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ORIGINAL ARTICLE

Alcohol Intake, Smoking, and Colorectal Adenoma

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Background: Colorectal cancer is the third most common cancer in Korea. Because colorectal adenoma is a precursor lesion of colorectal cancer, primary prevention of colorectal adenomas may be important for reducing morbidity and mortality from the disease. The aim of this study is to examine the association of alcohol consumption and cigarette smoking in relation with colorectal adenoma in a cross-sectional study of Korean adults.
Methods: A total of 366 participants who underwent colonoscopy were included (113 cases and 255 controls) in this study. Information on alcohol intake and cigarette smoking was collected from structured questionnaires. The odds ratio (ORs) and 95% confidence intervals (CIs) were calculated using the multivariate logistic regression models.
Results: Alcohol intake was associated with a higher prevalence of colorectal adenoma in men; compared to non-drinkers, ORs (95% CIs) were 11.49 (2.55-51.89) for 10-20 g/day of alcohol intake and 14.15 (3.31-60.59) for > 20 g/day of alcohol intake (P for trend = 0.003). There was a weaker association of alcohol intake for women than men; however, there was a suggestive increase in the prevalence of colorectal cancer in women. Cigarette smoking was not associated with colorectal adenoma, but we cannot rule out the possibility that this was due to low statistical power.
Conclusion: Our study provides evidence to suggest that alcohol intake may contribute to colorectal adenoma in the Korean population. Our study results demonstrate that a larger epidemiologic study is needed.
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Key Words: Colorectal adenoma, Cigarette smoking, Alcohol drinking, Cancer prevention

INTRODUCTION

Colorectal cancer is the third most common cancer in Korea, and its incidence has increased to an average of 5.9% per year from 1999 to 2010.[1] Colorectal adenoma is a precursor lesion of colorectal cancer,[2] which may have some shared etiological factors of colorectal cancer.[3,4] Identifying the possible risk factors associated with colorectal adenoma may help to prevent colorectal cancer.

Several studies have investigated the association of cigarette smoking[5-16] and alcohol intake[5,6,11,16-22] in relation to colorectal neoplasia, but the mechanisms remain unclear. The Continuous Update Project Report by the World Cancer Research Fund/ American Institute for Cancer Research has confirmed that alcohol intake is a convincing risk factor for colorectal cancer in men and a probable risk factor in women.[23] A meta-analysis of 42 epidemiologic studies reported that cigarette smoking was associated with a higher risk of colorectal adenoma development: compared to never smokers, the pooled relative risk estimate was 2.14 for current smokers, 1.47 for former smokers, and 1.82 for ever smokers.[13]

To examine whether alcohol intake and cigarette smoking are associated with colorectal adenoma in the Korean population, we evaluated these associations in a cross-sectional study of Korean men and women who had undergone colonoscopy.

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MATERIALS AND METHODS

1. Study population

A total of 382 men and women aged 45-71 years, who underwent colonoscopy between August 2011 and September 2012 at a University hospital in Daegu, Korea, were included in this study. All participants answered questionnaires about their socio- demographic status and risk factors for colorectal adenoma including family history of colorectal cancer, aspirin use, supplement use, physical activity, education level, smoking status, marital status, and menopausal status (only in women). Participants' height and weight were measured by trained health professionals, and body mass index (BMI [kg/m^2]) was calculated by dividing weight (kg) by height (m^2). After the exclusion of 14 participants who had a history of cancer, a total of 366 participants were included in our study. All of the participants provided written informed consent, and this study was approved by the Institutional Review Board of Daegu Catholic University Medical Center.

2. Ascertainment of colorectal adenoma

Colorectal polyps were classified as adenomatous, hyperplastic, and other non-adenomatous polyps through colonoscopy and histological examinations. Of the 366 participants who underwent colonoscopy, 58 men and 55 women had adenomatous polyps.

