Coffee, Tea, Tobacco, and Cancer of the Large Bowel[1]

John A. Baron, Maria Gerhardsson de Verdier, and Anders Ekbom

Cancer Epidemiology Unit, Uppsala University, Sweden [J. A. B., A. E.]; National Board of Health and Welfare, Centre for Epidemiology S-112 81 Stockholm, Sweden [M. G. de V.]; and Department of Psychiatry, Karolinska Institutet St. Göran's Hospital S-112 81 Stockholm, Sweden [M. G. de V.]

Abstract

The impact of tobacco use and coffee and tea intake on the risk of colorectal cancer is unclear. Previous research has suggested that coffee may be protective against these cancers, and investigation regarding tea or cigarette smoking has yielded inconsistent results. To clarify these issues, we evaluated coffee and tea intake and tobacco smoking as risk factors for cancer of the colon and rectum in a population-based case-control study from Stockholm, Sweden. Cases were ascertained from the regional cancer registry, and controls identified through population registers. Subjects completed a questionnaire requesting information regarding foods and beverages consumed, exercise, tobacco use, and personal characteristics. Logistic regression modelling was used to compute odds ratios.

A total of 352 cases of colon cancer, 217 cases of rectal cancer, and 512 controls took part. High coffee intake was negatively associated with the risk of colon cancer: the odds ratio for those drinking 6 or more cups per day was 0.55 (95% confidence interval, 0.31–0.96) compared to those drinking one or fewer. There was no association with rectal cancer. For tea, the associations were the opposite: there was no association with colon cancer risk, but the odds ratio for rectal cancer was 0.56 (95% confidence interval, 0.34–0.90) for those drinking 2 or more cups per day compared with those drinking none. Smokers of 11 or more cigarettes per day had a 20 to 30% reduction in the risk of colon and rectal cancer, but these findings were consistent with chance. There was no association of long-term cigarette smoking with risk.

Introduction

Cigarette smoking, coffee drinking, and tea drinking are three social habits that are common worldwide, but the effects of these exposures on the risk of colorectal cancer are not clear. In most studies, cigarette smoking has not been found to have a large effect on the risk of colorectal cancer (1, 2), but recent findings have suggested that long-term smoking may be a risk factor (3, 4). In contrast, it has been proposed that coffee consumption is protective against colorectal cancer, possibly through an effect on cholesterol metabolism (5). Several studies have reported findings consistent with such a protective effect, but in many of these, the findings were compatible with chance, the effects of covariates, or biases in the study design (5). Tea, another caffeine-containing beverage, has received less attention in this regard, but there are suggestions that it may be associated with a decreased risk of rectal cancer (6, 7).

To elucidate these issues, we report here the results from a population-based case-control study of colorectal cancer from Sweden.

Subjects and Methods

This case-control study was conducted in Stockholm, Sweden, with the approval of the institutional review board of the Karolinska Institute. Methods and other findings from the study have been previously described (8, 9). We attempted to include all cases of adenocarcinoma of colorectal cancer diagnosed in living patients in Stockholm County during the period January 22, 1986–March 15, 1988. Case ascertainment was based on a surveillance network established at the major hospitals in Stockholm, as well the Stockholm Regional Cancer Registry. Controls were selected during the study period from the computerized population register for the county, which is updated monthly. Potential participants were selected every 4 months, randomly selected within gender and four strata of year of birth (1907–1916; 1917–1926; 1927–1936; 1937–1946).

Information regarding diet, smoking, weight, and other personal characteristics was obtained from study subjects by means of a questionnaire. Area hospitals were visited weekly by a research assistant who handed out the questionnaire to potential cases in the study. Patients who were too ill to complete the questionnaire themselves were aided by the assistant; a few controls (less than 1%) also received such assistance. Cases found through the Cancer Registry (19%) and all controls were mailed the same questionnaire after an introductory letter and telephone call. If necessary, a telephone interview was used to obtain missing information from these subjects. Surrogate respondents were not used for potential subjects who had died, or who were too ill to participate.

