RESEARCH COMMUNICATION

Relation of Cigarette Smoking, Alcohol Use, and Dietary Habits to Colon Adenomas: A Case-Control Study in Saitama, Japan

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Abstract

   A case-control study of colon adenoma in relation to dietary habits was undertaken in Saitama, Japan. The population included 105 patients with newly diagnosed colon adenoma, 843 general population controls, and 84 hospital controls who had no pathologic lesions at colonoscopy. The adenoma patients and the hospital controls underwent total colonoscopy between November 1992 and March 1994. Information about diet, cigarette smoking and alcohol use were obtained with a self-administered questionnaire. Unconditional logistic regression analysis was used to compare adenoma patients with general population controls and with hospital controls. We found that current cigarette smokers had a higher risk (OR = 2.86, CI = 1.20-6.80) than did nonsmoking hospital controls. Current alcohol use did not affect the risk of colon adenoma. Ex-drinkers had a higher risk (OR = 2.36, CI = 1.02-5.45) than did nondrinking general population controls. The same tendency was observed in comparison with hospital controls. The consumption of raw vegetables was inversely related to the risk of colon adenoma when adenoma patients were compared with general population controls (P for trend = 0.02) or hospital controls (trend P=0.17). Having one bowel movement per day was associated with a lower risk than having less or more frequently bowel movements when adenoma patients were compared with either general population or hospital controls. The present study suggests that the high consumption of raw vegetables is important in the primary prevention of colon adenoma.

Key words: case-control study, colon adenoma, dietary habit

Introduction

  Colon cancer is one of the most common cancers in western countries, and mortality from this cancer has rapidly increased over the past few decades in Japan (Japanese Cancer Association, 1994; Kurihara et al.(ed.), 1984). Epidemiological studies have suggested that dietary factors are associated with the development of colorectal cancer (Burkitt, 1971; Armstrong and Doll, 1973; Kato et al., 1987). Dietary fat has been suspected as a causative factor due to the possible effects of oxidized fat and the elevated production of free bile acids, fecal mutagens, and ketosteroids (Hill et al., 1971; Creath, 1990). In contrast, dietary fiber is believed to decrease the risk of colorectal cancer (Trock et al., 1990). However, evidence for a relationship between dietary factors and colorectal cancer is not conclusive (Trock et al., 1990; Byers and Graham, 1984).

   Adenomatous polyps are well-established precursor lesions of adenocarcinoma of the large bowel (Morson, 1974), and multiple genetic alterations are observed in the transition from normal epithelium to adenoma to carcinoma (Vogelstein et al., 1988). For epidemiological studies, the use of this precursor lesion as an end-point preceding the development of colon cancer has the methodological virtues of a shorter period between exposure and outcome. However few epidemiological studies of colon adenoma, dietary habits, and physical activity have been conducted (Hoff et al., 1986; Macquart-Moulin et al., 1987; Stemmermann et al., 1988; Kono et al., 1991).

   The present study reports the findings for relationship of smoking, drinking, and dietary habits with the risk of colon adenoma, using data from a case-control study of patients undergoing total colonoscopy and general population controls.

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Table 1. Distribution of Adenoma Patients and Controls by Sex and Age

Age group	Adenoma Patients		General population controls		Hospital controls	
	Male	Female	Male	Female	Male	Female
40-49	15	12	171	170	7	27
50-59	31	16	198	159	10	20
60-69	21	10	84	61	9	11
Total	67	38	453	390	26	58

Materials and Methods

Seventeen provincial cities, 18 towns, and 3 villages near the Saitama Cancer Center Hospital were selected for this study. Patients were drawn from the Saitama Cancer Center Hospital and population controls were selected from the study area. A total of 105 patients with colon adenoma, 843 general population controls, and 84 hospital controls aged 40-69 years were studied (Table 1).

Cases and hospital controls

A total of 870 patients of the study area who had first undergone total colonoscopy at the Saitama Cancer Center Hospital between November 1992 and March 1994 were asked about lifestyle with a self-administered questionnaire. Of the 750 (86.2%) patients who replied, 105 were found on histological examination to have colon adenoma and 84 were found to have no pathologic lesions.

General population controls

Control subjects from the community were recruited from among 1,500 families randomly selected from telephone directories of the study areas. Of the 945 (63.0%) families who replied to lettered invitation, 612 agreed to participate in the lifestyle survey. Of the 868 persons who returned valid questionnaires, 25 were excluded because of a self-reported history of colorectal surgery or polypectomy. Therefore, 843 control subjects were included in the study.

