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Tea Consumption and Risk of Cancer of the Colon and Rectum

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Abstract: *The association between tea consumption and risk of colon and rectal cancers was investigated in a population-based case-control study conducted in Iowa (United States). Colon (*n = 685*) and rectal (n = 655) cancer cases age 40–85 yr were identified through the Iowa Surveillance, Epidemiology, and End Results (SEER) Cancer Registry (86% response rate); controls (*n = 2,434*) were frequency matched by sex and 5-yr age group (80% response rate). The usual adult consumption of tea (hot and iced), along with other information including dietary data, was self-reported using a mailed questionnaire. Total tea consumption (cups/day) was categorized as none (reference category), low (<3.1), medium (3.1–5.0), and high (>5.0), with cut points for tea consumers based on the 75th and 90th percentiles of use among controls. Unconditional logistic regression was used to estimate the odds ratios (ORs) and 95% confidence intervals. There was no association between total tea consumption and colon cancer (ORs = 1.0, 1.1, 1.3, and 0.7) or rectal cancer (ORs = 1.0, 0.9, 1.4, and 1.0) after adjustment for age, sex, education, physical activity, smoking history, and intake of coffee, fiber, and fruits and vegetables. Results were similar when hot tea and iced tea were evaluated individually. Further adjustment for other colorectal cancer risk factors did not alter these results. There was no association with proximal or distal colon cancer. There was also no interaction between tea consumption and any of the dietary variables or total fluid on risk of colon or rectal cancer, with the exception of a suggestive positive association between an increasing frequency of tea consumption and colon cancer risk among current smokers (multivariate ORs = 1.0, 1.4, 2.0, and 1.8;* P *for trend = 0.1), but not among never smokers (multivariate ORs = 1.0, 1.0, 1.1, and 0.4;* P *for trend = 0.3). These data do not support an overall association, either positive or negative, between tea consumption and risk of colon or rectal cancer in this Midwestern US population.*

Introduction

Tea (*camellia sinensis*) is one of the most commonly consumed beverages in the world. Tea contains several polyphenolic compounds with potent antioxidant properties that exert a protective effect in a number of experimental tumor models, including colorectal cancer (1–3). Whereas most experimental studies used green tea extracts, black tea, the form most commonly consumed in Western countries, also appears to show chemopreventive activities for a variety of tumor models (3–5). In contrast, epidemiological data are more limited and, to date, are equivocal regarding a protective association of tea consumption, black or green, and cancer risk in general (1,2).

Epidemiological studies have generally found no consistent association between risk of colorectal cancer and black tea consumption (6–20). However, of ≥15 studies evaluating the association of black tea and colorectal cancer, most have used relatively weak study designs, including ecological (difficulty extrapolating group data to individuals), hospital-based case-control (controls likely to be biased in tea consumption), or cohort studies with mortality end points (inability to distinguish effects on cancer incidence vs. survival). After these studies are excluded, there are only two population-based case-control studies and four cohort studies of colon or rectal cancer incidence, only two of which were conducted in the United States (Iowa and Hawaii), supporting the need for additional studies using stronger study designs to evaluate this association. Furthermore, most prior studies have not distinguished hot tea from iced tea consumption, and polyphenol content can vary between these beverages (21,22).

We evaluated consumption of hot and iced teas (assumed to be predominantly black tea) and risk of colon and rectal cancers in a population-based, case-control study. We were able to control for potential confounding by other colorectal

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cancer risk factors and evaluate potential interactions that have been previously reported or are biologically plausible, including those with age, smoking, dietary factors, and total fluid intake (10,14,19).

Subjects and Methods

Sample Population

This population-based case-control study was conducted between 1986 and 1989 with a major focus on the association of drinking water contaminants and cancer risk at six cancer sites. Further details of the study with regard to colon and rectal cancers are published elsewhere (23), as are the results for tea consumption and risk of bladder and kidney cancer (24). Briefly, incident cases of colon cancer (diagnosed March–December 1987) and rectal cancer (diagnosed January 1986–December 1987) were identified through the Iowa Cancer Registry, which is part of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program (25). After physician consent was obtained to contact cases, a letter was sent to each case or next of kin explaining the study. Eligibility criteria included Iowa residency at diagnosis, age at diagnosis between 40 and 85 yr, histological confirmation of the cancer, and no previous history of malignant neoplasms, excluding nonmelanoma skin cancers. The participation rate for the 685 colon cancer cases was 86%; 95 (14%) were proxy respondents. The participation rate for the 655 rectal cancer cases was also 86%; 115 (18%) were proxy respondents.

