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ORIGINAL CONTRIBUTION

Coffee consumption but not green tea consumption is associated with adiponectin levels in Japanese males

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Abstract
Purpose Coffee is among the most widely consumed beverages in the world. Numerous epidemiological studies have reported a significant inverse association between coffee consumption and risk of type 2 diabetes mellitus, but the underlying mechanisms are still not fully understood. Therefore, we conducted an epidemiological study to clarify the relationship between coffee consumption and adiponectin levels in Japanese males. We also evaluated whether green tea consumption affected adiponectin levels.
Methods We carried out a cross-sectional study. The subjects were 665 male employees in Japan. Coffee consumption was assessed, using a self-administered questionnaire, as the number of times per week and cups per day respondents drank, and subjects were grouped into four levels (non, 1–5 times/week, 1–2 cups/day and ≥3 cups/day).
Results The means of adiponectin levels were positively associated with coffee consumption. A dose–response relationship was found between coffee consumption and circulating adiponectin levels. The relationship remained significant after adjustment for potential confounding factors (P for trend <0.05). However, green tea consumption was not significantly associated with adiponectin levels (P for trend = 0.90).
Conclusions We not only revealed that habitual coffee consumption is associated with higher adiponectin levels in Japanese males but also found a dose-dependent association between coffee consumption and adiponectin levels. Therefore, our study suggested that coffee components might play an important role in the elevation of adiponectin level.

Keywords Adiponectin · Epidemiological study · Coffee · Green tea

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Introduction

Coffee is among the most widely consumed beverages in the world [1]. It is believed to have beneficial effects in the prevention and treatment of many diseases. The protective effect of coffee against many diseases such as various types of cancer [2, 3], cardiovascular diseases [4] and type 2 diabetes mellitus [5–8] has been investigated.

Adiponectin is an adipocyte-specific secretory protein [9]. Circulating adiponectin levels are lower in the obese and in type 2 diabetes subjects than in healthy controls. Many studies have demonstrated that adiponectin plays an important role in the regulation of insulin function and the development of type 2 diabetes mellitus [10]. To date, a few studies have reported a finding of this sort: Williams et al. [11] found that women drinking four or more cups of coffee per day had significantly higher adiponectin levels than those who did not drink coffee regularly. Kempf et al. [12] indicated a significant increase in adiponectin levels in response to increased coffee consumption in an intervention trial.

Recent studies have demonstrated that coffee consumption can affect blood pressure, cholesterol levels and

liver transaminase levels. Therefore, it might be expected that coffee consumption would affect adiponectin levels. It is possible to hypothesize that coffee may reduce the risk for certain chronic diseases, including diabetes mellitus, through its effects on glucose metabolism and lipid metabolism, and its protective action on the liver.

This study was conducted for the purpose of clarifying the associations of coffee consumption with adiponectin levels in Japanese males. We evaluated whether coffee consumption was associated with adiponectin, metabolic parameters including parameters of liver damage, lipoprotein and white blood cells. Moreover, the current study on adiponectin levels in Japanese males examined not only associations with coffee consumption but also associations with consumption of green tea.

Subjects and methods

Study subjects

Study subjects were male employees registered with a particular health insurance society in Fukuoka Prefecture, Japan. All employees were full-time, white-collar, daytime Japanese workers. Each subject received an annual health check-up in 2000. The study protocol was approved by the Ethics Committee of Fukuoka University. Consent was obtained from 671 people to use the data obtained during their annual health check-ups and to donate residual blood samples used for the examination. Individuals who had missing data for any of the exposure parameters were excluded ($n = 6$). Finally, 665 subjects were included in the present analysis.