A series of questions regarding tobacco use was included in the questionnaire. Ever-smoking of pipes or cigars was recorded, and detailed information on cigarette smoking was also requested, including the number of cigarettes currently smoked and the number smoked in each 5-year period beginning in 1950. The questionnaire also included quantitative food frequency items, focusing on average consumption during the past 5 years, excluding periods of altered diet due to illness. There were 55 food items, chosen

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to cover more than 80% of the foods in the Swedish diet. Response alternatives were never, less than once per month, 1–3 times per month, 1–4 times per week, and more than 4 times per week. Information on portion sizes was also requested, as "small," "standard," or "large," using a photographic guide. From the data provided, intake of total energy and nutrients was computed using the nutrient data base at the Swedish National Food Administration (10). Questions regarding beverage intake were also included in the food frequency questionnaire; for coffee and tea, these were framed in terms of usual number of cups or glasses drunk per day. For alcoholic beverages, categorical responses were sought, with 5 to 7 categories depending on the particular beverage. Additional questions regarded height and weight 5 years prior to the study, from which BMI[2] was calculated as weight/height^2. Other items focused on occupational and recreational exercise, and the two exercise responses were combined as previously described into a single scale as: very active (very active in either work and/or recreation); inactive (inactive in work and recreation); or moderately active (moderately active, but not very active, in work or recreation) (9). Cases were also questioned regarding their recent symptoms. Gastrointestinal complaints (*e.g.*, nausea, abdominal pain) were recorded separately from more general complaints (*e.g.*, weight loss, fatigue).

The odds ratio was used as a measure of association between the exposures of interest and cancer risk. These were calculated using likelihood ratio techniques with unconditional logistic regression (11) by the statistics package STATISTIX (12). In the analyses, coffee and tea consumption were considered in separate analyses as linear terms, and as categorical variables. The categories were selected according to the distribution of all cases and controls combined. To control for possible confounding, two sets of models were fit for each exposure. In the first, age (linear term) and gender (male versus female) were included as main effects along with the exposure. The second model also included terms for fat intake (approximate quintiles), fiber intake (approximate quintiles), BMI (approximate quintiles), and physical exercise (3 categories described above). Possible effect modification by sex and age was considered by fitting models within each sex separately, and within the age groups ≤69 and >69 years (representing two approximately equal-sized groups of subjects). The statistical significance of the possible effect modification was considered by introducing product terms into the logistic models (exposure*interaction factor), and examining the associated change in deviance (11). Because of the possibility of response bias, the variation in the relative risks according to the symptomatic status of the cases was investigated.

Results

A total of 452 colon cancer cases, 268 rectal cancer cases, and 624 controls was selected. Nonresponse was 21% among potential cases and 18% among potential controls, leaving 352 colon cancer cases, 217 rectal cancer cases, and 512 controls for analysis. Characteristics of cases and controls are summarized in Table 1. Of the 569 subjects in the combined case group, 177 reported recent gastrointestinal symptoms, and 346 reported some general symptoms. Two hundred forty cases and 4 controls received assistance with the questionnaire.

Table 1 Characteristics of cases and controls

	Rectal cancer	Colon cancer	Controls
Number	217	352	512
% Female	50.7	53.7	53.9
Mean age (yr)	66.9 ± 8.5[a]	68.4 ± 8.9	67.7 ± 9.0
Mean height (meters)	1.70 ± 9.2	1.69 ± 8.8	1.70 ± 0.9
Mean weight (kg)	70.5 ± 11.8	71.3 ± 13.0	69.1 ± 12.0
Mean BMI (kg/m^2)	24.3 ± 3.1	24.8 ± 3.5	24.0 ± 3.3
Mean fat intake (g/day)	68.3 ± 25.3	67.7 ± 24.7	63.3 ± 24.6
Mean fiber intake (g/day)	15.3 ± 5.4	15.5 ± 5.5	15.4 ± 5.2

[a] Mean ± SD.

Current coffee consumption was inversely associated with the risk of colon cancer (Table 2). Among subjects drinking 6 or more cups per day, the age- and sex-adjusted relative risk was 0.55 (95% CI, 0.31–0.96) compared to those drinking 1 cup daily or less. Analyzed as a continuous variable, each cup of coffee taken per day reduced the relative risk of colon cancer by a multiplicative factor of 0.93 (95% CI, 0.86–1.00). Further adjustment for physical exercise, BMI, and intake of fat and fiber yielded relative risk estimates that were slightly farther from unity. In contrast, rectal cancer appeared unrelated to coffee intake (Table 2). These effects were broadly similar in males and females, as well as in older and younger subjects (data not shown).