A single control series was used in the analysis for both cancer sites. Cases from all six cancer sites were frequency matched to controls by sex and 5-yr age group, with a case-control matching ratio of ~2.3:1. Controls <65 yr of age were selected from the state of Iowa driver's license records, whereas those aged 65–85 yr were selected from rosters of the US Health Care Financing Administration. Both sources have very high coverage of the Iowa population (26,27). The participation rate for the 2,434 controls was 80%; 2 were proxy respondents.

Data Collection

Eligible cases and controls (or their proxies) were contacted by telephone and invited to participate by completing a self-administered, mailed questionnaire. The questionnaire ascertained demographic data, occupational history, smoking history, familial history of cancer in first-degree relatives, and past medical conditions. A 55-item food frequency questionnaire (usual adult consumption) was also included, as well as detailed items regarding adult fluid consumption. Specific questions were asked about the usual adult consumption of iced tea and hot tea (cups/day) as well as coffee and other beverages at home and outside the home. Respondents were specifically asked to report what they had consumed over all their adult years and exclude any changes in the last couple of years. Total beverage consumption was estimated from usual adult fluid intake of drinking water, coffee, tea, fruit juices/drinks, soups, milk, soft drinks, and alcoholic beverages, as previously reported (24).

Subjects reluctant to complete the detailed questionnaire (7.7%) were offered a 15-min abbreviated telephone interview that included information on beverage (including tea) consumption, smoking, and other critical information for the analysis of water quality and cancer risk but excluded the detailed occupational history and food frequency questionnaire.

Statistical Analysis

Of the 3,774 participants who participated in the study, we excluded 102 (2.7%) who were missing data for tea consumption. Hot tea consumption was categorized as none, low (<1.9 cups/day), medium (1.9–3.0 cups/day), and high (>3 cups/day), with cut points for users based on the 75th and 90th percentiles of consumption among controls. Using the same percentiles, iced tea was categorized into no, low (<3.0 cups/day), medium (3–5 cups/day), and high (>5 cups/day) consumption. Because most previous studies did not distinguish hot tea and iced tea, we also created a total tea variable, which was the sum for consumption of hot and iced teas. This variable was categorized into no, low (<3.1 cups/day), medium (3.1–5.0 cups/day) and high (>5.0 cups/day) consumption, again based on the 75th and 90th percentiles of consumption among the controls.

Unconditional logistic regression was used to estimate the odds ratios (ORs) and corresponding 95% confidence intervals (CIs) for the association between tea consumption and risk of colon and rectal cancers. Colon cancer was further subdivided into proximal cancer (cancers of the cecum, ascending colon, hepatic flexure, and transverse colon) and distal cancer (cancers of the splenic flexure, descending colon, and sigmoid colon) and was based on the SEER ICD-O coding of the cancer site (28). Eighteen colon cancer cases were excluded from the subsite analysis, because their subsite was "appendix," "colon, not otherwise specified," or "overlapping lesions of the colon."

ORs were initially adjusted for age and sex. We also evaluated sex-specific models, but there was little heterogeneity in results (data not shown), so only models with both sexes combined are presented. All ORs were then adjusted for confounders in this data set (i.e., factors associated with tea consumption and colorectal cancer risk). Finally, models were fitted that included an extended number of other factors associated with tea consumption or risk factors for colorectal cancer.

We also evaluated the possible modifying effects of age (≤69 and >69 yr), first-degree family history of colorectal cancer (no or yes), smoking (never, former, and current), coffee consumption (no or yes), physical activity (inactive and active), red meat intake (≤5.9 and >5.9 servings/wk), fi-

ber intake (≤16 and >16 g/day), fruit and vegetable intake (≤40.7 and >40.7 servings/wk), and total beverage intake (≤2.6 and >2.6 l/day). All cut points used to create strata were based on the median value of continuous variables of the control series. These factors were evaluated because of their potential to modify the effect of tea consumption on colorectal cancer risk based on epidemiological or laboratory findings.

Results

Table 1 summarizes case-control differences for major colorectal cancer risk factors. Colon cancer cases were slightly heavier, consumed less fruits and vegetables and dietary fiber, and were more likely to have a first-degree family history of colorectal cancer and personal history of colitis than controls; differences were also noted for education level, tobacco use, and leisure physical activity. Similar patterns were noted for rectal cancer cases, although they also consumed less calcium and had more years of chlorinated water use than controls.

