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GREEN TEA AND RISK OF BREAST CANCER IN ASIAN AMERICANS

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There is substantial *in vitro* and *in vivo* evidence implicating tea polyphenols as chemopreventive agents against various cancers. However, epidemiologic data obtained from mainly Western populations are not supportive of a protective role of tea, mainly black tea, in the etiology of breast cancer. Much less is known about the relationship between green tea and breast cancer risk. During 1995–1998, we conducted a population-based, case-control study of breast cancer among Chinese, Japanese and Filipino women in Los Angeles County and successfully interviewed 501 breast cancer patients and 594 control subjects. Detailed information on menstrual and reproductive factors; dietary habits, including intake of black and green tea; and other lifestyle factors was collected. Risk of breast cancer was not related to black tea consumption. In contrast, green tea drinkers showed a significantly reduced risk of breast cancer, and this was maintained after adjusting for age, specific Asian ethnicity, birthplace, age at menarche, parity, menopausal status, use of menopausal hormones, body size and intake of total calories and black tea. Compared to women who did not drink green tea regularly (*i.e.,* less than once a month), there was a significant trend of decreasing risk with increasing amount of green tea intake, adjusted odds ratios being 1.00, 0.71 (95% confidence interval [CI] 0.51–0.99) and 0.53 (95% CI 0.35–0.78), respectively, in association with no, 0–85.7 and >85.7 ml of green tea per day. The significant inverse association between risk of breast cancer and green tea intake remained after further adjustment for other potential confounders, including smoking; alcohol, coffee and black tea intake; family history of breast cancer; physical activity; and intake of soy and dark green vegetables. While both green tea and soy intake had significant, independent protective effects on breast cancer risk, the benefit of green tea was primarily observed among subjects who were low soy consumers. Similarly, the protective effect of soy was primarily observed among subjects who were nondrinkers of green tea. In summary, our results point to an important role of both green tea and soy intake in relation to breast cancer risk in Asian-American women.

Key words: *breast cancer; green tea; Asian Americans*

Tea is derived from the leaf of the plant *Camellia sinensis.* Approximately 20% of the world's tea is consumed as green tea, which is popular in Japan and parts of China, whereas 80% of tea is consumed as black tea, which is the main tea beverage in the United Kingdom, United States and Europe. Leaves meant for green tea are picked by the same method as those picked for black tea. In the processing of green tea, fresh tea leaves are steamed or heated immediately after harvest, resulting in minimal oxidation of the naturally occurring polyphenols in the tea leaves. In the processing of black tea, the tea leaves are dried and crushed upon harvesting to encourage oxidation, which converts the indigenous tea polyphenols (primarily catechins and gallocatechins) to other polyphenols (mainly theaflavins and thearubigens). The oxidation of catechins to theaflavins and thearubigens gives it the characteristic red-brown color.[1,2]

There has been substantial interest in the role of tea in the risk of breast cancer since the mid-1980s.[3,4] In studies conducted in Western countries, where almost all tea consumed is black, the risk of breast cancer was not influenced by black tea consumption.[3–7] Although no association between green tea and breast cancer risk was reported in the cohort study of atomic bomb survivors,[8,9] 2 hospital-based studies from Japan suggested that green tea may favorably influence the risk of breast cancer recurrence.[10,11]

We report here an investigation of the risk of breast cancer in relation to both green and black tea consumption among Asian-American women who participated in a population-based, case-control study in Los Angeles County.[12]