Lifestyle questionnaire

A self-administered questionnaire was delivered to patients before colonoscopy, and was mailed to each of the control subjects.

Dietary questions included the average frequency and amount of consumption of three nonalcoholic beverages (green tea, coffee, and milk), rice, noodles, and miso soup, and the average frequency of consumption of bread, margarine, potatoes, pickled vegetables, raw vegetables, cocked vegetables, meat, fish, eggs, tofu, garlic, fruit, yogurt, ice cream, sweet beverages, and cake over the past year. Pre-coded answers were used for consumption frequency, and conventional serving units were used for quantity.

Information on smoking was requested to calculate lifetime consumption in cigarette-years. Information on alcohol consumption was also requested.

Subjects were requested to give information about previous colorectal polyps or polypectomy so that patients with a positive history could be excluded.

Data processing

The consumption of foods and beverages was classified into three levels (Appendix). Unconditional logistic regression analysis was used to compare patients with general population controls and with hospital controls (Breslow and Day, 1980).

The odds ratios (OR) and its 95% confidence interval (CI) were calculated on the basis of the regression coefficient and its standard error for an indicator term corresponding to a level of an independent variable. The trend of association was assessed by a logistic regression model that assigned scores to the level of an independent variable. Statistical significance (two-sided) was based on the ratio of the regression coefficient to its standard error. Statistical analysis (LOGISTIC) was performed with the Statistical Analysis System (SAS Institute Japan, 1994).

Results

Cigarette smoking tended to be associated positively with the risk of colon adenoma when adenoma patients were compared with either group of control subjects. Current cigarette smokers had a significantly increased risk (OR = 2.86, CI = 1.20-6.80) of colon adenoma than did nonsmokers among the hospital controls (Table 2). Alcohol consumption status did not affect the risk of colon adenoma, and no specific alcoholic beverage was associated with an increased risk of colon adenoma in either set of controls (Table 3).

The consumption of raw vegetables was inversely related to the risk of colon adenoma when adenoma patients were compared with general population controls. A dose-response relationship was also observed (P for trend = 0.02) (Table 4). The same tendency was also observed when adenoma patients were compared with hospital controls (Table 4). None of the other food items or food groups was associated with an increased risk of colon adenoma.

When adenoma patients were compared with hospital controls, no food item was associated with increased risk of

Table 2. Odds Ratios (OR) and 95% Confidence Intervals (CI) for the Relationship of Colon Adenoma and Cigarette Smoking in Adenoma Patients and Controls[a]

History	No. of cases/ controls	RR	CI upper	lower	Trend P-value[b]
Comparison with general population controls					-
Cigarette smoking					
Never	43/455	1.00			
Ex	23/126	1.81	0.95	3.45	
Current	39/262	1.54	0.88	2.71	
Cigarette years					0.23
Nonsmoker	43/455	1.00			
<=800	46/292	1.68	0.98.	2.90	
> 800	16/96	1.42	0.68	2.94	
Comparison with hospital controls					-
Cigarette smoking					
Never	43/60	1.00			
Ex	23/12	1.53	0.61	3.84	
Current	39/12	2.86	1.21	6.80	
Cigarette years					0.25
Nonsmoker	43/60	1.00			
<=800	46/21	2.01	0.93	4.32	
> 800	16/3	3.62	0.89	14.73	

a) Adjusted for sex and age.
b) Based on the logistic regression model with scores of 0-2 assigned to the three levels.

Table 3. Odds Ratios (OR) and 95% Confidence Intervals (CI) for the Relationship of Colon Adenoma and Alcohol Intake in Adenoma Patients and Controls[a]

History	No. of cases/ controls	RR	CI upper	lower	Trend *P*-value[b]
Comparison with general population controls					-
Alcohol drinking					
Never	44/417	1.00			
Ex	9/29	2.36	1.02	5.45	
Current	52/397	1.09	0.67	1.77	
Drinking days/week					0.98
Nondrinker	44/417	1.00			
1-3/week	24/131	1.57	0.90	2.75	
4-7/week	37/295	0.98	0.57	1.67	
Current drinkers vs. nondrinkers[c]					-
Nondrinker	44/417	1.00			
Sake	32/211	1.03	0.58	1.83	
Shochu	21/132	1.33	0.69	2.55	
Beer	44/44	0.99	0.59	1.65	
Whisky/brandy	19/44	1.15	0.59	2.26	
Comparison with hospital controls					-
Alcohol drinking					
Never	44/51	1.00			
Ex	9/3	2.61	0.62	10.90	
Current	52/30	1.01	0.48	2.10	
Drinking days/week					0.97
Nondrinker	44/51	1.00			
1-3/week	24/12	1.56	0.65	3.68	
4-7/week	37/21	0.91	0.39	2.10	
Current drinkers vs. nondrinkers[c]					-
Nondrinker	44/51	1.00			
Sake	32/15	0.86	0.32	2.32	
Shochu	21/8	1.54	0.53	4.51	
Beer	44/27	0.91	0.42	1.96	
Whisky/brandy	19/13	0.70	0.24	1.99	

