Short Communication

Tea Consumption and Risk of Breast Cancer

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Abstract

Objective: **The purpose of our study was to examine the association of regular tea consumption with the risk of breast cancer in a large population-based case-control study from the United States.**
Methods: **Five thousand and eighty-two women with incident breast cancer between the ages of 20 and 74 years old from population-based cancer registries in Wisconsin, Massachusetts, and New Hampshire and 4,501 age-matched controls from lists of licensed drivers and Medicare beneficiaries completed a structured telephone interview that included information on usual tea consumption 5 years prior to the interview and other breast cancer risk factors. Logistic regression was used to obtain covariate-adjusted odds ratios and 95% confidence intervals associated with quantities of tea consumed.**
Results: **Tea consumption was not related to breast cancer risk overall (*P* for trend = 0.18). However, when stratified by age, an inverse association was observed among women less than 50 years: those consuming three or more cups per day had a 37% reduced breast cancer risk when compared with women reporting no tea consumption (age and study site–adjusted odds ratios, 0.63; 95% confidence intervals, 0.44-0.89; *P* = 0.01) with a significant test for trend (*P* = 0.01). The inverse association noted among younger women was consistent for *in situ* and invasive breast cancer, and for ductal and lobular breast cancer. All results were unchanged after adjustment for established risk factors.**
Conclusion: **We observed evidence to support a potential beneficial influence for breast cancer associated with moderate levels of tea consumption (three or more cups per day) among younger women. Further research is needed to confirm this association.** (Cancer Epidemiol Biomarkers Prev 2009;18(1):341–5)

Introduction

Despite advances in early detection and treatment, the breast cancer mortality and morbidity burden remains significantly higher in the United States compared with Asian countries (1, 2). Recent research has attributed some of these differences to variations in the intake of phytochemicals specifically, polyphenols in tea, *Camelia sinensis* (3). Laboratory studies have shown that epigallocatechin gallate in green tea polyphenols (3-12) and theaflavin-3,3′-digallate in black tea polyphenols (12, 13) exert multifunctional inhibitory effects such as suppression of mammary tumors, inhibition of cell proliferation and angiogenesis, induction of apoptosis in 7,12-dimethylbenz(a)anthracene–induced mammary carcinogenesis (5-8), and suppressed proliferation and lipogenesis in MCF-7 breast cancers (9). Most black and green tea extracts strongly inhibited neoplastic transformation in mouse mammary organ cultures, providing evidence of antimutagenic, antiproliferative, and antineoplastic activities (10). Despite indications from laboratory studies, epidemiologic studies on the effects of green and black tea on breast cancer have been inconclusive (14-17). The conflicting results may be attributed to confounding factors that include the use of tobacco, alcohol and other nutrients, and lack of standardization of quantities and compositions of the tea products consumed. Considering that tea is the most common beverages consumed worldwide (3), with increasing consumption in the United States (18), and given the low toxicity profile of these beverages, green and black tea products are attractive candidates for breast cancer chemoprevention (19). We examined data from a large, population-based, case-control study to shed further light on the potential role of tea consumption on breast cancer risk.

Subjects and Methods

The case-control study has been described in detail in previous reports (20). In brief, cases were women with a first primary breast cancer diagnosis identified from population-based cancer registries in Wisconsin, Massachusetts, and New Hampshire according to protocols approved by institutional review boards at each site. Eligible cases included women who resided in Wisconsin, Massachusetts (excluding metropolitan Boston), or

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New Hampshire, were ages 20 to 74 years at diagnosis, had a listed telephone number, and were verified by self-report to have a driver's license for those less than 65 years of age. Approximately 80% of eligible case women were successfully interviewed. Within each state, controls frequency-matched to cases within 5-year age strata were randomly selected from lists of licensed drivers if less than 65 years of age, or a roster of Medicare beneficiaries compiled by the Centers for Medicare and Medicaid Services (formerly the Health Care Financing Administration) if 65 years of age and older. To be eligible as a control, a woman was required to have a listed telephone number, no personal history of breast cancer and, if less than 65 years of age, a driver's license. Approximately 76% of eligible case subjects were successfully interviewed. The present analysis is based on the 5,082 case women (3,944 invasive/1,138 *in situ*) and 4,501 control women interviewed between 1998 and 2001 during the era of the study when questions on tea consumption were incorporated in the study interview.

