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Jasmine tea consumption and upper gastrointestinal cancer in China

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Abstract

Epidemiological data on green/jasmine tea and esophageal as well as gastric cancer are limited and inconclusive. In order to study the effect of jasmine tea in upper gastrointestinal (UGI) cancers, we evaluated 600 esophageal squamous cell carcinoma (ESCC), 598 gastric cardia adenocarcinoma (GCA), and 316 gastric non-cardia adenocarcinoma (GNCA) cases and 1514 age-, gender-, and neighborhood-matched controls. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated from logistic regression adjusted for matching factors and potential confounders. Among controls, 35% of males and 8% of females reported consumption of jasmine tea; other tea consumption was rare. Consumption of jasmine tea (ever vs. never) was not associated with risk of ESCC (OR=1.15, 95% CI 0.92–1.44), GCA (OR=1.14, 95% CI 0.88–1.37), or GNCA (OR=0.85, 95% CI 0.64–1.15) in males and females combined. Among males, cumulative lifetime consumption showed a significant positive dose-response relation with ESCC risk, but not for GCA and GNCA. In exploratory analyses, occupation affected the relation between tea and ESCC such that consumption in males was associated with increased risk only in non-office workers. Overall, we found no evidence for a protective effect of tea in esophageal or gastric cancer. Further studies of the potential effects of thermal damage, tea quality, and water quality on UGI cancers are suggested.

Keywords

jasmine tea; esophageal cancer; gastric cancer

Background

Upper gastrointestinal (UGI) cancer, including esophageal and gastric cancer, are among the most common causes of cancer death in the world, with an estimated 385,000 esophageal and 700,000 gastric cancer deaths annually [1]. Shanxi Province in north central China has among the highest esophageal cancer rates in the world [2]. Because symptoms of UGI cancer usually appear only when disease is in an advanced stage, early detection is rare and the 5 year survival rate after diagnosis is low (http://www.cancer.org/docroot/cri/content/

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Competing interests
We declare that we have no conflict of interest.

cri_2_4_1x_what_are_the_key_statistics_for_esophagus_cancer_12.asp). Potential strategies to reduce the health burden of these diseases are needed.

Tea, the most popular beverage worldwide aside from water, is prepared from the young shoots of *Camellia sinensis*, and is rich in polyphenols (especially catechins), minerals, and amino acids. The strong antioxidant potential of catechins, particularly (−) epigallocatechin-3-gallate (EGCG), has been widely demonstrated *in vitro* and in animal studies [3–5]. In addition, anti-mutagenic, anti-diabetic, anti-inflammatory, anti-bacterial, and anti-viral effects of catechins have been reported [6, 7]. Cell culture studies have shown that oxidized EGCG inactivates epidermal growth factor receptor, which might subsequently reduce cancer development [8]. Studies in cells [9–11] and human tumor tissues [12] also suggest that tea may reduce cancer risk through modification of epigenetic pathways.

Tea and tea constituents have consistently shown inhibitory effects on carcinogenesis in animal studies at essentially all organ sites evaluated, including the esophagus and stomach [13]. Although many human epidemiologic studies on tea and cancer have been conducted, results have been inconsistent and must be considered inconclusive [13].

Jasmine tea is one type of green tea, which is scented and differs from general green tea because of an extra heat step in processing. Data from several animal studies suggest that jasmine tea may reduce the N-nitrosomethylbenzylamine-induced esophageal tumor burden [14–16]. However, none of the previously reported epidemiological studies on tea and cancer has specified an effect of jasmine tea.

We used a case-control study conducted in Shanxi Province, a high-risk region for these cancers in China, to further explore the association between jasmine tea consumption and UGI cancers.

