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Consumption of Coffee and Green Tea and the Risk of Colorectal Cancer in Korea: The Health Examinees Study

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Coffee and green tea may affect colorectal physiology and contain many bioactive components, such as polyphenol and caffeine, which have antioxidant and anti-carcinogenic activities. However, the association between coffee and green tea consumption and the risk of colorectal cancer (CRC) has been inconclusive. This study examined the association between coffee and green tea consumption and the risk of CRC in a large-scale prospective cohort study in Korea. Data from the Health Examinees study from 2004 to 2013 were analyzed, and 114,243 participants (39,380 men and 74,863 women) aged 40–79 years were included in the final analysis. A Cox proportional hazards regression model using age at time scale was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) of coffee and green tea consumption for the risk of CRC by sex. In both men and women, no significant association was found between coffee and green tea consumption and the risk of CRC. Among women, there was a significant increase in the risk of colon cancer (HR, 1.66; 95% CI, 1.13–2.44) in the black coffee drinker group. Our findings suggest that consumption of coffee and green tea may not be associated with the CRC incidence in Korea; instead, the association may differ depending on cancer subsites and coffee types.

Key Words Colorectal neoplasms, Coffee, Tea

INTRODUCTION

Colorectal cancer is estimated to be the third most common cancer in the world, accounting for 10% of all new cancer diagnoses in 2020 [1]. In Korea, colorectal cancer was the third most common cancer in both men and women in 2019 [2]. Due to the high incidence of colorectal cancer, it is important to identify modifiable risk factors for colorectal cancer and to prevent the incidence of colorectal cancer from a public health perspective [3].

Coffee and green tea are among the most widely consumed beverages in the world [4], and their consumption among Koreans has increased three fold over a decade [5]. Suggested mechanisms by which coffee may prevent colorectal cancer development include increasing large bowel motility in the rectosigmoid region [6] and reducing secretion of carcinogenic bile acid and sterol into the bowel [7]. Coffee and green tea also contain bioactive components, such as polyphenol and caffeine, which have antioxidant and antitumorigenic properties [8].

In previous epidemiological studies, however, inconsistent results have been reported regarding coffee and green tea consumption and the risk of colorectal cancer. Some previous studies have reported an inverse association between coffee [9-11] and green tea [12] consumption and the risk of colorectal cancer, whereas others reported no association [13-15]. Based on evidence from prospective studies, the World Cancer Research Fund/American Institute for Cancer Research concluded that the evidence linking the risk of colorectal cancer with coffee and green tea consumption was 'limited-no conclusion' [16].

The results of these previous studies were mostly reported from Western countries and Japan, and the culture of coffee and tea consumption may differ from country to country [17-

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19]. Lifestyle factors, such as smoking, alcohol consumption, and body mass index (BMI), were related to coffee and green tea consumption [20-24]. The variable results of epidemiological studies regarding the risk of colorectal cancer with coffee and green tea consumption could also be explained by a variety of lifestyle factors. Furthermore, different anatomical subsites of the colorectum have different clinical and biological characteristics [25,26], and the impact of various risk factors on colorectal cancer differs by sex [27].

A previous case-control study of colorectal cancer risk with coffee [10] and green tea [28] consumption in Korea showed that high coffee and green tea consumption may be associated with a lower risk of colorectal cancer. To the best of our knowledge, there are no large-scale population-based studies that have investigated the association between coffee and green tea consumption and the risk of colorectal cancer considering lifestyle factors in the Korean population. Therefore, the aim of this study was to examine the association between coffee and green tea consumption and the risk of colorectal cancer in the Health Examinees (HEXA) study.

MATERIALS AND METHODS

Study population

The HEXA study is a large-scale genomic cohort study with the Korean population [29]. Participants in the HEXA study were Korean adult men and women aged 40–79 and prospectively recruited from 38 health examination centers and training hospitals located in eight regions between 2004 and 2013 [29]. The selection criteria for the 38 centers participating in the HEXA study were as follows [30]: 1) the experience building a cohort and participating in multicenter network study; 2) the ability to recruit over 2,000 participants per year; 3) the health examination system representing the community; 4) the infrastructure for repeated surveys; and 5) a follow-up rate of over 50%. A total of 173,202 participants were recruited for the study. All participants voluntarily signed an informed consent before starting the study, and the protocol was approved by the Institutional Review Board (IRB) at Seoul National University Hospital (IRB No. E-2110-004-1257).

