Coffee and Tea and the Risk of Recurrent Colorectal Adenomas

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Abstract
Consumption of coffee has been associated with a reduction in the risk of the colon, and (less consistently) drinking tea has been associated with a reduction in the risk of rectal cancer. The effect of these beverages on the risk of colorectal adenomas, however, has not been well investigated.

We used data from an adenoma prevention trial to investigate these associations. Patients with at least one recent large bowel adenoma were followed with colonoscopy 1 and 4 years after their qualifying examinations. Adenomas detected at the year 4 colonoscopy were used as end points. A food frequency questionnaire was administered at study entry and study completion; average intake over the study period was used to estimate the exposures of interest.

There was no apparent association between the intake of regular coffee, decaffeinated coffee, or tea and the risk of recurrent colorectal adenomas. The relative risks and 95% confidence intervals per cup daily were 0.96 (0.87–1.05) for regular coffee, 0.97 (0.84–1.12) for decaffeinated coffee, and 1.02 (0.83–1.25) for tea. These negative findings were present both overall and for adenomas of the right and left large bowel.

Introduction
Colorectal adenomas (preneoplastic lesions of the large bowel) share many epidemiological characteristics with large bowel cancer, including the importance of diet (1). A diet low in fiber or high in dietary fat is associated with an increased risk of colorectal cancer, a finding that has also been reported (albeit less consistently) for adenomas (2).

A protective effect of coffee on the risk of colorectal neoplasia has been proposed, based on possible effects on cholesterol and bile acid balance (3). Tea may also lower the risk of cancer through the effects of the polyphenols contained in the beverage; these may be antioxidants and may affect the activation and detoxification of carcinogens (4). Many epidemiological studies have found that high coffee intake is associated with a decreased risk of colon (but not rectal) cancer (reviewed in Refs. 5 and 6). Tea drinking, on the other hand, seems unrelated to colon cancer risk, but in some studies it has been inversely associated with rectal cancer (5, 6). These associations have been poorly investigated for adenomas. We report here the relationship between coffee and tea intake, and recurrence of adenomas in an adenoma prevention clinical trial, which permitted the study of incident adenomas in subjects undergoing uniform colonoscopic surveillance.

Subjects and Methods
Subjects were participants in a clinical trial of β carotene and vitamins C and E in combination as preventive agents against recurrence of large bowel adenomas. The main results of the study have been published; the antioxidants had no impact on adenoma recurrence (7). Participants were recruited at six clinical centers in the United States; all participants had at least one large bowel adenoma excised within the 3 months before entry, with no known polyps left in the bowel. Patients with familial polyposis, a history of invasive colorectal cancer, or malabsorption syndromes were not included. Also excluded were subjects with conditions that could conceivably be worsened by vitamin C or E, such as renal calculi or thrombophlebitis. After entry, patients were enrolled in a 3-month placebo run-in to assess adherence to study procedures; 864 subjects were randomized. By protocol, both the qualifying endoscopy and an exam 1 year later left the subjects with a “clean colon,” cleared of known polyps in the bowel. The end point of the study was adenomas found after the year 1 exam, up to and including an exam at year 4.

A standardized food frequency questionnaire (with portion-size choices; Ref. 8) was administered at study entry and at the end of the trial. This requested information regarding usual diet over the past year and included 100 food items (plus open-ended questions for frequently eaten, unlisted foods). Nutrient intake was estimated using software developed by the National Cancer Institute in connection with the questionnaire. An individual’s questionnaire was deemed acceptable if no more than 50 food items on the questionnaire were skipped, at least three foods per day were eaten on average, and the estimated total caloric intake was between 500 and 5000 calories daily. To stabilize the dietary estimates and obtain information regarding diet during the period in which the adenomas were formed, the average of the baseline and year 4 nutrient intakes were used as the dietary exposure in the principal analyses. Associations with the baseline diet alone were also investigated.

Odds ratios of having at least one adenoma between the year 1 and the year 4 exam were used as the measure of association; these were calculated with unconditional logistic
regression (9). Models were fit after first adjusting for age (linear term), sex, study center, and the time interval between year 1 and year 4 colonoscopies. More detailed models included further adjustment for total caloric intake, dietary fat and dietary fiber [included as the residuals of the regression on calories (10)], cigarette smoking (never, former, or current smoker), and alcohol intake (linear term).