Tea consumption was not uncommon in this population, with 43% of the men and 51% of the women in the control group reporting any tea consumption (hot or iced). Equal numbers of men and women used iced tea (36%), whereas hot tea consumption was more common among women (32%) than men (21%). Among controls who drank tea, the median consumption of any tea was 2.0 cups/day. The respective medians for hot and iced teas were 1.0 and 1.3 cups/day, with no difference between men and women for hot tea but a higher median consumption of iced tea for women (2 vs. 1.1 cups/day). There was a weak correlation (Pearson correlation coefficient = 0.18) between consumption of hot and iced teas in the control group. Table 2 summarizes the relation between selected colorectal cancer risk factors and tea consumption in the control population. Greater tea consumption was positively associated with vegetable and fruit intake, fiber intake, total beverage intake, and a higher level of leisure physical activity; there was little evidence for systematic differences across the other risk factors included in Table 2.

After adjustment for age and sex, there was no evidence for a dose-response relation between any type of tea con-

Table 1. Relation of Selected Colorectal Cancer Risk Factors With Case-Control Status, Iowa, 1986–89

Risk Factor	Controls	Colon Cancer Cases		Rectal Cancer Cases	
		Value	*P*	Value	*P*
	Mean ± SD				
Age, yr	68.4 ± 9.9	69.0 ± 9.3	0.1	67.3 ± 10.0	0.01
BMI[a] at age 40 yr, kg/m^2	24.3 ± 3.5	24.8 ± 4.1	0.01	24.9 ± 3.8	0.002
Dietary intake					
Vegetables and fruits, servings/wk	44.0 ± 22.7	42.1 ± 23.1	0.09	43.2 ± 19.6	0.4
Red meat, servings/wk	6.9 ± 5.8	6.9 ± 4.8	0.9	7.0 ± 4.5	0.7
Calcium, mg/day	824 ± 473	800 ± 546	0.3	775 ± 428	0.02
Fiber, g/day	17.1 ± 7.5	15.7 ± 7.4	0.0003	16.4 ± 6.8	0.06
Years of chlorinated water	19.8 ± 18.3	21.1 ± 18.7	0.3	22.7 ± 20.5	0.05
Total beverage l/day	2.8 ± 1.2	2.8 ± 1.6	0.7	2.8 ± 1.5	0.8
	Percent distribution				
Family history of colorectal cancer (1st degree)	8.5	21	0.001	13	0.001
History of colitis	11	22	0.001	30	0.001
Education					
<High school	21	22	0.03	24	0.2
High school	51	56		52	
>High school	28	22		24	
Tobacco use					
Never	45	47	0.01	45	0.2
Former	39	42		42	
Current	16	11		13	
Leisure physical activity					
Inactive	50	55	0.007	55	0.03
Moderately active	30	23		25	
Highly active	20	22		20	
Coffee consumption					
None	13	13	0.1	10	0.2
1.0–1.9 cups/day	21	26		24	
2.0–3.3 cups/day	20	19		21	
3.4–6.0 cups/day	23	22		21	
>6.0 cups/day	23	20		24	

a: Body mass index.

Table 2. Relation of Selected Risk Factors With Level of Tea Consumption Among Controls, Iowa, 1986–89

Factor	Total Tea Consumption,[a] cups/day				*P*
	None (n = 1,297)	<3.1 (n = 840)	3.1–5.0 (n = 148)	>5.0 (n = 108)	
	Mean ± SD				
Age, yr	68.6 ± 9.9	68.6 ± 9.8	66.9 ± 10.6	66.5 ± 10.0	0.04
BMI at age 40 yr, kg/m^2	24.2 ± 3.5	24.4 ± 3.5	24.8 ± 4.0	25.2 ± 3.5	0.1
Dietary intake					
Vegetables and fruits, servings/wk	42.1 ± 23.1	45.4 ± 21.1	48.4 ± 25.6	50.2 ± 22.9	0.0001
Red meat, servings/wk	7.0 ± 5.8	6.6 ± 5.7	7.3 ± 7.4	6.9 ± 4.4	0.5
Calcium, mg/day	826 ± 457	814 ± 496	877 ± 460	824 ± 493	0.6
Fiber, g/day	16.8 ± 7.7	17.2 ± 6.8	18.1 ± 8.0	19.4 ± 9.1	0.006
Years of chlorinated water	20.6 ± 18.6	19.8 ± 18.4	16.1 ± 17.4	16.1 ± 17.2	0.2
Total beverage, l/day	2.6 ± 1.1	2.8 ± 1.0	3.4 ± 1.2	4.5 ± 1.7	0.0001
	Percent distribution				
Family history of colorectal cancer (1st degree)	8	10	8	7	0.6
History of colitis	11	11	9	12	0.9
Education					
<High school	24	18	18	20	0.001
High school	52	50	51	56	
>High school	24	32	31	24	
Tobacco use					
Never	42	50	52	42	0.002
Former	40	38	30	42	
Current	18	12	18	16	
Leisure physical activity					
Inactive	53	47	42	41	0.001
Moderately active	27	33	40	29	
Highly active	20	20	18	30	
Coffee consumption					
None	13	11	15	22	0.001
1.0–1.9 cups/day	18	25	25	24	
2.0–3.3 cups/day	20	23	18	13	
3.4–6.0 cups/day	22	25	23	17	
>6.0 cups/day	27	16	19	24	

