/day, 2–3 cups /day, ≥4 cups/day; and coffee, none, <1 cup/day, 1 cup/day, ≥2 cups/day. There were no questions about the consumption of decaffeinated or caffeinated drinks because decaffeinated beverages are uncommon in Japan.

Laboratory measurements

Blood samples were collected by venipuncture, and spot urine samples were obtained. Hemoglobin A_{1c} (HbA_{1c}) was determined by high-performance liquid chromatography (Tosoh Corp., Tokyo,). Serum low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, creatinine, and urinary creatinine

concentrations were measured using enzymatic methods. We measured urinary albumin using an immunonephelometry method (Medical and Biological Laboratories Co., Ltd., Nagoya). We calculated estimated glomerular filtration rates (eGFR) based on serum creatinine using the equation proposed by the Japanese Society of Nephrology.[26] Urinary albumin-creatinine ratio (UACR) levels were calculated by dividing the urinary albumin values by the urinary creatinine concentrations.

Mortality follow-up

The primary outcome in this study was all-cause mortality. Participants received an annual follow-up during their survival through interviews, medical records, letters, telephone calls, and municipal registration of residence. During the follow-up period (median, 5.3 years), 27 participants were lost to follow-up (follow-up rate, 99.5%). The underlying cause of death was determined based on medical records or death certificates: it was coded according to the International Classification of Diseases, 10th revision.

Statistical analysis

The age- and sex-adjusted mortality rate was calculated using the person-years method: we calculated mortality in each 10-year age-group by sex and then weighted it based on the distribution of all participants. The Cox proportional-hazards models were used to estimate the HRs and 95% CIs for mortality. In the multivariable-adjusted model, we selected the following covariates, known to be a potential risk or protective factors for mortality: age, sex, BMI, diabetes duration, current smoking habit, current alcohol intake, LTPA, sleep duration, HbA_{1c}, UACR, systolic blood pressure, LDL cholesterol, history of CVD, and cancer. We conducted further adjustment for the coffee-drinking habit to analyze the association between green tea and mortality, and vice versa. We confirmed the proportional hazard assumption graphically and using the Schoenfeld residual test: the P-value was 0.57 for the green tea category, 0.44 for the coffee category, and 0.15 for the green tea and coffee category. All statistical analyses were performed using Statistical Analysis Software (SAS) version 9.4 (SAS institute Inc., Cary, NC, USA). We considered values of P<0.05 statistically significant in all analyses.

RESULTS

Table 1 summarizes the baseline clinical characteristics of the four groups divided according to the amount of green tea or coffee consumed. With the green tea groups, mean age, duration of diabetes, sleep duration, HDL cholesterol, systolic blood pressure, and frequency of cancer history increased in participants with higher green tea consumption. By contrast, the proportion of males, current smokers and current drinkers, eGFR, and diastolic blood pressure decreased in participants with higher green tea consumption. With the coffee groups, mean age, sleep duration, UACR, systolic blood pressure, frequency of taking antihypertensive or antiplatelet drugs, history of CVD, and cancer decreased in participants with higher coffee consumption. Conversely, the proportion of males, current smokers and current drinkers, mean LTPA, HbA_{1c}, eGFR, LDL cholesterol, HDL cholesterol, and diastolic blood pressure increased in participants with higher coffee consumption.

During the follow-up period (median, 5.3 years; follow-up rate, 99.5%), 309 participants (218 men, 91 women) died. The main causes of death were cancer (n=114) and CVD (n=76). Table 2 presents the number of all-cause and cause-specific deaths, crude incidence, multivariable-adjusted HRs, and 95% CIs according to the green tea and coffee consumption groups. In the green tea groups, all-cause mortality significantly decreased according to the amount of green tea consumed (P for trend, 0.001). The multivariable-adjusted HR was significantly lower in participants who consumed ≥4 cups/day of green tea compared with those who did not drink green tea (HR, 0.60; 95% CI, 0.42 to 0.85). Further, the HR remained significant after additional adjustments for coffee consumption. Cause-specific mortality for cancer was not associated with the amount of green tea consumed: the association of the amount of green tea consumed with CVD was marginally insignificant (P for trend, 0.08). In the coffee groups, all-cause mortality was also significantly reduced according to the amount of coffee consumed (P for trend, 0.001). The multivariable-adjusted HR was significantly lower in participants who consumed ≥2 cups/day of coffee than in those who did not consume coffee (HR, 0.59; 95% CI, 0.42 to 0.82). That association remained significant after further adjustments for green tea consumption. Cause-specific mortality for cancer was not associated with the amount of coffee consumed: the association of the amount of coffee consumption with CVD was marginally insignificant (P for trend, 0.06).

