

Cigarette Smoking, Alcohol Use and Adenomatous Polyps of the Sigmoid Colon

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The relationship of adenomatous polyps of the sigmoid colon with cigarette smoking and alcohol use was investigated in male self-defense officials in Japan. In the comparison between 116 cases and 930 controls, total ethanol intake was not at all associated with the risk of adenomatous polyps, but cigarette smoking was strongly related to adenomatous polyps. After adjustment for total ethanol intake, body mass index and rank, odds ratios (and 95% confidence interval) for the categories of 0, 1-399, 400-799, and 800 or more cigarette-years were 1.0 (referent), 2.3 (1.1-4.6), 2.9 (1.5-5.4) and 3.2 (1.6-6.5), respectively. Among five alcoholic beverages (sake, shochu, beer, whiskey including brandy, and wine), only whiskey consumption was weakly related to the risk of adenomatous polyps. Because the present findings disagree with an earlier observation on self-defense officials, we examined the association with smoking and alcohol use separately for small (<5 mm) and large (≥5 mm) adenomas, combining data from these two studies. Cigarette smoking was more strongly associated with small adenomas while the positive association with certain alcoholic beverages were largely confined to large adenomas. These findings suggest that cigarette smoking and alcohol use may be linked with the development of adenoma at different stages of colon tumorigenesis.

Key words: Colon polyp — Smoking — Alcohol — Japanese men

Adenomatous polyps of the large bowel are considered to be a potential precancerous lesion, and their presence is associated with an increased risk of colorectal cancer,^{1,2)} although some cases of adenocarcinomas may develop *de novo* in the absence of adenomas.^{3,4)} Apart from the theory of adenoma-adenocarcinoma sequence, adenomas and cancers of the large bowel have similar epidemiologic features, and may share a common etiology.^{5,6)}

In conjunction with a controversial association between alcohol drinking and colorectal cancer,⁷⁻¹⁶⁾ several studies have recently examined the relation between alcohol and polyps of the large bowel.¹⁷⁻¹⁹⁾ An autopsy study showed a significant association of alcohol intake with the number of adenomatous polyps of the colon, but not with the prevalence of this condition.¹⁷⁾ A case-control study based on men and women referred for colonoscopy found a significant association between colonic adenomas and cumulative beer consumption.¹⁸⁾ In a case-control study in Japan, past and daily drinkers had an elevated risk of colon adenomas as compared with non-drinkers.¹⁹⁾

Cigarette smoking is rarely associated with colorectal cancer.²⁰⁾ Several studies of colorectal polyps, however, observed a positive association between cigarette smoking and adenomatous polyps^{18,21-23)} although this was not always the case.^{17,19)}

Analyzing the earlier data of the on-going study of male self-defense officials retiring from Self-Defense Forces (SDF) in Japan, it was reported that the consumption of alcoholic beverages, especially sake and beer, was associated with an increased risk of adenomatous polyps of the sigmoid colon and that cigarette smoking was not related to adenomatous polyps.²⁴⁾ This study aimed to examine whether the previous findings on alcohol use, smoking and polyps could be reproduced in a subsequent set of data in a population of male self-defense officials.

MATERIALS AND METHODS

Study subjects were 1296 male self-defense officials who received a retirement health examination at the SDF Fukuoka Hospital between January 1989 and December 1990. Details of the health examination and lifestyle survey have been described elsewhere.²⁴⁾ In brief, routine colonoscopy is conducted to examine the rectum and sigmoid colon, and the distance of intubation and the nature of polyps were recorded if available. In this analysis, colonoscopy with intubation of less than 40 cm was regarded as unsatisfactory unless any pathological lesions were found in the rectum or colon. Histological diagnosis of a biopsied or polypectomized specimen was referred to the pathology department of a university hospital.

In a series of 1296 men, 93 refused colonoscopy. Results of the colonoscopy were as follows; unsatisfac-

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tory 19, normal colonoscopy 946, at least one polyp 222, macroscopic carcinoma 2, and other non-polypoid lesions 14. Histological examination was done with 207 out of 222 men with colorectal polyps, and 118 men were found to have adenomatous polyps at a depth of 11–60 cm, which was defined as the sigmoid colon here. Two cases of the adenomatous polyps of the sigmoid colon and 16 men with normal colonoscopy were excluded from the analysis because of a prior history of colorectal polypectomy (9), colectomy (3) or malignant neoplasms (7), and having concurrently adenocarcinoma of the large bowel (1), gastric cancer (1) or polycythemia vera (1) (some had two or more reasons for exclusion). Thus 116 men having adenomatous polyps of the sigmoid colon and 930 men with normal colonoscopy were used in the present analysis.