3. Assessment of alcohol intake and cigarette smoking

Participants were asked about the age at which they started and/or quit drinking, and the amount and frequency of intake of alcoholic beverages, such as rice wine (makgeolli), wine, beer, and liquor. We calculated daily ethanol intake (g/day) based on the equivalent of ethanol grams for each alcoholic beverage. Questions regarding cigarette smoking habits included lifetime experience of more than 20 packs of cigarettes, age of smoking at initiation and cessation, the number of cigarettes smoked per day during regular smoking, and total number of years of regular cigarette smoking. Participants who reported smoking at least 100 cigarettes in their lifetime and who smoked currently were defined as current smoker; those who reported smoking at least 100 cigarettes in their lifetime, but did not smoke were defined as former smoker; and those who reported never having smoked 100 cigarettes were defined as never smoker. Total pack years of smoking was calculated based on the total duration of regular cigarette smoking and amount of cigarettes smoked per day during regular smoking.

4. Statistical analysis

To compare the distribution of characteristics between the cases and controls, we used the Chi-square test for categorical variables and t test for continuous variables. We also calculated the mean and standard deviation for continuous variables and percentages for categorical variables. We used the multivariate logistic regression models to investigate the associations between risk factors and prevalence of colorectal adenoma. In these multivariate logistic regression models, age, BMI, family history of colorectal cancer, history of colorectal polyps, aspirin use, supplement use, energy intake, physical activity, education level, marital status, and menopausal status (only in women) were adjusted. We categorized alcohol intake or smoking status using uniform cut points across studies based on the distribution of each exposure level in women or men.

We also examined the joint association of alcohol intake and smoking status with colorectal adenoma prevalence. We examined whether the associations differed by age ($<$ 60 and $\geq$ 60 years) and BMI ($<$ 25 and $\geq$ 25 kg/m^2). We used the likelihood ratio test to test the null hypothesis that there was no interaction of potential effect modifiers of colorectal adenoma.

A P-value of less than 0.05 was considered statistically significant, and all statistical analyses were conducted with SAS, version 9.3, software (SAS Institute, Inc., Cary, NC, USA).

RESULTS

Table 1 presents the participants' characteristics. Participants with colorectal adenoma, in comparison to colorectal adenoma-free controls, were older and more likely to be men. However, the proportion of supplement use was lower in cases than controls.

Alcohol intake was significantly associated with colorectal adenoma prevalence in men (Table 2). When we adjusted for age and supplement use, compared to non-drinkers, the ORs (95% CIs) were 4.37 (1.23-15.55) for $\leq$ 10 g/day, 6.23 (1.80-21.62) for 10-20 g/day, and 8.32 (2.60-26.61) for $>$ 20 g/day of alcohol intake (P for trend = 0.003) in men; and the ORs (95% CIs) were 0.72 (0.31-1.70) for 0 $<$ $-$5 g/day, and 1.60 (0.66-3.91) for $>$ 5 g/day of alcohol intake (P for trend = 0.35) in women. In the fully-adjusted multivariate model, compared with non-drinkers, the ORs (95% CIs) were 6.95 (1.49-32.51) for $\leq$ 10 g/day, 11.49 (2.55-51.89) for 10-20 g/day, and 14.15 (3.31-60.59) for $>$ 20 g/day of alcohol intake (P for trend = 0.003). A positive association was unclear for women, albeit with a suggestive increase in the prevalence of

Table 1. Characteristics of participants

	Cases (n = 113)	Controls (n = 255)	P-value
Age (mean ± SD [yr])	60.29 ± 5.28	59.08 ± 5.05	0.040
Sex (n [%])			< 0.001
Men	58 (51.33)	69 (27.06)	
Women	55 (48.67)	186 (72.94)	
BMI (mean ± SD [kg/m^2])	24.53 ± 2.66	24.29 ± 2.58	0.410
Family history of colorectal cancer (n [%])			0.320
Yes	6 (5.31)	8 (3.16)	
No	107 (94.69)	245 (96.84)	
History of colorectal polyps (n [%])			0.800
Yes	6 (5.31)	12 (4.71)	
No	107 (94.69)	243 (95.29)	
Aspirin use (n [%])			0.580
User	7 (6.19)	20 (7.84)	
Nonuser	106 (93.81)	235 (92.16)	
Supplement use (n [%])			0.010
User	43 (38.39)	130 (52.63)	
Nonuser	69 (61.61)	117 (47.37)	
Alcohol intake (mean ± SD [g/day])	16.43 ± 25.24	6.58 ± 18.78	< 0.001
Pack-years of smoking (mean ± SD)	8.51 ± 5.99	4.32 ± 2.93	0.005
Energy Intake (mean ± SD [kcal/day])	1728.70 ± 718.10	1666.90 ± 618.10	0.400
Physical activity (mean ± SD [MET-hr/wk])	29.31 ± 32.03	25.86 ± 24.01	0.310
Education level status (n [%])			0.230
Less than elementary graduate	16 (14.16)	33 (13.04)	
Middle school graduate	25 (22.12)	82 (32.41)	
High school graduate	51 (45.13)	102 (40.32)	
College or more	21 (18.58)	36 (14.23)	
Marital status (n [%])			0.100
Spouseless	6 (5.36)	27 (10.67)	
Spouse	106 (94.64)	226 (89.33)	
Menopausal status in Women (n [%])			0.790
Premenopause	3 (5.45)	12 (6.45)	
Postmenopause	52 (94.55)	174 (93.55)	