Figure 1 shows the multivariable-adjusted HRs of all-cause mortality according to combined green tea and coffee consumption. When the mortality in participants drinking neither green tea nor coffee was set as the referent, multivariable-adjusted HRs were significantly reduced as follows: in those consuming 2–3 cups of green tea with ≥2 cups/day of coffee (HR, 0.49; 95% CI, 0.24 to 0.99); consuming ≥4 cups/day of green tea with 1 cup/day of coffee (HR, 0.42; 95% CI, 0.20 to 0.88); and drinking ≥4 cups of green tea with ≥2 cups/day of coffee (HR, 0.37; 95% CI, 0.18 to 0.77) (table 3).

CONCLUSIONS

In this prospective study, we found that higher green tea and coffee consumption was significantly associated with decreased all-cause mortality in patients with type 2 diabetes. This association remained significant after adjusting for potential confounders: the impact of each beverage on mortality was independent. Similar trends were evident in analyzes of CVD-specific mortality.

Table 1 Baseline clinical characteristics according to amount of green tea or coffee consumed among Japanese participants with type 2 diabetes

	Green tea consumption				Coffee consumption			
	None	≤1 cup /d	2–3 cups/d	≥4 cups/d	None	<1 cup /d	1 cup/d	≥2 cups/d
N	607	1143	1389	1784	994	1306	963	1660
Age (years)	64.6±10.2	62.5±10.8	65.7±9.8	67.3±9.7	69.0±10.0	66.4±10.2	65.6±10.1	62.3±9.5
Male sex (%)	60.3	64.3	60.5	47.6	50.6	54.7	53.3	63.9
Duration of diabetes (years)	14.9±10.3	14.8±10.4	15.9±10.6	16.0±10.6	16.3±10.9	15.5±10.6	15.5±10.3	15.2±10.4
BMI (kg/m^2)	23.9±3.4	24.1±3.8	23.5±3.7	23.7±3.9	23.7±3.7	23.9±3.8	23.9±4.0	23.6±3.6
Current smoker (%)	24.9	20.7	18.85	15.1	12.6	12.1	15.1	29.2
Current alcohol intake (%)	40.5	45.7	42.6	31.8	30.5	38.8	40.9	43.5
Depressive symptoms (%)	10.2	9.6	7.5	8.7	9.7	9.3	7.5	8.6
LTPA (MET h/week)	12.3±16.1	11.2±14.7	11.5±14.0	12.0±15.3	11.3±14.8	11.3±14.9	12.5±15.2	11.8±14.8
Sleep duration (h/day)	6.8±1.4	6.7±1.3	6.9±1.3	6.9±1.5	7.0±1.6	6.9±1.4	6.9±1.3	6.7±1.3
HbA_{1c} (%)	7.4±1.0	7.4±1.0	7.4±1.0	7.5±1.1	7.4±1.1	7.4±1.0	7.4±1.0	7.5±1.1
HbA_{1c} (mmol/mol)	57.3±10.8	57.4±11.2	57.4±10.7	58.4±12.2	57.4±11.8	57.1±11.2	57.8±11.0	58.5±11.6
eGFR (ml/min/1.73 m^2)	73.3±23.7	78.6±21.8	74.2±21.4	73.5±20.9	69.7±23.1	73.5±21.0	75.5±22.2	78.6±20.4
UACR (mg/g·Cr)	246±780	175±690	178±583	195±620	251±771	209±666	189±695	145±509
LDL cholesterol (mmol/l)	2.9±0.7	2.8±0.7	2.9±0.7	2.9±0.7	2.8±0.7	2.8±0.7	2.8±0.7	2.9±0.7
HDL cholesterol (mmol/l)	1.4±0.4	1.5±0.4	1.5±0.4	1.5±0.4	1.4±0.4	1.4±0.4	1.5±0.4	1.5±0.4
Systolic blood pressure (mmHg)	130±18	130±17	130±17	132±17	131±18	132±17	131±17	129±16
Diastolic blood pressure (mmHg)	75±11	75±11	75±11	74±11	73±11	74±11	75±11	75±10
History of CVD (%)	24.2	22.1	20.7	21.4	25.7	22.8	20.9	18.9
History of cancer (%)	7.1	8.5	9.4	10.7	11.1	9.4	10.4	7.7
Insulin therapy (%)	32.8	27.7	27.0	29.6	30.4	24.9	28.7	31.1
Oral hypoglycemic agent (%)	59.6	64.2	65.5	62.3	61.2	64.9	64.1	62.9
Antihypertensive drugs (%)	55.7	51.6	54.6	54.4	61.9	57.4	56.5	45.1
Antiplatelet drugs (%)	28.2	22.9	24.1	25.8	29.4	26.9	25.2	20.6
Statin (%)	43.0	44.4	41.0	44.7	43.9	40.8	48.4	42.3
Coffee drinker (>0 cup/d, %)	75.1	87.0	81.5	75.5	–	–	–	–
Green tea drinker (>0 cup/d, %)	–	–	–	–	84.8	89.6	88.5	87.4