MATERIAL AND METHODS

This population-based, case-control study included women who were identified as Chinese, Japanese or Filipino, between the ages of 25 and 74 years at the time of diagnosis of an incident breast cancer on or after 1 January 1995. Cases were identified through the Los Angeles County Cancer Surveillance Program, the population-based cancer registry that is a member of the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) program and the statewide California Cancer Registry. Of the 871 Chinese, Japanese and Filipino women identified, 523 were interviewed (22 interviews were incomplete and consequently excluded from the final analysis), 244 declined to be interviewed (46 physicians declined to give permission to contact the patient, and 198 patients declined), 11 had died and 93 could not be located or had moved outside of Los Angeles County. Five hundred and ninety-four controls were selected from the neighborhoods where cancer cases resided at the time of diagnosis, using a well-established, standard algorithm to identify neighborhood controls that the University of Southern California Epidemiology Program has used in numerous case-control studies.[13] This algorithm defined a specified sequence of houses to be visited in the neighborhood where the case lived at diagnosis. We sought to interview as the control the first eligible resident in the sequence. If the first eligible control subject refused to participate, the second eligible one in the sequence was asked, and so on. Letters were left when no one was home, with follow-up by mail and telephone (if a number could be determined). Controls were frequency-matched to cases on specific Asian ethnicity and 5-year age group. On average, a suitable control was identified after walking 67 houses. Sixty-eight percent of controls interviewed represented the first eligible control identified (18% of controls had one refusal and 14% had 2 or more refusals).

In-person interviews were conducted using a standardized, structured questionnaire that covered demographic characteristics and migration history, menstrual and reproductive history, body size, physical activity and diet history. The diet questionnaire was developed by Dr. J. Hankin (University of Hawaii) and modeled after the validated diet instrument used in the Multiethnic Cohort

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Study being conducted in Hawaii and Los Angeles.[14,15] Dietary intake during the year prior to cancer diagnosis (for cases) or during the past year (for controls) was determined. In our food-frequency questionnaire, separate questions were asked regarding intake of black tea, green tea, herbal tea, regular coffee and decaffeinated coffee. The frequency of intake (never, 1 or 2 times/month, 3 times/month, 1–3 times/week, 4–6 times/week, once/day, 2 times/day and 3 or more times/day) for each beverage and the usual amounts (in units of one-half or 1 measuring cup) drunk each time were determined (one-half measuring cup is equivalent to 1 tea cup, which contains 4 fluid ounces or 120 ml). Measuring cups were displayed during the interview to facilitate estimation of amounts. We estimated consumption (in ml/day) of green and black tea separately and for the 2 teas combined. Because herbal teas are not processed from leaves of *C. sinensis,*[3] we did not include herbal tea in our composite index of tea.

We used ANOVA and analysis of covariance to compare among control subjects mean levels of tea intake between different categories of age, Asian ethnicity, birthplace and other potential predictors and to derive statistical significance levels (*p* values) (Table I). Based on 501 cases and 594 controls, we calculated odds ratios (ORs, relative risk estimates), their corresponding 95% confidence intervals (95% CIs) and *p* values by conditional logistic regression methods, with matched sets defined jointly by age (<39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70+ years), specific Asian ethnicity (Chinese, Japanese, Filipino) and birthplace (US-born, non-US-born). We conducted our case-control comparisons of tea consumption in 2 ways. First, we treated each type of tea separately so that the baseline group was comprised of individuals who were nondrinkers of that specific type of tea. Second, nondrinkers of black and green tea served as the baseline group, and they were compared to women who drank black tea or green tea. All regression models also included as covariates education (less than high school, high school, some college, college graduate, postgraduate), age at menarche (<12, 12–13, 14–15, 16+ years), parity (never pregnant, ever pregnant but no live births, 1+ live birth; categorical), current body mass index (in quartiles), total caloric intake (continuous), menopausal status (premenopausal, postmenopausal) and use of menopausal hormones (never, former, current) (referred to as model A adjusted ORs in Table II). Age at first pregnancy was not included in the baseline model since there was no significant improvement in the fit of the regression model with this variable. We considered additional lifestyle factors, including smoking habits; intake of alcohol, coffee, soy and dark leafy greens; family history of cancer; and physical activity, as they were found to be associated with tea consumption in this study (Table I) and in some previous studies or emerged as significant risk factors in this population[12,16] (referred as model B adjusted ORs in Table II). All *p* values are 2-sided.

