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The Relation of Smoking, Alcohol Use and Obesity to Risk of Sigmoid Colon and Rectal Adenomas

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We conducted a case-control study, using 429 cases with histologically confirmed sigmoid adenoma, 75 cases with rectal adenoma, and 3101 controls showing normal colonoscopy at least up to 60 cm from the anus. The subjects were male Self-Defense Forces personnel aged 48–56 who received a retirement health examination including a routine sigmoid- or colonoscopy. Lifestyle characteristics were ascertained by a self-administered questionnaire. Smoking in the recent past ($\leq$10 years preceding the colonoscopy) and smoking in the remote past (>10 years before the colonoscopy) were both significantly associated with risk of sigmoid adenoma but not with rectal adenoma as a whole. After reciprocal adjustment for smoking in the two periods, only smoking in the recent past was associated with both sigmoid colon and rectal adenomas. Odds ratios (OR) of sigmoid adenoma (and 95% confidence interval) for the categories of 0, 1–150, 151–250 and $\geq$251 cigarette-years were 1.0 (reference), 1.9 (1.3–2.8), 2.1 (1.4–3.0) and 3.0 (1.9–4.7), respectively (P for trend <0.01), and those for rectal adenoma were 1.0 (reference), 1.2 (0.4–3.2), 3.5 (1.4–8.5) and 2.0 (0.6–6.7), respectively (P for trend $=0.03$). Alcohol use was significantly positively associated with sigmoid adenoma, and insignificantly associated with rectal adenoma. Body mass index was significantly positively associated with sigmoid adenoma, especially large ones. No such association was found for rectal adenoma. These findings suggest that smoking, especially in the recent past, and alcohol use are common risk factors for sigmoid colon and rectal adenomas while obesity may be exclusively related to the growth of sigmoid adenoma.

Key words: Colorectal adenoma — Smoking — Alcohol use — Obesity — Japanese men

Colorectal adenoma is a well-established precursor lesion of adenocarcinoma,[1] and multiple genetic alterations are observed in the transition from normal epithelium to carcinoma via adenoma.[2] However, environmental factors linked to the development of colorectal tumor at different stages of tumorigenesis are not yet understood, although ecological and migrant studies strongly suggest an environmental influence.[3]

The relation of cigarette smoking and risk of colorectal adenoma has been one of the primary focuses in epidemiologic investigations.[4–13] We previously reported that smoking was associated with risk of sigmoid colon adenoma[14, 15] and suggested that smoking was linked to colon tumorigenesis in the early stages.[14] Though smoking has not generally been implicated in the etiology of colorectal cancer,[16] Giovannucci and co-workers recently demonstrated a positive association of cigarette smoking with risk of colorectal cancer as well as colorectal adenoma after allowance for the induction periods.[17, 18] Thus, it is necessary to study the relation between smoking and risk of colorectal adenoma in terms of adenoma size as done in our previous study[14] and in terms of smoking in different time periods as done by Giovannucci and co-workers.[17, 18] The relation between alcohol use and risk of colorectal cancer has been investigated in many studies, but no conclusion has been drawn.[19] Several studies have investigated the association between alcohol use and risk of colorectal adenoma, and their results are also inconsistent.[10, 11, 20–23] Our earliest study of male Self-Defense Forces personnel showed a positive association between sigmoid adenoma and specific alcoholic beverages,[24] but the association was not necessarily reproduced in our later studies,[14, 15] although the later findings were not contradictory. The inconsistent results may be due to the small number of cases in each analysis, especially regarding the small elevation of risk associated with alcohol use. Obesity is another matter of interest in the epidemiology of colorectal cancer.[3] However, studies addressing the relation between obesity and colorectal adenoma are very few.[25–28]

Although both epidemiological and genetic studies[29, 30] of colorectal cancer are suggestive of a difference in etiology between colon and rectal cancers, few studies

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have investigated risk factors for adenomas of these anatomic sites separately. We therefore in the present study examined the relations of smoking, alcohol use and obesity to risk of adenomas of the sigmoid colon and rectum separately. Independent analyses of these factors and sigmoid colon adenoma for different periods have been published elsewhere.[14, 15, 24, 28]

MATERIALS AND METHODS

Study subjects were 429 men having histologically confirmed sigmoid colon adenomas, 75 men with rectal adenomas and 3101 men with normal colonoscopy at least up to 60 cm from the anus. They were identified among 4981 male Self-Defense Forces personnel who received a retirement health examination at the Self-Defense Forces Fukuoka Hospital between October 1986 and December 1992, at the Kumamoto Hospital between January 1991 and December 1992 and at the Sapporo Hospital from April to December 1992. Personnel retiring from Self-Defense Forces are admitted to one of the Self-Defense Forces hospitals across the nation for a free comprehensive medical examination. The above three hospitals cover Kyushu and Hokkaido islands. Details of the health examination and the life-style survey have been described elsewhere.[14, 24, 28] Examinations relevant to the present study are described below.