a: Cut points for tea consumers based on 75th and 90th percentile distribution of consumption among controls.

sumption (hot, iced, and total) and risk of cancers of the colon (all, proximal, or distal) or rectum (Table 3). Adjustment for potential confounding factors in these data (age, sex, education, leisure physical activity, smoking history, and intake of dietary fiber and fruits and vegetables; see **Methods**) did not materially change the results (Table 3). At the highest levels of tea consumption, there was a weak positive association with hot tea (OR = 1.4, 95% CI = 0.8–2.5) and an inverse association with iced tea (OR = 0.5, 95% CI = 0.2–1.1) and total tea (OR = 0.7, 95% CI = 0.4–1.3), but none of the point estimates was statistically significant. Further adjustment of the associations in Table 3 for body mass index, family history of colorectal cancer, history of colitis, total beverage consumption, years of chlorinated water consumption, and intake of red meat, calcium, and coffee also did not alter the results (data not shown). Adjustment for season of return of the questionnaire (which could influence reporting of tea consumption) also did not alter the results (data not shown).

We next evaluated the interaction between selected colorectal cancer risk factors and tea consumption on the risk of colon and rectal cancers. There was no evidence for an interaction with sex, first-degree family history of colorectal cancer, physical activity, or red meat, fiber, fruit and vegetable, coffee, or total beverage consumption (data not shown). However, there was a suggestive interaction with smoking status for colon, but not rectal, cancer. Among never smokers, there was a suggestive inverse association with tea consumption at the highest level of use, no association of tea consumption among former smokers, and a positive association among current smokers (Table 4). However, the CIs for all point estimates included 1.0, and the trend tests were not statistically significant except for the age/sex model for current smokers.

Discussion

We found little evidence for an association, either positive or negative, between tea consumption and risk of colon or rectal cancer in this Midwestern US population. This was true for hot tea and iced tea consumption, among men and

Table 3. ORs and 95% CIs for Cancer of the Colon (All, Proximal, Distal) and Rectum According to Level of Tea Consumption, Iowa, 1986–89[a]

Tea Consumption,[b] cups/day	Controls	All Colon Cancer				Proximal Colon Cancer				Distal Colon Cancer				Rectal Cancer			
		Cases	OR1	OR2	95% CI	Cases	OR1	OR2	95% CI	Cases	OR1	OR2	95% CI	Cases	OR1	OR3	95% CI
Hot tea																	
None	1,804	462	1	1	Ref	177	1	1	Ref	272	1	1	Ref	466	1	1	Ref
<1.9	407	136	1.2	1.1	0.9–1.4	55	1.2	1.1	0.8–1.7	77	1.2	1.1	0.8–1.7	101	0.9	0.9	0.7–1.2
1.9–3.0	126	32	0.9	0.9	0.6–1.4	12	0.8	0.6	0.3–1.3	19	0.8	0.6	0.3–1.3	45	1.4	1.3	0.9–1.9
>3.0	56	20	1.2	1.4	0.8–2.5	9	1.4	1.6	0.7–3.4	11	1.4	1.6	0.7–3.4	17	1.1	1.1	0.6–1.9
Iced tea																	
None	1,537	405	1	1	Ref	165	1	1	Ref	234	1	1	Ref	410	1	1	Ref
<3.0	693	209	1.1	1.1	0.9–1.3	80	1.1	1.0	0.7–1.4	119	1.1	1.0	0.7–1.4	178	0.9	1.0	0.8–1.2
3.0–5.0	99	28	1.1	1.1	0.7–1.8	7	0.7	1.0	0.4–2.1	20	0.7	1.0	0.4–2.1	23	0.8	1.0	0.6–1.6
>5.0	64	8	0.5	0.5	0.2–1.1	1				6	0.2	0.2	0.03–1.5	18	1.0	1.0	0.5–1.8
Total tea																	
None	1,297	321	1	1	Ref	130	1	1	Ref	185	1	1	Ref	335	1	1	Ref
<3.1	840	261	1.2	1.1	0.9–1.4	101	1.1	1.0	0.8–1.4	151	1.1	1.0	0.8–1.4	214	1.0	0.9	0.8–1.2
3.1–5.0	148	48	1.2	1.3	0.9–1.9	13	0.8	0.9	0.5–1.8	33	0.8	0.9	0.5–1.8	52	1.3	1.4	1.0–2.1
>5.0	108	20	0.7	0.7	0.4–1.3	9	0.8	0.9	0.9–1.9	10	0.8	0.9	0.4–1.9	28	1.0	1.0	0.6–1.5