Figure 1 shows the flow chart of the study population. In this study, we used the data on HEXA-Gem (HEXA-G) participants provided with additional qualification criteria on the participating sites: 1) Eight sites that participated in the pilot study only during 2004–2006; 2) Eight sites that did not meet the HEXA standards for biospecimen quality control; and 3) Five sites that participated in the study for less than two years [31]. After excluding participants recruited at 21 centers based on HEXA recruitment criteria, a total of 141,893 participants remained. Among the participants, we excluded participants who did not consent to data linkage with the cancer registry and death data (n = 24,000), had death information at baseline (n = 2), self-reported a history of colorectal cancer

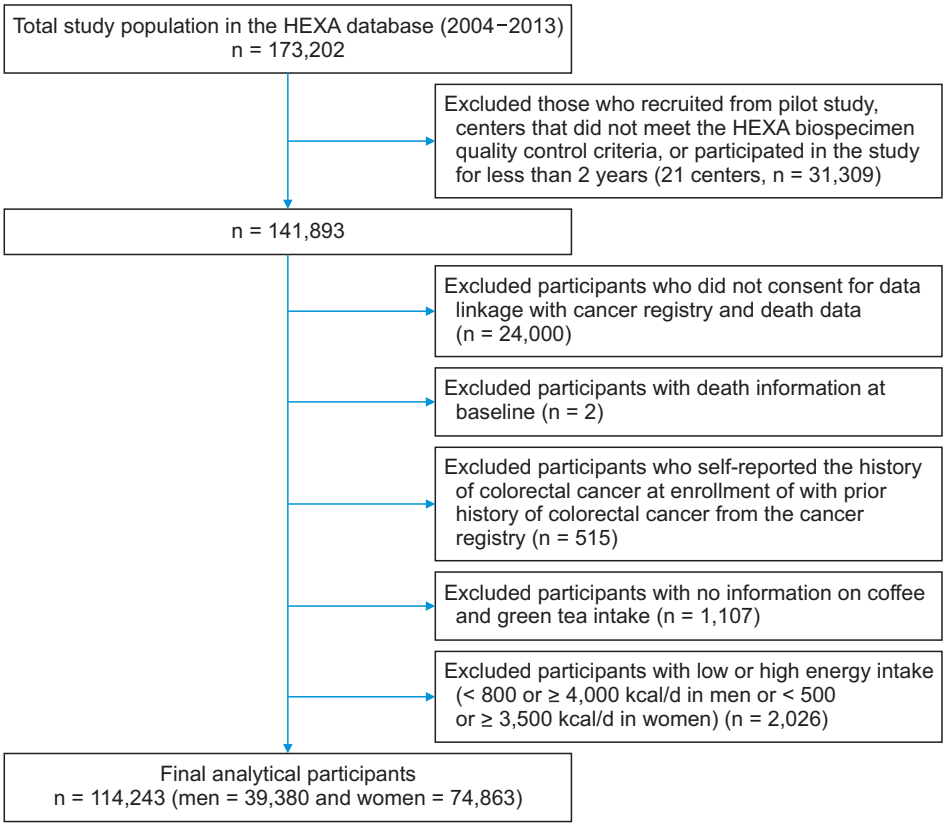

Figure 1. Flow chart for study population. HEXA, Health Examinees.

at enrollment or had a prior history of colorectal cancer from the cancer registry (n = 515), had no information on coffee and green tea intake (n = 1,107), and had implausible energy intake (n = 2,026) (< 800 or ≥ 4,000 kcal/d in men; < 500 or ≥ 3,500 kcal/d in women [31]).

After these exclusions, 114,243 participants (39,380 men and 74,863 women) were included in the final analysis.

Assessment of coffee and green tea consumption

Coffee consumption was evaluated as a semiquantitative food frequency questionnaire (FFQ) consisting of 106 food items designed for the Korean population [30]. The reproducibility and validity of the FFQ were previously evaluated in a prior study [32]. Participants were asked how often they consumed coffee and green tea on average over the past 12 months before baseline. Participants had a choice of 9 frequency levels of coffee and green tea consumption (none, once per month, 2 to 3 times per month, once to 2 times per week, 3 to 4 times per week, 5 to 6 times per week, once to 2 times per day, 3 to 4 times per day, and more than 5 times per day) and 3 choices for the average amount of coffee and green tea consumption per drink from three categories ("1/2 cup", "1 cup", and "2 cups"). Participants were also asked a question about the portion sizes of sugar and creamer added to coffee if they used them. Coffee and green tea consumption was categorized as none, < 1 cup/d, 1 to < 2 cups/d, and ≥ 2 cups/d.