Values are expressed as means±SD or percentages.
BMI, body mass index; Cr, creatinine; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rates; HbA_{1c}, hemoglobin A_{1c}; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LTPA, leisure-time physical activity; MET, metabolic equivalent; UACR, urinary albumin creatinine ratio.

Further, the combination of higher green tea and coffee consumption significantly reduced all-cause mortality risk by 63%.

Hitherto, little research has investigated the association between green tea consumption and mortality in diabetic patients. Some epidemiological studies from Japan and China have reported the association between green tea consumption and mortality in the general population, including diabetic and non-diabetic individuals. The Ohsaki Study was the first large-scale investigation on this subject: among 40 530 Japanese men and women, it found that those who consumed ≥5 cups/day of green tea had a 15% lower risk of all-cause mortality than those drinking <1 cup/day.[6] A meta-analysis of five cohort studies of the general population (including diabetic and non-diabetic individuals) demonstrated that the HRs (95% CIs) of the highest vs the lowest green tea consumption were 0.80 (0.68–0.93) for all-cause mortality and 0.67

Table 2 All-cause and cause-specific mortality according to amount of green tea or coffee consumed among Japanese participants with type 2 diabetes

	Green tea consumption					Coffee consumption				
	None (n=607)	≤1 cup/d (n=1143)	2–3 cups/d (n=1384)	≥4 cups/d (n=1784)	P for trend	None (n=994)	<1 cup/d (n=1306)	1 cup/d (n=963)	≥2 cups/d (n=1660)	P for trend
All-cause mortality										
No of death	50	74	87	98		94	91	58	66	
Incidence (/1000PYs)	15.8	12.3	11.9	10.4		18.2	13.2	11.5	7.5	
HR (95% CI)										
Age- and sex-adjusted	1.0 (ref.)	0.87 (0.61–1.24)	0.71 (0.50–1.00)	0.60 (0.43–0.85)	0.001	1.0 (ref.)	0.81 (0.60–1.08)	0.76 (0.55–1.05)	0.58 (0.41–0.80)	0.001
Multivariable-adjusted	1.0 (ref.)	0.85 (0.60–1.22)	0.73 (0.51–1.03)	0.60 (0.42–0.85)	0.002	1.0 (ref.)	0.88 (0.66–1.18)	0.81 (0.58–1.13)	0.59 (0.42–0.82)	0.002
+Coffee	1.0 (ref.)	0.88 (0.61–1.26)	0.73 (0.51–1.03)	0.60 (0.42–0.85)	0.001	–	–	–	–	
+Green tea	–	–	–	–		1.0 (ref.)	0.88 (0.66–1.18)	0.81 (0.58–1.13)	0.58 (0.42–0.81)	0.002
Cancer mortality										
No of death	16	26	39	33		32	33	22	27	
Incidence (/1000PYs)	5.1	4.3	5.4	3.5		6.2	4.8	4.4	3.1	
HR (95% CI)										
Age- and sex-adjusted	1.0 (ref.)	0.96 (0.52–1.80)	0.98 (0.55–1.76)	0.63 (0.34–1.15)	0.09	1.0 (ref.)	0.87 (0.53–1.41)	0.86 (0.50–1.49)	0.72 (0.43–1.23)	0.26
Multivariable-adjusted	1.0 (ref.)	0.96 (0.52–1.80)	1.02 (0.57–1.83)	0.65 (0.35–1.19)	0.12	1.0 (ref.)	0.92 (0.56–1.49)	0.94 (0.54–1.62)	0.78 (0.45–1.34)	0.41
+Coffee	1.0 (ref.)	0.98 (0.53–1.84)	1.02 (0.57–1.84)	0.65 (0.35–1.19)	0.11	–	–	–	–	
+Green tea	–	–	–	–		1.0 (ref.)	0.92 (0.56–1.50)	0.94 (0.54–1.62)	0.77 (0.45–1.33)	0.39
Cardiovascular mortality										
No of deaths	13	22	15	26		23	23	14	16	
Incidence (/1000PYs)	4.1	3.7	2.1	2.8		4.5	3.3	2.8	1.8	
HR (95% CI)										
Age- and sex-adjusted	1.0 (ref.)	0.97 (0.49–1.93)	0.47 (0.23–1.00)	0.62 (0.32–1.22)	0.06	1.0 (ref.)	0.82 (0.46–1.46)	0.72 (0.37–1.40)	0.52 (0.27–1.01)	0.049
Multivariable-adjusted	1.0 (ref.)	1.03 (0.51–2.05)	0.53 (0.25–1.13)	0.66 (0.33–1.31)	0.09	1.0 (ref.)	0.92 (0.51–1.65)	0.83 (0.42–1.62)	0.53 (0.27–1.04)	0.06
+Coffee	1.0 (ref.)	1.06 (0.53–2.12)	0.54 (0.25–1.14)	0.65 (0.33–1.29)	0.08	–	–	–	–	
+Green tea	–	–	–	–		1.0 (ref.)	0.92 (0.51–1.64)	0.82 (0.42–1.61)	0.52 (0.26–1.02)	0.055