A self-administered questionnaire inquired about smoking habit, alcohol use, the consumption of 13 foods and non-alcoholic beverages and other lifestyle characteristics before colonoscopy was done. The questionnaire was slightly different from that used in the previous study, but drinkers were defined, in the same way as in the previous one, as those who had ever drunk once per week or more over a period of one year or longer. Regarding five alcoholic beverages, i.e., sake (fermented product of rice), shochu (distilled spirit made from rice or other grains), beer, whiskey including brandy, and wine, current and past drinkers were asked about the number of days in the week when they drank and the amount consumed per day on average in the past one year or in the year prior to the cessation of drinking. If the consumption was limited to certain seasons, the frequency and amount were reported for specified seasons. Ethanol intake was estimated from the reported frequency and amount of consumption of each beverage using the approximate volume concentration of ethanol (sake 16%, shochu 25%, beer 4.5%, whiskey 40% and wine 12%). Body mass index (BMI) (kg/m^2) was used as a measure of obesity.

The estimated alcohol intake was closely related to serum high-density lipoprotein (HDL)-cholesterol, and gamma-glutamyltransferase. After adjustment for smoking (classified into never, past and current; <25 or ≥ 25 cigarettes per day) and BMI (continuous variables), adjusted mean concentrations of HDL-cholesterol were 48, 48, 52, 57 and 59 mg/dl, and the adjusted odds ratios (ORs) for abnormal gamma-glutamyltransferase (>50 units) were 1.0, 3.7, 4.1, 6.0 and 11.0 for never-drinkers, past drinkers, and current drinkers consuming <30 , 30–59 and ≥ 60 ml of ethanol per day, respectively.

In both case and control groups, age ranged from 48 to 54, and about 70% were aged 52 years. Thus we did not allow for age in the analysis. SDF rank and BMI were taken into consideration as potential confounders. Unlike

the previous study,²⁴⁾ rice consumption was not materially related to the risk of adenomatous polyps and was not taken into account in the present analysis.

Unconditional logistic regression analysis²⁵⁾ was used to estimate crude and adjusted ORs. ORs and 95% confidence intervals (CI) were calculated based on the regression coefficient and its standard error for an indicator term corresponding to a level of independent variable. Trend of the association was assessed by using the logistic regression model with ordinal scores assigned to levels of independent variables. All the computations were done by using the Statistical Analysis System.²⁶⁾

RESULTS

There was virtually no association between total ethanol intake and adenomatous polyps in either univariate or multivariate analysis (Table I). However, the risk of adenomatous polyps was positively associated with cigarette smoking. There was an increasing gradient in the

Table I. Risk of Adenomatous Polyps of the Sigmoid Colon According to Categories of Smoking, Alcohol Use, Rank and Body Mass Index

Variable	No.	Crude OR	Adjusted OR ^{a)} (95% CI)
Smoking (cigarette-years) ^{b)}			
0	13/244	1.0	1.0 (Referent)
1–399	23/189	2.3	2.3 (1.1–4.6)
400–799	56/359	2.9	2.9 (1.5–5.4)
≥ 800	24/138	3.3	3.2 (1.6–6.5)
Alcohol use			
Never	19/176	1.0	1.0 (Referent)
Past	4/25	1.5	1.3 (0.4–4.0)
Current (ml ^{c)} /day)			
<30	31/283	1.0	1.0 (0.6–1.9)
30–59	35/257	1.3	1.2 (0.7–2.2)
≥ 60	27/189	1.3	1.2 (0.6–2.2)
SDF rank			
Low	81/625	1.0	1.0 (Referent)
Middle	20/181	0.9	0.8 (0.5–1.4)
High	15/124	0.9	0.9 (0.5–1.6)
Body mass index			
<22.5	39/297	1.0	1.0 (Referent)
22.5–25.0	43/372	0.9	0.9 (0.6–1.5)
≥ 25.0	34/261	1.0	1.0 (0.6–1.7)

OR: odds ratio, CI: confidence interval.

No. are cases/controls.

a) Adjusted for the other three variables in each analysis.

b) Cigarettes smoked per day multiplied by years of smoking.

c) Total ethanol intake.

risk according to level of cigarette smoking in terms of cigarette-years (Table I). The trend in the multivariate analysis was highly significant ($P = 0.0006$). When analyzed with respect to current smoking status, both past and current smokers had a significantly elevated risk of adenomatous polyps (Table II).

We also examined the association between the risk of adenomatous polyps and each of the five alcoholic beverages with respect to the average amount of ethanol consumed per day (Table III). Shochu, sake and beer

showed no measurable association with the risk of adenomatous polyps, but the risk was moderately elevated among men with high consumption of whiskey. Wine drinkers were too few to justify separate analysis; one case and 19 controls drank wine at least once per week or more on average in the year or in certain seasons.