Materials and methods

Study population

Patients presenting to the Shanxi Cancer Hospital in Taiyuan, Shanxi, People's Republic of China between 1997 and 2005 were potentially eligible for inclusion in this case-control study of upper gastrointestinal (UGI) tract cancers. The Shanxi Cancer Hospital, the largest cancer hospital in Shanxi, performed surgery on approximately 2000 new esophageal and 1800 new gastric cancers annually during the study period. We included cases in this study who: (i) were males or females 20 years of age or older, (ii) resided in of one of five geographic regions in relatively close proximity to the hospital (Taiyuan, Linfen, Jinzhong, Chanzi, and Xinzhou), (iii) had newly diagnosed (incident) cancer of the esophagus or stomach without previous treatment (ie, no surgery, chemotherapy, or radiotherapy), (iv) underwent surgical resection of their tumor at the Shanxi Cancer Hospital, and (v) had their diagnosis histologically confirmed. During the study period, about two-thirds of new UGI cancers presenting to the Shanxi Cancer Hospital came from the five geographic regions we designated. Since one objective of our study was to evaluate somatic changes in tumors in UGI cancer cases, we limited recruitment to patients who had surgical resection of their tumor as their primary therapy. We invited a systematic sample (eg, all patients from selected days of selected weeks) of new UGI cancer patients from our designated geographic regions who underwent surgical resection (approximately 50% of such patients from these regions) to join the study; 98% of invitees accepted enrollment in the study.

Esophageal cancer cases were limited to those with histological esophageal squamous cell carcinoma (ESCC), which included nearly all esophageal cancers since adenocarcinoma of the esophagus is essentially nonexistent in this high-risk population. Gastric cardia

adenocarcinoma (GCA) included adenocarcinomas located in the top three centimeters of the stomach, while gastric non-cardia adenocarcinoma (GNCA) included gastric cancers located in the remainder of the stomach. All histological diagnoses were made initially by pathologists at the Shanxi Cancer Hospital and confirmed by pathologists at the National Cancer Institute.

One control was enrolled for each case matched on age (± 5 years), gender, and neighborhood of residence. To identify potential controls, each case was asked to identify a neighbor of approximately the same age and gender. When the initial suggested neighbor could not be enrolled (ie, unavailable, ineligible, or refused), other neighbors, or the village doctor were asked to suggest another neighbor of the same age and gender. Potential controls were asked if they had any cancer or UGI disease, and were considered ineligible if they reported affirmatively to either question. In addition, the interview for the control had to be completed within six months of its matched case to be included. Over 75% of all identified potential controls were enrolled, including 95% of available and eligible controls (ie, the ones actually invited). The primary reason for non-enrollment among available/eligible controls was refusal to give a blood sample.

After obtaining informed consent, cases (while in the hospital but before their surgery) and controls (in their homes) were interviewed to obtain information on demographics and lifestyle. Questionnaire-based information on occupation, tobacco smoking, alcohol use, source of drinking water, family history of cancer, dietary pattern, and tea consumption were collected. For each type of tea, questions were asked about consumption habits before illness: Before you became ill, how much jasmine or green tea did you usually drink per month in grams (intensity)? At what age did you start drinking jasmine or green tea regularly? For how many years did you drink jasmine or green tea regularly (duration)? What was the usual strength of the jasmine or green tea that you drank (weak, medium, strong)?

A pilot study conducted during 1995–1998, in which separate questions on green, jasmine, black, and other tea consumption were asked found that, among ESCC patients who reported any use of either green or jasmine tea, 96% used jasmine tea (N=186), while only 4% used other green tea (N=8). As a result of this data, the questionnaire for the current study asked a single, combined question about the use of jasmine and green tea. For purposes of simplicity, throughout the current manuscript, we refer to this category as jasmine tea.

Statistical analysis

Odds ratios (OR) and 95% confidence intervals (CI) were calculated from logistic regressions. Before proceeding, we confirmed that conditional logistic regression with 600 ESCC-only controls (OR=1.41, 95% CI 1.04–1.91), unconditional logistic regression adjusted for matching factors with 600 ESCC-only controls (OR=1.41, 95% CI 1.04–1.91), and unconditional logistic regression adjusted for matching factors with 1514 pooled controls from all three cancer sites studied (OR=1.35, 95% CI 1.06–1.73) produced essentially similar point estimates for jasmine tea use and ESCC risk. To optimize power, all subsequent analyses employed unconditional logistic regression models adjusted for matching factors and used the 1514 pooled controls. Geographic region was used as a surrogate for neighborhood matching factor in the unconditional logistic regression models. We first examined the association between ever (vs. never) tea consumption and UGI cancer risk; then we examined the association between quantitative variables (intensity, duration, total amount, strength, and age started) regarding jasmine tea use and UGI cancer risk.