Variables

Height and weight were measured to calculate body mass index (BMI = weight in kilograms divided by the square of height in meters). The systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured once using a standard mercury sphygmomanometer with the cuff on the right arm and the subjects in a sitting position. Smoking status, alcohol drinking status, physical activity, and coffee and green tea consumption were assessed through a self-administered questionnaire. Coffee or green tea consumptions were categorized into four levels, respectively (coffee: non, 1–5 times/week, 1–2 cups/day and ≥3 cups/day; green tea: non, 1–5 times/week, 1–3 cups/day and ≥4 cups/day). The standard serving size was assigned on the questionnaire as 1 cup. Participants were classified as never, ex-, and current smokers. Alcohol-drinking status was classified into four categories: never, ex-, 1–6 times/week and regular alcohol drinkers. We defined physically activity as over 30 min of leisure time physical activity. Frequency of physical activity was divided two categories by the number of times (less than once a week, once a week or more) Hypertension was defined as a SBP of ≥140 mmHg and/or a DBP of ≥90 mmHg and/or taking antihypertensive medication. Hypercholesterolemia was defined as total cholesterol (TC) of ≥240 mg/dL and/or taking anti-hyperlipidemic medication. Type 2 diabetes mellitus was defined as taking anti-diabetic medication.

Adiponectin levels were determined in 2006 in spare serum samples that had been stored at −80 °C. All of the subjects agreed to have their serum adiponectin levels measured. Adiponectin levels were determined by enzyme-linked immunosorbent assay (Otsuka Pharmaceutical Co., Ltd, Japan). Serum total cholesterol and LDL cholesterol (LDL-C) were measured enzymatically using commercial enzyme kits (Wako, Osaka, Japan and Daiichi Kagaku, Tokyo, Japan, respectively). HDL cholesterol (HDL-C) was measured using the direct method. Triglyceride (TG) was measured using the glycerol removal method. White blood cell counts were measured by flow cytometry. Aspartate aminotransferase (AST), alanine aminotransferase (ALT) and γ-glutamyl transpeptidase (GGT) were measured using the Japan Society of Clinical Chemistry (JSCC) consensus method. The basic characteristics of the subjects are shown in Table 1.

Statistical analysis

AST, ALT, GGT, TG and serum adiponectin levels were converted into logarithms to approximately normalize the distribution and used in one-way analysis of variance (ANOVA) and analysis of covariance (ANCOVA). Comparison of continuous variables including adiponectin levels against coffee-drinking status was conducted using ANOVA. Post hoc comparison was conducted using Tukey's method. ANCOVA was used to test differences and to estimate adjusted means across categories of coffee-drinking status or green tea drinking status after adjustment for covariates. These estimated means were adjusted for age (continuous), BMI (continuous), smoking status (never, ex-, current), physical activity (less than once a week, once a week or more) and taking anti-hypertensive medication (yes or no). The geometric means with adjustment for covariates are shown. Trends were tested for using the contrast method. Categorical variables were compared using the chi-square test. A P value of less than 0.05 was considered statistically significant. All statistical analyses were conducted using SAS for WINDOWS version 9.1 (SAS Institute, Cary, NC).

Table 1 Basic characteristics of participants

Variables	$n = 665$
Age (years), mean (SD)	48.3 (5.3)
Body mass index (kg/m^2), mean (SD)	23.4 (2.9)
Systolic blood pressure (mmHg), mean (SD)	125.0 (14.6)
Diastolic blood pressure (mmHg), mean (SD)	78.0 (10.7)
Smoking status, *n* (%)	
Non-smoker	196 (43.1)
Ex-smoker	57 (11.5)
Current smoker	412 (45.4)
Drinking status, *n* (%)	
Alcohol	
Non-drinker	112 (16.8)
Ex-drinker	10 (1.5)
1–6 times/week	158 (23.8)
Regular drinker	385 (57.9)
Coffee	
Non-drinker	130 (19.5)
1–5 times/week drinker	181 (27.2)
1–2 cups/day drinker	220 (33.1)
≥3 cups/day drinker	134 (20.2)
Green tea	
Non-drinker	113 (17.0)
1–5 times/week drinker	113 (17.0)
1–3 cups/day drinker	267 (40.2)
≥4 cups/day drinker	172 (25.9)
Physical activity, *n* (%)	
Less than once a week	522 (78.5)
Once a week or more	143 (21.5)
Hypertension, *n* (%)	112 (16.8)
Hypercholesterolemia, *n* (%)	185 (27.8)
Diabetes mellitus, *n* (%)	27 (4.1)