RESULTS

This analysis included 501 breast cancer patients (160 Chinese, 146 Japanese and 195 Filipinos) and 594 controls (228 Chinese, 175 Japanese, 191 Filipinos). As we have reported previously,[12,16] cases and controls were similar in terms of birthplace, education, age at menarche and body size but cases were significantly more likely to be nulliparous, had fewer live births, had lower consumption of soy and were less physically active than controls (data not shown).

Table I shows the age-adjusted mean daily intake of black and green tea separately and the 2 teas combined by demographic and various lifestyle factors. Among controls, the respective average intake of black tea, green tea and the 2 teas combined was 107.2, 93.9 and 201.0 ml/day (120 ml/day is equivalent to 4 fluid ounces/day or 1 tea cup), respectively. Intake of black tea was almost 3 times higher in Chinese (181.1 ml/day) than in Japanese (66.3 ml/day) and Filipino (56.6 ml/day) women. Non-US-born Chinese and Filipino women had much higher black tea intake than their respective US-born counterparts, but this was not true of Japanese-American women. Intake patterns of black tea did not differ significantly by other lifestyle factors after adjustment for Asian ethnicity and birthplace (Table I).

Intake of green tea was highest in Japanese (159.6 ml/day), intermediate in Chinese (102.0 ml/day) and lowest in Filipino (24.0 ml/day) women. In each Asian ethnic group, intake of green tea was at least 2-fold higher among non-US-born women compared to US-born women. Intake of green tea also tended to

TABLE I – AGE-ADJUSTED MEANS OF BLACK TEA AND GREEN TEA INTAKE (IN ML/DAY) AMONG 594 CONTROL WOMEN BY VARIOUS CHARACTERISTICS, LOS ANGELES COUNTY

	Black tea	Green tea
Race and birthplace[1]		
Chinese		
US-born	105.6	58.3
Non-US-born	189.2	114.5
Japanese		
US-born	69.6	116.6
Non-US-born	62.1	239.1
Filipino		
US-born	31.6	4.1
Non-US-born	57.9	24.6
p for ethnicity effect	<0.0001	<0.0001
p for birthplace effect	0.22	0.0003
Regular coffee (ml/day)[2]		
None	81.1	103.2
<0–≤120	106.3	112.7
>120–≤240	78.4	99.0
>240	101.5	98.1
p	0.65	0.96
Smoking status[2]		
Never[3]	94.1	122.7
Ever	81.0	52.0
p	0.57	0.001
Alcohol[2]		
No[4]	91.8	111.6
Yes	82.7	53.7
p	0.71	0.01
Adult soy (mg isoflavones/1,000 kcal)[2]		
≤ 1.79	75.5	42.7
>1.79–6.24	120.9	58.6
>6.24–12.68	93.8	141.9
>12.68	65.8	149.3
p	0.13	<0.0001
Dark leafy green vegetables[2,5]		
≤3 ×/week	66.8	77.3
4+/week	95.6	109.9
p	0.11	0.09
Body mass index at reference date[2, 6]		
≤20.9	65.1	111.5
>20.9 to ≤22.8	99.8	97.6
>22.8 to ≤24.95	91.5	125.6
>24.95	96.7	68.9
p	0.50	0.10
Lifetime physical activity[2,7]		
No	58.6	92.3
1–19 years	85.1	106.0
20 + years	101.3	96.5
p	0.47	0.84
Family history of breast cancer[2, 8]		
No	95.0	99.7
Yes	52.3	115.6
p	0.19	0.61

[1]Adjusted for age (≤39, 40–44, 45–49, 50–54, 60–64, 65–69, 70+ years). –[2]Adjusted for age (≤39, 40–44, 45–49, 50–54, 60–64, 65–69, 70+ years), Asian ethnicity and birthplace (Chinese US-born, Chinese non-US-born, Japanese US-born, Japanese non-US-born, Filipino US-born, Filipino non-US-born). –[3]*Never-smoker* is defined as smoking fewer than 100 cigarettes in a lifetime. –[4]*No alcohol* is defined as drinking fewer than 26 drinks/year. –[5]Intake during adolescence. –[6]Calculated as weight in kilograms divided by square of height in meters. –[7]Calculated by accumulating all years in which the subject reported any recreational physical activity of at least 1 hr/week. –[8]In mothers and sisters.