The participants' type of coffee consumption was also analyzed (none, black coffee, sugar coffee, cream coffee, and 3-in-1 coffee) according to coffee additives. People who did not drink coffee at baseline were classified as none. Coffee consumers who added sugar were classified as sugar coffee. Coffee consumers who added cream were classified as cream coffee. Coffee consumers who added or did not add

Table 1. General characteristics of the study population by daily coffee consumption in men

Variables	Daily coffee consumption, no. of cups				
	None (n = 4,807)	< 1 (n = 7,515)	1 to < 2 (n = 14,553)	≥ 2 (n = 12,505)	*P*-value[a]
Age, yr	55.6 ± 8.7	54.6 ± 8.6	54.8 ± 8.7	52.4 ± 8.5	< 0.01
Education level (yr)					< 0.01
< 10	1,142 (23.8)	1,474 (19.6)	2,952 (20.3)	2,515 (20.1)	
10–12	1,870 (38.9)	2,923 (38.9)	5,823 (40.0)	5,331 (42.6)	
12	1,738 (36.2)	3,035 (40.4)	5,614 (38.6)	4,536 (36.3)	
Missing	57 (1.2)	83 (1.1)	164 (1.1)	123 (1.0)	
Body mass index (kg/m^2)					< 0.01
< 18.5	115 (2.4)	108 (1.4)	160 (1.1)	146 (1.2)	
18.5–22.9	1,688 (35.1)	2,122 (28.2)	4,003 (27.5)	3,466 (27.7)	
23–24.9	1,446 (30.1)	2,241 (29.8)	4,448 (30.6)	3,767 (30.1)	
≥ 25	1,558 (32.4)	3,044 (40.5)	5,942 (40.8)	5,126 (41.0)	
Smoking status					< 0.01
Non-smoker	1,962 (40.8)	2,562 (34.1)	4,061 (27.9)	2,241 (17.9)	
Ex-smoker	2,103 (43.7)	3,239 (43.1)	6,504 (44.7)	4,444 (35.5)	
Current smoker	730 (15.2)	1,698 (22.6)	3,957 (27.2)	5,800 (46.4)	
Missing	12 (0.2)	16 (0.2)	31 (0.2)	20 (0.2)	
Alcohol consumption					< 0.01
Non-drinker	1,268 (26.4)	1,378 (18.3)	2,725 (18.7)	2,543 (20.3)	
Ex-drinker	540 (11.2)	578 (7.7)	943 (6.5)	768 (6.1)	
Current drinker	2,985 (62.1)	5,542 (73.7)	10,844 (74.5)	9,172 (73.3)	
Missing	14 (0.3)	17 (0.3)	41 (0.3)	22 (0.2)	
Regular exercise					< 0.01
No	1,854 (38.6)	2,835 (37.7)	5,871 (40.3)	6,034 (48.3)	
Yes	2,939 (61.1)	4,660 (62.0)	8,641 (59.4)	6,448 (51.6)	
Missing	14 (0.3)	20 (0.3)	41 (0.3)	23 (0.2)	
First-degree family history of colorectal cancer					< 0.01
No	4,589 (95.5)	7,163 (95.3)	13,968 (96.0)	11,864 (94.9)	
Yes	118 (2.5)	192 (2.6)	341 (2.3)	296 (2.4)	
Missing	100 (2.1)	160 (2.1)	244 (1.7)	345 (2.8)	
Red and processed meat intake (g/d)	34.7 ± 40.8	37.1 ± 39.3	41.1± 40.0	46.9 ± 42.5	< 0.01
Vegetable and fruits intake (g/d)	454.9 ± 292.6	387.3 ± 272.6	457.1 ± 272.4	461.0 ± 277.6	< 0.01
Energy intake (kcal/d)	1,746.8 ± 474.1	1,734.4 ± 467.7	1,856.1 ± 467.8	1,955.7 ± 501.4	< 0.01

Values are presented as mean ± standard deviation or number (%).
[a]Analysis of Variance test for continuous variables; Chi-square test for categorical variables.

sugar and cream were classified as 3-in-1 and black coffee, respectively.

Identification of colorectal cancer cases

The cases of colorectal cancer were identified in linkage with the Korea Central Cancer Registry data by the end of December 2018. The Korea Centers for Disease Control and Prevention requested data connection to Korea Central Cancer Registry after obtaining prior consent from the study participants. We defined colorectal cancer as C18 to C20, colon cancer as C18, and rectal cancer as C19 and C20 according to the 2021 International Classification of Diseases, 10th Revision code.

Statistical analysis

For each participant, person-years of follow-up was calculated from baseline to the first of the diagnosis of colorectal cancer, the end of follow-up observation (December 31, 2018), or the date of death recorded in the Causes of Death Statistics of Statistics Korea, whichever came first. The chi-square test for categorical variables and Analysis of Variance for continuous variables were used to analyze the general characteristics of the participants at baseline based on their coffee and green tea consumption. A Cox proportional hazards regression model using age at time scale was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) to investigate the association between coffee, green tea consumption and the risk of colorectal, colon, and rectal cancer by sex.