Multivariate adjustments included age, sex, BMI, diabetes duration, current smoking habit, current alcohol intake, LTPA, sleep duration, HbA_{1c}, UACR, systolic blood pressure, LDL cholesterol, history of CVD and cancer.

BMI, body mass index; CVD, cardiovascular disease; HbA_{1c}, hemoglobin A_{1c}; LDL, low-density lipoprotein; LTPA, leisure-time physical activity; UACR, urinary albumin creatinine ratio.

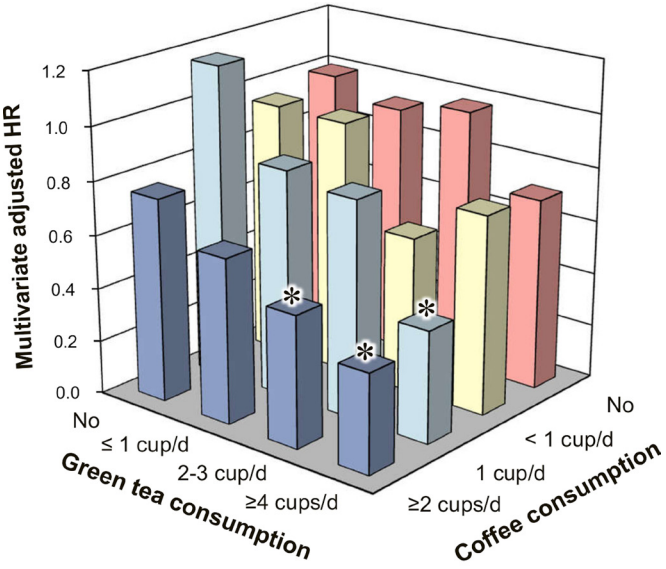

Figure 1 Combined effects of green tea and coffee consumption on all-cause mortality in patients with type 2 diabetes. The estimates are adjusted for age, sex, BMI, diabetes duration, current smoking habit, current alcohol intake, LTPA, sleep duration, HbA_{1c}, UACR, systolic blood pressure, LDL cholesterol, history of CVD and cancer. *P<0.05 vs the reference group (NO consumption of green tea and coffee). BMI, body mass index; CVD, cardiovascular disease; HbA_{1c}, hemoglobin A_{1c}; LDL, low-density lipoprotein; LTPA, leisure-time physical activity; UACR, urinary albumin creatinine ratio.

