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Association Between Coffee Consumption and Circulating Levels of Adiponectin and Leptin

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ABSTRACT Coffee has been proposed to have benefits for chronic diseases; however, the relevant mechanism remains to be elucidated. We conducted a cross-sectional study and evaluated the levels of adiponectin and leptin in relation to coffee consumption. We included a total of 4406 individuals (men = 2587 and women = 1819) for adiponectin analysis and 2922 individuals (men = 1731 and women = 1191) for leptin analysis. Participants answered number of cups of coffee per week and types of coffee they consumed and their serum levels of adiponectin and leptin were measured using an enzyme-linked immunosorbent assay. We found that increasing coffee consumption was associated with increased levels of adiponectin among women; geometric means of adiponectin were 8.0 (95% CI: 7.2–8.9 μg/mL) among women who regularly consumed 15 or greater cups/week, but 7.5 (95% CI: 6.8–8.4 μg/mL) among women who did not consume coffee (P for trend = .009). Leptin levels were inversely associated with coffee consumption among both men and women (P for trend = .04 for men and 0.04 for women); geometric means of 15 or greater cups of coffee per week were 2.6 (95% CI: 2.4–2.8 ng/mL) among men and 5.1 (95% CI: 4.5–5.8 ng/mL) among women, but for noncoffee drinkers, geometric means were 3.0 (95% CI: 2.7–3.3 ng/mL) for men and 5.8 (95% CI: 5.1–6.6 ng/mL) for women. Coffee consumption was associated with higher circulating levels of adiponectin and lower circulating levels of leptin. Our study may suggest that improvement in adipocyte function contributes to the beneficial metabolic effects of coffee consumption.

KEYWORDS: • ***adiponectin*** • ***coffee*** • ***leptin***

INTRODUCTION

Coffee is one of the most consumed beverages worldwide. Coffee consumption has been suggested to decrease the risk of type 2 diabetes,[1] coronary heart disease, and stroke in women[2,3] and improve cognitive function.[4] However, the mechanism of its actions is not clear.

Adipose tissue is not only a storage of excess energy but also has other important function as an endocrine organ.[5] Adipose tissue secretes more than one hundred adipose tissue secretion products (adipokine). Among these adipokines, adiponectin and leptin are most widely researched. Previous studies showed antiatherosclerotic[6,7] and antidiabetic effects[7–9] of adiponectin. Low concentrations of adiponectin were observed in obese and diabetic individuals,[10,11] as well as patients who have coronary artery disease[12,13] or metabolic syndrome.[14] Leptin was originally discovered through positional cloning of *ob/ob* mice, of which a recessive mutation causes abnormalities in food intake and energy expenditure,[15] and its level is positively correlated with body fat mass[10] and inversely correlated with adiponectin.[16,17]

According to a few epidemiological studies, adiponectin or leptin has been proposed to be one of the key metabolites in the mechanism through which coffee is associated with lower risk of several chronic diseases, as suggested by the observation that coffee consumption may alter levels of adiponectin and leptin.[18–21] A recent U.S. clinical trial reported no changes in glycemia and/or insulin sensitivity, but a significant increase in adiponectin levels after 8-week coffee consumption.[22]

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Coffee consumption has markedly increased over the past years in Korea. The frequency data of coffee in the Korean National Health and Nutrition Examination Survey showed that the proportion of Korean adults who consumed coffee two or more times per day increased from 29.1% in 2001 to 43.3% in 2011 and this increasing trend was statistically significant ($P < .0001$).[23] That study also observed that higher socioeconomic status such as education and income levels were associated with higher frequency of coffee consumption in Korean adults. Given that coffee has become a popular beverage and its health benefit and possible risk are of great interest in Korea, epidemiologic studies on coffee and risks of chronic diseases are needed to elucidate their associations and the potential mechanism among Korean populations.

To our knowledge, there is no study that has yet jointly evaluated adiponectin and leptin levels in relation to coffee consumption in the Korean population. Therefore, we investigated whether coffee consumption was associated with levels of adiponectin and leptin in a cross-sectional study of Korean men and women.