Results

The basic characteristics of subjects in relation to their coffee consumption are shown in Table 2. Subjects who consumed more coffee tended to be younger. Increasing coffee consumption was associated with lower SBP and DBP. Coffee-drinking was associated with smoking and drinking status. Current smokers and non-alcohol drinkers were more likely to consume coffee frequently. There were no significant differences between coffee consumption and BMI or frequency of physical activity.

Biological characteristics by consumption of coffee are shown in Table 3. Higher coffee consumption was significantly associated with lower levels of AST, ALT and GGT. As coffee consumption increased, white blood cell counts were higher. There were no associations between coffee consumption and TC, LDL-C or HDL-C levels. The respective means of adiponectin in those drinking coffee non-, 1–5 times/week, 1–2 cups/day and ≥3 cups/day were, respectively, 5.95, 6.51, 7.05 and 6.89 μg/mL. The difference was significant ($P < 0.01$, one-way ANOVA).

Next, we performed ANCOVA to estimate adjusted means and to test the differences (Table 4). The logarithm-transformed means of adiponectin level rose as coffee consumption increased. The means were positively associated with coffee consumption even after confounding factors, such as age, BMI, smoking status, anti-hypertensive medication and physical activity, were adjusted for ($P < 0.01$, P for trend < 0.05). Though a significant dose–response relationship was observed between coffee consumption and adiponectin levels, there were no significant differences in adiponectin levels between 1 and 2 cups/days and ≥3 cups/day ($P = 0.58$). On the other hand, drinking green tea was not associated with higher adiponectin levels ($P = 0.89$, P for trend = 0.90).

Discussion

This study was conducted to examine the association between coffee consumption and circulating adiponectin level. The main findings of the present study are that the adiponectin levels of those drinking 1 or more cups of coffee per day were significantly higher than those of subjects who drank coffee occasionally or never. Moreover, a significant dose–response relationship was observed.

Some previous studies demonstrated a relationship between coffee consumption and adiponectin level. Williams et al. [11] reported that subjects with and without diabetes who drank four or more cups of coffee per day had significantly higher adiponectin levels than those who did not drink coffee regularly. Moreover, similar findings were observed for caffeine intake. The study included women only. Kempf et al. [12] reported that coffee consumption led to increased adiponectin levels in an interventional study. Although adiponectin strongly correlated with BMI, the interventional study did not consider weight change. Though their studies had several limitations, our findings are consistent with theirs and suggest that coffee has a beneficial effect on blood adiponectin levels in Japanese men.

Moreover, we investigated whether coffee consumption was related to metabolic parameters. Our results indicated that higher coffee consumption was associated with lower levels of parameters of liver damage, including AST, ALT and GGT. Several studies reported that coffee consumption inhibited elevation of liver transaminases [13] and was associated with a lower risk of liver cirrhosis [14]. Although our study did not observe the association between