a) Adjusted for sex and age.
b) Based on the logistic regression model with scores of 0-2 assigned to the three levels.
c) At least 1/week during a certain season.

Table 4. Odds Ratios (OR) and 95% Confidence Intervals (CI) of Colon Adenoma by Dietary Items in Food Frequency Questionnaire: Comparison with General Population Controls[a]

	Low	Intermediate			High			Trend P-value[b]
		RR	CI		RR	CI		
Rice	1.00	1.25	0.64	2.42	1.38	0.74	2.57	0.94
Noodles	1.00	0.78	0.49	1.24	0.87	0.48	1.57	0.51
Miso soup	1.00	1.14	0.69	1.86	1.02	0.62	1.71	0.91
Green tea	1.00	0.74	0.43	1.28	1.07	0.61	1.85	0.40
Coffee	1.00	0.92	0.55	1.51	0.72	0.43	1.18	0.35
Milk	1.00	1.03	0.62	1.72	0.80	0.47	1.34	0.61
Bread	1.00	1.24	0.78	1.99	1.03	0.60	1.77	0.66
Margarine	1.00	1.40	0.88	2.24	1.06	0.58	1.94	0.44
Potatoes	1.00	0.87	0.50	1.49	0.92	0.55	1.52	0.96
Pickled vegetables	1.00	0.79	0.50	1.26	0.78	0.46	1.34	0.36
Raw vegetables	1.00	1.02	0.58	1.78	0.52	0.31	0.85	0.02
Cooked vegetables[c]	1.00	0.97	0.62	1.51	1.46	0.73	2.91	0.48
Seaweed	1.00	0.93	0.55	1.58	0.86	0.48	1.52	0.59
Meat[d]	1.00	1.37	0.78	2.39	1.05	0.65	1.70	0.86
Fish[e]	1.00	1.08	0.63	1.86	1.19	0.74	1.91	0.46
Eggs	1.00	0.67	0.39	1.13	0.82	0.48	1.41	0.61
Tofu dishes	1.00	0.71	0.43	1.17	0.82	0.47	1.46	0.53
Garlic[f]	1.00	0.87	0.51	1.47	0.91	0.56	1.47	0.68
Fruits	1.00	0.70	0.44	1.11	1.69	0.86	3.33	0.73
Yogurt	1.00	1.21	0.76	1.92	1.06	0.59	1.93	0.62
Ice cream	1.00	0.73	0.40	1.34	0.57	0.28	1.13	0.10
Soft drinks	1.00	1.22	0.77	1.93	1.03	0.49	2.17	0.54
Cake	1.00	1.14	0.72	1.80	1.56	0.84	2.90	0.14

a) Adjusted for sex and age.
b) Based on the logistic regression model with scores of 0-2 assigned to the three consumption levels.
c) Including boiled vegetables, fried vegetables, and Tempura.
d) Including chicken, chicken dishes, beef/pork, beef/pork dishes, and ham/sausages.
e) Including boiled fish, broiled fish, and sashimi(raw fish).
f) Including garlic dishes.

Table 5. Odds Ratios (OR) and 95% Confidence Intervals (CI) of Colon Adenoma by Dietary Items in Food Frequency Questionnaire: Comparison with Hospital Controls