We adjusted the risk factors for colorectal cancer assessed at baseline, including education level (< 10 years, 10–12 years, > 12 years, and missing), BMI (< 18.5 kg/m^2, 18.5–22.9 kg/m^2, 23–24.9 kg/m^2, ≥ 25 kg/m^2, and missing), smoking status (non-smoker, ex-smoker, current smoker,

Table 2. General characteristics of the study population by daily coffee consumption in women

Variables	Daily coffee consumption, no. of cups				
	None (n = 13,535)	< 1 (n = 16,778)	1 to < 2 (n = 31,074)	≥ 2 (n = 13,476)	*P*-value[a]
Age, years	55.4± 7.8	53.1± 7.9	52.3 ± 7.9	49.8 ± 7.2	<0.01
Education level (yr)					<0.01
< 10	6,260 (46.3)	6,240 (37.2)	10,762 (34.6)	3,663 (27.2)	
10–12	5,049 (37.3)	7,182 (42.8)	13,646 (43.9)	6,322 (46.9)	
> 12	2,076 (15.3)	3,180 (19.0)	6,364 (20.5)	3,381 (25.1)	
Missing	150 (1.1)	176 (1.0)	302 (1.0)	110 (0.8)	
Body mass index (kg/m^2)					<0.01
< 18.5	414 (3.1)	335 (2.0)	551 (1.8)	268 (2.0)	
18.5–22.9	6,339 (46.8)	7,228 (43.1)	13,009 (41.9)	5,710 (42.4)	
23–24.9	3,508 (25.9)	4,572 (27.2)	8,333 (26.8)	3,496 (25.9)	
≥ 25	3,274 (24.2)	4,643 (27.7)	9,181 (29.5)	4,002 (29.7)	
Smoking status					<0.01
Non-smoker	13,225 (97.7)	16,272 (97.0)	29,991 (96.5)	12,436 (92.3)	
Ex-smoker	105 (0.8)	187 (1.1)	392 (1.3)	255 (1.9)	
Current smoker	151 (1.1)	224 (1.3)	567 (1.8)	750 (5.6)	
Missing	54 (0.4)	95 (0.6)	124 (0.4)	35 (0.3)	
Alcohol consumption					<0.01
Non-drinker	11,140 (82.3)	11,647 (69.4)	19,878 (64.0)	7,619 (56.5)	
Ex-drinker	221 (1.6)	382 (2.3)	522 (1.7)	263 (2.0)	
Current drinker	2,118 (15.6)	4,651 (27.7)	10,565 (34.0)	5,562 (41.3)	
Missing	56 (0.4)	98 (0.6)	109 (0.4)	32 (0.2)	
Regular exercise					<0.01
No	6,401 (47.3)	7,518 (44.8)	15,129 (48.7)	7,358 (54.6)	
Yes	7,109 (52.5)	9,213 (54.9)	15,866 (51.1)	6,105 (45.3)	
Missing	25 (0.2)	47 (0.3)	79 (0.3)	13 (0.1)	
First-degree family history of colorectal cancer					<0.01
No	12,867 (95.1)	15,884 (94.7)	29,657 (95.4)	12,673 (94.0)	
Yes	337 (2.5)	456 (2.7)	843 (2.7)	331 (2.5)	
Missing	331 (2.4)	438 (2.6)	574 (1.8)	472 (3.5)	
Red and processed meat intake (g/d)	22.1 ± 28.6	27.9 ± 34.3	30.5 ± 32.2	36.7 ± 39.8	<0.01
Vegetable and fruits intake (g/d)	492.8 ± 318.7	464.3 ± 313.3	504.8 ± 301.0	502.4 ± 316.5	<0.01
Energy intake (kcal/d)	1,582.2 ± 465.6	1,604.3 ± 487.3	1,715.3 ± 470.9	1,782.1 ± 514.3	<0.01

Values are presented as mean ± standard deviation or number (%).
[a]Analysis of Variance test for continuous variables; Chi-square test for categorical variables.

and missing), alcohol consumption (non-drinker, ex-drinker, current drinker, and missing), regular exercise (no, yes, and missing), first-degree family history of colorectal cancer (no, yes, and missing), total energy intake (kcal/d, continuous), red and processed meat intake (g/d, continuous), and vegetable and fruit intake (g/d, continuous). For all covariates, missing values were treated as additional categories of variables and included in the model.