Table 2 Basic characteristics by consumption of coffee

Variables	Non ($n = 130$)	1–5 times/week ($n = 181$)	1–2 cups/day ($n = 220$)	≥3 cups/day ($n = 134$)	*P* value
Age (year), mean (SD)	49.9 (5.0)	48.0 (5.4)	47.7 (5.3)	48.2 (5.1)	**<0.001**
Body mass index (kg/m^2), mean (SD)	23.7 (2.9)	23.8 (3.1)	23.1 (2.8)	23.2 (2.9)	0.06
Systolic blood pressure (mmHg), mean (SD)	129.5 (13.6)	124.6 (13.7)	123.1 (15.2)	124.6 (14.8)	**<0.001**
Diastolic blood pressure (mmHg), mean (SD)	80.7 (9.7)	77.7 (10.6)	76.7 (10.7)	77.9 (11.1)	**<0.01**
Smoking status, *n* (%)					**<0.001**
Non-smoker	56 (43.1)	69 (38.1)	54 (24.6)	17 (12.7)	
Ex-smoker	15 (11.5)	14 (7.7)	18 (8.2)	10 (7.5)	
Current smoker	59 (45.4)	98 (54.1)	148 (67.3)	107 (79.9)	
Alcohol drinking status, *n* (%)					**<0.05**
Non-drinker	13 (10.0)	24 (13.3)	42 (19.1)	33 (24.6)	
Ex-drinker	2 (1.5)	2 (1.1)	4 (1.8)	2 (1.5)	
1–6 times/week	26 (20.0)	52 (28.7)	48 (21.8)	32 (23.9)	
Regular drinker	89 (68.5)	103 (56.9)	126 (57.3)	67 (50.0)	
Physical activity, *n* (%)					0.72
Less than once a week	103 (79.2)	141 (77.9)	177 (80.5)	101 (75.4)	
Hypertension, *n* (%)	38 (29.2)	22 (12.2)	33 (15.0)	19 (14.2)	**<0.001**
Hypercholesterolemia, *n* (%)	40 (30.8)	51 (28.2)	59 (26.8)	35 (26.1)	0.83
Diabetes mellitus, *n* (%)	7 (5.4)	3 (1.7)	12 (5.5)	5 (3.7)	0.22

P value by one-way analysis of variance for continuous variables and χ^2 tests for categorical variables

Table 3 Biological characteristics by consumption of coffee

Variables	Non ($n = 130$)	1–5 times/week ($n = 181$)	1–2 cups/day ($n = 220$)	≥3 cups/day ($n = 134$)	*P* value
AST (IU/L), mean (SD)	34.6 (25.8)	29.1 (14.8)	28.5 (16.0)	29.1 (17.6)	**<0.01**
ALT (IU/L), mean (SD)	98.0 (97.1)	77.8 (82.9)	62.0 (68.4)	60.4 (75.7)	**<0.01**
GGT (IU/L), mean (SD)	37.4 (22.4)	34.2 (37.8)	32.1 (24.7)	32.3 (36.6)	**<0.001**
Cholesterol level (mg/dL)					
TC, mean (SD)	199.9 (34.4)	202.7 (33.3)	200.1 (33.5)	202.9 (35.0)	0.78
LDL-C, mean (SD)	103.2 (30.5)	109.2 (29.0)	110.3 (26.8)	110.8 (28.7)	0.10
HDL-C, mean (SD)	61.9 (14.7)	59.0 (15.2)	60.3 (14.5)	58.3 (14.0)	0.17
Triglyceride (mg/dL), mean (SD)	195.8 (169.0)	203.0 (210.8)	156.3 (113.8)	194.5 (312.3)	**<0.01**
White blood cell count (/μL), mean	6420.8 (1689.5)	6577.4 (1749.2)	6818.6 (1734.0)	7164.2 (1884.4)	**<0.01**
Adiponectin level (μg/mL)					**<0.01**
Mean (SD)	6.0 (2.6)	6.5 (3.0)	7.1 (3.2)	6.9 (3.3)	
Median (IQR)	5.3 (4.1–7.3)	6.0 (4.3–8.0)	6.5 (4.6–8.7)	6.2 (4.5–8.6)	

ALT Alanine aminotransferase, *AST* aspartate aminotransferase, *GGT* γ-glutamyl transpeptidase, *TC* total cholesterol, *LDL-C* LDL cholesterol, *HDL-C* HDL cholesterol, *IQR* inter quartile range

P values refer to overall differences across groups as derived from one-way analysis of variance

coffee consumption and cholesterol levels, recent studies showed that coffee consumption increased HDL-C levels [12, 15].