Abbreviations: SD, standard deviation; MET, metabolic equivalent.

Table 2. ORs and 95% CIs for colorectal adenoma according to alcohol intake in men and women

	OR (95% CI)				P for Trend
	Alcohol intake (g/day)				
Men	0	0 < −10	10 < −20	> 20	
No. of cases/controls	5/26	11/13	15/12	26/18	
Model 1[a]	1.00	4.16 (1.18-14.60)	6.74 (1.96-23.11)	8.31 (2.62-26.33)	0.002
Model 2[b]	1.00	6.95 (1.49-32.51)	11.49 (2.55-51.89)	14.15 (3.31-60.59)	0.003
Women	0	0 < −5	> 5		
No. of cases/controls	38/128	8/36	9/19		
Model 1[a]	1.00	0.76 (0.33-1.78)	1.66 (0.68-4.01)		0.300
Model 2[b]	1.00	0.82 (0.33-2.07)	1.71 (0.67-4.41)		0.280

[a]Model 1 was adjusted for age (continuous [yr]), [b]Model 2 was adjusted for age (continuous [yr]), BMI (continuous [kg/m^2]), family history of colorectal cancer (yes/no), history of colorectal polyps (yes/no), aspirin use (user/nonuser), supplement use (user/nonuser), energy intake (continuous [kcal/day]), physical activity (continuous [MET-hr/wk]), education level status (less than elementary graduate, middle school graduate, high school graduate, and college or more), pack years of smoking (continuous), marital status (spouse/spouseless), and menopausal status (only in women: premenopausal, postmenopausal without hormone therapy, postmenopausal with hormone therapy, and postmenopausal with nonresponse).

Table 3. ORs and 95% CIs for colorectal adenoma according to duration of alcohol intake in men and women

	OR (95% CI)			P for Trend
	Duration of alcohol intake (yr)			
Men	0	0 < −30	> 30	
No. of cases/controls	4/23	25/12	29/34	
Model 1[a]	1.00	15.19 (4.03-57.23)	4.63 (1.42-15.11)	0.008
Model 2[b]	1.00	32.28 (5.77-180.56)	7.83 (1.59-38.49)	0.009
Women	0	0 < −10	> 10	
No. of cases/controls	37/126	9/25	8/33	
Model 1[a]	1.00	1.27 (0.54-2.99)	0.84 (0.36-1.99)	0.700
Model 2[b]	1.00	1.86 (0.70-4.94)	0.81 (0.32-2.05)	0.650

[a]Model 1 was adjusted for age (continuous [yr]), [b]Model 2 was adjusted for age (continuous [yr]), BMI (continuous [kg/m^2]), family history of colorectal cancer (yes/no), history of colorectal polyps (yes/no), aspirin use (user/nonuser), supplement use (user/nonuser), energy intake (continuous [kcal/day]), physical activity (continuous [MET-hr/wk]), education level status (less than elementary graduate, middle school graduate, high school graduate, and college or more), pack years of smoking (continuous), marital status (spouse/spouseless), and menopausal status (only in women: premenopausal, postmenopausal without hormone therapy, postmenopausal with hormone therapy, and postmenopausal with nonresponse).