TABLE II – RISK OF BREAST CANCER IN ASSOCIATION WITH INTAKE OF TEA AND COFFEE, LOS ANGELES COUNTY

	Cases	Controls	Adjusted OR[1] (95% CI)	Adjusted OR[2] (95% CI)
Black tea (ml/day)[3]				
Non-black tea drinker	202	230	1.00	1.00
>0 to 85.7	189	228	1.04 (0.77–1.40)	1.02 (0.76–1.39)
>85.7	110	135	1.08 (0.76–1.54)	1.13 (0.78–1.62)
p_{trend}			0.65	0.55
Green tea (ml/day)[4]				
Non-green tea drinker	299	303	1.00	1.00
>0–85.7	123	168	0.71 (0.51–0.99)	0.74 (0.52–1.04)
>85.7	79	122	0.53 (0.35–0.78)[5]	0.61 (0.40–0.93)
p_{trend}			0.001	0.01
Non-tea drinker	138	131	1.00	1.00
Black tea only	161	172	1.00 (0.71–1.42)	0.96 (0.67–1.37)
Green tea only	64	99	0.57 (0.36–0.90)	0.58 (0.36–0.93)
Black and green tea	138	191	0.69 (0.47–1.00)	0.73 (0.49–1.09)
p (3 df)			0.03	0.08
Non-tea drinker	138	131	1.00	1.00
Black tea only				
≤85.7 ml/day	112	108	1.09 (0.74–1.60)	1.03 (0.70–1.53)
>85.7 ml/day	49	64	0.84 (0.51–1.36)	0.81 (0.49–1.34)
Green tea only				
≤85.7 ml/day	32	41	0.75 (0.42–1.33)	0.73 (0.40–1.32)
>85.7 ml/day	32	58	0.44 (0.25–0.78)	0.47 (0.26–0.85)
Black and green tea				
≤85.7 ml/day	55	88	0.65 (0.41–1.03)	0.62 (0.38–1.00)
>85.7 ml/day	83	103	0.71 (0.46–1.10)	0.84 (0.53–1.32)
p (6 df)			0.05	0.12
Herbal tea[3,4]				
None	361	419	1.00	1.00
Yes	140	174	0.88 (0.65–1.19)	0.93 (0.69–1.27)
p_{trend}			0.40	0.67
Regular coffee (ml/day)[3,4]				
None	193	224	1.00	1.00
>0–120	96	86	1.18 (0.80–1.73)	1.16 (0.78–1.72)
>120–≤240	107	130	0.93 (0.65–1.32)	0.90 (0.63–1.29)
>240	105	153	0.80 (0.56–1.14)	0.77 (0.53–1.12)
p_{trend}			0.18	0.14
Decaffeinated coffee[3,4]				
None	343	431	1.00	1.00
Yes	158	162	1.06 (0.79–1.43)	0.98 (0.72–1.33)
p_{trend}			0.69	0.88
Regular and decaffeinated coffee (ml/day)[3,4]				
None	135	154	1.00	1.00
>0–120	94	102	0.91 (0.61–1.36)	0.91 (0.60–1.38)
>120 to ≤ 240	120	141	0.86 (0.59–1.26)	0.80 (0.55–1.19)
>240	152	196	0.81 (0.56–1.18)	0.77 (0.52–1.13)
p_{trend}			0.26	0.14