MATERIALS AND METHODS

Study participants

The Korean Metabolic Syndrome Research Initiative was composed of 9995 participants aged 20 years and over who underwent regular health examinations from January to June, 2007 at the Health Promotion Center at University Hospitals. As a part of regular health examination, clinical, biochemical, and anthropometric measures were determined among participants. Participants were asked about their demographic factors and smoking status, physical activity, family history of diseases, medical history, and their regular alcohol. We included only participants who answered the coffee questions ($n = 4502$). We excluded participants whose sex is reported with error ($n = 5$) and those who had missing information about leptin levels ($n = 1528$) for leptin analysis or top 1% and bottom 1% of adiponectin or leptin levels to remove the influence of the outliers ($n = 93$ for adiponectin and $n = 47$ for leptin). As a result, we included 4406 (men = 2587 and women = 1819) for adiponectin analysis and 2922 (men = 1731 and women = 1191) for leptin analysis. The study protocol was approved by the Institutional Review Board at the Yonsei University College of Medicine (4-20050197) and all participants provided written informed consent.

Assessment of coffee consumption

Participants were asked about the number of cups of coffee per week and types of coffee they consumed. Participants were asked, ''Do you drink coffee?'', ''How many cups of coffee per day or per week do you drink?'', and ''What types of coffee do you usually drink?''

Assessment of clinical, biochemical, and anthropometric measures

Fasting peripheral venous blood samples of participants were obtained at each health promotion center at university hospitals. Serum adiponectin levels were measured in a central laboratory using an enzyme-linked immunosorbent assay (ELISA) (Mesdia Co., Ltd., Seoul, Korea). Leptin levels were measured by the same company (Mesdia Co., Ltd.) and also by the same method (ELISA). The intra- and interassay variances for adiponectin and leptin were 7.5% to 13.8% and 4.6% to 8.6%; 7.5% to 13.8% and 6.1% to 8.6%, respectively. Systolic and diastolic blood pressure, height, and weight were directly measured by health professionals. Participants wore light clothing when their weights and heights were measured. Height and weight were measured using the DS-103M (Dong Sahn Jenix Co., Ltd., Seoul, Korea) or InBody 720 (Inbody Co., Ltd., Seoul, Korea). Body mass index (BMI, kg/m^2) was calculated as weight (kg) divided by height squared (m^2). Blood pressure was measured in a seated position after a 15-min rest by a registered nurse or blood pressure technician using EASY × 800 (R/L) (Jawon Medical Co., Ltd., Daejeon, Korea). Participants' demographic factors, smoking status, physical activity, family history of diseases, medical history, and their regular alcohol intake were assessed by trained interviewers using structured questionnaires. We asked participants whether they engaged in regular exercise and, if they answered yes, administered additional questions, including type of exercise, frequency, duration, and starting time. Age at starting smoking, duration, and dose of smoking for smoking status, type of alcoholic beverage, and frequency and the quantity for alcohol intake were also asked.

Statistical analysis

Participants' baseline characteristics were compared using a chi-square test for categorical variables and analysis of variance for continuous variables. We log transformed values of variables if those were not normally distributed. Geometric means and 95% CI of adiponectin and leptin levels were calculated based on exponentiation of log-transformed values according to coffee consumption per week (cups/week, none, ≤7, 8–14, ≥15) using the Generalized Linear Model (GLM). We adjusted for age (years, continuous), BMI (kg/m^2, continuous), smoking (men: never, past, current; women: never, ever), alcohol (g/day, continuous), marital status (married, others), and education (high school, college or higher studies). To test for trends across quartiles, participants were assigned the median value of their quartile level. This ordinal variable of coffee category was treated as a continuous variable in the GLM. We performed the sensitivity analysis by including and excluding study participants with hyperlipidemia, hypertension, and diabetes (men = 325 and women = 182 for adiponectin analysis; men = 160 and women = 92 for leptin analysis) and found no significant differences in the results (data not shown); therefore, we included them in the analysis. We also did a sensitivity analysis by excluding participants (6% for both men and women) who reported that they consume decaffeinated coffee and found no significant differences in the associations between adiponectin or leptin and coffee consumption compared to the results of the analysis, including those individuals (data not shown). We examined whether the associations between groups varied by

smoking status, alcohol intake, exercise, BMI, or having hyperlipidemia, high blood pressure, or diabetes. The software used throughout all statistical analysis was SAS version 9.4 software package (SAS Institute, Inc., Cary, NC, USA).