Unlike coffee, tea consumption showed no hints of an inverse association with cancer of the colon (Table 2). However, subjects drinking 2 or more cups of tea daily did have a reduced risk of cancer of the rectum compared to nondrinkers (OR, 0.56; 95% CI, 0.35–0.89). Considered as a linear effect in the regression models, each cup of tea reduced the relative risk of rectal cancer by a multiplicative factor of 0.90 (95% CI, 0.76–1.07). Further adjustment for physical exercise, BMI, and intake of fat and fiber did not materially alter these estimates. The associations were similar in men and women (data not shown), but the inverse relationship between tea intake and rectal cancer risk was more pronounced for older subjects. Among subjects ≤69 years, the OR of rectal cancer for drinking 2 or more cups of tea daily (*versus* none) was 0.84 (95% CI, 0.46–1.55), while for those over 69 years of age, it was 0.31 (95%, CI 0.14–0.67). The corresponding interaction terms in the logistic models provided a statistically significant improvement in fit over the model without them (χ^2 = 8.67 on 2 degrees of freedom for the models with age and sex as covariates).

The relative risks for current cigarette smoking were below unity for both cancer of the colon and rectum, but the differences from 1.0 were consistent with chance, and there was no pattern with amount of smoking (Table 3). Although these relationships were broadly similar in older and younger subjects (data not shown), there was a suggestion that the effects differed by sex. Among men, current smoking of 11 or more cigarettes a day had, if anything, a positive association with colon cancer risk (age-adjusted OR, 1.26; 95% CI, 0.66–2.37). Among women, the asso-

[2] The abbreviations used are: BMI, body mass index; CI, confidence interval; OR, odds ratio.

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Table 2 Multivariate logistic odds ratios for coffee and tea drinking and colorectal cancer[a]

		Cancer site		
		Colon	Rectum	Colorectal
Current coffee drinking				
0–1 cups/day	57/23/61[b]	1.0	1.0	1.0
2 cups/day	83/55/120	0.72	1.17	0.85
		0.45–1.15	0.65–2.12	0.56–1.30
3 cups/day	89/56/120	0.82	1.23	0.93
		0.51–1.31	0.68–2.22	0.61–1.42
4–5 cups/day	89/56/143	0.63	0.96	0.73
		0.40–1.01	0.53–1.74	0.48–1.12
6+ cups/day	34/27/68	0.48	0.86	0.60
		0.27–0.86	0.43–1.73	0.36–1.00
Current tea drinking				
None	161/109/237	1.0	1.0	1.0
1 cup/day	112/79/160	1.02	1.06	1.02
		0.74–1.41	0.74–1.52	0.77–1.35
2+ cups/day	79/29/115	0.96	0.56	0.79
		0.67–1.37	0.34–0.90	0.57–1.10

[a] Adjusted for intake of fat and fiber, BMI, and exercise.
[b] Number of colon cancer cases/rectal cancer cases/controls.

Table 3 Multivariate logistic odds ratios for cigarette smoking and colorectal cancer[a]

		Cancer site		
		Colon	Rectum	Colorectal
Cigarette smoking status				
Never	163/101/233[b]	1.0	1.0	1.0
Former	93/58/138	0.94	0.88	0.92
		0.66–1.34	0.58–1.32	0.67–1.25
Current	78/51/125	0.91	0.84	0.89
		0.63–1.31	0.55–1.28	0.65–1.22
1–10 cigarettes/day	39/26/57	1.08	1.01	1.06
		0.67–1.73	0.59–1.74	0.70–1.61
11+ cigarettes/day	39/25/68	0.77	0.70	0.75
		0.48–1.24	0.40–1.20	0.50–1.13
Duration of cigarette smoking after 1950				
Never smoker	163/101/233	1.00	1.00	1.00
Up to 20 years	56/38/83	0.98	0.97	0.99
		0.65–1.49	0.60–1.56	0.69–1.42
25–35 years	52/33/79	0.91	0.83	0.88
		0.60–1.32	0.51–1.36	0.60–1.28
40+ years	63/38/101	0.89	0.79	0.87
		0.60–1.32	0.49–1.25	0.61–1.22
Pack-years of cigarette smoking after 1950				
Never smoker	164/101/233	1.00	1.00	1.00
<11.05	51/39/89	0.83	0.91	0.86
		0.55–1.26	0.57–1.45	0.60–1.23
≥11.05; <22.74	62/34/84	1.04	0.85	0.99
		0.70–1.56	0.52–1.30	0.70–1.42
≥22.74	58/36/90	0.90	0.81	0.87
		0.59–1.36	0.50–1.31	0.61–1.25