(0.46–0.96) for CVD mortality.[7] The results of the present study are consistent with those of previous studies of the general population (including diabetic and non-diabetic individuals): however, we found the impact of green tea consumption to be even greater (HR for the highest vs lowest consumption, 0.60). To our knowledge, this is the first study to identify an association between higher green tea consumption and decreased all-cause mortality in type 2 diabetes patients.

The association between coffee consumption and mortality has been controversial in diabetic patients, although most studies have described beneficial effects in general populations (including diabetic and non-diabetic individuals). This association with diabetic patients was initially investigated with a Finnish diabetic population (3837 individuals) in 2006: a 30% significant reduction in all-cause mortality was observed in those who consumed ≥7 cups/day of coffee compared with those drinking 0–2 cups/day.[16] However, the Health Professionals Follow-up Study of 3497 male diabetic patients found no association between coffee consumption and all-cause or CVD mortality.[17] The National Health and Nutrition Examination Survey recently found that ≥200 mg/day of caffeine from coffee reduced all-cause mortality among 1974 women with diabetes, but not among men.[19] Some large-scale studies of general populations have attempted to identify associations in subgroup analyses of diabetic patients. The National Institutes of Health-American Association of Retired Persons Diet and Health Study (total n=2 46 433) found that consuming ≥4 cups/day of coffee was associated with a 19% significant reduction of all-cause mortality in men and 14% insignificant reduction in women with self-reported diabetes.[12] Similarly, in a US prospective cohort with 90 317 participants, drinking ≥4 cups/day of coffee was significantly associated with reduced all-cause mortality in diabetic patients.[13]

Table 3 Multivariate-adjusted HR and 95% CIs of green tea and coffee consumption for all-cause mortality in patients with type 2 diabetes

	Coffee consumption			
Green tea consumption	**No**	**<1 cup/d**	**1 cup/d**	**≥2 cups/d**
No				
Event no. /at risk	14/151	13/136	11/111	12/209
HR (95% CI)	1.0 (ref.)	0.95 (0.45–2.04)	1.17 (0.53–2.59)	0.76 (0.35–1.66)
≤1 cup/d				
Event no. /at risk	17/149	22/305	15/230	20/459
HR (95% CI)	0.93 (0.45–1.92)	0.95 (0.48–1.86)	0.85 (0.41–1.77)	0.62 (0.31–1.23)
2–3 cups/d				
Event no. /at risk	30/257	20/361	18/271	19/500
HR (95% CI)	0.98 (0.52–1.86)	0.59 (0.30–1.16)	0.81 (0.40–1.64)	0.49 (0.24–0.99)
≥4 cups/d				
Event no. /at risk	33/437	36/504	14/351	15/492
HR (95% CI)	0.72 (0.38–1.35)	0.74 (0.40–1.38)	0.42 (0.20–0.88)	0.37 (0.18–0.77)

Multivariate adjustments include age, sex, BMI, diabetes duration, current smoking habit, current alcohol intake, LTPA, sleep duration, HbA_{1c}, UACR, systolic blood pressure, LDL cholesterol, history of CVD and cancer.
BMI, body mass index; CVD, cardiovascular disease; HbA_{1c}, hemoglobin A_{1c}; LDL, low-density lipoprotein; LTPA, leisure-time physical activity; UACR, urinary albumin creatinine ratio.

Conversely, in a Dutch population, the Alpha Omega Study involving 4837 patients with prior myocardial infarction determined that consuming more than four cups/day of coffee increased mortality by 24% in diabetic patients, whereas it decreased mortality by 27% in those without diabetes.[14] In the Nurses' Health Study (7170 female patients with diabetes), habitual coffee consumption was not found to be associated with increased risk of mortality.[18] The UK Biobank (total n=498 134 participants) failed to identify a significant association between coffee consumption and mortality in diabetic patients.[15] Most of the above studies were conducted in developed country populations, which have a higher risk of CVD than those in Asia.[20] To our knowledge, the present investigation is the first prospective study to demonstrate a significant association between coffee consumption and reduced mortality in an Asian population with type 2 diabetes.