RESULTS

Baseline characteristics according to coffee consumption in 2587 men and 1819 women were presented (Table 1). Moderate or heavy coffee consumers (≥8 cups per week) were more likely to be younger and to have professional/administrative jobs compared to no coffee or light coffee consumers in both men and women. Regular coffee consumers were more likely to be educated at college or higher compared to nonconsumers in both men and women. Men who regularly consumed coffee were more likely to smoke and consumed lower amount of alcohol compared to non-coffee consumers. Women who regularly consumed coffee

Table 1. Baseline Characteristics According to Total Coffee Consumption in Men and Women

	Total coffee consumption (cups/week)				
	None	*≤7*	*8–14*	*≥15*	P
Men					
Total no. of participants, *n* (%)	168 (6.5)	1461 (56.5)	403 (15.6)	555 (21.4)	
Age (years), mean (SD)	47.1 (9.9)	45.1 (9.5)	44.8 (9.6)	43.2 (7.9)	<.001
BMI (kg/m^2), mean (SD)	24.6 (3.0)	24.4 (2.7)	24.5 (2.7)	24.7 (2.8)	.17
Alcohol intake(g/day), mean (SD)	31.7 (43.0)	25.6 (27.4)	19.5 (22.1)	22.6 (30.8)	<.001
Education, %					<.001
High school	25.3	9.9	14.7	12.4	
College/graduate school	74.7	90.1	85.3	87.6	
Marital status, %					.87
Others	7.1	7.1	7.5	6.2	
Married	92.9	92.9	92.5	93.8	
Smoking status, %					<.001
Never	32.7	23.0	24.1	16.4	
Past	36.9	37.8	40.4	31.7	
Current	30.4	39.2	35.5	51.9	
Jobs, %					<.001
Professional/administrative	61.9	67.9	73.0	73.9	
Sales/service	10.2	7.8	12.1	8.2	
Manufacturing/technical/agriculture	12.2	15.1	6.7	9.4	
Others	15.7	9.2	8.2	8.5	
Exercise, %					<.001
Yes	67.5	57.0	68.6	60.0	
No	32.5	43.0	31.4	40.0	
Women					
Total no. of participants, *n* (%)	186 (10.2)	1110 (61.0)	325 (17.9)	198 (11.9)	
Age (years), mean (SD)	51.0 (11.8)	45.4 (10.1)	43.1 (9.4)	42.3 (7.4)	<.001
BMI (kg/m^2), mean (SD)	22.4 (2.8)	22.6 (2.9)	22.6 (3.1)	22.6 (2.8)	.75
Alcohol intake (g/day), mean (SD)	5.4 (10.2)	6.9 (11.1)	6.7 (16.3)	7.7 (13.1)	.80
Education, %					.008
High school	35.4	23.6	28.2	21.9	
College/graduate school	64.6	76.4	71.8	78.1	
Marital status, %					<.001
Others	21.1	9.7	14.7	7.1	
Married	78.9	90.3	85.3	92.9	
Smoking, %					.15
Never	96.2	95.7	96.0	92.5	
Past	1.6	2.0	1.5	1.5	
Current	2.2	2.3	2.5	3.0	
Jobs, %					.001
Professional/administrative	18.1	20.9	30.4	31.2	
Sales/service/manufacturing/technical/agriculture	11.8	8.3	9.0	11.5	
Housewife	63.2	64.9	53.9	50.0	
Others	6.9	5.9	6.7	7.3	
Regular exercise, %					.04
Yes	56.6	51.4	58.0	46.6	
No	43.4	48.6	42.0	53.4	

Number of participants were not equal because information on some factors was not available for a few participants. Values are mean ± standard deviation and % for categorical variables.

BMI, body mass index.

were more likely to be married compared to noncoffee consumers. Men and women who consumed 15 or more cups per week were less likely to exercise compared to noncoffee consumers.