a: OR1 adjusted for age and sex, OR2 adjusted for age, sex, education, smoking history (never, former, current ≤20 cigarettes/day, current >20 cigarettes/day), leisure physical activity, and intake of dietary fiber and fruits and vegetables with accompanying 95% confidence interval (CI); OR3 adjusted for the above factors plus coffee consumption with accompanying 95% CI. OR, odds ratio; Ref, reference.

b: Cut points for tea consumption based on 75th and 90th percentile distribution of consumption among controls.

Table 4. ORs and 95% CIs for Cancer of the Colon According to Level of Total Tea Consumption, Stratified by Smoking History, Iowa, 1986–89[a]

	Total Tea Intake, cups/day				
	None	<3.1	3.1–5.0	>5.0	*P* (trend)
Never smokers					
n, cases/controls	143/547	129/418	25/77	6/46	
OR1	1	1.1	1.2	0.5	0.7
OR2	1	1.0	1.1	0.4	0.3
95% CI	Ref	0.7–1.3	0.6–1.9	0.2–1.2	
Former smokers					
n, cases/controls	145/523	106/319	15/45	9/45	
OR1	1	1.1	1.2	0.7	0.9
OR3	1	1.2	1.3	0.8	0.6
95% CI	Ref	0.9–1.7	0.7–2.5	0.4–1.8	
Current smokers					
n, cases/controls	33/227	26/103	8/26	5/17	
OR1	1	1.7	1.9	2.1	0.3
OR3	1	1.4	2.0	1.8	0.1
95% CI	Ref	0.7–2.8	0.7–5.4	0.5–6.1	

a: OR1 adjusted for age and sex; OR2 adjusted for age, sex, education, leisure physical activity, and intake of dietary fiber and fruits and vegetables; OR3 adjusted for the above factors plus pack-years of smoking.

women, and for proximal and distal colon cancer. Multivariate adjustment did not alter these results. There was also no interaction between tea consumption and other colorectal cancer risk factors, including sex, age, family history of the disease, physical activity, and consumption of red meat, fiber, fruit and vegetables, or coffee. A possible exception to the latter findings was a weak positive association of tea consumption and risk of colon cancer among current smokers, which was not seen in former smokers (no association) or never smokers (suggestive inverse association at highest level of consumption).

Strengths of this study include the population-based design, relatively large sample size, high participation rates, assessment of hot and iced teas consumed at home and at work, and availability of data on a large number of potential confounders. There are also several limitations to this study that warrant comment. We did not have data on type of tea consumed. However, during the time frame of this study (late 1980s), the vast majority of tea consumed in Iowa is expected to have been black tea (1,2). A more serious limitation is the lack of method of tea preparation; specifically, whether the tea was made strong or weak and, for iced tea, whether it was brewed, sun tea, or instant tea. Recent studies have shown that the total polyphenol and total flavonoid content are highest in brewed hot tea (1 tea bag/cup) brewed ≥2 min (reference level), followed by brewed iced tea (~22% lower), hot tea brewed 1 min (~36% lower), sun tea (~41% lower), dilute hot tea (0.5 bag/cup, ~66% lower), and instant tea (~85% lower) (21,22). In addition, instant tea has low or no catechins, theaflavins, or gallic acid but does have significant quantities of thearubigens.

As with all case-control studies, there is also a potential for selection and recall bias. Given the population-based design and high participation rates of cases and controls, severe selection bias seems unlikely. With respect to recall bias, the lack of a wide knowledge of the potential chemoprotective effects of tea in the 1980s makes it unlikely that cases would differentially report tea consumption relative to controls. The presence of gastrointestinal symptoms in colorectal cancer patients could lead to changes in tea consumption (particularly hot tea), leading to bias away from the null. However, a standardized questionnaire was used for data collection, and participants were told to report usual adult consumption and to exclude any changes in the last couple of years, reducing the likelihood of this potential bias. In contrast, nondifferential misclassification of exposure due to inaccurate reporting of tea consumption would be expected to bias our results toward the null.