[a] Adjusted for intake of fat and fiber, BMI, and exercise.
[b] Number of cancer cases/rectal cancer cases/controls.

ciation tended to be a protective one, albeit consistent with chance (OR, 0.57; 95% CI, 0.30–1.10). However, the interaction terms were not close to statistical significance (χ^2 = 3.65 on 3 degrees of freedom for the models with age and sex as covariates).

Even after a long latency, smoking was unassociated with risk. Subjects who had been smoking in 1950–1955 had, if anything, a slightly decreased age-and sex-adjusted risk of cancer of the colon (OR, 0.81; 95% CI, 0.61–1.08) and of cancer of the rectum (OR, 0.87; 95% CI, 0;63–1.22).

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Long-term smoking also did not affect risk; the relative risk for smoking 40 or more years was 0.85 (95% CI, 0.59–1.23) for colon cancer and 0.85 (95% CI, 0.55–1.32) for rectal cancer. Adjustment for diet, BMI, and exercise did not materially change these odds ratios.

Subjects who had ever smoked a pipe had a reduced risk of cancers of the colon (age-and sex-adjusted OR, 0.72; 95% CI, 0.46–1.13) but this reduction was consistent with chance. There were similar findings for rectal cancer (age- and sex-adjusted OR, 0.76; 95% CI, 0.45–1.26). The ever-smoking of cigars was associated with a more substantial reduction in the risk of cancer of the colon (age- and sex-adjusted OR, 0.48; 95% CI, 0.24–0.95), and a more modest inverse relationship with the risk of cancer of the rectum (age- and sex-adjusted OR, 0.69; 95% CI, 0.34–1.41).

There was no evidence of mutual confounding among the exposures investigated. In multivariate models including age, sex, coffee and tea intake, and cigarette smoking, the odds ratios for the exposures under study were essentially unchanged from the other analyses. Similar findings were found for models with cigar smoking (data not shown).

After exclusion of the cases who reported gastrointestinal or other symptoms, the relative risks for all of the exposures investigated were similar to those calculated from the entire data set (data not shown). Exclusion of the subjects who received assistance in completing the questionnaire also did not affect the findings regarding tobacco use or tea consumption, but the inverse association of coffee intake with risk was weaker. Compared to subjects drinking 0 or 1 cup of coffee, subjects drinking 6 or more cups per day had an odds ratio of 0.86 (95% CI, 0.43–1.70) (other data not shown).

Such an impact on the relative risks associated with coffee might be expected if the nurse assistance tended to minimize the reporting of socially discouraged habits. The percentage of cases who reported ever smoking cigarettes was lower among those who received nurse assistance (49.8%) than among those who did not (56.4%), and the mean daily coffee intake was slightly lower as well (3.0 ± 1.9 *versus* 3.4 ± 1.9 cups/day). However, the prevalence of reported current smokers was slightly higher in the nurse assistance group (25.8% *versus* 22.2%). Thus, there were no consistent differences in the reporting of personal habits between the self-respondent group, and those who received nurse assistance.

Discussion

In this population-based case-control study, usual coffee intake was associated with a decreased risk of colon (but not rectal) cancer. For tea, the data indicate a protective effect on cancer of the rectum. There was no substantial association of cigarette smoking with risk of either colon or rectal cancer, even among long-term smokers.