The relationship between coffee and green tea consumption and the risk of colorectal cancer was examined in the nonsmokers and nondrinkers group and the group with a body mass index (BMI) less than 25 stratified according to smoking, drinking status, and BMI among lifestyle factors.

All statistical analyses were conducted using SAS software version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

The distribution of the general characteristics of the study population according to the frequency of coffee consumption is shown in Table 1, 2. In both men and women, people who consumed more than 2 cups of coffee per day tended to be younger (52.4 years for men, 49.8 years for women), current smokers (46.4% in men, 5.6% in women) and had a higher BMI range of ≥ 25 kg/m^2 (41.0% in men, 29.7% in women), lower regular physical activity (48.3% in men, 54.6% in women), consumed higher amounts of red and processed meat (46.9 g/d in men, 36.7 g/d in women), and energy intake (1,955.7 kcal/d in men, 1,782.1 kcal/d in women) than people who did not consume coffee. The distribution of the general characteristics of the study population according to the frequency of green tea consumption is shown in Table S1, S2.

The HRs and 95% CIs for colorectal cancer according to

Table 3. Hazard ratios (HRs) and 95% confidence intervals (CIs) for colorectal cancer incidence according to daily coffee consumption

Variables	Daily coffee consumption, no. of cups			
	None	< 1	1 to < 2	≥ 2
Men (n = 39,380)				
Number	4,807	7,515	14,553	12,505
Person-years	43,883.9	69,925.9	131,542.0	112,616.0
Colorectal cancer				
No. of event	62	90	174	137
Crude HR	1.00 (reference)	0.95 (0.69–1.32)	0.98 (0.73–1.31)	1.03 (0.76–1.39)
aHR[a]	1.00 (reference)	0.93 (0.67–1.29)	0.96 (0.71–1.28)	1.01 (0.74–1.38)
Colon cancer				
No. of event	38	51	92	73
Crude HR	1.00 (reference)	0.89 (0.59–1.36)	0.86 (0.59–1.25)	0.94 (0.63–1.39)
aHR[a]	1.00 (reference)	0.85 (0.56–1.30)	0.82 (0.56–1.20)	0.91 (0.61–1.37)
Rectal cancer				
No. of event	24	39	82	64
Crude HR	1.00 (reference)	1.05 (0.63–1.75)	1.17 (0.74–1.85)	1.17 (0.73–1.87)
aHR[a]	1.00 (reference)	1.05 (0.63–1.75)	1.17 (0.74–1.86)	1.17 (0.72–1.90)
Women (n = 74,863)				
Number	13,535	16,778	31,074	13,476
Person-years	125,268.0	159,250.0	280,035.0	122,126.0
Colorectal cancer				
No. of event	81	118	188	78
Crude HR	1.00 (reference)	1.31 (0.99–1.75)	1.26 (0.97–1.63)	1.42 (1.03–1.94)
aHR[a]	1.00 (reference)	1.27 (0.95–1.69)	1.21 (0.93–1.58)	1.34 (0.97–1.86)
Colon cancer				
No. of event	52	80	128	51
Crude HR	1.00 (reference)	1.41 (0.99–2.00)	1.36 (0.99–1.89)	1.52 (1.02–2.25)
aHR[a]	1.00 (reference)	1.36 (0.96–1.94)	1.33 (0.95–1.84)	1.43 (0.96–2.14)
Rectal cancer				
No. of event	29	38	60	27
Crude HR	1.00 (reference)	1.14 (0.70–1.85)	1.06 (0.68–1.66)	1.23 (0.72–2.10)
aHR[a]	1.00 (reference)	1.10 (0.68–1.80)	1.01 (0.64–1.59)	1.18 (0.68–2.05)

Values are present as number only or HR (95% CI).
aHR, adjusted HR.
[a]Adjusted for education level (<10 yr, 10–12 yr, >12 yr, and missing), body mass index (< 18.5 kg/m^2, 18.5–22.9 kg/m^2, 23–24.9 kg/m^2, ≥ 25 kg/m^2, and missing), smoking status (non-smoker, ex-smoker, current smoker, and missing), alcohol consumption (non-drinker, ex-drinker, current drinker, and missing), regular exercise (no, yes, and missing), first-degree family history of colorectal cancer (no, yes, and missing), red and processed meat intake (g/d, continuous), vegetable and fruits intake (g/d, continuous), and energy intake (kcal/d, continuous).

coffee consumption are presented by sex in Table 3. In both men and women, no significant association was found between coffee consumption and the risk of colorectal cancer (HR: 1.01, 95% CI: 0.74–1.38 for men; HR: 1.34, 95% CI: 0.97–1.86 for women). In site-specific analyses, no significant association was found between coffee consumption and the risk of colon cancer (HR: 0.91, 95% CI: 0.61–1.37) and rectal cancer (HR: 1.17, 95% CI: 0.72–1.90) in men. Among women, no significant association was found between coffee consumption and the risk of colon cancer (HR: 1.43, 95% CI: 0.96–2.14) or rectal cancer (HR: 1.18, 95% CI: 0.68–2.05).