Of the originally randomized patients, 44 died before the end of the study, 32 elected not to have the follow-up colonoscopy, 19 could not be examined because they had moved or were too ill, and 18 did not complete the final colonoscopy for unknown reasons, leaving 751 patients who completed the trial. Of these, 666 completed satisfactory baseline and year 4 dietary questionnaires and are included in this analysis. The age and sex distribution and the adenoma recurrence risk of subjects who did not provide complete dietary information was similar to that of these 666 subjects (data not shown).

Results
The subjects included in the analysis were predominantly (78%) male, with a mean age at study entry of 61.3 (SD, 8.3). The overall adenoma recurrence risk was 37%. Over the course of the study, the changes in the reported diet and beverage intake of the subjects were small (Table 1) and similar in those with and without a recurrence (data not shown).

There was no clear relationship between adenoma risk and consumption of coffee or tea (Table 2). The multivariate odds ratios for intake of coffee and decaffeinated coffee were slightly lower than 1.0, but these small reductions were consistent with chance. Even the heaviest drinkers had relative risks close to 1.0, and there were no apparent trends of risk with increasing amounts usually drunk. The odds ratios for tea intake tended to be slightly higher than 1.0, but these elevations were also consistent with chance. Similar results for both coffee and tea were obtained for the right and left bowel (Table 1), for the end point of adenomas 0.5 cm or greater in estimated diameter, and when baseline intake was used for coffee, tea, and diet (data not shown).

These effects of coffee and tea were examined in a series of subgroup analyses: within sexes, above and below median subject age, above and below median fat and fiber intake, alcohol drinkers and nondrinkers, and smokers and nonsmokers. Generally, there were no indications of meaningful differences (data not shown). However, there was a suggestion that coffee might have an inverse association with adenoma recurrence among subjects who drank alcohol (odds ratio per cup per day, 0.88; 95% CI, 0.78–1.00), whereas among those who did not, coffee conferred a slight increase in risk (odds ratio per cup per day, 1.15; 95% CI, 0.97–1.37). The corresponding linear interaction term was not statistically significant, however (P = 0.51). There were also suggestions of an interaction by age of the effect of tea. For subjects younger than the median age (63 years), tea was associated with an increase in risk (odds ratio per cup per day, 1.32; 95% CI, 0.96–1.81). Among those over 63, tea exerted a nonsignificant inverse association with risk (odds ratio per cup per day, 0.81; 95% CI, 0.61–1.08). The corresponding interaction term achieved borderline statistical significance (P = 0.04). A similar interaction was seen with respect to dietary fat. Among subjects whose calorie-adjusted dietary fat was below the median, tea had an inverse relationship with risk (odds ratio per cup per day, 0.79; 95% CI, 0.57–1.09), whereas among those with calorie-adjusted fat above the median, tea tended to increase risk (odds ratio per cup per day, 1.22; 95% CI, 0.90–1.66). The corresponding interaction term was not statistically significant, however (P = 0.23).

Discussion
We found no relationship between drinking coffee or tea and the recurrence of adenomas in a population at high risk for these neoplasms. The substantial sample size brought considerable statistical stability to the risk estimates; it is unlikely that by chance we overlooked a substantial effect. Suggestions of inverse associations in subgroups were found, but they were accompanied by indications of modest increases in risk in other groups. Without prior hypotheses, it seems most reasonable to ascribe these interactions to chance.

There is little previous research regarding consumption of coffee or tea and the risk of large bowel adenomas. In a Japanese study of sigmoid adenomas in males, drinking coffee (brewed or instant) tended to be associated with a reduced risk, but the results were consistent with chance (11). Nonsignificantly lower coffee consumption in adenoma cases than in controls was also reported in a case-control study among patients presenting for endoscopic evaluation (12). A marked reduction in risk of bowel adenomas associated with drinking 8 or more cups of coffee per day was reported from a screening trial in Denmark (13). In contrast, a study from New York City reported a nonsignificant increase in risk with coffee consumption of 6 cups per day or more (14). Data regarding colorectal cancer risk and coffee intake are more extensive and are more consistent (although not entirely so) in suggesting an inverse relationship with colon cancer risk (reviewed in Ref. 5).

A few studies have considered the association between tea consumption and adenoma risk. There were nonsignificant suggestions of a protective association of the intake of green tea with the risk of sigmoid adenomas among Japanese males (11). However, studies in England and Denmark found, if anything, a greater tea intake among adenoma cases than controls (12, 13). The data regarding the association of tea intake with cancer of the colon and rectum does not suggest any effect in the colon. In the rectum, however, there have been indications of an inverse association with cancer risk (5).