As very few women drank tea, analyses were stratified by gender and adjusted for the other two matching factors (age and geographic region) in all models. In addition, potential

confounding effects were explored using selected *a priori* risk factors, including occupation, ever (vs. never) tobacco smoking, ever alcohol drinking (vs. non-drinker), source of drinking water, ever (vs. never) scalding-hot food consumption, and family history of esophageal and gastric cancer in any first degree relative. Occupation was classified as either office worker or non-office worker (including farmer and industrial worker); drinking water was classified as either pipe water (as occurs in cities, and is treated) or non-pipe water (including water from shallow or deep wells, ponds, rivers, and spring water, all untreated sources). Both simple (adjusted only for matching factors), and full (further adjusted for all six potential confounders) models were determined. Additional adjustment for more detailed smoking exposure (ie, cumulative lifetime tobacco use) was also performed, but as results did not differ from those using the simpler ever tobacco smoking variable, only the simpler variable was used in the models presented here. Effect modification of the tea-ESCC association was explored in males for the six *a priori* risk factors with fully adjusted models.

For quantitative tea variables (intensity, duration, total amount, strength, and age started), analyses were conducted among all males with never drinkers as the reference group. Cumulative lifetime total jasmine tea consumption was calculated as the product of intensity (grams/month) and duration (years).

All p-values were two-sided and a p-value <0.05 was considered statistically significant. We used SAS version 9.1 software for all statistical analyses.

This study was approved by the institutional review boards of the Shanxi Cancer Hospital in Taiyuan, and the National Cancer Institute in Bethesda, Maryland.

Results

A total of 600 ESCC, 598 GCA, and 316 GNCA matched case-control pairs were included in the current analyses. Among ESCC cancers, 7% were anatomically located in the upper third of the esophagus, 70% in the middle, and 23% in the lower third. Gender, age, geographic region, and distribution of the potential risk factors of study subjects are shown in Table I. Among the potential risk factors, tobacco smoking and alcohol consumption were *a priori* risk factors, although neither was a significant independent risk factor for UGI cancer in the present study; occupation, drinking water source, scalding-hot food consumption, and family history of esophageal cancer were selected because they were significantly associated with risk of one or more of the three UGI cancers evaluated here in simple models. Overall, nearly three-quarters of cases were males and the median age of all cases was 59 years.

Tea consumption is shown in Table II. Overall, 31% of controls reported ever drinking any tea, and jasmine was the only commonly-used tea (28%). Any tea use in all UGI cancer cases combined was slightly more frequent than in controls (35% vs. 31% respectively). Use of black (2%) and other tea (2%) were infrequent, not associated with UGI cancer, and not analyzed further. Tea consumption was predominantly a male habit: among controls, 35% of males versus 8% of females ever used jasmine tea. Ever use of jasmine tea was associated with increased cancer risk only for ESCC (OR=1.31, 95% CI 1.04–1.64), an effect restricted to males (OR=1.35, 95% CI 1.06–1.73). Notably, after further adjustment for potential confounders (occupation, smoking, alcohol use, drinking water source, scalding- hot food consumption, and family history of esophageal cancer) in the full model, the association was diluted and no longer significant (OR=1.23, 95% CI 0.98–1.002). Due to limited power for evaluation of tea in females, further analyses were conducted only in males.

Jasmine tea use and risk of UGI cancers by intensity, duration, cumulative lifetime consumption (gram-years), tea strength, and age started tea use are shown in Table III for male subjects. Moderate (100–199 grams/month) and high (>200 grams/month) intensity were associated with an approximately 40% increased risk for ESCC compared to never tea drinkers in the full model. Higher lifetime total tea consumption was associated with a statistically significant 68% increased ESCC risk, a relation that increased monotonically (p trend=0.007). Each higher gram-year category (equivalent to an increase of approximately 2–3 cups of tea per day for 10 years) was associated with an 8% increase in risk of ESCC (OR=1.07, 95% CI 0.98–1.17). Individuals who preferred their tea strong had a 34% increased ESCC risk compared to never drinkers, and tea strength showed a marginally insignificant dose-response trend (p=0.054).

Ever vs. never tea consumption was not associated with either GCA or GNCA risk (Table II). More detailed analyses of quantitative tea consumption did not show significant results for either GCA or GNCA (Table III).