We found that women who regularly consumed moderate or heavy amounts of coffee had higher levels of adiponectin compared to none or light coffee consumers (Table 2). Geometric means of adiponectin were 8.0 (95% CI: 7.2–8.9 μg/mL) among women who regularly consumed 15 or more cups per week, but 7.5 (95% CI: 6.8–8.4 μg/mL) among women who did not consume coffee (P for trend = .009). However, there was not a statistically significant inverse association between adiponectin levels and coffee consumption among men. Leptin levels were significantly inversely associated with coffee consumption among both men and women (P for trend = .04 for men and .04 for women). Geometric means of 15 or more cups per week were 2.6 (95% CI: 2.4–2.8 ng/mL) among men and 5.1 (95% CI: 4.5–5.8 ng/mL) among women, but for noncoffee drinkers, geometric means were 3.0 (95% CI: 2.7–3.3 ng/mL) for men and 5.8 (95% CI: 5.1–6.6 ng/mL) for women.

When we additionally adjusted for physical activity, the results were similar. Geometric means of adiponectin were 8.5 (95% CI: 7.6–9.5 μg/mL) among women who regularly consumed 15 or more cups per week, but 7.9 (95% CI: 7.1–8.9 μg/mL) among women who did not consume coffee (P for trend = .01). However, there was not a statistically significant inverse association for adiponectin levels among men (P for trend = .45). For leptin levels, significant inverse trends were observed for both men (P for trend = .04) and women (P for trend = .03).

When we examined whether caffeinated coffee was associated with circulating levels of adiponectin and leptin, we found decreasing levels of adiponectin with increasing caffeinated coffee consumption in women (P for trend = .001). Caffeinated coffee consumption was not associated with leptin levels.

In the sensitivity analysis, we excluded participants who ever had cardiovascular disease or cancer and found that coffee consumption was inversely associated with adiponectin levels in women, but not in men; for women, geometric means of adiponectin were 7.9 (95% CI: 6.7–9.0 μg/mL) among women

Table 2. Geometric Mean (95% Confidence Interval) of Adiponectin and Leptin Levels in Men and Women According to Total or Caffeinated Coffee Consumption

		Coffee consumption (cups/week)			
	None	*≤7*	*8–14*	*≥15*	P *for trend*
Total coffee					
Men					
Adiponectin (μg/mL)	168	1461	403	555	
Age-adjusted	4.8 (4.4–5.2)	4.1 (4.0–4.2)	4.7 (4.5–4.9)	4.3 (4.1–4.4)	.09
MV-adjusted[a]	5.2 (4.6–5.9)	4.5 (4.0–4.9)	4.9 (4.4–5.5)	4.6 (4.1–5.1)	.31
Leptin (ng/mL)	82	1184	151	314	
Age-adjusted	3.1 (2.8–3.5)	2.9 (2.8–3.0)	2.7 (2.5–3.0)	2.8 (2.7–3.0)	.22
MV-adjusted[a]	3.0 (2.7–3.3)	2.8 (2.6–3.0)	2.8 (2.5–3.1)	2.6 (2.4–2.8)	.04
Women	186	1110	325	198	
Adiponectin (μg/mL)					
Age-adjusted	7.0 (6.5–7.6)	6.5 (6.3–6.7)	7.0 (6.6–7.5)	7.2 (6.7–7.7)	.006
MV-adjusted[a]	7.5 (6.8–8.4)	7.2 (6.7–7.9)	7.7 (7.0–8.4)	8.0 (7.2–8.9)	.009
Leptin (ng/mL)	114	837	137	103	
Age-adjusted	5.1 (4.5–5.7)	5.5 (5.3–5.7)	4.9 (4.4–5.4)	5.1 (4.5–5.8)	.10
MV-adjusted[a]	5.8 (5.1–6.6)	5.5 (5.0–6.0)	5.1 (4.5–5.8)	5.1 (4.5–5.8)	.04
Caffeinated coffee					
Men	332	795	262	327	
Adiponectin (μg/mL)					
Age-adjusted	4.2 (4.0–4.5)	4.4 (4.2–4.5)	4.9 (4.7–5.3)	4.4 (4.2–4.7)	.05
MV-adjusted[a]	4.6 (3.9–5.3)	4.6 (3.9–5.3)	5.1 (4.4–6.0)	4.7 (4.0–5.4)	.10
Leptin (ng/mL)	243	584	81	181	
Age-adjusted	3.8 (3.6–4.0)	3.9 (3.7–4.0)	4.0 (3.6–4.4)	3.7 (3.5–4.0)	.40
MV-adjusted[a]	3.9 (3.6–4.3)	4.0 (3.7–4.3)	4.0 (3.6–4.5)	3.9 (3.5–4.2)	.63
Women	286	732	212	143	
Adiponectin (μg/mL)					
Age-adjusted	6.6 (6.2–7.0)	6.6 (6.4–6.9)	7.5 (7.0–8.1)	7.3 (6.7–8.0)	.001
MV-adjusted[a]	6.9 (6.1–7.8)	7.1 (6.3–8.0)	7.9 (7.0–9.0)	7.9 (6.8–9.1)	.001
Leptin (ng/mL)	212	547	80	77	
Age-adjusted	5.9 (5.5–6.3)	5.9 (5.7–6.1)	5.9 (5.3–6.5)	6.2 (5.6–6.9)	.51
MV-adjusted[a]	6.2 (5.6–6.8)	6.4 (5.8–6.9)	6.1 (5.4–7.0)	6.7 (5.9–7.6)	.50