DISCUSSION

Using the same design and methodology as employed in the previous study, the present study failed to reproduce the association between adenomatous polyps and alcohol use. Questions on the consumption of alcoholic beverages were slightly modified in the current series, but it is unlikely that the lack of association was due to different accuracy in ascertainment of alcohol consumption. The estimated intake of alcohol was considered to be as valid in the present study as in the previous one. Further, there was no difference in the consumption of five alcoholic beverages between the two periods. Current drinkers took 61% of total ethanol intake from shochu, 20% from beer, 12% from sake, 6% from whiskey, and 0.1% from wine. These figures were essentially the same as those in the previous study.²⁴⁾

Unlike the previous study,²⁴⁾ the present study found a positive association between cigarette smoking and ad-

Table II. Current Smoking Status and the Risk of Adenomatous Polyps of the Sigmoid Colon

Smoking status	No.	Adjusted OR ^{a)} (95% CI)
Never	13/244	1.0 (Referent)
Past	33/276	2.2 (1.1-4.3)
Current ^{b)}		
< 25	50/280	3.3 (1.8-6.3)
≥ 25	20/130	2.8 (1.3-5.9)

OR: odds ratio, CI: confidence interval.

No. are cases/controls.

a) Adjusted for drinking, rank and body mass index as categorized in Table I.

b) Cigarettes smoked per day.

Table III. Relationship between the Consumption of Alcohol Beverages and Adenomatous Polyps of the Sigmoid Colon

Beverage	Ethanol (ml/day)	No.	Adjusted OR ^{a)} (95% CI)	Trend ^{b)}
Shochu	0	41/347	1.0 (Referent)	$P=0.55$
	1-14	18/163	0.9 (0.5-1.5)	
	15-29	9/115	0.6 (0.3-1.4)	
	≥ 30	44/280	1.2 (0.7-1.9)	
Beer	0	29/252	1.0 (Referent)	$P=0.92$
	1-14	66/503	1.1 (0.7-1.8)	
	15-29	16/133	1.0 (0.5-1.9)	
	≥ 30	1/17		
Sake	0	76/583	1.0 (Referent)	$P=0.80$
	1-14	23/250	0.7 (0.4-1.2)	
	15-29	7/38	1.4 (0.7-2.6)	
	≥ 30	6/34		
Whiskey	0	79/649	1.0 (Referent)	$P=0.41$
	1-14	24/222	0.9 (0.5-1.4)	
	15-29	7/26	2.0 (0.9-4.4)	
	≥ 30	2/8		

OR: odds ratio, CI: confidence interval.

No. are cases/controls excluding past drinkers.

a) Adjusted for smoking history, rank and body mass index as categorized in Table I.

b) Scores 0-3 were assigned to the four consumption levels.

Table IV. Adjusted Odds Ratios (and 95% Confidence Intervals) for Small (<5 mm) and Large (≥5 mm) Adenomas of the Sigmoid Colon According to Smoking and Alcohol Use^{a)}

Variable	Small adenoma (n=86)	Large adenoma (n=72)
Smoking (cigarette-years) ^{b)}		
0	1.0 (Referent)	1.0 (Referent)
1-399	1.5 (0.7-3.3)	1.7 (0.8-3.8)
400-799	2.1 (1.1-4.1)	1.7 (0.8-3.4)
≥800	2.5 (1.2-5.3)	1.4 (0.6-3.3)
Alcohol Use		
Never	1.0 (Referent)	1.0 (Referent)
Past	1.5 (0.5-4.7)	1.7 (0.5-5.6)
Current (ml ^{c)} /day)		
<30	1.0 (0.5-2.0)	1.0 (0.5-2.3)
30-59	1.5 (0.7-2.9)	1.2 (0.5-2.7)
≥60	1.0 (0.5-2.1)	2.1 (0.9-4.6)

a) Based on logistic regression analysis controlling for rank and body mass index as categorized in Table I, period (1986-88 versus 1989-90), and either smoking or alcohol use. No. of controls=2114.

b) Cigarettes smoked per day multiplied by years of smoking.

c) Total ethanol intake.

enomatous polyps. Again, the ascertainment of cigarette smoking did not differ much between the two periods. Current smoking status was strongly associated with HDL-cholesterol in both studies. In the present study, after adjustment for alcohol use and BMI, mean concentrations of HDL-cholesterol, which is known to be decreased by smoking,²⁷⁾ were 56, 56, 50 and 49 mg/dl for never-smokers, past smokers and current smokers consuming <25 or ≥25 cigarettes per day, respectively. Further, subjects were almost equally distributed in terms of the current smoking status and cigarette-years in the two series (data not shown).