Table 4. ORs and 95% CIs for colorectal adenoma according to smoking status in men and women

	OR (95% CI)		
	Never smoker	Former smoker	Current smoker
Men			
No. of cases/controls	13/26	29/30	16/13
Model 1[a]	1.00	1.93 (0.83-4.46)	2.53 (0.94-6.85)
Model 2[b]	1.00	1.93 (0.77-4.84)	2.35 (0.80-6.90)
Women	Never smoker	Ever smoker	
No. of cases/controls	50/179	5/7	
Model 1[a]	1.00	2.59 (0.79-8.52)	
Model 2[b]	1.00	3.07 (0.82-11.50)	

[a]Model 1 was adjusted for age (continuous [yr]), [b]Model 2 was adjusted for age (continuous [yr]), BMI (continuous [kg/m^2]), family history of colorectal cancer (yes/no), history of colorectal polyps (yes/no), aspirin use (user/nonuser), supplement use (user/nonuser), energy intake (continuous [kcal/day]), physical activity (continuous [MET-hr/wk]), education level status (less than elementary graduate, middle school graduate, high school graduate, and college or more), alcohol drinking (continuous [g/day]), marital status (spouse/spouseless), and menopausal status (only in women: premenopausal, postmenopausal without hormone therapy, postmenopausal with hormone therapy, and postmenopausal with nonresponse).

colorectal adenomas. For the duration of alcohol intake, the highest prevalence of colorectal adenoma was observed for men who drank for up to 30 years, compared to non-drinkers (OR, 32.28; 95% CI, 5.77-180.56) (Table 3).

The associations for former or current smokers were not statistically significant for either men or women (Table 4). When we examined duration, amount and pack years of smoking, a higher, but not statistically significant, prevalence of colorectal adenoma was observed in men (Table 5).

Table 6 shows the joint association of alcohol intake and smoking status in relation to colorectal adenoma. The highest prevalence of colorectal adenoma was found in ever smokers who consumed 0 < −10 g/day of alcohol, compared to never smokers who did not drink alcohol. However, this interaction was not statistically significant (P for heterogeneity = 0.808). There were no significant modifying association between smoking status and alcohol intake: neither age (≤ 60 years and > 60 years) nor BMI (≤ 25 kg/m^2 and > 25 kg/m^2) significantly modified associations for smoking status or alcohol intake (P for heterogeneity > 0.400).

DISCUSSION

We found that a higher amount and longer duration of alcohol intake was associated with a higher prevalence of colorectal adenoma in Korean men. There was a weaker association for women than men, although increased prevalence of colorectal adenoma was suggested among alcohol drinkers. Cigarette smoking was not significantly associated with the prevalence of colorectal adenoma, however, we cannot rule out the possibility that the lack of association we observed was partially due to the small sample size. We did not find any statistically significant joint effect of alcohol intake and smoking status for colorectal adenoma. Although the combination of alcohol intake and smoking causes cancers of mouth or throat than either alcohol intake or smoking alone,[24,25] it remains equivocal whether the effects of alcohol intake and smoking together are worse than either alone for colorectal cancer development.

Table 5. ORs and 95% CIs for colorectal adenoma according to duration and amount of smoking in men

	OR (95% CI)			P for Trend
	Duration of smoking (yr)			
	0	0 < −25	> 25	
No. of cases/controls	13/26	12/13	29/28	
Model 1[a]	1.00	1.91 (0.68-5.43)	2.05 (0.88-4.77)	0.090
Model 2[b]	1.00	1.76 (0.55-5.63)	2.05 (0.81-5.17)	0.380
	Amount of smoking (cigarettes/day)			
	0	0 < −15	> 15	
No. of cases/controls	13/26	21/16	24/26	
Model 1[a]	1.00	2.66 (1.05-6.78)	1.85 (0.77-4.40)	0.210
Model 2[b]	1.00	2.69 (0.98-7.41)	1.81 (0.71-4.62)	0.260
	Pack years of smoking			
	0	0 < −20	> 20	
No. of cases/controls	13/26	22/17	19/23	
Model 1[a]	1.00	2.65 (1.05-6.68)	1.63 (0.66-4.03)	0.420
Model 2[b]	1.00	2.81 (1.02-7.74)	1.51 (0.56-4.09)	0.570

[a]Model 1 was adjusted for age (continuous [yr]), [b]Model 2 was adjusted for age (continuous [yr]), BMI (continuous [kg/m^2]), family history of colorectal cancer (yes/no), history of colorectal polyps (yes/no), aspirin use (user/nonuser), supplement use (user/nonuser), energy intake (continuous [kcal/day]), physical activity (continuous [MET-hr/wk]), education level status (less than elementary graduate, middle school graduate, high school graduate, and college or more), and alcohol drinking (continuous [g/day]).