The associations between jasmine tea use and ESCC risk increased as anatomic location moved caudal: OR=0.49 (95% CI=0.19–1.24) for the upper third, OR=1.30 (95% CI 0.98–1.73) for the middle third, and OR=1.76 (95% CI 1.14–2.74) for the lower third. Further adjustment for potential confounders (full model) did not substantially modify the results.

We tested effect modification of the jasmine tea - ESCC association among males by the *a priori* risk factors (occupation, tobacco smoking, alcohol drinking, water source, scalding-hot food consumption, and family history of UGI cancer). A statistically significant interaction was seen only for occupation (p=0.026), and stratified analyses showed a significant tea - ESCC association among non-office workers (OR=1.40, 95% CI 1.05–1.86) but not for office workers (OR=0.73, 95% CI 0.43–1.86). Although the interaction was not significant, a suggestive positive association was observed in smokers (OR=1.28, 95% CI 0.98–1.67) but not smokers (OR=0.76, 95% CI 0.33–1.76); no clear difference between alcohol drinkers (OR=1.14, 95% CI 0.85–1.53) and non-drinkers (OR=1.43, 95% CI 0.88–2.34) was seen. Interactions between jasmine tea consumption (ever vs. never) and the other *a priori* risk factors were not significant (results not shown).

Discussion

We found no evidence for a protection effect of jasmine tea consumption on UGI cancers in this large case-control study. While there was some evidence that higher lifetime tea consumption was associated with increased risk for ESCC in males, and that occupation modified the tea-ESCC association to show increased risk in non-office workers, overall, this study provided only limited evidence for a relation between jasmine tea consumption and UGI cancer risk.

We identified fifteen epidemiological studies from the literature, as shown in Table IV, that have reported results on tea consumption and esophageal cancer risk, including thirteen case-control studies [17–29], two cohort studies [30, 31], and one small intervention trial [32]. Among these, two case-control studies [24, 29] and one cohort study [31] reported only the effect of hot tea consumption but not general tea consumption. Three of the eight case-control studies showed a protective effect of green tea drinking on esophageal cancer [20, 27, 28], but statistically significant effects were only observed among women in two of the studies [20, 27]. In contrast, tea consumption was associated with a significantly increased risk for esophageal cancer in two other studies [21, 25]. The remaining six case-control studies were null [17–19, 22, 23, 26]. Both cohort studies were conducted in Japan: the larger study (440 esophageal cancer cases) showed an increased risk (RR=1.5, 95% CI 1.1–

1.9) for hot versus non-hot tea drinking [31], while the smaller cohort (78 esophageal cancer cases) observed a dose-response (p for trend=0.04) for increasing green tea use [30]. The intervention trial gave decaffeinated green tea for one year to subjects with esophageal precancerous lesions, but no difference in precancerous lesions between the intervention (N=100) and placebo groups (N=100) was observed [32]. Our results, therefore, appear to be consistent with the preponderance of the evidence in the literature, which is most consistent with a null effect for esophageal cancer among tea drinkers, and does not support the application of jasmine tea as a chemo-prevention agent for esophageal cancer.

Confounding by poorly measured or unmeasured variables is always a concern in epidemiologic studies. Smoking and drinking are the dominant risk factors for ESCC in the West, however, smoking and alcohol exposures confer little or no risk for ESCC in the areas of the world where this disease occurs in epidemic proportions with rates in excess of 100 per 100,000 (ie, the Taihang mountain region of northcentral China which includes Shanxi and Linxian in adjacent Henan Province, northern Iran around the Caspian Littoral). In these high-risk areas, women have rates that are as high as men (ie, northern Iran) or nearly as high as men (Taihang mountain region of China), despite the fact that the women are virtually all non-smokers and non-drinkers. Analytic epidemiologic studies from these areas confirm that increased ESCC risk from smoking is minimal, on the order of a 30–60% increase, and that alcohol use is not associated with risk [33]. Similar to other studies on ESCC from this high-risk region, we found no significant associations between smoking or alcohol use and ESCC cancer in our study, and adjustment for these exposures, including more detailed consideration of cumulative lifetime smoking exposure, did not appreciably affect our estimates of the tea-ESCC relation. Thus, we have no evidence that either smoking or drinking influenced the results of our analyses here. Potential confounding by other risk factors described below could, however, be operational.