[a]Adjusted for age (years, continuous), smoking (men; never, past, and current smokers, women; never and ever smokers), BMI (kg/m^2, continuous), alcohol (g/day, continuous), marital status (married and others), and education (≤12 and >12 years).

MV, multivariate.

who regularly consumed 15 or more cups per week, but 7.2 (95% CI: 6.3–8.2 μg/mL) among women who did not consume coffee (*P* for trend = .002). For leptin levels, lower levels of leptin were observed among men or women who regularly consumed 15 or more cups per week compared to noncoffee consumers, but the trend was not statistically significant.

When we examined the proportion of participants who drank 15 or more cups per day in a joint strata of levels of adiponectin (tertiles) and leptin (tertiles), we found the highest proportion among men and women who had high adiponectin levels, but low leptin levels; 16.2% of men were coffee consumers of 15 or more cups per day and 18.8% of women were coffee consumers of 15 or more cups per day among those who had the highest tertile levels of adiponectin, but the lowest tertile levels of leptin.

When we examined the association between adiponectin levels and coffee consumption according to smoking status, alcohol intake, exercise, presence of hypertension or diabetes, and BMI, the positive association was limited to women who were never smokers (*P* for trend = .04), women who exercised regularly (*P* for trend = .004), women who did not have hyperlipidemia, hypertension, or diabetes (*P* for trend = .03), or women who had a BMI of ≥25 kg/m^2 (*P* for trend = .02), but the interaction was not statistically significant (Table 3). For leptin levels, the inverse association was limited to women who did not exercise regularly (*P* for interaction = .09) (Table 4). Other factors did not modify the associations for adiponectin or leptin levels (*P* for interaction ≥.24).

DISCUSSION

In our cross-sectional study, we found that Korean women who regularly consumed coffee had higher levels of

Table 3. Geometric Mean (95% Confidence Interval) of Adiponectin Levels (μg/mL) According to Total Coffee Consumption and by Other Factors