The health examination was done during a five-day admission. The routine sigmoidoscopy or colonoscopy was to examine the rectum and sigmoid colon. More proximal sites were examined at the Fukuoka Hospital if the subjects tolerated the procedure, and at the Sapporo Hospital if they had a positive fecal occult blood test or a prior history of large bowel diseases. The distance of intubation and the nature of polyps were recorded. In this analysis, colonoscopy with an intubation of less than 60 cm from the anus and not reaching the sigmoid-descending junction was regarded as unsatisfactory unless a pathological lesion was found.

In total, 4981 men were admitted to the three hospitals during the study period, with exclusion of three men who had been enumerated in duplicate as exceptional second admissions; none of them was used in duplicate in the previous studies dealing with data in different time periods.[14, 15, 24, 28] Out of the 4981 men, 264 refused colonoscopy and the study was unsatisfactory with 586 men. Of the remaining 4131 men, 3185 had normal colonoscopy at least up to 60 cm from the anus, and 569 were found to have adenomatous polyps in the absence of colorectal adenocarcinoma. Of the latter, 449 men had adenomatous polyps at a depth of 11–60 cm from the anus (defined as the sigmoid colon), and 79 men had them at a depth of 10 cm or less from the anus (defined as the rectum). Twenty-three men with sigmoid or rectal adenoma and 84 men with normal colonoscopy were excluded because of a prior history of colorectal polyp, polypectomy, colectomy, inflammatory bowel diseases, or malignant neoplasms; concurrent non-colorectal malignant neoplasms; or contracting polyposis. Thus, 429 cases with sigmoid adenoma, 75 cases with rectal adenoma, and 3101 controls remained for the present study. Size of adenoma was available for 374 cases with sigmoid adenoma and 64 cases with rectal adenoma. Mean diameters were 4.7 mm for sigmoid adenoma and 5.5 mm for rectal adenoma. Among adenoma cases, 17 had both sigmoid and rectal adenomas. Since analyses excluding these 17 subjects with multiple loci produced the same results, these 17 men were included in the group of sigmoid adenoma cases and in that of rectal adenoma cases.

A self-administered questionnaire inquired about smoking habit, alcohol use, consumption of selected foods and nonalcoholic beverages, and other life-style characteristics before the colonoscopy was done. The questionnaires have been revised biennially and differed slightly in form from each other, especially with respect to dietary items. Ever-smokers were defined as those who were smoking or had smoked daily at least for one year. The average number of cigarettes smoked per day and the total years of smoking were obtained from both current and past smokers. Past smokers also reported the time when they had finally ceased smoking. Ever-drinkers were defined as those who were drinking or had drunk once per week or more over a period of one year or longer; for each of five alcoholic beverages (shochu, beer, sake, whiskey or brandy, and wine), current drinkers reported the number of days on which they had drunk each per week and the amount consumed per day on average in the past one year; if the consumption was limited to certain seasons, the frequency and the 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.

Age ranged from 48 to 56 years, and all cases and 98% of controls were 51 to 53 years old. Thus, age was omitted in the analysis. The rank in the Self-Defense Forces as classified into three categories, study periods (1986–1988, 1989–1990, or 1991–1992) and hospitals were always allowed for in the analysis. In the period 1991 to 1992, estimated alcohol consumption was slightly affected by study seasons.[15] Inclusion of this variable in the analysis, however, hardly changed the results. Therefore the results not allowing for seasons are presented in this paper.

Cigarette-years (numbers of cigarettes smoked per day multiplied by years of smoking) of the ever-smokers and total alcohol intake of the current drinkers were cate-

gorized into three levels at the nearest tertiles in control subjects. Body mass index (kg/m^2) was classified into four categories with cut-off points at the 30th, 60th, and 90th percentiles in the control group.