Thermal irritation has been hypothesized to be involved in esophageal carcinogenesis for a long time [34]. Tea drunk at high temperature was a risk factor in nine of the above case-control studies [17–19, 21, 22, 24–26, 29] and one of the cohort studies [31] (Table 1). Further, hot food consumption has also consistently been associated with increased risk of esophageal cancer [17, 35], particularly when consumed in large amounts. Though we do not have information on tea temperature from our subjects, we did ask about scalding- hot food consumption, a potential surrogate for hot tea. Consumption of scalding- hot food by itself was associated with an increased risk of ESCC (OR=2.10, 95% CI 1.52–2.90) in the current study, and adjustment for this variable attenuated the tea-ESCC association slightly. This result is consistent with a potential role, albeit modest, for thermal damage in our study as well. Physiological studies suggested that food and liquid need longer time to pass the lower part of esophagus than to pass the upper and middle parts [36] (http://www.nature.com/gimo/contents/pt1/full/gimo3.html). We found that the tea-ESCC association was substantially increased in the lower third of esophagus compared with the upper parts, an observation consistent with a potential thermal effect due to longer dwell time in the lower esophagus.

Occupation has been reported to be associated with increased risk of ESCC [37, 38], which could be explained by occupational exposures or other lifestyle factors. Our study showed that ESCC risk was increased only among tea drinkers who were non-office workers (i.e., farmers and industrial workers). Unlike office workers, this group was more likely to be exposed to pesticides or industrial pollution, and had lower socio-economic status (SES), which may have resulted in the use of lower quality tea, poorer nutrition, and poorer general health.

The non protective effect of tea consumption could be due to contamination of the water used to make tea. Water from open sources may be contaminated by air pollution, industrial discharge, or human waste [39, 40]. In addition, source of drinking water could be an indicator of SES, potentially reflecting aspects of SES not captured otherwise. The suggestive association between tea drinking and ESCC risk could also be due to contamination of the tea itself by carcinogens and/or other toxic substances. Several studies have shown that tea is liable to contamination and consequent accumulation of heavy metals, fluoride, and pesticides [41–43]. Notably, polycyclic aromatic hydrocarbons (PAHs), known esophageal carcinogens in animals and suspected carcinogens in humans [44, 45], have also been detected in teas [46–51].

Jasmine tea is made from green tea scented with jasmine flowers, and is usually classified as green tea. Green tea is made from fresh *Camellia sinensis* leaves through 3 main process steps: steaming or pan frying to inactivate the polyphenol oxidase and keep the pleasant green color; kneading to form the commercial shape; and roasting followed by frying or air drying to dry it. The heating processes usually involve burning wood, oil, or coal. Lin et al suggested that the manufacturing process for tea leaves might be the main source of the observed PAH contamination of tea [50]. In order to remove the moisture introduced by fresh jasmine flowers, jasmine tea may go through additional heating process, and subsequently be exposed to more PAH contamination than regular green tea. Lin and colleagues examined the concentrations of 16 PAHs in green, oolong, Puerh, black, and jasmine tea, and found that jasmine tea had much higher total PAH contents (1220ug/kg) than regular green tea (323 – 566ug/kg), as well as higher BaP content (28 μg BaP/kg in jasmine tea, not detected in green tea, 5 μg BaP/kg in oolong tea, 8 μg BaP/kg in Puerh tea, and 39 μg BaP/kg in black tea) [49]. Tea infusion studies have shown that PAHs in teas were released into water and increased with each refill and longer brewing time [48, 49, 51]. Because PAH concentrations in jasmine tea (28ng BaP/gram) are comparable to those in cigarettes (25ng BaP/cigarette) [52, 53], it is plausible that PAH exposure may have a role in the tea-ESCC relation observed here.