The mechanisms underlying reduced mortality with green tea and coffee consumption are not fully understood. Green tea contains a number of beneficial substances, including phenolic compounds, theanine, and caffeine.[4 8] Epigallocatechin gallate is the most prevalent phenolic compound: it has been shown to have antioxidant, anti-inflammatory, and anti-mutagenic properties.[27] Coffee also contains numerous bioactive components, including phenolic compounds and caffeine, which have been suggested as contributing to the associated favorable effects.[9] Phenolic compounds, such as chlorogenic acid, have been reported to have a health impact through various mechanisms, such as antioxidant and anti-inflammatory actions.[9 28]

Caffeine is one of the components in green tea and coffee that could contribute to their favorable effects. The beneficial effects of caffeine on insulin sensitivity and glucose-induced insulin secretion have been suggested[29] through several mechanisms, including weight loss and thermogenesis.[30 31] However, previous studies have found that consumption of both caffeinated and decaffeinated coffee was associated with reduced mortality.[12] That could mean that caffeine does not play a beneficial role in the association between coffee consumption and risk of mortality. Caffeine has also been reported to stimulate sympathetic activity and increase serum catecholamine levels,[32] leading to increased blood pressure or CVD risk.[11 33] The impact of coffee consumption on mortality was greater in the present study (HR 0.58) than that previously reported in developed country diabetic patients: HR 0.81 in men,[12] HR 0.76,[13] HR 0.70,[16] and HR 0.53 in women.[19] The difference may be explained by coffee having harmful effects among patients at higher CVD risk: that is based on findings that higher coffee consumption increased mortality among diabetic patients with previous myocardial infarction.[14] Japanese type 2 diabetes patients are generally at lower CVD risk than developed ones:[20] thus, caffeine may exert less detrimental effects on the vasculature, resulting in enhanced beneficial effects of coffee.

To date, no study has investigated the combined effect of green tea and coffee consumption on all-cause mortality. The present study determined that combined higher green tea and coffee consumption markedly reduced mortality. The Japan Public Health Center-Based Study found that the combination of ≥2 cups/day of green tea and ≥1 cup/day of coffee significantly reduced the risk for cerebral infarction and intracerebral hemorrhage.[34] However, that effect did not apply to CHD: the study found no impact on CHD mortality. We found that the relative risk reduction of mortality (HR, 0.37) was greater than when consuming only green tea (HR, 0.72) or only coffee (HR, 0.76; figure 1, table 3), thus, the protective mechanisms of the two beverages may differ. In addition to CVD and cancer, coffee reportedly confers health benefits with liver disease and dementia,[10] however, reduced mortality associated with green tea is mostly explained with respect to CVD or cancer.[7 8] Green tea and coffee consumption may be associated with different disease incidence or severity.

One strength of the present study is the high follow-up rate (99.5%), which enabled us to accurately investigate the association among green tea and coffee consumption and mortality. Further, this cohort study included potential confounders, such as sleep duration, diabetic complications, lifestyle, physical activity, laboratory data, and medications.

Some limitations of this study deserve mention. First, green tea and coffee consumption was assessed using single, self-reported data, which raises the problem of potential misclassification. However, the green tea and coffee consumption evaluated using our questionnaire showed high correlation with that found with 16 non-consecutive dietary records in a Japanese population.[25] Second, we did not obtain information about some other confounding factors, such as educational and socioeconomic levels. Higher educational or income levels may be associated with greater coffee consumption:[35] they may also be related to lower mortality risk.[36] Those factors may be considered by adjusting for physical activities or smoking status, which could be associated with higher educational or income levels.[36] However, a universal health insurance system has been established in Japan, thus, medical care is supposedly received regardless of educational or socioeconomic states. Third, the CVD medications differed among the coffee groups (table 1). Those medications were not considered in the analyses, however, history of CVD was included as a confounding factor. Fourth, we did not assess whether coffee was caffeinated or decaffeinated. However, decaffeinated coffee is uncommon in Japan. Previous studies have found a similar association between caffeinated or decaffeinated coffee and mortality.[12 13] Fifth, owing to the observational nature of the present study, we cannot conclude that consuming green tea or coffee reduces mortality. But long-term interventional studies of this kind may be difficult to implement: green tea and coffee are typically consumed as part of daily life. Sixth, the

number of cause-specific deaths was relatively small. That could lead to low statistical power in detecting significant associations. Seventh, there may have been multiple testing problems in our statistical analyses. Multiple testing corrections were not conducted in the present study, however, the results of table 2 are evidently consistent with those of previous studies.[15 37 38] Finally, this study was conducted only among a Japanese population. The ingredients of Japanese green tea could differ from those in green tea in other countries.[39] Accordingly, the findings of this study may not apply to other populations.