The HRs and 95% CIs for colorectal cancer according to green tea consumption are presented by sex in Table 4. We found no evidence of an association between green tea consumption and the risk of colorectal cancer in men (HR: 0.90, 95% CI: 0.56–1.45) or women (HR: 1.04, 95% CI: 0.62–1.74). In site-specific analyses, no significant association was found between green tea consumption and the risk of colon cancer (HR: 0.58, 95% CI: 0.27–1.26) and rectal cancer (HR: 1.32, 95% CI: 0.71–2.45) in men. Among women, no significant association was found between green tea consumption and the risk of colon cancer (HR: 1.11, 95% CI: 0.60–2.07) and rectal cancer (HR: 0.92, 95% CI: 0.37–2.29).

The HRs and 95% CIs for colorectal cancer according to coffee types are presented by sex in Table 5. In men, no significant association was found between coffee types and the risk of colorectal cancer. Among women, there was a significant increase in the risk of colorectal cancer (HR: 1.42, 95% CI: 1.03–1.95) and colon cancer (HR: 1.66, 95% CI: 1.13–2.44) in the black coffee drinker group, but we found no association between coffee types and the risk of rectal cancer.

Table 4. Hazard ratios (HRs) and 95% confidence intervals (CIs) for colorectal cancer incidence according to daily green tea consumption

	Daily green tea consumption, no. of cups			
	None	< 1	1 to < 2	≥ 2
Men (n = 39,380)				
Number	15,638	16,655	5,310	1,777
Person-years	136,468.0	153,977.0	49,931.2	17,195.8
Colorectal cancer				
No. of event	198	189	57	19
Crude HR	1.00 (reference)	0.90 (0.74–1.10)	0.88 (0.66–1.18)	0.88 (0.55–1.40)
aHR[a]	1.00 (reference)	0.91 (0.74–1.12)	0.89 (0.66–1.21)	0.90 (0.56–1.45)
Colon cancer				
No. of event	116	98	33	7
Crude HR	1.00 (reference)	0.81 (0.62–1.06)	0.90 (0.61–1.32)	0.57 (0.27–1.23)
aHR[a]	1.00 (reference)	0.81 (0.61–1.06)	0.90 (0.60–1.33)	0.58 (0.27–1.26)
Rectal cancer				
No. of event	82	91	24	12
Crude HR	1.00 (reference)	1.03 (0.76–1.39)	0.86 (0.55–1.36)	1.28 (0.70–2.34)
aHR[a]	1.00 (reference)	1.06 (0.78–1.43)	0.90 (0.56–1.43)	1.32 (0.71–2.45)
Women (n = 74,863)				
Number	32,324	31,924	8,173	2,442
Person-years	281,591.0	300,302.0	78,776.0	24,922.5
Colorectal cancer				
No. of event	199	206	42	16
Crude HR	1.00 (reference)	1.04 (0.85–1.26)	0.84 (0.60–1.17)	1.03 (0.62–1.71)
aHR[a]	1.00 (reference)	1.03 (0.84–1.25)	0.83 (0.59-1.17)	1.04 (0.62–1.74)
Colon cancer				
No. of event	131	138	30	11
Crude HR	1.00 (reference)	1.07 (0.84–1.36)	0.92 (0.62–1.37)	1.10 (0.59–2.03)
aHR[a]	1.00 (reference)	1.06 (0.83–1.35)	0.92 (0.61–1.38)	1.11 (0.60–2.07)
Rectal cancer				
No. of event	68	68	12	5
Crude HR	1.00 (reference)	0.98 (0.70–1.38)	0.68 (0.37–1.26)	0.91 (0.37–2.25)
aHR[a]	1.00 (reference)	0.97 (0.69–1.37)	0.67 (0.36–1.24)	0.92 (0.37–2.29)

Values are present as number only or HR (95% CI).
aHR, adjusted HR.
[a]Adjusted for education level (< 10 yr, 10–12 yr, > 12 yr, and missing), BMI (< 18.5 kg/m^2, 18.5–22.9 kg/m^2, 23–24.9 kg/m^2, ≥ 25 kg/m^2, and missing), smoking status (non-smoker, ex-smoker, current smoker, and missing), alcohol consumption (non-drinker, ex-drinker, current drinker, and missing), regular exercise (no, yes, and missing), first-degree family history of colorectal cancer (no, yes, and missing), red and processed meat intake (g/d, continuous), vegetable and fruits intake (g/d, continuous), and energy intake (kcal/d, continuous).