	Low	Intermediate			High			Trend P-value[b]
		RR	CI		RR	CI		
Rice	1.00	1.21	0.46	3.19	1.54	0.63	3.77	0.50
Noodles	1.00	1.57	0.78	3.16	1.72	0.64	4.57	0.15
Miso soup	1.00	0.72	0.35	1.49	0.90	0.40	2.00	0.76
Green tea	1.00	0.61	0.26	1.44	0.62	0.26	1.47	0.46
Coffee	1.00	1.24	0.57	2.70	0.91	0.43	1.91	0.99
Milk	1.00	0.86	0.37	2.02	0.45	0.20	1.01	0.08
Bread	1.00	1.53	0.72	3.24	0.80	0.37	1.73	0.71
Margarine	1.00	1.74	0.81	3.76	0.56	0.25	1.30	0.39
Potatoes	1.00	0.76	0.32	1.79	0.77	0.35	1.70	0.66
Pickled vegetables	1.00	1.21	0.60	2.42	1.45	0.64	3.31	0.34
Raw vegetables	1.00	0.85	0.36	1.98	0.57	0.28	1.18	0.17
Cooked vegetables[c]	1.00	0.76	0.39	1.50	0.70	0.26	1.87	0.96
Seaweed	1.00	1.27	0.58	2.79	1.19	0.52	2.72	0.72
Meat[d]	1.00	1.78	0.74	4.28	1.00	0.50	2.02	0.82
Fish[e]	1.00	0.66	0.30	1.46	0.90	0.43	1.88	0.78
E+A36ggs	1.00	0.67	0.29	1.53	0.80	0.34	1.87	0.70
Tofu dishes	1.00	1.27	0.59	2.71	1.32	0.56	3.12	0.54
Garlic[f]	1.00	0.87	0.40	1.88	1.33	0.63	2.76	0.49
Fruits	1.00	0.65	0.32	1.31	0.72	0.29	1.80	0.36
Yogurt	1.00	1.27	0.62	2.63	0.78	0.34	1.80	0.73
Ice cream	1.00	1.97	0.71	5.44	1.53	0.51	4.61	0.20
Sweet beverages	1.00	1.31	0.64	2.68	2.20	0.60	8.13	0.18
Cake	1.00	1.13	0.55	2.29	1.00	0.42	2.41	0.90

* See footnotes for Table 4.

Table 6. Odds Ratios (OR) and 95% Confidence intervals (CI) for the Relationship of Colon Adenomas and Bowel Movements in Adenoma Patients and Controls

History	No. of cases/ controls	RR	CI upper	lower
Comparison with general population controls				
Bowel Movements				
1 or less per 2 days	13/103	1.00		
about 1 per day	59/589	0.70	0.36	1.34
2 or more per day	33/151	1.38	0.67	2.85
Comparison with hospital controls				
Bowel Movements				
1 or less per 2 days	13/18	1.00		
about 1 per day	59/54	0.84	0.35	2.04
2 or more per day	33/12	2.19	0.77	6.19

a) Adjusted for sex and age.
b) Based on the logistic regression model with scores of 0-2 assigned to the three levels.

Appendix. Definition of "Frequency of consumption" in Tables 4 and 5

	Frequency of consumption		
	Low	Intermediate	High
Rice	<1 bowl/day	1-2 bowls/day	>=3 bowls/day
Noodles	<=1 bowl/week	2-4 bowls/week	>=5 bowls/week
Miso sou	<1 bowl/day	1 bowl/day	>=2 bowls/day
Green tea	<1 cup/day	1-4 cups/day	>=5 cups/day
Coffee	<1 cup/week	1-6 cups/week	>=1 cup/day
Milk	<1 glass/week	1-6 glasses/week	>=1 glass/day
Bread	<1 /week	1-4 /week	>=5 /week
Margarine	<1 /week	1-4 /week	>=5 /week
Potatoes	<1 /week	1 /week	>=2 /week
Pickled vegetables	<=4 /week	5-7 /week	>=2 /day
Raw vegetables	<=4 /week	5-6 /week	>=1 /day
Cooked vegetables[a]	<=6 /week	7-13 /week	>=2 /day
Seaweed	<=1 /week	2-4 /week	>=5 /week
Meat[b]	<=4 /week	5-6 /week	>=1 /day
Fish[c]	<=4 /week	5-6 /week	>=1 /day
Eggs	<=1 /week	2-4 /week	>=5 /week
Tofu dishes	<=1 /week	2-4 /week	>=5 /week
Garlic[d]	<1 /week	1 /week	>=2 /week
Fruits	<=4 /week	5-7 /week	>=2 /day
Yogurt	<1 /week	1-4 /week	>=5 /week
Ice cream	<1 /week	1 /week	>=2 /week
Sweet beverages	<1 /week	1-4 /week	>=5 /week
Cake	<1 /week	1-4 /week	>=5 /week

a) Including boiled vegetables, fried vegetables, and Tempura.
b) Including chicken, chicken dishes, beef/pork, beef/pork dishes, and ham/sausages.
c) Including boiled fish, broiled fish, and sashimi(raw fish).
d) Including garlic dishes.

adenoma (Table 5). However, a slight inverse relation (P for trend = 0.08) with the consumption of milk was observed.