			Total coffee consumption (cups/week)				
	No.	*None*	*≤7*	*8–14*	*≥15*	P *for trend*	P *for interaction*
Men							
Smoking status							.88
Never	579	5.9 (4.9–7.1)	4.7 (4.1–5.5)	5.0 (4.2–6.0)	4.8 (4.1–5.7)	.43	
Past	953	5.0 (4.1–6.2)	4.2 (3.6–5.0)	4.7 (3.9–5.7)	4.6 (3.8–5.5)	.31	
Current	1055	4.4 (3.9–5.1)	4.2 (3.9–4.4)	4.6 (4.2–5.1)	4.1 (3.8–4.5)	.83	
Alcohol intake							.19
Nondrinkers	264	5.0 (4.0–6.3)	4.3 (3.8–4.9)	4.6 (3.7–5.6)	3.9 (3.2–4.7)	.13	
Drinkers	2296	5.1 (4.6–5.5)	4.3 (4.1–4.5)	4.8 (4.5–5.1)	4.5 (4.2–4.8)	.57	
Exercise							.76
Yes	1531	5.5 (4.8–6.4)	4.5 (4.0–5.0)	5.0 (4.4–5.6)	4.6 (4.0–5.2)	.51	
No	1017	4.2 (2.6–6.8)	4.1 (2.6–6.4)	4.4 (2.8–7.1)	4.2 (2.6–6.6)	.47	
Have hyperlipidemia or high BP or diabetes							
Yes	325	3.8 (2.7–5.4)	3.5 (2.6–4.7)	3.3 (2.5–4.5)	3.7 (2.7–5.1)	.78	
No	2262	5.5 (4.8–6.2)	4.6 (4.1–5.1)	5.2 (4.6–5.9)	4.8 (4.3–5.3)	.69	
BMI							.67
<25 kg/m^2	1558	5.3 (4.5–6.2)	4.5 (3.9–5.1)	4.9 (4.2–5.7)	4.6 (4.0–5.3)	.97	
25+ kg/m^2	1029	4.8 (4.0–5.8)	4.3 (3.7–4.9)	4.8 (4.1–5.7)	4.4 (3.8–5.1)	.71	
Women							
Smoking status							.84
Never	1736	7.7 (7.0–8.5)	7.4 (6.9–7.9)	7.8 (7.2–8.4)	8.2 (7.4–9.0)	.04	
Ever	83	6.8 (4.3–10.7)	7.8 (5.3–11.6)	7.9 (5.1–12.1)	7.9 (5.1–12.2)	.73	
Alcohol intake							.69
Nondrinkers	876	6.4 (5.5–7.4)	6.1 (5.4–6.9)	6.4 (5.5–7.5)	6.8 (5.7–8.1)	.29	
Drinkers	849	7.7 (6.5–9.1)	7.2 (6.5–7.9)	7.6 (6.8–8.5)	7.6 (6.7–8.6)	.31	
Exercise							.47
Yes	931	6.6 (5.7–7.6)	6.6 (5.9–7.4)	7.1 (6.2–8.1)	7.9 (6.8–9.2)	.004	
No	840	8.5 (7.1–10.1)	8.0 (6.9–9.2)	8.1 (6.9–9.4)	8.3 (7.1–9.8)	.87	
Have hyperlipidemia or high BP or diabetes							.65
Yes	182	9.0 (6.7–11.9)	8.3 (6.4–10.7)	10.0 (7.3–13.7)	8.5 (5.8–12.3)	.71	
No	1637	7.3 (6.5–8.2)	7.1 (6.5–7.8)	7.4 (6.7–8.2)	7.9 (7.1–8.9)	.03	
BMI							.37
<25 kg/m^2	1484	7.8 (6.9–8.8)	7.7 (7.0–8.4)	8.0 (7.2–8.9)	8.2 (7.3–9.2)	.18	
25 + kg/m^2	335	6.6 (5.1–8.6)	5.8 (4.8–7.1)	6.5 (5.2–8.0)	7.8 (6.1–9.9)	.02	

Adjusted for age (years, continuous), smoking (men; never, past, and current smokers, women; never and ever smokers), BMI (kg/m^2, continuous), alcohol (g/day, continuous), marital status (married and others), and education (≤12 and >12 years).

BP, blood pressure.

Table 4. Geometric Mean (95% Confidence Interval) of Leptin Levels (ng/mL) According to Total Coffee Consumption and by Other Factors