Unconditional logistic regression analysis was used to estimate an odds ratio (OR).[31] The OR and 95% confidence interval (CI) were calculated based on the regression coefficient and its standard error for an indicator term corresponding to a level of an independent variable. The trend of the association was assessed by applying the logistic regression model with ordinal scores assigned to levels of independent variables. All the computations were done by using the Statistical Analysis System (SAS).[32]

RESULTS

Total cumulative cigarette smoking was strongly associated with an increased risk of sigmoid colon adenoma, but not with risk of rectal adenoma as a whole, although moderate smoking (451–660 cigarette-years) was insignificantly associated with an increased risk of rectal adenoma (Table I). Although elevations in risk were moderate, total alcohol intake was significantly positively associated with risk of sigmoid adenoma. There was also a tendency of positive association between alcohol and rectal adenoma with almost the same magnitude as that noted for sigmoid adenoma (Table I). Men in the highest category of body mass index had a significantly increased risk of sigmoid adenoma, while they had a somewhat decreased risk of rectal adenoma (Table I).

We then examined the relationship between smoking during different time periods and adenoma risk. We defined here smoking in the recent past as that within 10 years prior to colonoscopy, and smoking in the remote past as that until the time of 10 years before colonoscopy, regardless of current smoking status. Cigarette smoking was significantly associated with an increased risk of sigmoid adenoma regardless of the period which had elapsed before the endoscopy. There was no dose-dependent association with rectal adenoma, but the risk was significantly elevated for moderate smoking in the recent past (Table II). After reciprocal adjustment for smoking habits during the two periods, only smoking in the past 10 years was significantly associated with both sigmoid colon and rectal adenomas (Table III). Adjustment for recent smoking resulted in approximately 50% decrease in rectal adenoma risk associated with smoking in the remote past regardless of exposure levels, but the decrease was far from significance.

We further examined the association between each type of alcoholic beverage and adenoma risk (Table IV).

Table I. Risk of Adenoma of the Sigmoid Colon and Rectum According to Smoking, Alcohol Use and Obesity[a]

Variables	Controls No.	Sigmoid adenoma		Rectal adenoma	
		No.	OR (95% CI)	No.	OR (95% CI)
Smoking (cigarette-years[b])					
0	795	59	1.0 (Reference)	17	1.0 (Reference)
1–450	801	102	1.7 (1.2–2.3)	10	0.6 (0.3–1.2)
451–660	811	143	2.3 (1.7–3.2)	32	1.7 (0.9–3.2)
≥661	694	125	2.3 (1.6–3.2)	16	1.0 (0.5–2.0)
		P for trend <0.01		P for trend $=0.28$	
Alcohol use (ml/day)					
Never	528	54	1.0 (Reference)	10	1.0 (Reference)
Past	109	16	1.4 (0.8–2.5)	5	2.5 (0.8–7.8)
Current					
0–25.6	809	93	1.2 (0.8–1.7)	16	1.0 (0.5–2.3)
25.7–51.2	829	132	1.6 (1.1–2.2)	21	1.4 (0.6–3.0)
≥51.3	826	134	1.5 (1.1–2.1)	23	1.5 (0.7–3.2)
		P for trend[c] $=0.01$		P for trend[c] $=0.21$	
Body mass index (kg/m^2)					
≤22.3	897	124	1.0 (Reference)	27	1.0 (Reference)
22.4–24.1	914	127	1.1 (0.8–1.4)	17	0.6 (0.3–1.2)
24.2–26.7	965	116	0.9 (0.7–1.2)	25	0.9 (0.5–1.5)
≥26.8	325	62	1.5 (1.0–2.0)	6	0.6 (0.3–1.5)
		P for trend $=0.25$		P for trend $=0.42$	

OR, odds ratio; CI, confidence interval.
a) Adjusted for rank, hospital, study period and the other two variables in the table.
b) Cigarettes smoked per day multiplied by years of smoking.
c) Excluding past drinkers.