The frequency of bowel movement was associated with colon adenoma risk when adenoma patients were compared with general population controls. The relative risks of one bowel movement per day were less than unity when adenoma patients were compared with either group of control subjects (Table 6).

Discussion

Previous studies have shown that cigarette smoking is associated with increased risks of both colorectal cancer (Doll and Peto, 1976; Hirayama, 1990; Kune et al., 1992) and

colorectal adenoma (Monnet et al, 1991; Zahm et al., 1991; Lee et al., 1993; Olsen et al., 1993). On the other hand, we found that cigarette smoking was inversely related to colon cancer risk in our previous study (Hoshiyama et al., 1993) Honjo et al. (Honjo et al., 1995) found that recent, but not lifetime, smoking was significantly associated with the development of colorectal adenoma. Their data strongly suggest that smoking in the recent past is associated with a risk of colorectal adenoma and agree with the finding in American men that smoking within the past two decades is strongly associated with a risk of small (<10 mm) adenoma (Giovannucci et al., 1994). We also found that current cigarette smokers had a higher risk (OR = 2.86, CI = 1.20-6.80) than did nonsmoking hospital controls. However, in this study the proportions of current smokers were 14% in hospital controls and 31% in general population controls (Table 2). Such a proportion was very low compared with the whole Japanese population aged 40-69 in which approximately 50% in male and 10% in female are smokers. Thus, our data may not confirm that cigarette smoking is associated with an increased risk of colon adenoma. However, the reason for this association remains to be elucidated.

In the present study, we found no increased risk of colon adenoma associated with alcohol use. Several previous studies (Cope et al., 1991; Giovannuci et al., 1993) have found alcohol use and colon or colorectal adenoma to be positively associated, but several studies have not (Lee et al., 1993; Olsen et al., 1993). Among specific alcoholic beverages, beer has been reported to be associated with adenoma of the colon or colorectums (Kikendall et al., 1989; Scandler et al., 1993; Kune et al., 1991). A cohort study (Hirayama, 1989) found a striking association of beer drinking with sigmoid colon cancer but not with rectal cancer. These findings are consistent with a possible carcinogenic effect of nitrosoamines (Goff and Fine, 1989; Spiegelhalder et al., 1979). However, other studies failed to show a specific association between consumption of beer and increased risk of cancer of the rectum (Manousos et al., 1983; Tajima and Tominaga, 1985; Kabat et al., 1986; Adami et al., 1992). Therefore, a clear association of alcohol with colon adenoma or colorectal cancer has not yet been shown.

Most fiber in the Japanese diet comes from vegetables (Shimbo et al., 1995). Vegetables are also an important source of vitamins A and C. Our analysis comparing the general population controls and adenoma patients showed an inverse relation between raw vegetable intake and colon adenoma. The same tendency was also observed when adenoma patients were compared with hospital controls. On the other hand, the consumption of rice and cooked vegetables did not affect the risk of colon adenoma. Whether the protective effects of raw vegetable intake are due to fiber or vitamin C is uncertain. Experimental and clinical metabolic studies have shown that potential carcinogens in the intestinal lumen can be diluted, bound, and more rapidly eliminated with the presence of a diet rich in fiber (Reddy, 1987). Postulated mechanisms are the dilution or absorption of fecal

carcinogens, the alteration in bile acid metabolism, and the production of short-chain fatty acids (Kritchevsky, 1995); these effects probably differ by the type of fiber, i.e. soluble and non-soluble fiber. However, several studies (Trock et al., 1990; Benito et al., 1990; Bidoli et al., 1992) have failed to show that fruit consumption has any effect on the risk of colorectal cancer. These findings suggest that certain forms of fiber and/or vitamin C have at most a slight effect on the risk of colon adenoma.

The relation between frequency of bowel movement and colorectal cancer or adenoma has not been thoroughly investigated. We found that the relative risk for persons having one bowel movement per day was less than unity and that the relative risk for persons having two or more bowel movements per day was more than unity when adenoma patients were compared with either group of control subjects. Although the decrease in risk among those having one bowel movement per day was not significant, similar findings in the two comparisons support the view that persons who continue to have one bowel movement per day share a common characteristic that decreases their risk, but is likely to be independent of the effects of bowel movement.

Acknowledgment

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Personal Profile: Overleaf

Personal Profile: **Yoshiharu Hoshiyama**

Apart from his duties in the Department of Public Health at Showa University Dr Hoshiyama is very keen on jazz, golf and mystery - and of course his family. A relaxed moment with his daughter is illustrated below.