Information on tea consumption was ascertained in a structured telephone interview. Women were asked how often, on average, they consumed a cup of black or green tea, not herbal tea, approximately 5 years before the breast diagnosis in cases, or a comparable reference period in controls. Women were permitted to report their usual consumption per day, week, month, or year. The interview also elicited information on known and suspected breast cancer risk factors including reproductive and menstrual history, alcohol consumption, physical activity, height, weight, exogenous hormone use, family history of breast cancer, screening mammography history, and demographic characteristics.

Among the 5,082 cases and 4,501 controls that were asked to report usual tea consumption, data were missing for 23 cases and 15 controls. After excluding these women, a total of 5,059 cases and 4,486 controls were included in the present analysis, of whom 98% were Caucasian. Unconditional logistic regression was used to estimate odds ratios (OR) and Wald 95% confidence intervals (CI) for the risk of breast cancer associated with tea consumption. All models included terms for referent age (in 5-year categories) and study site (Wisconsin, Massachusetts, or New Hampshire). We considered potential confounding by established breast cancer risk factors including menopausal status/age at menopause, parity/age at first birth, body mass index, recency of postmenopausal hormone use, education, alcohol consumption, physical activity, history of benign breast disease, and history of screening mammogram in the 5 years before the reference age. However, results were essentially unchanged after further adjustment for these factors and only age/residence-adjusted results are shown. Tests for linear trend were done by including an ordinal variable for cups per day (0, <1, 1<2, 2<3, 3 or more) in logistic regression models that also included terms for age and state of residence, and in multivariate models, all other covariates.

Results

The characteristics of cases and controls included in the analysis are shown in Table 1. When compared with controls, cases were younger at menarche, were more educated, were of lower parity and older age at first child birth, and were more likely to have a first-degree family history of breast cancer, to have ever used postmenopausal hormones, and to have had a mammogram in the preceding 5 years.

Associations according to consumption of tea (cups per day) are shown in Table 2. Overall, 44.7% of cases and 45.7% of controls reported any tea consumption 5 years before the reference date. We observed a weak inverse association with a greater number of cups consumed per day (P for trend = 0.18). However, the inverse association was limited to younger women (ages 50 years and younger): those reporting three or more cups per day 5 years prior to the interview had a 37% reduced breast cancer risk when compared with women reporting no tea consumption (age and study site–adjusted OR, 0.63; 95% CI, 0.44-0.89; P = 0.01) and the test for trend with increasing cups per day was statistically significant (P = 0.01). No similar inverse association was observed in women ages 51 to 65 years (P trend = 0.56) or in older women (P trend = 0.50; Table 2). An inverse association with greater tea consumption was also observed among premenopausal women (median age, 45.0 years in cases and 44.8 years in controls), although the results were somewhat attenuated (age and study site–adjusted OR, 0.71; 95% CI, 0.50-0.1.01 for three or more cups per day versus zero cups per day), with a borderline test for trend (P = 0.05).

When examined according to breast cancer subtypes, the inverse relationship noted with greater tea consumption among younger women (ages up to 50 years) was consistent for *in situ* and invasive breast cancer, and for ductal and lobular invasive breast cancer (data not shown), although stratified results were based on small numbers. The age and study site–adjusted OR for high tea consumption (three or more cups per day) was 0.41 (95% CI, 0.20-0.83) for *in situ* breast cancer (test for trend = 0.01); 0.71 (95% CI, 0.49-1.02) for invasive breast cancer (test for trend = 0.08); 0.69 (95% CI, 0.48-0.99) for invasive ductal breast cancer (test for trend = 0.03), and 0.33 (95% CI, 0.10-1.07) for invasive lobular breast cancer (test for trend = 0.03). Data were too sparse to consider associations for *in situ* breast cancer according to histology. No significant relationships according to tea consumption were observed in older women, regardless of breast cancer subtype (data not shown).

All results were essentially unchanged after adjusting for other established breast cancer risk factors (data not shown): the multivariate-adjusted OR for three or more cups per day in women ages 50 years or younger was 0.62 (95% CI, 0.43-0.88) for all breast cancers combined (test for trend = 0.004), 0.38 (95% CI, 0.19-0.78) for *in situ* breast cancer (test for trend = 0.002), and 0.71 (95% CI, 0.49-1.02) for invasive breast cancer (test for trend = 0.05).