In conclusion, this prospective cohort study demonstrated that greater consumption of green tea and coffee was significantly associated with reduced all-cause mortality: the effects may be additive. Our results suggest that consuming green tea and coffee may have beneficial effects on the longevity of Japanese people with type 2 diabetes.

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Contributors YK and MI were responsible for the study concept and design. YK, MI, and HF conducted the analysis. TO, HI, TJ-K, MY, YO, TH, UN, and TK interpreted the data and contributed to the discussion. YK and MI drafted the manuscript. All authors participated in critically revising the manuscript and approved the final version. MI is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Drinking green tea and coffee daily linked to lower death risk in people with diabetes

4 or more cups of green tea + 2 or more of coffee linked to 63% lower all cause mortality

Drinking plenty of both green tea and coffee is linked to a lower risk of dying from any cause among people with type 2 diabetes, suggests research published in the online journal ***BMJ Open Diabetes Research & Care.***

Drinking 4 or more daily cups of green tea plus 2 or more of coffee was associated with a 63% lower risk of death over a period of around 5 years, the findings show.

People with type 2 diabetes are more prone to circulatory diseases, dementia, cancer, and bone fractures. And despite an increasing number of effective drugs, lifestyle modifications, such as exercise and diet, remain a cornerstone of treatment.

Previously published research suggests that regularly drinking green tea and coffee may be beneficial for health because of the various bioactive compounds these beverages contain.

But few of these studies have been carried out in people with diabetes. The researchers therefore decided to explore the potential impact of green tea and coffee, separately and combined, on the risk of death among people with the condition.

They tracked the health of 4923 Japanese people (2790 men, 2133 women) with type 2 diabetes (average age 66) for an average of just over 5 years.

All of them had been enrolled in The Fukuoka Diabetes Registry, a multicentre prospective study looking at the effect of drug treatments and lifestyle on the lifespan of patients with type 2 diabetes.

They each filled in a 58-item food and drink questionnaire, which included questions on how much green tea and coffee they drank every day. And they provided background information on lifestyle factors, such as regular exercise, smoking, alcohol consumption and nightly hours of sleep.

Measurements of height, weight and blood pressure were also taken, as were blood and urine samples to check for potential underlying risk factors.

Some 607 of the participants didn't drink green tea; 1143 drank up to a cup a day; 1384 drank 2-3 cups; and 1784 drank 4 or more. Nearly 1000 (994) of the participants didn't drink coffee; 1306 drank up to 1 cup daily; 963 drank a cup every day; while 1660 drank 2 or more cups.

During the monitoring period, 309 people (218 men, 91 women) died. The main causes of death were cancer (114) and cardiovascular disease (76).

Compared with those who drank neither beverage, those who drank one or both had lower odds of dying from any cause, with the lowest odds associated with drinking higher quantities of both green tea and coffee.

Drinking up to 1 cup of green tea every day was associated with 15% lower odds of death; while drinking 2-3 cups was associated with 27% lower odds. Getting through 4 or more daily cups was associated with 40% lower odds.

Among coffee drinkers, up to 1 daily cup was associated with 12% lower odds; while 1 cup a day was associated with 19% lower odds. And 2 or more cups was associated with 41% lower odds.

The risk of death was even lower for those who drank both green tea and coffee every day: 51% lower for 2-3 cups of green tea plus 2 or more of coffee; 58% lower for 4 or more cups of green tea plus 1 cup of coffee every day; and 63% lower for a combination of 4 or more cups of green tea and 2 or more cups of coffee every day.

This is an observational study, and as such, can't establish cause. And the researchers point to several caveats, including the reliance on subjective assessments of the quantities of green tea and coffee drunk.

Nor was any information gathered on other potentially influential factors, such as household income and educational attainment. And the green tea available in Japan may not be the same as that found elsewhere, they add.

The biology behind these observations isn't fully understood, explain the researchers. Green tea contains several antioxidant and anti-inflammatory compounds, including phenols and theanine, as well as caffeine.

Coffee also contains numerous bioactive components, including phenols. As well as its potentially harmful effects on the circulatory system, caffeine is thought to alter insulin production and sensitivity.

"This prospective cohort study demonstrated that greater consumption of green tea and coffee was significantly associated with reduced all-cause mortality: the effects may be additive," the researchers conclude.