Table 6. ORs and 95% CIs for colorectal adenoma in a joint combination of alcohol intake and smoking status

	ORs (95% CIs)			P for heterogeneity
	Alcohol intake (g/day)			
	0	0 < −10	> 10	
Smoking status				0.808
Never smoker	1.00	1.23 (0.58-2.63)	3.16 (1.15-8.73)	
Ever smoker	1.54 (0.47-5.08)	6.20 (1.96-19.60)	5.84 (2.16-15.82)	

Adjusted for age (continuous [yr]), sex, BMI (continuous [kg/m^2]), family history of colorectal cancer (yes/no), history of colorectal polyps (yes/no), aspirin use (user/nonuser), supplement use (user/nonuser), energy intake (continuous [kcal/day]), physical activity (continuous MET-hr/wk), education level status (less than elementary graduate, middle school graduate, high school graduate, and college or more), marital status (spouse/spouseless), and menopausal status (premenopausal, postmenopausal without hormone therapy, postmenopausal with hormone therapy, and postmenopausal with nonresponse).

The hypothesis that high alcohol intake increases the risk of colorectal cancer has been supported by several studies.[18] For colorectal adenoma, an increased risk or prevalence associated with alcohol intake has been observed in some epidemiologic studies,[6,19,26,27] but not in all.[5,28-30] The mechanism through which alcohol induces carcinogenesis remains unknown, but a few mechanisms have been suggested. Alcohol, by generating acetaldehyde, may lead to DNA damage[31] and increase oxidative stress through ethanol-induced cytochrome P-450.[32] Alcohol intake inhibits folate-mediated methionine synthesis, and thus may impair DNA methylation, which is linked to carcinogenesis.[32,33]

A meta-analysis of 42 epidemiologic studies (20 conducted in the United States, 12 in Europe, 8 in Asia, 1 in South America, and 1 in Australia) provided evidence that cigarette smoking is a strong risk factor for colorectal adenoma development; the pooled relative risk estimate was 2.14 (95% CI, 1.86-2.46) for current smokers, 1.47 (95% CI, 1.29-1.67) for former smokers, and 1.82 (95% CI, 1.65-2.00) for ever smokers, compared to never smokers.[13] Smoking appeared to be associated with an early stage of colorectal carcinogenesis.[34,35] Cigarette smoking generates DNA adducts and potentially causes irreversible genetic damage to the cells. Although we did not find a significantly higher prevalence of colorectal adenoma, a larger study may be warranted.

The limitations of our study are as follows: (1) because this is a cross-sectional study, we cannot infer a causal relationship between alcohol intake/smoking status and colorectal adenoma development; (2) some misclassification of information on alcohol intake and smoking from questionnaires may exist; (3) the sample size was small; and (4) because the study was conducted

in a specific region of Korea, the result of our study may not be generalizable to the general Korean population.

Our study has several strengths. We observed a strong association between alcohol intake and colorectal adenoma prevalence in Korean men, indicating that the potential large contribution of alcohol intake to the development of colorectal cancer in the Korean populations. Given a high alcohol intake in Korean men (21.4% of Korean adult men drink 10 or more drinks per occasion),[36] our findings suggest that a key obstacle to preventing colorectal neoplasia in men is high alcohol intake. Because we assessed various risk factors for colorectal neoplasia, we were able to adjust for potential confounding factors. Also, detailed questions on alcohol intake and smoking status enabled us to examine the amount and duration of each exposure level.

In summary, we found that high amount of alcohol intake and longer duration of alcohol intake were associated with a higher prevalence of colorectal adenoma in Korean men. Further Korean epidemiologic studies with a larger study populations are needed to examine the association of alcohol intake and smoking status with colorectal adenoma, especially in women.

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CONFLICTS OF INTEREST

No potential conflicts of interest were disclosed.

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