Table II. Risk of Adenoma of the Sigmoid Colon and Rectum According to Smoking in the Recent and Remote Past[a)]

Cigarette-years[b)]	Controls No.	Sigmoid adenoma		Rectal adenoma	
		No.	OR (95% CI)	No.	OR (95% CI)
Smoking in the past 10 years					
0	1277	102	1.0 (Reference)	23	1.0 (Reference)
1–150	535	88	2.1 (1.5–2.8)	7	0.8 (0.3–1.8)
151–250	863	150	2.2 (1.7–2.9)	36	2.2 (1.3–3.8)
≥251	426	89	2.5 (1.8–3.4)	9	1.1 (0.5–2.5)
		P for trend <0.01		P for trend $=0.06$	
Smoking until 10 years ago					
0	832	63	1.0 (Reference)	18	1.0 (Reference)
1–340	769	112	1.9 (1.4–2.6)	14	0.8 (0.4–1.6)
341–460	753	130	2.2 (1.6–3.0)	26	1.5 (0.8–2.7)
≥461	747	124	2.1 (1.5–2.9)	17	1.0 (0.5–1.9)
		P for trend <0.01		P for trend $=0.65$	

OR, odds ratio; CI, confidence interval.
a) Adjusted for alcohol use, body mass index as categorized in Table I, rank, hospital and study period.
b) Cigarettes smoked per day multiplied by years of smoking.

Table III. Risk of Adenoma of the Sigmoid Colon and Rectum According to Smoking in the Recent and Remote Past after an Additional Reciprocal Adjustment for Smoking during the Two Periods[a)]

Cigarette-years[b)]	Controls No.	Sigmoid adenoma		Rectal adenoma	
		No.	OR (95% CI)	No.	OR (95% CI)
Smoking in the past 10 years					
0	1277	102	1.0 (Reference)	23	1.0 (Reference)
1–150	535	88	1.9 (1.3–2.8)	7	1.2 (0.4–3.2)
151–250	863	150	2.1 (1.4–3.0)	36	3.5 (1.4–8.5)
≥251	426	89	3.0 (1.9–4.7)	9	2.0 (0.6–6.7)
		P for trend <0.01		P for trend $=0.03$	
Smoking until 10 years ago					
0	832	63	1.0 (Reference)	18	1.0 (Reference)
1–340	769	112	1.2 (0.8–1.8)	14	0.5 (0.2–1.3)
341–460	753	130	1.2 (0.8–1.8)	26	0.5 (0.2–1.5)
≥461	747	124	0.9 (0.5–1.4)	17	0.4 (0.1–1.3)
		P for trend $=0.38$		P for trend $=0.22$	

OR, odds ratio; CI, confidence interval.
a) Adjusted for alcohol use, body mass index as categorized in Table I, rank, hospital, study period and the other variable in the table.
b) Cigarettes smoked per day multiplied by years of smoking.

Wine drinkers were too few to justify separate analysis; 11 sigmoid adenoma cases, one rectal adenoma case and 63 controls drank wine at least once per week or more on average in the year or in certain seasons. Men who did not drink a certain alcoholic beverage but consumed other types of alcoholic beverages generally had an increased risk of sigmoid adenoma as compared to lifelong nondrinkers regardless of the type of beverage. Only men with high whiskey consumption showed a prominent increase in the risk of sigmoid adenoma (Table IV). We did an additional analysis in which four alcoholic beverages were mutually adjusted for, and found that only men with high consumption of whiskey had a significantly increased risk of sigmoid adenoma (data not shown). Although statistically insignificant, the associations of alcoholic beverages with rectal adenoma were similar to those noted for sigmoid colon adenoma; men with high whiskey consumption tended to have an increased risk of rectal adenoma (Table IV).

Finally we repeated the same analyses for large (≥5 mm, n=174) and small (<5 mm, n=200) adenomas of the sigmoid colon, separately. No material difference was

Table IV. Risk of Adenoma of the Sigmoid Colon and Rectum According to Alcoholic Beverages[a)]

Beverage (ml[b)]/day)	Controls No.	Sigmoid adenoma		Rectal adenoma	
		No.	OR (95% CI)	No.	OR (95% CI)
Shochu					
Never	528	54	1.0 (Reference)	10	1.0 (Reference)
0[c)]	634	97	1.5 (1.1–2.2)	18	1.4 (0.6–3.1)
0.1–25.6	739	87	1.2 (0.8–1.7)	13	1.0 (0.4–2.3)
25.7–51.2	624	97	1.5 (1.1–2.2)	16	1.5 (0.6–3.3)
≥51.3	467	78	1.5 (1.0–2.2)	13	1.6 (0.7–3.7)
Beer					
Never	528	54	1.0 (Reference)	10	1.0 (Reference)
0[c)]	296	49	1.6 (1.0–2.4)	5	0.9 (0.3–2.7)
0.1–25.6	1957	283	1.4 (1.0–2.0)	52	1.5 (0.7–2.9)
25.7–51.2	189	24	1.3 (0.8–2.1)	3	0.8 (0.2–2.8)
≥51.3	22	3		0	
Sake					
Never	528	54	1.0 (Reference)	10	1.0 (Reference)
0[c)]	1592	227	1.4 (1.0–2.0)	35	1.2 (0.6–2.5)
0.1–25.6	743	113	1.5 (1.0–2.1)	22	1.6 (0.7–3.4)
25.7–51.2	84	11	1.3 (0.7–2.3)	2	1.0 (0.3–3.8)
≥51.3	45	8		1	
Whiskey					
Never	528	54	1.0 (Reference)	10	1.0 (Reference)
0[c)]	1700	235	1.4 (1.0–1.9)	38	1.2 (0.6–2.5)
0.1–25.6	712	105	1.4 (1.0–2.0)	20	1.5 (0.7–3.3)
25.7–51.2	43	14	3.3 (1.8–6.1)	1	2.1 (0.4–10.0)
≥51.3	9	5		1	