		Total coffee consumption (cups/week)				
	No.	*None*	*≤7*	*8–14*	*≥15*	P *for trend*	P *for interaction*
Men							
Smoking status							.24
Never	368	1.8 (1.4–2.3)	1.8 (1.6–2.1)	1.7 (1.4–2.2)	1.6 (1.3–1.9)	.08	
Past	663	2.1 (1.7–2.5)	1.9 (1.7–2.2)	2.0 (1.7–2.4)	2.0 (1.7–2.3)	.53	
Current	700	2.3 (1.8–3.0)	2.0 (1.8–2.2)	1.7 (1.4–2.0)	1.7 (1.5–2.0)	.006	
Alcohol intake							.25
Nondrinkers	209	1.9 (1.4–2.7)	1.8 (1.6–2.1)	2.6 (2.0–3.5)	1.9 (1.5–2.4)	.30	
Drinkers	1522	2.1 (1.8–2.4)	2.0 (1.8–2.1)	1.8 (1.6–2.0)	1.8 (1.6–2.0)	.007	
Exercise							.46
Yes	903	2.0 (1.7–2.4)	1.9 (1.8–2.1)	1.9 (1.6–2.2)	1.7 (1.5–2.0)	.02	
No	828	2.1 (1.7–2.6)	1.9 (1.8–2.1)	1.8 (1.6–2.1)	1.9 (1.7–2.1)	.26	
Have hyperlipidemia or high BP or diabetes							.58
Yes[a]	160	2.6 (1.8–3.8)	2.3 (1.8–2.9)	—	—	.39	
No	1571	2.0 (1.7–2.3)	1.9 (1.8–2.0)	1.8 (1.6–2.0)	1.8 (1.6–1.9)	.05	
BMI							.26
<25 kg/m^2	1078	1.5 (1.3–1.8)	1.5 (1.3–1.6)	1.4 (1.3–1.6)	1.4 (1.3–1.6)	.38	
25+ kg/m^2	653	3.3 (2.7–4.0)	3.1 (2.8–3.4)	2.8 (2.4–3.4)	2.7 (2.4–3.1)	.01	
Women							
Smoking status							.99
Never	1137	5.5 (4.9–6.1)	5.3 (5.0–5.6)	4.9 (4.4–5.5)	4.8 (4.2–5.4)	.03	
Ever	54	10.3 (4.5–23.6)	4.8 (3.5–6.5)	4.1 (2.3–7.4)	5.5 (3.4–8.7)	.76	
Alcohol intake							.63
Nondrinkers	703	5.6 (4.8–6.7)	5.3 (4.7–6.1)	5.1 (4.2–6.1)	5.0 (4.1–6.1)	.21	
Drinkers	488	5.7 (4.4–7.3)	5.3 (4.6–6.0)	4.8 (4.0–5.7)	4.8 (4.0–5.7)	.09	
Exercise							.09
Yes	542	5.6 (4.7–6.7)	5.5 (4.8–6.2)	5.4 (4.4–6.6)	5.7 (4.6–7.1)	.84	
No	649	6.1 (5.1–7.2)	5.5 (4.9–6.1)	4.9 (4.2–5.7)	4.7 (4.0–5.5)	.002	
Have hyperlipidemia or high BP or diabetes							.51
Yes[a]	92	10.8 (5.6–20.7)	10.3 (5.5–19.4)	—	—	.72	
No	1099	5.7 (4.9–6.5)	5.3 (4.9–5.8)	5.0 (4.4–5.6)	5.0 (4.4–5.7)	.06	
BMI							.99
<25 kg/m^2	1003	5.1 (4.5–5.9)	4.8 (4.4–5.3)	4.4 (3.8–5.0)	4.5 (3.9–5.2)	.06	
25+ kg/m^2	188	10.0 (7.0–14.2)	10.2 (8.0–13.1)	10.9 (7.6–15.7)	8.2 (5.7–11.8)	.33	

Adjusted for age (years, continuous), smoking (men; never, past, and current smokers, women; never and ever smokers), BMI (kg/m^2, continuous), alcohol (g/day, continuous), marital status (married and others), and education (≤12 and >12 years).

[a]Cutoff of quartile was not available due to the skewed distribution.

adiponectin with an increase of adiponectin after consuming eight cups of coffee per week. However, we did not observe a significant association between coffee consumption and adiponectin levels in men. We observed that increase in coffee consumption was associated with lower levels of leptin in both men and women.

Our results support the evidence from the previous prospective cohort study and clinical trial[18–21,24] that coffee consumption was positively associated with adiponectin. The Nurses' Health Study found an increase of adiponectin with increased coffee consumption in both diabetic and nondiabetic women with an apparent increase after consuming ≥4 cups per day.[20] In addition, a crossover clinical trial, which provided packages of coffee and instructed participants (77% women) to stop drinking coffee in the first month, four cups per day in the second month, and eight cups per day for the third month, showed an increase in adiponectin levels when they drank eight cups per day.[24] Coffee consumption was also associated with increases in adiponectin levels in Japanese men[21] or women.[18] An 8-week randomized trial of 45 healthy overweight adults showed increased levels of adiponectin and decreased levels of fetuin-A for the caffeinated coffee drinkers compared to noncoffee drinkers.[22]

We found a positive association of adiponectin levels in relation to coffee consumption only among women. The gender difference could be partly explained by the effect of residual confounding by smoking in men compared to women, which is highly correlated with coffee consumption. In addition, the effects of coffee consumption on adipokines could differ by gender, possibly because of the different numbers and sizes of fat cells between men and women, which are the possible determinants of adiponectin production rates.[25] Adiponectin levels decrease significantly in

men during the pubertal stage[26] and the interaction between estrogen and *CYP1A1* enzymes, which metabolizes caffeine[27] may also be responsible for the potential gender difference.