[1]Conditional logistic regression models with matched sets defined jointly by age (≤39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70+ years), Asian ethnicity (Chinese, Japanese, Filipino) and birthplace (US-born, non-US-born) were employed. Education, age at menarche, pregnancy, current body mass index, total caloric intake, menopausal status and use of menopausal hormones were included as covariates in all models. –[2]Further adjusted for intake of soy (≤1.79, >1.79–6.24, >6.24–12.68, >12.68 mg isoflavones/day), dark green vegetables (≤3 times *vs.* 4+ times/week), smoking history (no/yes), alcohol intake (no/yes), physical activity (0, 1–19, 20+ years), and family history of breast cancer (no/yes). In analysis on tea, coffee intake (0, >0–120, >120–240, >240 ml/day) was also included. –[3]Intake of green tea was included in these models. –[4]Intake of black tea was included in these models. –[5]We further categorized green tea intake of >85.7 ml into >85.7–209.4 ml and >209.4 ml; the respective ORs were 0.41 (95% CI 0.21–0.81) and 0.58 (95% CI 0.37–0.89) compared to non-green tea drinkers.

be higher among never-smokers (*i.e.,* fewer than 100 cigarettes lifetime), non-alcohol drinkers (fewer than 26 drinks per year) and high (above median) consumers of soy after adjustment for birthplace and Asian ethnicity (χ^2 adjusted p values < 0.05). Green tea intake was not significantly influenced by intake of other dietary factors, including red meat, processed meat, poultry, shellfish/fish or milk (data not shown) or by intake of coffee, physical activity pattern or family history of breast cancer (Table I).

Risk patterns by tea intake among cases and controls are shown in Table II. Risk of breast cancer did not differ between black tea drinkers and non-black tea drinkers. In contrast, green tea drinkers showed a significantly reduced risk of breast cancer compared to non-green tea drinkers even after adjusting for age, Asian ethnicity, birthplace, age at menarche, parity, total caloric intake, body size, menopausal status and use of menopausal hormones. This significant inverse association between green tea and risk remained unchanged after adjusting for black tea intake ($p_{trend} = 0.001$). Compared to women who did not drink tea (either black or green) regularly (*i.e.,* less than once a month), risk of breast cancer was lowest among those who drank green tea only (OR = 0.57, 95% CI 0.36–0.90), intermediate among those who drank both green and black tea (OR = 0.69, 95% CI 0.47–1.00) and unchanged among those who drank black tea only (OR = 1.00, 95% CI 0.71–1.42) after adjustment for the covariates mentioned above. The reduced risk associated with green tea only remained statistically significant after further adjustment for other lifestyle factors, including physical activity; family history of breast cancer; smoking; and intake of alcohol, coffee, soy and dark leafy greens (adjusted OR = 0.58, 95% CI 0.36–0.93). Risk of breast cancer was not related to intake of herbal tea, regular coffee or decaffeinated coffee (Table II).

The association between breast cancer risk and intake of green tea was examined separately by various subgroups, including Asian ethnicity, place of birth, smoking, alcohol use and intake of coffee (Table III). In each subgroup analysis, risk of breast cancer was consistently reduced among women who drank green tea. The risk reduction associated with green tea was statistically significant in Japanese, alcohol drinkers and daily coffee drinkers (Table III). Risk of breast cancer was not significantly lowered among women who drank black tea in these subgroup analyses (data not shown).

Table IV shows the risk of breast cancer in relation to the combined effects of intake of green tea and intake of soy during adolescence and adult life; this summary index of soy intake has been strongly associated with breast cancer risk.[12] The protective effect of green tea was influenced by dietary soy level. Similarly, the protective effect of soy was dependent on green tea intake. Specifically, the protective effect of soy on breast cancer risk was clearly observed only among non-green tea drinkers and *vice versa.* However, green tea intake offered no further protection among high soy consumers and *vice versa.* High intake of soy alone, green tea alone or both factors together was associated with a statistically significant 40–50% reduction in breast cancer risk (Table IV). Similar patterns of results were observed when we considered adult soy intake and intake of green tea (data not shown).