OR, odds ratio; CI, confidence interval.
a) Adjusted for smoking, body mass index as categorized in Table I, rank, hospital and study period.
b) Ethanol consumed.
c) Drinkers who never drank the alcoholic beverage under study but drank other alcoholic beverages.

noted between small and large adenomas as regards the association with smoking and alcohol use (data not shown). Obesity was, however, significantly associated only with large adenoma; OR (and 95% CI) for the categories of body mass index≤22.3, 22.4–24.1, 24.2–26.7, and ≥26.8 were 1.0 (reference), 1.1 (0.8–1.7), 0.8 (0.5–1.2), and 1.6 (1.0–2.6), respectively. Corresponding figures for small adenoma were 1.0 (reference), 1.0 (0.7–1.5), 0.9 (0.6–1.4), and 1.3 (0.8–2.1), respectively.

DISCUSSION

Studies relating smoking to risk of colorectal cancer have been rare,[33–35] while smoking has been associated with an increased risk of colorectal adenoma in many studies[4–11] but not in all.[12, 13] This pooling analysis consolidated the positive association between smoking and colorectal adenoma and further suggested that recent, not lifetime, smoking was important in the occurrence of colorectal adenoma. Since the earliest study in our series failed to find any association between smoking and sigmoid colon adenoma,[24] we reanalyzed the data in the same manner employed in the present study. There was a significant positive association between smoking in the recent past and sigmoid colon adenoma; OR (95% CI) for the categories of 0, 1–150, 151–250, and ≥251 cigarette-years within 10 years prior to the endoscopy were 1.0 (reference), 3.4 (1.3–8.5), 2.4 (0.9–6.8), and 4.4 (1.3–15.1), respectively (P for trend=0.08). On the other hand, there was no such association with smoking in the remote past (data not shown). Our data thus strongly indicate that smoking in the recent past is related to risk of colorectal adenoma, and is in agreement with the finding among U.S. men that smoking within the past two decades was strongly associated with risk of small (<10 mm) adenomas.[17]

We arbitrarily divided cumulative smoking exposure into that until 10 years ago and that within the past 10 years. Nevertheless, if an adenoma grows linearly with respect to time, our division is not unreasonable if we compare adenoma size in our study with that in the study of Giovannucci and co-workers.[17] Adenomas in their study were much larger than those in our study; adenomas less than 10 mm and greater than 10 mm numbered 262 and 174, respectively, in Giovannucci *et al.*'s study, while the corresponding numbers were 375 and 49 in our

study. Most adenomas (53%) in our study were less than 5 mm in size. Giovannucci *et al.* found an odds ratio of 2.96 for adenomas of less than 10 mm in the category of $\geq$700 cigarette-years within the past 20 years, adjusting for smoking until 20 years ago.[17] The association between smoking and adenoma seems stronger in our study than in their study. However, precise comparison would be invalid bacause of the differences in adenoma size and time period under study.

The findings that adenoma risk was associated with recent smoking, but not with smoking in the distant past, suggest that smoking is primarily involved in the initiation of adenomas. However, since we did not ascertain the intervals of possible smoking cessation, our estimation of cigarette-smoking in the distant past (until 10 years ago) may not have been precise enough to detect a positive association with adenoma risk. We should also be cautious in interpreting the findings of multivariate analyses mutually adjusting for cigarette smoking during the two periods (within 10 years versus >10 years prior to the endoscopy); the two variables were highly correlated with each other ($r=0.77$).