Since it is unlikely that methods of ascertaining cigarette smoking and alcohol use differed between the two studies, reasons for the difference should exist elsewhere. Detected polyps may have differed in nature between the two series. Because diagnostic skill in colonoscopy seems to have improved recently, it is possible that smaller polyps were more frequently detected in the current series. Thus we *a posteriori* reviewed the size of polyps detected in the earlier and present series. Although the size was not always recorded, polyps of the current series were indeed much smaller than those of the earlier series; mean diameters of the largest polyps were 4.0 mm (n=180) in the current series and 5.3 mm (n=104) in the earlier series (Wilcoxon rank sums test $P=0.0001$).

Classifying men with adenomas of the sigmoid colon by the size of the largest one, analysis was done for small

Table V. Adjusted Odds Ratios (and 95% Confidence Intervals) for Small (<5 mm) and Large (≥5 mm) Adenoma of the Sigmoid Colon According to Consumption of Alcoholic Beverages^{a)}

Beverage	Ethanol (ml/day)	Small adenoma (n=82)	Large adenoma (n=68)
Shochu	0	1.0 (Referent)	1.0 (Referent)
	1-14	1.4 (0.8-2.5)	0.7 (0.3-1.4)
	15-29	0.4 (0.2-1.1)	0.5 (0.2-1.3)
	≥30	1.0 (0.6-1.8)	1.1 (0.6-1.9)
	Trend ^{b)}	$P=0.70$	$P=0.91$
Beer	0	1.0 (Referent)	1.0 (Referent)
	1-14	1.1 (0.7-1.9)	1.2 (0.7-2.3)
	≥15	1.1 (0.5-2.2)	1.9 (0.9-4.0)
	Trend ^{b)}	$P=1.00$	$P=0.08$
Sake	0	1.0 (Referent)	1.0 (Referent)
	1-14	1.0 (0.6-1.7)	0.9 (0.5-1.7)
	≥15	1.5 (0.7-3.1)	2.1 (1.0-4.4)
	Trend ^{b)}	$P=0.50$	$P=0.08$
Whiskey	0	1.0 (Referent)	1.0 (Referent)
	1-14	1.0 (0.6-1.7)	0.7 (0.3-1.3)
	≥15	1.9 (0.8-4.4)	2.9 (1.4-6.1)
	Trend ^{b)}	$P=0.32$	$P=0.04$

a) Based on logistic regression analysis controlling for rank and body mass index as categorized in Table I, period (1986-88 versus 1989-90), and smoking. No. of controls=2026. Past drinkers were excluded.

b) Scores 0-3 were assigned to the categories of 0, 1-14, 15-29 and ≥30 ml/day.

(<5 mm) and large (≥5 mm) adenomas using the whole data from October 1986 to December 1990. Cases with small adenomas and those with large adenomas numbered 22 and 35, respectively, in the previous series while the corresponding figures in the current series were 64 and 37, respectively. There was no measurable difference between adenoma cases of known size (n=158) and those of unknown size (n=44) with respect to smoking and alcohol use as well as to age, rank and BMI. As shown in Table IV, the association with cigarette smoking was more striking for small adenomas, and a marginally increased risk related to heavy alcohol use (≥60 ml of ethanol per day) was observed only for large adenomas. With regard to type of alcoholic beverage, the consumption of beer, sake and whiskey was positively associated with large adenomas but hardly so with small adenomas (Table V). Thus, the discrepancy between the earlier and present studies can be largely ascribed to a different composition of small and large adenomas.

The apparent difference in the association with smoking and alcohol use between small and large adenomas seems to be compatible with the idea that different factors

act in the course of adenoma from the initiation of adenoma through the growth of adenoma to the transition to carcinoma.^{28, 29)} Although we have no immediate explanation as to the underlying mechanisms for the observed association between certain alcoholic beverages and large adenomas, as discussed before,²⁴⁾ it is likely that the consumption of these alcoholic beverages is involved in the growth of adenomas rather than in the stage of initiation if they are etiologically linked with colon adenomas. On the other hand, cigarette smoking may be responsible for the development of adenomas in the early stage. It could be argued that the association with cigarette smoking should be as strong for large adenomas as for small adenomas if smoking is related to the initiation of adenomas. The association between smoking and large adenomas was less evident, but smoking history determined at the time of colonoscopic examination would be less relevant to large adenomas. In this regard, the general lack of an association between smoking and colon

cancer²⁰⁾ does not necessarily rule out a possible involvement of smoking in colon tumorigenesis.

Our study subjects were men who had served in the SDF until the age of retirement, and therefore were mostly in their early 50s. It might be difficult to generalize the present findings to the male Japanese population. Further study allowing for the size of adenomas is needed to consolidate a differential relationship of smoking and alcohol use to colon adenomas of different sizes.

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