Studies on tea consumption and gastric cancer have been conducted mainly in Japan and China. No significant associations were observed in eight cohort studies from Japan [54], where relative risk estimates were all close to one; while eight case-control studies from China and Japan showed mixed results (three studies showed protective effects, one study showed risk, and four studies were null) [55]. Our null results for jasmine tea and gastric cancer, therefore, are consistent with previously published data, particularly the prospective studies [55]. One explanation that has been suggested to potentially explain the inconsistent results for tea consumption in epidemiologic studies is low quantity of tea consumption [13]. However, the median tea consumption in our study subjects was over 200 grams per month, an amount that is higher than the dose (150 grams per month) reported by Gao et al [20]. as associated with reduced risk of gastric cancer, which suggests that our null result is unlikely to be due to low quantity of tea consumption.

There are several advantages to our study: We had a large sample size, neighborhood-matched controls, quantitative assessment of lifetime tea exposure, detailed information on many potential confounders and effect modifiers, and we were able to simultaneously evaluate relations with cancer at three adjacent but anatomically different sites using identical study methods. Some limitations to our study are also evident: As with all case-control studies, our study is susceptible to recall bias, we had incomplete information on known potential confounders (most notably tea temperature, but also tea and water quality), there may be other confounders unknown to us, and our sample size was limited for the evaluation of effect modification.

In conclusion, this first large study focused on jasmine tea consumption found no evidence for a protective effect of tea on UGI cancers. Cumulative lifetime consumption showed a significant positive dose-response relation with ESCC risk, but not for GCA or GNCA. Studies are needed to further evaluate our results and to integrate more precise measurements of thermal damage, contamination of tea leaves, and the water used in making the tea.

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TABLE I

CHARACTERISTICS OF SUBJECTS

		Controls	Esophageal cancer Cases	Gastric cardia adenocarcinoma Cases	Gastric non-cardia adenocarcinoma Cases
N		1514	600	598	316
Gender					
	Male (%)	1107 (73)	376 (63)	491 (82)	239 (76)
	Female (%)	407 (27)	224 (37)	107 (18)	77 (24)
Age (median)		59 (52–65)	58 (51–64)	61 (55–66)	57.5 (50–63)
	Male	60 (53–65)	59 (52–64)	61.5 (55–66)	58 (51–63)
	Female	57 (50–63)	57 (50.5–63)	60 (54–64)	54 (44–63)
Geographic regions					
	Taiyuan (%)	524 (35)	212 (35)	199 (33)	113 (36)
	Linfen (%)	266 (18)	94 (16)	118 (20)	54 (17)
	Jinzhong (%)	294 (19)	153 (26)	104 (18)	37 (12)
	Chanzi (%)	274 (18)	90 (15)	121 (20)	63 (20)
	Xinzhou (%)	156 (10)	51 (8)	56 (9)	49 (15)
Occupation	Office worker	239 (16)	108 (18)	147 (24)	83 (26)
Tobacco smoking	Smoker	980 (65)	350 (58)	412 (69)	218 (69)
Alcohol consumption	Drinker	766 (51)	287 (48)	325 (54)	179 (57)
Water source	Pipe water	813 (54)	327 (54)	307 (51)	180 (57)
Scalding-hot food	Consumer	1145 (76)	513 (86)	506 (84)	283 (90)
Family history	UGI cancer	170 (11)	131 (22)	104 (17)	53 (17)

TABLE II

TEA CONSUMPTION (EVER vs. Never) AND UGI CANCERS IN MALES AND FEMALES [a]