Discussion

In this large case-control study, we observed no overall association between tea consumption and breast cancer risk, although results were consistent with a possible inverse association for younger-onset breast cancer. The results among younger women were consistent regardless of breast cancer subtypes defined by breast cancer stage (invasive and *in situ*) and histology (ductal and

Table 1. Selected characteristics of breast cancer cases and controls: Collaborative Breast Cancer Study (1998-2001)

Characteristic	Cases (n = 5,059)	Controls (n = 4,486)	P*
	No. (%)	No. (%)	
Education			0.012
Less than high school	308 (6.1)	320 (7.2)	
High school graduate	1,969 (39.1)	1,769 (39.6)	
Some college	1,309 (26.0)	1,208 (27.1)	
College graduate	1,448 (28.8)	1,168 (26.2)	
Age at menarche (y)			<0.0001
<13	2,323 (46.6)	1,911 (43.1)	
13 to <14	1,434 (28.8)	1,239 (27.9)	
≥14	1,229 (24.7)	1,286 (29.0)	
Parity			<0.0001
Nulliparous	692 (13.7)	506 (11.3)	
1-2	2,243 (44.3)	1,836 (41.0)	
3-4	1,672 (33.1)	1,610 (35.9)	
≥5	452 (8.9)	534 (11.9)	
Age at first birth (y)			<0.0001
<20	760 (17.4)	814 (20.5)	
20-24	1,639 (37.6)	1,618 (40.8)	
25-29	1,305 (29.9)	1,042 (26.3)	
≥30	657 (15.1)	494 (12.5)	
Age at menopause (y) †			<0.0001
<45	403 (18.7)	496 (24.7)	
45-49	589 (27.5)	547 (27.2)	
50-54	861 (40.0)	748 (37.2)	
≥55	298 (13.9)	221 (11.0)	
Menopausal status			0.1
Premenopausal	1,962 (38.8)	1,674 (37.3)	
Postmenopausal	2,750 (54.4)	2,531 (56.4)	
Unknown	347 (6.9)	281 (6.3)	
Use of postmenopausal hormone therapy †			0.0017
Never	3,100 (61.7)	2,883 (64.6)	
Former	264 (5.3)	255 (5.7)	
Current	1,659 (33.0)	1,322 (29.6)	
First-degree family history of breast cancer			<0.0001
No	3,845 (78.4)	3,796 (86.8)	
Yes	1,058 (21.6)	579 (13.2)	
Body mass index (kg/m^2)			0.36
<25	2,418 (48.2)	2,085 (46.9)	
25 to <30	1,575 (31.4)	1,410 (31.7)	
≥30	1,021 (20.4)	949 (21.4)	
Screening mammography history ‡			<0.0001
Never	747 (14.9)	625 (14.1)	
Less than annual	1,354 (27.1)	1,690 (38.1)	
At least annual	2,904 (58.0)	2,126 (47.9)	
State			
Wisconsin	3,128 (61.8)	2,507 (55.9)	
Massachusetts	1,435 (28.4)	1,418 (31.6)	
New Hampshire	496 (9.8)	561 (12.5)	

*χ^2 test for differences in cases and controls.
†Among postmenopausal women only.
‡For the 5-y time period before the reference age.

lobular), although the number of younger women consuming large quantities of tea (three or more cups per day) was limited in all analyses. Our results provide some support for the hypothesis that regular tea consumption, particularly at moderately high levels, might reduce breast cancer risk in younger women.

Our results are consistent with some, although not all, previous research on the possible association of tea consumption and breast cancer risk. In a meta-analysis including 13 studies, Sun et al. (3) examined populations in eight countries and provided summary results for tea consumption overall, and for green tea and black tea, separately, in relation to breast cancer risk. For black tea, which most likely comprised most of the tea consumed in the current study of primarily Caucasian women, the combined results from the eight case-control studies showed a modest inverse association between consumption and risk of breast cancer (OR, 0.91; 95% CI, 0.84-0.98), whereas combined results in five cohort studies showed a modest increase in risk associated with higher levels of black tea intake (OR, 1.15; 95% CI, 1.02-1.31), variously defined as any daily consumption to a minimum of five cups per day. For green tea, results indicated a significantly reduced risk of breast cancer for highest versus non/lowest intake (OR, 0.78; 95% CI, 0.61-0.98); high intake in these studies ranged from