### Table 1 Characteristics of subjects (means ± SD)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>At study entry</th>
<th>At study completion</th>
<th>Correlation&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coffee intake, cups/day</td>
<td>1.5 ± 2.3</td>
<td>1.6 ± 2.2</td>
<td>0.52</td>
</tr>
<tr>
<td>Decaffeinated coffee intake, cups/day</td>
<td>0.8 ± 1.5</td>
<td>0.7 ± 1.4</td>
<td>0.49</td>
</tr>
<tr>
<td>Tea intake, cups/day</td>
<td>0.4 ± 0.9</td>
<td>0.4 ± 0.9</td>
<td>0.54</td>
</tr>
<tr>
<td>Total caloric intake, Kcal/day</td>
<td>1977 ± 752</td>
<td>2016 ± 756</td>
<td>0.50</td>
</tr>
<tr>
<td>Total fat intake, g/day</td>
<td>87.0 ± 43.2</td>
<td>86.0 ± 41.0</td>
<td>0.52</td>
</tr>
<tr>
<td>Total carbohydrate intake, g/day</td>
<td>204.5 ± 79.1</td>
<td>217.9 ± 82.5</td>
<td>0.43</td>
</tr>
<tr>
<td>Total protein intake, g/day</td>
<td>76.3 ± 29.3</td>
<td>77.3 ± 29.7</td>
<td>0.49</td>
</tr>
<tr>
<td>Total dietary fiber intake, g/day</td>
<td>14.5 ± 7.4</td>
<td>16.5 ± 7.2</td>
<td>0.46</td>
</tr>
</tbody>
</table>

<sup>a</sup>Product moment correlation between measurements at study entry and study completion.
On the whole, the available data show only inconsistent suggestions of a protective effect of coffee on the risk of large bowel adenomas and little indication of a protective effect of tea. Differences between these findings and those for Frank cancer could derive from several sources. The data available regarding adenomas are relatively limited, and conceivably, different findings might emerge after further investigation. Most of the studies regarding adenomas have estimated prevalence odds ratios and therefore are potentially susceptible to distortions from prevalence-incidence bias (15). (For example, an exposure that both causes adenomas and hastens their progression to cancer might not be associated with prevalent adenomas.) Finally, adenomas and cancer could have different risk factors: e.g., coffee or tea might affect late stages of carcinogenesis, such as the transition from a small adenoma to cancer.

Our study has several important strengths. Patients were endoscoped at prescribed intervals, largely avoiding bias introduced when patients seek medical care or screening for reasons related to exposures and adenoma outcomes. Patients had two colonoscopies with the removal of all known polyps before the start of the risk period; in contrast to most previous adenoma research, the adenomas observed were truly incident, and we were able to avoid potential problems associated with prevalent lesions. A large number of subjects were observed, and the study had adequate power to investigate moderately strong relationships.

There are also several limitations to our analysis. All of the subjects in the study had at least one adenoma during their lifetime; we analyzed risk factors for subsequent neoplasms. Consequently, it is possible that our findings do not describe risk factors for the occurrence of adenomas more generally (in particular, first adenomas). Also, the end points observed in this study were generally small polyps. These neoplasms are relatively common and probably do not confer a markedly increased risk of colorectal cancer (16). In a multistage process such as cancer, it is possible that the epidemiology of these adenomas will not directly clarify the etiology of cancer. However, since most cancers probably begin as small adenomas, these data do describe the earliest visible stages of carcinogenesis. In general, the epidemiology of these lesions seems to resemble that of colorectal cancer itself (1).

We administered two food frequency questionnaires during our study: at entry into the trial and at year 4. Because it is not entirely clear when dietary influences on adenoma formation actually occur, it is correspondingly not clear which of the two dietary questionnaires would most appropriately be used to assess possible risk factors. We chose the average of the baseline and year 4 assessments, because the reference period for these questionnaires bracketed the risk period of the study. In any case, baseline data led to the same findings as the averages. Moreover, there was no evidence of biased reporting of diet: the changes in reported diet between baseline and year 4 were small and very similar in those with and without a recurrence.

In summary, we found no evidence of a protective effect of coffee or tea on the risk of large bowel adenomas. If these exposures affect the risk of colorectal cancer, it is likely that they do so at later stages of carcinogenesis than those represented by small adenomas.

### References


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