There was no material difference in the risk associated with smoking between small (<5 mm) and large ($\geq$5 mm) sigmoid adenomas, whether smoking exposure was divided into recent and remote past exposures or not. Giovannucci and co-workers reported that smoking within the 20 years preceding the endoscopy was only associated with 'small' adenoma (<10 mm) in men[17] and was more strongly associated with 'small' adenoma than with 'large' adenoma ($\geq$10 mm) in women.[18] It may be difficult to find a difference in the risk associated with smoking between adenomas less than 5 mm and greater than 5 mm. That is, dividing adenoma size at 5 mm may run the risk of misclassification.

We found a positive association of smoking in the recent past with rectal adenoma. Smoking has rarely been investigated in association with risk of rectal adenoma. A case-control study in Japan showed no association of either past or current smoking with risk of rectal adenoma.[12] Further studies allowing for the time period of smoking are needed to consolidate our reported positive association between smoking and rectal adenoma.

Although underlying mechanisms of the association between smoking and an increased risk of adenoma remain elusive, carcinogens which are formed during combustion of cigarettes seem likely to be involved. Epidemiologic studies measuring DNA-adducts of carcinogens in adenoma tissue will be useful to investigate the etiological role of smoking.

A positive association of alcohol use with colon or colorectal adenoma was found in some studies,[20–23] but not in others.[10, 11] In a Japanese study, a positive association was found for proximal colon adenoma but not for distal colon or rectal adenoma.[12] No measurable association was found for colon or rectal adenoma in a French study.[36] Our observed association with rectal adenoma might be due to chance, but the magnitude of the association expressed in terms of OR was similar to that noted for sigmoid colon adenoma. Our findings suggest that alcohol *per se* rather than a specific beverage is related to an increased risk of adenoma. In our previous study,[24] alcoholic beverages other than shochu were positively associated with sigmoid adenoma, even though shochu was the largest source of ethanol intake. It is difficult to address the relation between a specific alcoholic beverage and any disease condition when subjects consume different types of alcoholic beverages. In general, previous studies including our earlier ones[14, 15, 24] have not examined the association with a specific beverage with never-drinkers as a reference group; the reference group in those studies included drinkers who consumed alcoholic beverages other than the beverage under study.

Among specific alcoholic beverages, beer has been associated with an increased risk of rectal cancer, although inconclusively,[19] and a positive association of beer with adenoma of the colon or colorectum was observed in some studies[4, 13, 37] but not in all.[36] In the present study, only whiskey drinking seemed to confer an additional excess risk of sigmoid and rectal adenomas. In a Japanese case-control study whiskey drinking was associated with risk of proximal colon but not with risk of distal colon or rectal adenoma.[12] In a French study, distillates were not associated with colon or rectal adenoma.[36] The association with whiskey in the present study may be due to chance, because the number of men with high whiskey consumption was small. Alternatively, the association may be confounded by diet and other environmental factors.

Regarding obesity and colorectal cancer, a positive association has been observed for colon cancer,[38–41, 43] but not always,[44–46] though more consistently in men[38–41, 43] than in women,[40, 41] while no material association has been found for rectal cancer in most studies.[38, 40–44] Even an inverse association between obesity and rectal cancer was found in two studies.[45, 46] In these studies, body mass index[38, 40–46] or percent of desirable weight[39] was used for an index of obesity. The few studies of colorectal adenoma have resulted in inconsistent findings regarding the association with body mass index.[25–27] Incorporating waist-hip circumference ratio as a measure of obesity, our latest study evidently showed a positive association between waist-hip circumference ratio, rather than body mass index, and large sigmoid adenoma.[28] This pooling analysis used only body mass index, because waist-hip circumference ratio data were not available in the earlier series. Nevertheless the present findings are in agreement with those noted for colon and rectal cancer and suggest

that obesity is related to the growth of colon adenoma.

Finally, strengths and weaknesses in the present study should be mentioned. A strength of this study was the high rate of participation in endoscopic examination (95%) among a homogeneous population. Furthermore, questionnaires were completed before the endoscopy. The probability that control subjects in our study had adenomas at the unexamined proximal sites might have resulted in dilution, leading to an underestimation of the strength of the associations. A weakness was that the estimation of alcohol intake was limited to current drinkers over the past one year. We could not evaluate the influence of cumulative alcohol intake on adenoma risk. Another drawback was the small number of rectal adenoma cases. Due to the limited study power, the findings on rectal adenoma are necessarily inconclusive. A larger number of cases is needed to address the association of smoking, alcohol use and obesity with rectal adenoma.

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