Table 2. Relative risk of breast cancer according to tea consumption by age: Collaborative Breast Cancer Study (1998-2001)

Tea consumption	≤50		51-65		>65		Total	
	Case/control	OR (95% CI)	Case/control	OR (95% CI)	Case/control	OR (95% CI)	Case/control	OR (95% CI)
0 cups/d	1,186/1,015	1.00 Ref	1,306/1,140	1.00 Ref	306/281	1.00 Ref	2,798/2,436	1.00 Ref
<1 cup/d	475/431	0.95 (0.81-1.11)	757/625	1.07 (0.94-1.22)	189/161	1.09 (0.83-1.42)	1,421/1,217	1.03 (0.93-1.13)
1 to <2 cups/d	150/147	0.91 (0.71-1.16)	215/209	0.94 (0.76-1.16)	67/65	1.06 (0.72-1.57)	432/421	0.94 (0.81-1.09)
2 to <3 cups/d	67/70	0.86 (0.61-1.22)	117/97	1.11 (0.83-1.47)	30/37	0.87 (0.52-1.45)	214/204	0.97 (0.79-1.18)
≥3 cups/d	59/82	0.63 (0.44-0.89)	109/93	1.08 (0.81-1.45)	26/33	0.78 (0.45-1.35)	194/208	0.86 (0.70-1.05)
P trend		0.01		0.56		0.50		0.18

NOTE: ORs and 95% CIs adjusted for age and study site.

approximately one-half to five cups per day. Results of the meta-analysis are difficult to interpret given the wide range of, and often modest definitions used for, high intake (as low as one or fewer cups per day; refs. 15-17) in the component studies. As the half-life of tea catechins is only 6 to 8 hours in the plasma (8, 21), consistent intake and higher minimum levels of exposures might be necessary for a protective association to be observed. Although the frequency of tea consumption throughout the day was not available in our study, a clear inverse association was evident only for daily consumption of three or more cups.

Our study suggests that a benefit of tea consumption might be limited to younger-onset breast cancer. Age-specific breast cancers may vary greatly in clinical behavior, histopathologic characteristics and molecular alterations, and may develop through different etiologic pathways (22, 23). In laboratory studies, the bioactive components of tea have multifunctional inhibitory effects such as inhibition of cell proliferation and angiogenesis, and induction of apoptosis via different pathways (5-10) in addition to effects on ovarian steroidogenesis. These factors may have contributed to the observed variations in associations with tea consumption according to age (our data was too sparse to distinguish whether the interaction was limited to age or menopausal status). To our knowledge, only one previous study examined associations according to age/menopausal status. In a hospital-based case-control study, Baker and colleagues found no clear associations between intake of black tea and breast cancer risk overall (13); however, they reported a stronger protective effect in a subsample of premenopausal women with lobular histology. This finding is consistent with the current results in which we observed a suggestion of a stronger inverse association for high levels of tea consumption in lobular (OR, 0.33) than ductal (OR, 0.69) young-onset breast cancer.

Our study had a few limitations to consider. Although response rates were reasonably high, we cannot exclude the possibility of selection bias in the data. Furthermore, we could not distinguish black from green tea consumption. However, given the years of data collection (1998 and 2001), and that the great majority of women were Caucasian and residents of nonmetropolitan areas in the United States, we assume that results apply mainly to the consumption of black tea. As green tea may offer greater benefit (3, 10, 14), the current results may underestimate possible chemopreventive effects of tea on breast carcinogenesis. Random measurement error may also have attenuated associations. Recall bias is a possibility if cases and controls reported tea consumption differentially based on their prior beliefs about the benefits of tea on health. Although we cannot rule out recall bias in the data, it is unclear how such bias would account for the age-specific associations suggested in the present data. Finally, we had no information on the steroid receptor status of breast cancers among case women in the study, which some research suggests, might influence associations of breast cancer with tea consumption (24).

The findings in this large case-control study suggest a potential inverse association of tea consumption with younger-onset breast cancer, particularly for the lobular subtype. Further studies are needed to explore tea consumption patterns according to age and breast cancer histologic subtypes.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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