A mechanistic interest in the protective effects of tea consumption has focused on the polyphenolic compounds in tea (1). Most laboratory research has focused on the major polyphenols in green tea extracts, including the flavanols (catechins, 30–40% dry weight tea) and flavonols (5–10% of dry weight). These compounds have been shown to be protective against tumor initiation and progression in a variety of experimental tumor models (1–3), including some (29,30), but not all (31), models of colon tumorigenesis. Mechanisms by which tea might protect against carcinogenesis include modulation of carcinogen activation and detoxification enzymes, suppression of nitrosation reactions, inhibition of heterocyclic amine production, general antioxidant properties due to the ability to scavenge free radicals, and anti-inflammatory effects (1–3).

Black tea, in contrast to green tea, contains a different profile of polyphenols due to fermentation. In particular, the flavanols and some of the other polyphenols are oxidized to theaflavins and thearubigens, whereas the other components are virtually unchanged (32). The theaflavins and thearubi-

gens, although less well characterized, also appear to have chemopreventive properties (3–5). The major flavanols in green tea may be oxidized in vivo into these compounds (5), suggesting that they might possess parallel biological properties. However, an older literature suggests that black tea consumption may promote cancer. Black tea is mutagenic in some in vitro assays (33,34). Black tea also contains small amounts of tannins, and subcutaneous injection of tannin induced tumors at the injection site in a mouse model, although there was no effect in rats treated with a total aqueous extract from black tea, a more relevant model system (35). A comprehensive review by the International Agency for Research on Cancer concluded that there was inadequate evidence for the carcinogenicity of tea in experimental animals or humans (36).

Our results of no overall association of black tea and risk of colon or rectal cancers are in agreement with most published studies (6–17,19,20). However, most of these studies had design limitations (see **Introduction**). Of two published population-based case-control studies, a study from Sweden (n = 352 cases and 512 controls) found no association of black tea with colon cancer and an inverse association with rectal cancer (OR = 0.56 for 2 cups/day vs. none, 95% CI = 0.34–0.90) (12). The other study, from Japan (n = 132 cases and 578 controls), found a positive association for black tea consumption and colon cancer (OR = 2.5 for daily vs. less than daily consumption, 95% CI = 1.2–5.3) and no association for rectal cancer (17). In contrast, the Japanese data revealed an inverse association for green tea consumption with colon cancer but no association with rectal cancer.

Of four published cohort studies of tea and colon cancer incidence, three (10,13,14) found no association for colon cancer. The single positive study was a cohort analysis of the α-Tocopherol, β-Carotene (ATBC) trial (19), which found a positive association between black tea consumption and risk of colon cancer. The ATBC cohort was conducted in >29,000 male smokers between the ages of 50 and 69 yr (avg >37 pack-yr at baseline), and during the follow-up from 1985 to 1993, 111 colon cancers were identified. Compared with those who did not consume tea, men who drank <1 cup/day [relative risk (RR = 1.40, 95% CI = 0.84–2.33) or ≥1 cup/day (RR = 2.09, 95% CI = 1.34–3.26)] were at increased risk of colon cancer after adjustment for age, intervention group, calcium intake, body mass, and occupational physical activity. Our positive finding of increased risk of colon cancer among smokers is consistent with the ATBC trial results, although the association in our study was somewhat weaker and not statistically significant. Thus chance remains a potential explanation. In addition, from a mechanistic perspective, one might predict a protective effect of tea consumption in smokers, since green tea has been shown to decrease micronucleus formation in peripheral lymphocytes of smokers (37), as well as the frequency of sister chromatid exchange in mitogen-stimulated peripheral lymphocytes of smokers (38). However, these data may not generalize to black tea.

For rectal cancer, the incidence studies have mainly reported no association (13,14,19), although a cohort study of men of Japanese ancestry in Hawaii reported a graded, positive association with black tea consumption (10). Compared with never users of black tea, men using tea two to four times per week (RR = 2.0), almost daily (RR = 2.1), and once a day or more (RR = 4.2) were at elevated risk of rectal cancer.

Only the ATBC study (19) has evaluated the association of tea consumption and risk of proximal or distal colon cancer, and a positive association was reported for both subsites, consistent with their overall findings for colon cancer. We found no association of tea consumption with either subtype. We were not able to evaluate subtypes of colon cancer among smokers because of limited sample size.