DISCUSSION

Our case-control study was designed specifically to identify lifestyle determinants that influence risk of breast cancer among Asian-American women in Los Angeles County. Although previous studies have investigated the influence of black tea[3–7,17–22] and green tea[8,9] in relation to the risk of developing breast cancer, very few studies have examined the separate effects of black and green tea in the same study population.[8] Our results in Asian-American women suggest that the inverse association with tea is apparent primarily for green tea. This pattern of risk reduction was consistently observed in each of the 3 Asian ethnic groups studied, in US-born women and migrants, in ever-smokers and never-smokers, in alcohol drinkers and nondrinkers and in daily coffee drinkers and non-daily coffee drinkers. Risk of breast cancer was not statistically associated with black tea intake in any of the subgroup analyses.

TABLE III – RISK OF BREAST CANCER IN ASSOCIATION WITH INTAKE OF GREEN TEA BY ASIAN ETHNICITY, BIRTHPLACE, SMOKING, ALCOHOL USE AND INTAKE OF COFFEE

	Cases/ controls	Non-green tea drinker	Green tea drinker Adjusted OR[1] (95% CI)
Asian ethnicity			
Chinese	160/228	1.00	0.92 (0.55–1.53)
Japanese	146/175	1.00	0.38 (0.19–0.77)
Filipino	195/191	1.00	0.58 (0.31–1.10)
Birthplace			
US-born	126/163	1.00	0.52 (0.25–1.08)
Non-US-born	375/431	1.00	0.71 (0.49–1.04)
Smoker			
Never-smoker	382/468	1.00	0.72 (0.50–1.03)
Ever-smoker	108/124	1.00	0.41 (0.16–1.06)
Alcohol			
Nondrinker	422/492	1.00	0.74 (0.52–1.05)
Drinker	68/99	1.00	0.20 (0.06–0.66)
Coffee drinker			
Nondaily	193/224	1.00	0.72 (0.42–1.22)
Daily	308/369	1.00	0.58 (0.38–0.90)

[1]Conditional logistic regression models with matched sets defined jointly by age (≤39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70+ years), Asian-ethnicity (Chinese, Japanese, Filipino) and birthplace (US-born, non-US-born) were employed. Education, age at menarche, pregnancy, current body mass index, menopausal status, use of menopausal hormones, intake of soy (≤ 1.79, > 1.79–6.24, >6.24–12.68, >12.68 mg isoflavones/day), dark green vegetables (≤3 times *vs.* 4+ times/week), smoking history (no/yes), alcohol intake (no/yes), coffee intake (0, >0–120, > 120–240, > 240 ml/day), physical activity (0, 1–19, 20+ years), family history of breast cancer (no/yes) and intake of black tea (0, > 0–85.7, > 85.7 ml) were included as covariates. In analyses that were stratified by specific variables, the specific stratifying variable was excluded accordingly.

Previous case-control[17–22] and cohort[5–7] studies conducted in Western populations have found no association between tea consumption and risk of breast cancer. Because Western populations drink mainly black tea, the influence of green tea was not examined in these studies. The role of green tea in relation to risk of breast cancer was investigated in a Japanese cohort study. In an analysis of 270 breast cancer cases identified in a cohort of atomic bomb survivors in Hiroshima and Nagasaki, Nagano *et al.*[9] reported no association between breast cancer risk and green tea intake. Compared to women who drank green tea 0–1 times/day, relative risks of 1.2 and 1.0 were found in association with drinking green tea 2–4 times and 5+ times/day, respectively. In another analysis, which included a larger number of primary breast cancers ($n = 427$) in the same cohort, Key *et al.*[8] found no significant association between breast cancer risk and intake of either green or black tea (see below for a possible explanation of the differences in results between the Japanese cohort and our study). A few studies have also investigated the role of green tea in relation to risk of breast cancer recurrence. Two studies conducted in Japan suggested that green tea consumers with stage I or II breast cancer experienced a lower risk of recurrence than women with low daily intake of green tea.[10,11] The comparison was between very high daily *vs.* lower daily green tea intake in these studies (5 or more cups/day *vs.* 4 or fewer cups/day in one study;[10] 3 or more cups/day *vs.* 0–2 cups/day in another study[11]). Better understanding of the amount of green tea needed to confer a beneficial effect on breast cancer is needed. Although some 50% of the Asian-American controls in our study were at least monthly drinkers of green tea, only 21% drank green tea at least 5 times/week. Thus, the level of green tea intake among drinkers in this Los Angeles population was still 4–5 times lower than that in Japan, where the usual intake is several cups of green tea per day (approx. 400–500 ml/day).[23] In addition to the amount of tea consumption, the concentrations of tea polyphenols consumed will likely vary, depending on the type of tea and preparation methods. Geographic area, growing conditions and preparation methods, including the amount of tea used, temperature and brewing time, are known to influence the levels of tea polyphenols.[24,25]