Table 5. Hazard ratios (HRs) and 95% confidence intervals (CIs) for colorectal cancer incidence according to coffee types

	Coffee types			
	None	Black	Sugar	3-in-1
Men (n = 39,380)				
Number	4,807	4,727	3,984	25,302
Person-years	43,849.3	41,703.2	36,377.6	230,383.0
Colorectal cancer				
No. of event	62	65	46	283
Crude HR	1.00 (reference)	1.26 (0.89–1.78)	0.94 (0.64–1.38)	0.95 (0.72–1.25)
aHR[a]	1.00 (reference)	1.21 (0.85–1.73)	0.91 (0.62–1.33)	0.93 (0.70–1.23)
Colon cancer				
No. of event	38	38	27	145
Crude HR	1.00 (reference)	1.25 (0.79–1.96)	0.92 (0.56–1.51)	0.82 (0.57–1.17)
aHR[a]	1.00 (reference)	1.17 (0.74–1.84)	0.87 (0.53–1.42)	0.78 (0.54–1.13)
Rectal cancer				
No. of event	24	27	19	138
Crude HR	1.00 (reference)	1.29 (0.74–2.23)	0.99 (0.54–1.80)	1.16 (0.75–1.80)
aHR[a]	1.00 (reference)	1.29 (0.74–2.24)	0.97 (0.53–1.78)	1.16 (0.75–1.81)
Women (n = 74,863)				
Number	13,535	12,609	9,442	38,352
Person-years	125,161.0	110,570.0	87,901.5	353,231.0
Colorectal cancer				
No. of event	80	79	64	231
Crude HR	1.00 (reference)	1.47 (1.07–2.01)	1.36 (0.98–1.89)	1.24 (0.96–1.61)
aHR[a]	1.00 (reference)	1.42 (1.03–1.95)	1.33 (0.95–1.85)	1.18 (0.91–1.53)
Colon cancer				
No. of event	52	57	42	151
Crude HR	1.00 (reference)	1.69 (1.16–2.47)	1.40 (0.93–2.11)	1.28 (0.94–1.76)
aHR[a]	1.00 (reference)	1.66 (1.13–2.44)	1.39 (0.92–2.10)	1.22 (0.89–1.69)
Rectal cancer				
No. of event	28	22	22	80
Crude HR	1.00 (reference)	1.07 (0.61–1.89)	1.27 (0.72–2.22)	1.16 (0.75–1.79)
aHR[a]	1.00 (reference)	1.02 (0.58–1.81)	1.21 (0.69–2.14)	1.11 (0.71–1.72)

Values are present as number only or HR (95% CI).
aHR, adjusted HR.
[a]Adjusted for education level (< 10 yr, 10–12 yr, > 12 yr, and missing), body mass index (< 18.5 kg/m^2, 18.5–22.9 kg/m^2, 23–24.9 kg/m^2, ≥ 25 kg/m^2, and missing), smoking status (non-smoker, ex-smoker, current smoker, and missing), alcohol consumption (non-drinker, ex-drinker, current drinker, and missing), regular exercise (no, yes, and missing), first-degree family history of colorectal cancer (no, yes, and missing), red and processed meat intake (g/d, continuous), vegetable and fruits intake (g/d, continuous), and energy intake (kcal/d, continuous).

DISCUSSION

In this study, we analyzed the association between coffee and green tea consumption and the risk of colorectal cancer by using data from a large-scale cohort study. We found no clear association between coffee or green tea consumption and the risk of colorectal cancer in either men or women. Stratifying by the type of coffee, there was a significant increase in the risk of colorectal cancer and colon cancer in the black coffee drinker group among women, but we found no evidence of an association between coffee types and the risk of rectal cancer in men and women.

In a meta-analysis of 26 prospective studies, no association was reported between coffee consumption and the risk of colorectal cancer in men (Relative risk [RR]: 0.96, 95% CI: 0.88–1.04) and women (RR: 1.06, 95% CI: 0.97–1.14) [33]. A meta-analysis [12] identified an inverse association between green tea consumption and the risk of colorectal cancer in only women (OR: 0.68, 95% CI: 0.56–0.81). These sex differences in the results for the association between green tea consumption and the risk of colorectal cancer are not clearly known. It is thought that differences in physiological [34], physical [35], hormonal [36], and lifestyle [37] characteristics according to sex may have influenced green tea consumption, and further studies on the mechanistic basis of sex differences are needed.