		Esophageal cancer			Gastric cardia adenocarcinoma			Gastric non-cardia adenocarcinoma		
	Control (%)	Case (%)	OR (95% CI)*	OR (95% CI)#	Case (%)	OR (95% CI)*	OR (95% CI)#	Case (%)	OR (95% CI)*	OR (95% CI)#
Any tea	473 (31)	196 (33)	**1.26 (1.01–1.57)**	1.17 (0.94–1.47)	228 (38)	1.21 (0.98–1.49)	1.15 (0.92–1.43)	100 (32)	1.04 (0.78–1.37)	0.88 (0.66–1.17)
Jasmine tea										
Overall	422 (28)	182 (30)	**1.31 (1.04–1.64)**	1.15 (0.92–1.44)	199 (33)	1.16 (0.94–1.45)	1.14 (0.92–1.44)	88 (28)	1.03 (0.77–1.37)	0.85 (0.64–1.15)
Male	390 (35)	163 (43)	**1.35 (1.06–1.73)**	1.23 (0.96–1.59)	195 (40)	1.24 (0.99–1.55)	1.18 (0.94–1.50)	86 (36)	1.10 (0.82–1.49)	0.92 (0.67–1.26)
Female	32 (8)	19 (8)	1.05 (0.58–1.91)	1.08 (0.59–1.98)	4 (4)	0.46 (0.16–1.35)	0.48 (0.16–1.40)	2 (3)	0.32 (0.07–1.36)	0.36 (0.08–1.571)
Black tea										
Overall	29 (2)	6 (1)	0.63 (0.26–1.55)	0.57 (0.23–1.41)	17 (3)	1.33 (0.71–2.48)	1.26 (0.67–2.37)	6 (2)	0.86 (0.34–2.14)	0.76 (0.30–1.90)
Male	28 (2)	6 (2)	0.66 (0.26–1.62)	0.58 (0.23–1.45)	17 (3)	1.38 (0.74–2.59)	1.31 (0.69–2.47)	6 (2)	0.91 (0.36–2.28)	0.79 (0.31–2.01)
Female	1 (<1)	0	-	-	0	-	-	0	-	-
Other tea										
Overall	37 (2)	10 (2)	0.80 (0.39–1.64)	0.85 (0.41–1.76)	16 (3)	0.94 (0.51–1.72)	0.97 (0.53–1.80)	9 (3)	1.17 (0.55–2.51)	1.22 (0.56–2.68)
Male	34 (3)	8 (2)	0.73 (0.33–1.61)	0.82 (0.37–1.84)	16 (3)	1.02 (0.55–1.90)	1.07 (0.57–2.00)	8 (3)	1.06 (0.47–2.38)	1.12 (0.48–2.58)
Female	3 (1)	2 (1)	-	-	0	-	-	1 (1)	-	-

[a] Reference group is never consumption. Gender was adjusted in the analyses of overall subjects (males and females combined).

* ORs adjusted for age at interview, geographic regions;

ORs adjusted for age at interview, geographic regions, occupation, ever tobacco smoking, ever alcohol drinking, drinking water source, ever scalding-hot food consumption, and family history of esophageal or gastric cancer.

TABLE III

JASMINE TEA CONSUMPTION AND ESCC RISK IN MALES

			Esophageal cancer		Gastric cardia adenocarcinoma		Gastric non-cardia adenocarcinoma	
		Control (%)	Case (%)	OR (95% CI)[#]	Case (%)	OR (95% CI)[#]	Case (%)	OR (95% CI)[#]
Intensity (gram/month) [a]	Never	717 (65)	213 (57)	1	297 (60)	1	153 (64)	1
	50–99	94 (8)	28 (7)	0.88 (0.55–1.40)	39 (8)	0.90 (0.59–1.36)	20 (8)	0.82 (0.48–1.41)
	100–199	156 (14)	72 (19)	1.36 (0.94–1.97)	100 (20)	**1.51 (1.08–2.11)**	45 (19)	1.17 (0.74–1.85)
	200–1000	140 (13)	63 (17)	1.36 (0.77–2.43)	56 (11)	0.90 (0.51–1.57)	21 (9)	0.64 (0.27–1.49)
	P for trend			0.146		0.201		0.936
Duration (years) [a]	Never	717 (65)	213 (57)	1	297 (60)	1	153 (64)	1
	1–14	127 (11)	48 (13)	1.06 (0.72–1.57)	56 (11)	1.11 (0.78–1.59)	30 (13)	1.02 (0.64–1.62)
	15–28	125 (11)	64 (17)	1.40 (0.92–2.11)	71 (5)	1.43 (0.98–2.09)	31 (13)	1.04 (0.62–1.76)
	29–69	138 (13)	51 (14)	0.94 (0.55–1.61)	68 (14)	1.15 (0.72–1.84)	25 (10)	0.90 (0.45–1.79)
	P for trend			0.603		0.225		0.906
Lifetime consumption (gram-year)[b]	Never	717 (65)	213 (57)	1	297 (60)	1	153 (64)	1
	50–1499	121 (11)	37 (10)	0.88 (0.59–1.34)	59 (12)	1.16 (0.82–1.64)	32 (13)	1.10 (0.70–1.72)
	1500–3749	141 (13)	55 (14)	1.16 (0.81–1.66)	73 (15)	1.24 (0.89–1.72)	32 (13)	0.90 (0.58–1.40)
	3750–24750	128 (11)	71 (19)	**1.68 (1.19–2.39)**	63 (13)	1.15 (0.81–1.63)	22 (9)	0.75 (0.45–1.25)
	P for trend			**0.007**		0.221		0.302
Strength	Never	717 (65)	213 (57)	1	297 (60)	1	153 (64)	1
	Weak	157 (14)	58 (15)	1.07 (0.76–1.52)	80 (16)	1.15 (0.84–1.57)	36 (15)	0.91 (0.60–1.38)
	Medium	114 (10)	51 (14)	1.36 (0.93–1.989)	51 (10)	1.08 (0.75–1.57)	27 (11)	1.04 (0.65–1.67)
	Strong	118 (11)	54 (14)	1.34 (0.92–1.95)	64 (13)	1.35 (0.95–1.91)	23 (10)	0.82 (0.49–1.36)
	P for trend			0.054		0.112		0.556
Age started	Never	717 (65)	213 (57)	1	297 (60)	1	153 (64)	1
	42–70	131 (12)	42 (11)	0.96 (0.65–1.43)	76 (15)	1.31 (0.94–1.82)	26 (11)	0.96 (0.59–1.55)
	27–41	136 (12)	69 (18)	**1.55 (1.10–2.18)**	70 (14)	1.25 (0.90–1.74)	39 (16)	1.16 (0.76–1.77)
	5–26	123 (11)	52 (14)	1.18 (0.80–1.71)	49 (10)	0.97 (0.67–1.41)	21 (9)	0.64 (0.38–1.07)
	P for trend			0.074		0.539		0.314