In summary, we found no association of black tea, either hot or iced, and risk of colon or rectal cancer. There was no effect modification by dietary or other lifestyle factors, with the possible exception of smoking, where current smokers who drank tea were at modestly elevated risk of colon cancer, although risk estimates were not precise. Whereas the latter finding is congruent with a single study that was conducted among male smokers, it will require verification in other studies.

Acknowledgments and Notes

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References

1. Katiyar SK and Mukhtar H: Tea in chemoprevention of cancer: epidemiologic and experimental studies. *Int J Oncol* **8,** 221–238, 1996.
2. Yang CS and Wang ZY: Tea and cancer. *JNCI* **85,** 1038–1049, 1993.
3. Ho C-T, Chen C-W, Wanasundara UN, and Shahidi F: Natural antioxidants from tea. In *Natural Antioxidants: Chemistry, Health Effects, and Applications*, Shahidi F (ed). Champaign, IL: Am Oil Chem Soc, 1997, pp 213–223.
4. Yang G, Wang ZY, Kim S, Liao J, Seril DN, et al.: Characterization of early pulmonary hyperproliferation and tumor progression and their inhibition by black tea in a 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone-induced lung tumorigenesis model with A/J mice. *Cancer Res* **57,** 1889–1894, 1997.
5. Shi ST, Wang ZY, Smith TJ, Hong JY, Chen WF, et al.: Effects of green tea and black tea on 4-(methylnitrosamino)-1-(3-pyridyl)-1-