In stratified analyses by anatomical subsites, an inverse association between coffee consumption and colon cancer was found in European men (RR: 0.85, 95% CI: 0.72–0.99) and Asian women (RR: 0.73, 95% CI: 0.58–0.88). In rectal cancer, no association was found [33]. A prospective cohort in Japan showed a significant inverse association between

coffee consumption and the risk of colon cancer among women only (RR: 0.44, 95% CI: 0.19–1.04; *P* for trend = 0.04). In men, no significant association was observed in any colorectal cancer sites [38]. In a population-based prospective cohort study, no significant association was found between green tea consumption and the risk of colon and rectal cancer [39]. These subsite differences in the effect of coffee consumption on colorectal cancer might be explained by various mechanisms. A previous study found that coffee increased colon motility, especially the distal colon [6]. Our results from Korean are consistent with previous studies [38,39] in that they showed no association between consumption of coffe or green tea and the risk of rectal cancer, but the result from Korean women is inconsistent with previous studies [33,38] in that they showed an inverse association between coffee consumption and the risk of colon cancer.

Inconsistency with previous studies may be due to complex biological effects, such as caffeine levels [40] and differences in tea drinking culture and ethnicity. Western countries [17] and Japan [18] prefer filtered or brewed coffee, while Koreans prefer instant mixes of coffee containing nondairy creamer and sugar over brewed ones [19]. It is possible to consider the difference in the average intake of tea and the difference in absorption and metabolic rate by ethnicity [41]. In the analysis of coffee types, there was a significant increase in the risk of colorectal cancer and colon cancer in the black coffee drinker group among women only. It was suggested that the risk of colorectal cancer may be increased in 3-in-1 coffee, sugar coffee, or cream coffee because coffee additives could increase the risk of obesity [42,43], but the risk of colorectal cancer and colon cancer increased in the black coffee drinker group among women. When the black coffee group was categorized again according to coffee consumption frequency, only 'intake <1 cup/d' significantly increased the risk of colon cancer (HR: 2.00; 95% CI: 1.22–3.28) (Table S3).

Overall, most studies have consistently expressed the opinion that caffeine and polyphenols in coffee have a protective effect on colorectal cancer [8]. On the other hand, coffee contains mutagens, such as methylglyoxal [44] and tannins [45], which could counteract coffee's protective effects against colorectal cancer. In addition, it is estimated that inconsistent conclusions can be drawn from epidemiological studies in humans because the amount of caffeine [46] and polyphenols [47] in coffee differs depending on whether coffee is filtered or unfiltered, the degree of roasting of beans, brewing method, and species of coffee beans, and standardization is difficult. The results of our present study presumably suggest that black coffee consumption may increase the risk of colorectal cancer in women. Caution should be needed in the interpretation of the results in the black coffee drinker group among women.

Coffee and green tea drinkers are more likely to smoke and consume alcohol [20]. Previous studies have reported that smoking confers a significant effect modifier on the association between tea consumption and the risk of esophageal cancer [48] and lung cancer [49]. Coffee consumption increased the risk of rectal cancer among never smokers in women (HR: 1.44, 95% CI: 1.06–1.95) [50]. According to our results, no significant difference was found between coffee and green consumption and the risk of colorectal cancer stratified according to smoking (Table S4) and drinking status (Table S5).

A hospital-based case–control study of colorectal cancer risk with coffee consumption in Korea showed that high coffee consumption may be associated with a lower risk of colorectal cancer among nonobese (HR: 0.24, 95% CI: 0.14–0.41) and obese people (HR: 0.21, 95% CI: 0.10–0.45) [10]. In our study, however, no significant difference was found between coffee and green consumption and the risk of colorectal cancer stratified according to BMI (Table S6).

The strength of this study is the elucidation of the association between coffee or green tea consumption and colorectal cancer incidence using a large population-based cohort of Korean adults. We conducted an analysis of the association between coffee and green tea consumption and the risk of colorectal cancer according to the coffee type and stratification analysis to explain it in various ways. The limitation of this study is that it could not be investigated considering the amount of intake and additives according to the type of coffee. Further research is needed to investigate the relationship between the consumption of coffee and the risk of colorectal cancer according to the type and the amount of coffee additive. Data on coffee and green tea consumption and lifestyle factors were collected through surveys, which may be limited by measurement error. The amount of caffeine in coffee and green tea varies depending on the type of coffee and green tea mixture [51], which was also not investigated in this study.

In conclusion, no association was found between coffee and green tea consumption and colorectal cancer incidence in Korea. Among women, however, there was a significant increase in the risk of colorectal cancer and colon cancer in the black coffee drinker group.

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CONFLICTS OF INTEREST

No potential conflicts of interest were disclosed.

SUPPLEMENTARY MATERIALS

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