Our study strengthens the overall evidence on green tea because a large number of potential dietary and nondietary risk factors were adjusted for, whereas only nondietary potential confounders were considered in one of the previous studies.[9] Tea drinking in Asian populations, as in Western populations, is associated positively and negatively with certain lifestyle habits.[5] Tea drinking (particularly green tea) was very strongly associated with soy intake (Table I). Our results suggest that risk of breast cancer is significantly influenced by intake of both green tea and soy. Interestingly, the inverse association between breast cancer risk and green tea intake was found primarily among women who were low consumers of soy during both adolescence and adult life (Table IV). Similarly, the reduced risk associated with high soy intake during adolescence and adult life was observed primarily among non-green tea drinkers (Table IV). If our results on the joint effects of green tea and soy on breast cancer risk can be confirmed, they may explain, in part, the lack of association between breast cancer risk and intake of soy and green tea in the Japanese cohort study[8,9] since levels of both soy and green tea tended to be high in the Japanese population. One interpretation of this dietary soy/green tea relationship with breast cancer risk is that the 2 chemopreventive agents share anticarcinogenic pathways and there may be a threshold effect on risk from these mechanistically similar agents. Antioxidation may be one such common pathway. Tea polyphenols[1,24,25] as well as isoflavones and their metabolites are powerful antioxidants.[26,27] There is corroborative evidence for this

TABLE IV – RISK OF BREAST CANCER IN ASSOCIATION WITH INTAKE OF GREEN TEA AND SOY

Soy intake during adolescence/ adult life[1]	Non-green tea drinker		Green tea drinker	
	Case/ control	OR[2] (95% CI)	Case/ control	OR[2] (95% CI)
Both low	154/126	1.00	36/56	0.45 (0.26–0.78)
Low/high	79/74	0.81 (0.52–1.27)	61/75	0.52 (0.31–0.85)
Both high	59/102	0.40 (0.24–0.66)	105/159	0.41 (0.25–0.65)

[1]Soy intake during adolescence: low intake was defined as less than weekly intake; high intake was defined as weekly or more frequent. Adult soy intake: low intake was defined as ≤6.24 mg isoflavones/1,000 kcal; high intake was defined as >6.24 mg isoflavones/1,000 kcal.[12] –[2]Conditional logistic regression models with matched sets defined jointly by age (≤39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70+ years), Asian ethnicity (Chinese, Japanese, Filipino) and birthplace (US-born, non-US-born) were employed. Education, age at menarche, pregnancy, current body mass index, menopausal status, use of menopausal hormones and black tea intake were included as covariates.

antioxidant model from another study of ours, in which presence of urinary green tea polyphenols was linked to reduced risk of gastric and esophageal cancers.[2] In that prospective cohort study of Chinese men in Shanghai, the inverse association between urinary epigallocatechin and risk of gastric and esophageal cancers was observed only among subjects with low serum carotenes (below population median), suggesting that the anticarcinogenic activity of tea and the carotenoids may be closely related to their shared antioxidant properties.[2]