We also examined whether green tea consumption was associated with higher adiponectin levels. Green tea is a beverage that is commonly consumed in Japan. Though some animal studies [16, 17] have demonstrated that green tea extract can increase the levels of adiponectin, in human studies [18–20], the effects of green tea on adiponectin levels are not clear. In our study, no association between green tea consumption and adiponectin levels was found. Ryu et al. [20] reported that serum adiponectin levels were

Table 4 Crude and adjusted means of adiponectin levels by consumption of coffee

	n (%)	Adiponectin level (μg/mL)		
		Crude	Model 1	Model 2
Coffee consumption				
Non	130 (19.6)	5.47	5.49	5.48
1–5 times/week	181 (27.2)	5.91	6.03	6.03
1–2 cup/day	220 (33.1)	6.43	6.33	6.32
≥3 cups/day	134 (20.2)	6.19	6.16	6.17
P value[a]		**<0.01**	**<0.01**	**<0.01**
P for trend		**<0.01**	**<0.05**	**<0.05**
Green tea consumption				
Non	113 (17.0)	6.09	6.16	6.15
1–5 times/week	113 (17.0)	5.82	5.91	5.90
1–3 cup/day	267 (40.2)	5.99	6.04	6.04
≥4 cups/day	172 (25.9)	6.23	6.05	6.06
P value[a]		0.61	0.89	0.89
P for trend		0.55	0.82	0.90

Geometric means are shown

Model 1: Age (continuous), Body mass index (continuous), Smoking status (never, ex-, current)

Model 2: Age (continuous), Body mass index (continuous), Smoking status (never, ex-, current), Anti-hypertensive medication (yes or no), Physical activity (less than once a week, once a week or more)

[a] *P* value by one-way ANOVA or ANCOVA

unchanged after long-term green tea consumption [20]. Our data support their findings.

Numerous recent epidemiological studies indicate that regular coffee intake may have beneficial effects including decreased risk of type 2 diabetes mellitus [5–7, 21–23]. Several plausible mechanisms for the beneficial effect of coffee have been examined. The possibility that coffee lowers the levels of inflammatory markers such as C-reactive protein has been considered [24, 25]. It has also been suggested that coffee has antioxidant activities. It was reported that caffeine is the most plausible functional component in regular coffee to cause the increase in serum adiponectin levels in women. Since coffee contains about twice as much caffeine as green tea [26], the observed difference of adiponectin levels between coffee and green tea may depend on the caffeine content. However, it was reported that decaffeinated coffee consumption was associated with a lower risk of type 2 diabetes [27]. Apart from caffeine, coffee contains hundreds of other functional components, including phenolic compounds (chlorogenic acid and quinides), minerals (magnesium, potassium, manganese and chromium), vitamins (niacin) and fibers [28, 29]. Hence, the other components of coffee except caffeine may have beneficial effects. The exact underlying mechanisms are not yet completely clear.

There are several limitations to our study. First, we have no data about other lifestyle factors such as diet. Heavy coffee consumption tends to be strongly associated with cigarette smoking and, in many populations, with a generally less health-conscious lifestyle and lower socioeconomic status [30]. Though it is important to take into account the possible confounding role of other lifestyle factors, our study subjects had relatively similar lifestyle and socioeconomic factors. Therefore, we considered that the effects of residual confounding are relatively small. Second, we have no data on types of coffee, or whether sugar, milk or cream was added. Because the amount of sugar and milk added to coffee is probably insignificant compared to the consumption of other food, it seems that these are unlikely to have affected the metabolism. Inverse association with risk of type 2 diabetes mellitus was observed for coffee with or without milk/cream [31]. Third, because ours was a cross-sectional study, we did not deal with any temporal relationship between higher serum adiponectin levels and coffee consumption.

In conclusion, coffee consumption was found to be related to adiponectin levels in Japanese males. Adiponectin levels increased with higher coffee consumption in a graded manner. On the other hand, the benefits of green tea consumption on adiponectin levels were not confirmed in our study. The consumption of coffee, but not of green tea, appears to have benefits to adiponectin levels. Further studies are necessary to confirm our results in various populations and to determine whether the benefits of coffee consumption to circulating adiponectin level are causal.

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Conflict of interest The authors declare no conflict of interest.

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