Our findings of a lack of substantial relationship between cigarette smoking and the risk of large bowel cancer are similar to most previously published studies (1, 2, 13–18). Contrary to recent report (3, 4), we found no suggestion that long-term smoking conferred an increased risk. The relatively little other data available regarding this point also do not suggest an association (17, 18). The differing results could be due to several factors. Uncontrolled confounding is one possibility, although our analysis, as well as the recent positive reports (3, 4), controlled for all of the important known risk factors for large bowel cancer. There is some evidence that cigarette smokers with colorectal cancer present at a later stage than nonsmokers (19–21), but our case ascertainment largely through hospitals is likely to have been rapid enough to avoid bias from early fatality among smoking cases. However, it is possible that the choice of controls in the hospital-based studies (17, 18), or selective nonresponse in any of the case-control investigations could have affected the results.

There is little indication from the published literature that pipe or cigar smokers have a decreased risk of colorectal cancer; the previous studies that have focused on this topic have generally found, if anything, cigar smoking to be a risk factor (1, 2, 14, 15). Unfortunately, our data did not include details on the recency or amount of cigar and pipe smoking, so more detailed analysis from our data is not possible.

For coffee, the presence of a dose-response pattern and the preservation of the pattern of findings after exclusion of cases with various types of symptoms are compatible with a true protective effect against colon cancer. Indeed, our inquiries regarding such symptoms is a strength of the study. The lack of effect among subjects responding without nurse assistance could indicate a response bias. However, there was no general pattern suggesting different responses among those who received help with the questionnaire, and the limitation of the coffee effect to tumors in the colon would not be expected if there was such a bias. Consequently, the changes in the relative risks after exclusion of subjects with this assistance are most likely due to chance. The possible inverse association of coffee with colorectal cancer risk was not widely publicized in Sweden, and therefore response bias is also an unlikely explanation for our findings. However, coffee is routinely served to patients in Swedish hospitals 3 times a day, and this modest encouragement could have biased the cases to report more coffee intake, thereby leading us to underestimate the strength of the association.

The high coffee consumption in Sweden had a dual impact on our study. On the one hand, we had substantial numbers of heavily exposed subjects who drank 6 or more cups of coffee daily. However, so few subjects drank no coffee that our reference group had to include subjects who drank 1 cup per day. If coffee has a graded effect on risk, this difficulty should lead us to underestimate the true impact of coffee.

Previous studies have repeatedly suggested that coffee (or caffeine) intake may be inversely related to the risk of large bowel cancer (6, 22–27), although the data are not entirely consistent (6, 15, 28, 29). The possible confounding effects of diet or other lifestyle factors have not been extensively considered, and these could explain some of these differences in results. Also, it is possible that coffee may have effects that differ according to factors such as fat intake (5). Finally, there are several varieties of coffee beans and several methods of coffee preparation, which could have different effects on risk (30).

There is less published data regarding the association of tea intake with the risk of colorectal cancer (6, 7). Two Japanese studies have reported a possible inverse association with rectal cancer (7, 27), although other studies (one among Hawaiian Japanese) found tea drinking to be either a risk factor for cancer of the rectum (31, 32) or unrelated to it (33). For cancer of the colon, the findings have been mixed (6, 27, 31–33). Aside from the possibilities of con-

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founding by diet and lifestyle, there is no clear reason for the differences in findings: many of these studies also focused on the dark teas which are drunk in Sweden.

Experimental data can be invoked to support both an adverse and a protective effect of coffee on carcinogenesis. Constituents of coffee such as chlorogenic acid have been shown to be mutagens, and caffeine may impede DNA repair (34–37). On the other hand, in rodents, coffee and caffeine have generally either had no effect, or been protective against experimental carcinogenesis (38–44). Similar findings have been reported for tea (3, 31).

There is evidence supporting the hypothesis that coffee affects the risk of large bowel cancer by decreasing the concentration of stool lipids. Coffee, particularly unfiltered or boiled, appears to increase serum cholesterol (30, 45–47). This may decrease the stool concentrations of cholesterol and bile acids, which can act as cancer promoters in the large bowel (5). Caffeine is not involved in this effect (47); a lipid-soluble fraction appears to be the active moiety (48, 49).

In summary, our findings indicate that cigarette smoking, even long-term, does not have a substantial association with the risk of colorectal cancer. However, coffee consumption appears to be protective against colon cancer, and tea against rectal tumors. Further epidemiological research with careful consideration of confounding and response biases is warranted, and experimental studies regarding the effect of coffee constituents on the large bowel mucosa and bile acids seem warranted.

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