butanone bioactivation, DNA methylation, and lung tumorigenesis in A/J mice. *Cancer Res* **54,** 4641–4647, 1994.
6. Higginson J: Etiological factors in gastrointestinal cancer in man. *JNCI* **37,** 527–545, 1966.
7. Dales L, Friedman G, Ury H, Grossman S, and Williams S: A case-control study of relationships of diet and other traits to colorectal cancer in American blacks. *Am J Epidemiol* **109,** 132–144, 1978.
8. Watanabe Y, Tada M, Kawamoto K, Uozumi G, Kajiwara Y, et al.: A case-control study of cancer of the rectum and colon (Japan). *Nippon Shokakibyo Gakkai Zasshi* **81,** 185–193, 1984.
9. Phillips R and Snowdon D: Dietary relationships with fatal colorectal cancer among Seventh-Day Adventists. *JNCI* **74,** 307–317, 1985.
10. Heilbrun LK, Nomura A, and Stemmermann GN: Black tea consumption and cancer risk: a prospective study. *Br J Cancer* **54,** 677–683, 1986.
11. Olsen J and Kronborg O: Coffee, tobacco, and alcohol risk factors for cancer and adenoma of the large intestine. *Int J Epidemiol* **22,** 398–402, 1993.
12. Baron JA, Gerhardsson de Verdier M, and Ekbom A: Coffee, tea, tobacco, and cancer of the large bowel. *Cancer Epidemiol Biomarkers Prev* **3,** 565–570, 1994.
13. Zheng W, Doyle TJ, Kushi LH, Sellers TA, Hong C-P, et al.: Tea consumption and cancer incidence in a prospective cohort study of postmenopausal women. *Am J Epidemiol* **144,** 175–182, 1996.
14. Goldbohm RA, Hertog MGL, Brants HAM, van Poppel G, and van den Brandt PA: Consumption of black tea and cancer risk: a prospective cohort study. *JNCI* **88,** 93–100, 1996.
15. Stocks P: Cancer mortality in relation to national consumption of cigarettes, solid fuel, tea and coffee. *Br J Cancer* **24,** 215–225, 1970.
16. Tajima K and Tominaga S: Dietary habits and gastro-intestinal cancers: a comparative case-control study of stomach and large intestinal cancers in Nagoya, Japan. *Jpn J Cancer Res* **76,** 705–716, 1985.
17. Kato I, Tominaga S, Matsuura A, Yoshii Y, Shirai M, et al.: A comparative case-control study of colorectal cancer and adenoma. *Jpn J Cancer Res* **81,** 1101–1108, 1990.
18. La Vecchia C, Negri E, Franceschi S, D'Avanzo B, and Boyle P: Tea consumption and cancer risk. *Nutr Cancer* **17,** 27–31, 1992.
19. Hartman TJ, Tangrea JA, Pietinen P, Malila N, Virtanen M, et al.: Tea and coffee consumption and risk of colon and rectal cancer in middle-aged Finnish men. *Nutr Cancer* **31,** 41–48, 1998.
20. Kinlen LJ, Willows AN, Goldblatt P, and Yudkin J: Tea consumption and cancer. *Br J Cancer* **58,** 397–401, 1988.
21. Hakim IA, Weisgerber UM, Harris RB, Balentine D, van-Mierlo CAJ, et al.: Preparation, composition and consumption patterns of tea-based beverages in Arizona. *Nutr Res* **20,** 1715–1724, 2000.
22. Hakim IA, Hartz V, Harris RB, Balentine D, Weisgerber UM, et al.: Reproducibility and relative validity of a questionnaire to assess intake of black tea polyphenols in epidemiological studies. *Cancer Epidemiol Biomarkers Prev* **10,** 667–678, 2001.
23. Hildesheim ME, Cantor KP, Lynch CF, Dosemeci M, Lubin J, et al.: Drinking water source and chlorination by-products. II. Risk of colon and rectal cancers. *Epidemiology* **9,** 29–35, 1998.
24. Bianchi GD, Cerhan, JR, Parker AS, Putnam SD, See WA, et al.: Tea consumption and risk of bladder and kidney cancers in a population-based case-control study. *Am J Epidemiol* **151,** 377–383, 2000.
25. Ries LAG, Kosary CL, Hankey BF, Miller BA, and Clegg LX: *SEER Cancer Statistics Review, 1973–1996*. Bethesda, MD: National Cancer Institute, 1999.
26. Hartge P, Cahill JI, West D, Hauck M, Austin D, et al.: Design and methods in a multi-center case-control interview study. *Am J Public Health* **74,** 52–56, 1984.
27. Lynch CF, Logsden-Sackett N, Edwards SL, and Cantor KP: The driver's license list as a population-based sampling frame in Iowa. *Am J Public Health* **84,** 469–472, 1994.
28. Percy C, Van Holten V, and Muir C: *International Classification of Diseases for Oncology*, 2nd ed. Geneva, Switzerland: World Health Organization, 1990.
29. Yamane T, Hagiwara N, Tateishi M, Akachi S, Kim M, et al.: Inhibition of azoxymethane-induced colon carcinogenesis in rat by green tea polyphenol fraction. *Jpn J Cancer Res* **82,** 1336–1339, 1991.
30. Narisawa T and Fukaura Y: A very low dose of green tea polyphenols in drinking water prevents *N*-methyl-*N*-nitrosourea-induced colon carcinogenesis in F344 rats. *Jpn J Cancer Res* **84,** 1007–1009, 1993.
31. Hirose M, Hoshiya T, Akagi K, Takahashi S, Hara Y, et al.: Effects of green tea catechins in a rat multi-organ carcinogenesis model. *Carcinogenesis* **14,** 1549–1553, 1993.
32. Millin DJ: Factors affecting the quality of tea. In *Quality Control in the Food Industry*, Herschdoerfer SM (ed). London: Academic, 1987, pp 127–160.
33. Nagao M, Fujita Y, Wakabayashi K, Nukaya H, Kosuge T, et al.: Mutagens in coffee and other beverages. *Environ Health Perspect* **67,** 89–91, 1986.
34. Ariza RR, Dorado G, Barbancho M, and Pueyo C: Study of the causes of direct-acting mutagenicity in coffee and tea using the Ara test in *Salmonella typhimurium*. *Mutat Res* **201,** 89–96, 1988.
35. Kapadia GJ, Paul BD, Chung EB, Ghosh B, and Pradhan SN: Carcinogenicity of *Camellia sinensis* (tea) and some tannin-containing folk medicinal herbs administered subcutaneously in rats. *JNCI* **57,** 207–209, 1976.
36. International Agency for Research on Cancer: *IARC Monographs on the Evaluation of the Carcinogenic Risks to Humans. Coffee, Tea, Mate, Methylxanthines and Methylglyoxal*. Lyon, France: Int Agency Res Cancer, 1991.
37. Xue KX, Wang S, Ma GJ, Zhou P, Wu PQ, et al.: Micronucleus formation in peripheral-blood lymphocytes from smokers and the influence of alcohol- and tea-drinking habits. *Int J Cancer* **50,** 702–705, 1992.
38. Shim JS, Kang MH, Kim YH, Roh JK, Roberts C, et al.: Chemopreventive effect of green tea (*Camellia sinensis*) among cigarette smokers. *Cancer Epidemiol Biomarkers Prev* **4,** 387–391, 1995.