Results from the present study suggest no significant association between intake of black tea and breast cancer risk, but we cannot rule out a small beneficial effect in association with high intake. We observed a nonsignificant reduced risk (relative risk = 0.81) among women who were high consumers of black tea (>85.7 ml/day) compared to women who were non-tea drinkers (Table II). Reasons for a stronger cancer-protective effect of green tea but not black tea are not well understood. In studies on the inhibition of cancer formation by tea in animal models, the effective components appear to be catechins, theaflavins, thearubigens and caffeine. Although black tea contains all 3 classes of compounds, its catechin content is one-third to one-fourth that of green tea.[24,28] Thus, the lower catechin content in black tea compared to green tea may help explain the weak cancer-preventive activity of the former. The bioavailability and biologic activities of thearubigens, the major components of black tea, are also not known.[1,24]

There is some supportive evidence in rodent breast cancer models that green tea catechins fed in the diet are associated with a reduction of chemically induced mammary gland carcinogenesis.[29,30] In addition, female rats given green tea as their drinking fluid displayed a significant decrease in carcinogen-induced mammary tumor burden and invasiveness and significantly delayed latency to first tumor.[31] Tea polyphenol may influence breast cancer risk *via* various mechanisms. As mentioned above, the antioxidant properties of tea polyphenols may explain some of the anticarcinogenic activities of tea.[24,25] In addition, both green tea extract and its individual catechin components inhibited breast cancer and vascular endothelial cell proliferation, suppressed breast cancer xenograft size and decreased tumor vessel density.[32,33] In an MCF-7 breast cell-line study, epigallocatechin gallate, a main constituent of the polyphenols, inhibited binding of estrogen with its receptors, suggesting that green tea polyphenols may interfere with estrogen metabolism.[34] Few studies have evaluated the relationship between tea intake and circulating hormone levels, and we are aware of only one study which has analyzed green and black tea separately.[35] In that small study of premenopausal women in Japan, green tea was significantly inversely correlated with circulating follicular estradiol levels. Although black tea was also inversely associated with follicular phase estradiol levels, the relationship was weaker and not statistically significant. However, there was no significant association between luteal phase estradiol levels and intake of green or black tea.[35]

There are several limitations with this case-control study. We were able to interview only 60% of the reported cases. The largest loss was due to refusal by cases (23%) or their physicians (5%) or due to subjects (11%) moving outside of Los Angeles County. This modest interview rate raises several methodologic questions, a critical one being the comparability of interviewed and noninterviewed cases in terms of tea intake. The specificity of our finding with green tea only and not with black tea, herbal tea and coffee is reassuring, though there is no guarantee that some unmeasured difference exists between those interviewed and those not interviewed that could impact our results. A second limitation is that green tea drinking (similarly for soy intake) may be a general marker of Asian lifestyle and degree of acculturation. Although we adjusted for the known potential confounders in this study population, it is possible that residual effects remained that could not be completely controlled. In addition, our questions on prediagnostic tea drinking assessed the typical adult consumption patterns, and we did not ask about lifetime tea-drinking patterns or changes in tea-drinking habits. While we cannot be certain that cases did not change their dietary habits after their cancer diagnosis, we did not find any significant differences in intake of green tea or other dietary factors in relation to time between cancer diagnosis and interview.

In conclusion, our study shows that green tea may act as a chemopreventive agent against breast cancer development. Confirmation of these findings is needed. We also need, in particular, a better understanding of the dose–response relationships since our findings are based on modest amounts of green tea intake. We have found an intriguing interrelationship between intake of green tea and soy that points to the possibility of a shared anticarcinogenic mechanism between these 2 commonly consumed elements in the traditional Asian diet. Further studies designed to sort out definitively the separate and joint effects of green tea and soy intake on breast cancer risk in each of the Asian ethnic groups will provide insight regarding their respective roles in breast health.

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