Circulating leptin levels serve as a gauge for energy reserves and directs the central nervous system to adjust food intake and energy expenditure accordingly.[15] Coffee consumption was inversely associated with leptin ($P < .001$) in a cross-sectional study comprising 2554 male and 763 female Japanese workers.[19] Another Japanese study found lower levels of leptin among those consuming four or more cups per day compared to those consuming <1 cup per day.[28] In a randomized placebo-controlled double-blind parallel trial with overweight and moderately obese subjects, high coffee/caffeine consumption yielded to significantly low leptin levels in women, which agrees with our study.[29]

The underlying mechanism regarding the associations of adiponectin and leptin to coffee consumption is not yet clearly understood. It is possible that antioxidants found in coffee may play a role. Chlorogenic acid, an antioxidant found in coffee, increased adiponectin and decreased leptin levels in mice.[30] Results from a clinical study proposed that the inhibitory effect of chlorogenic acid on the glucose absorption in the small intestine and the inhibitory effect of glucose-6-phosphate in releasing glucose to the general circulation led to the usage of the stored fats from adipose tissue as an energy source.[31] High caffeine intake was associated with weight loss through thermogenesis and fat oxidation and it decreased leptin levels.[29] Several studies suggested that coffee and/or caffeine likely inhibit the inflammatory processes[24,32,33] and improves insulin sensitivity.[34] Caffeine and coffee-derived metabolites inhibited inflammasome activation.[32] Coffee consumption was inversely associated with circulating levels of E-selection or C-reactive protein among diabetic women.[33] A cross-sectional study of the Singaporean population found an inverse association between coffee consumption and homeostatic model assessment for insulin resistance.[34]

Korea has experienced a growing popularity of coffee. Korean National Health and Nutrition Examination Survey data showed increasing trend of coffee consumption over the past decade, with increase in the prevalence of daily coffee consumption by 20.3% from year 2001 to 2011.[23] The proportion of Korean adults who consumed two or more cups per day increased from 29.1% to 43.3% from 2001 to 2011 (P for trend <.0001). Our cross-sectional study suggests the possibility that coffee consumption confers potential benefits for Koreans. Further prospective studies are needed to explore whether coffee intake decreases or increases the risk of chronic disease and mortality among Korean population.

Our study has several limitations. First, this was a cross-sectional study where we were not able to infer temporal relationships. Second, residual or unmeasured confounding factors could partly explain our observation, but we adjusted for the potential confounding factors and performed stratified analyses, suggesting that our observations may not be fully explained by confounding bias. Third, we were not able to calculate energy intake because of lack of dietary assessment. Although anthropometric measures and physical activity may reflect long-term intake and expenditure of energy, energy intake calculated from well-designed dietary assessment may need to be considered to eliminate a potential confounding factor. Fourth, the proportion of non-coffee drinkers in our study were lower than the general population (14.4% in 2007)[23] partly because of higher social economic status in this study than the general population. High coffee consumption in this population may be limited by the generalizability, but the association between coffee consumption and adiponectin and leptin levels that we observed may also apply to other populations. The strengths of our study might include a relatively large number of participants and, to our knowledge, the first study that examined the association between coffee consumption and adiponectin and leptin levels in the Korean population, who are experiencing dramatic increase in coffee consumption during the last decade.

We found elevated adiponectin levels among regular female coffee consumers and lower levels of leptin among both male and female coffee consumers. Given the limited evidence on the benefit of coffee consumption for chronic diseases like diabetes, metabolic syndrome, and cardiovascular diseases in Korea, our study provides evidence for a benefical metabolic effect of coffee and demonstrates the need for further prospective cohort and mechanistic studies.

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AUTHOR DISCLOSURE STATEMENT

No competing financial interests exist.

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