[##]ORs adjusted for age at interview, geographic regions, occupation, ever tobacco smoking, ever alcohol drinking, drinking water source, ever scalding-hot food consumption, and family history of esophageal or gastric cancer;

[a] Further adjusted for total tea consumption

[b] Gram-year is an estimate of lifetime tea consumption, which was calculated as the product of intensity (gram/month) and duration (years). 1 gram-year is equivalent to 1 gram/month for 1 year. The medians for the 4 categories were 0, 750, 2400, and 7500 gram-years respectively.

TABLE IV

EPIDEMIOLOGICAL STUDIES: TEA EFFECT ON ESOPHAGEAL CANCER

Study	Country	Design	N*	Tea type	Tea effect	Hot tea effect	Comments
Decreased risk							
Gao, 1994 [20]	China	Case-control	734/1552	Green tea	♂OR=0.8 (0.6–1.1) ♀**OR=0.5 (0.3–0.8)**		
Wang, 1999 [28]	China	Case-control	68/68	Green tea	**OR=0.2 (0.1–0.7)**		
Wang, 2007 [27]	China	Case-control	355/408	Green tea	♂OR=1.4 (0.9–2.0) ♀**OR=0.3 (0.1–0.9)**		
Null effect							
Dejong, 1974 [19]	Singapore	Case-control	131/262	Not specified	♂OR=0.99 ♀OR=0.8	♂**OR=3.0 (p<0.01), P trend <0.01**	Hospital control
Cook-Mozaffari, 1979 [18]	Iran	Case-control	344/181	Not specified	Authors mentioned no difference	♂**OR=1.6 (1.1–2.3)** ♀**OR=1.9 (1.2–2.9)**	Only hot tea reported
Castellsague 2000 [17]	South America	Case-control	830/1779	Not specified	♂OR=0.8 (0.6–1.1) ♀OR=0.7 (0.4–1.2) Total 0.8 (0.6–1.1)	Very hot **3.7 (1.4–9.9)** **P trend=0.11**	
Sharp 2001 [26]	UK	Case-control	159/159	Not specified	3.0 (0.8–10.6) P global=0.198	**P trend=0.030** Warm 0.3 (0.1–0.9) P global=0.066	Women only; Very hot tea/coffee as reference
Mu, 2003 [23]	China	Case-control	218/415	Green tea	OR=0.7 (0.5–1.02), P=0.798		
Wang, 2002 [32]	China	Intervention trial	100/100	Green tea	No effect on precancerous lesion for 1 year intervention		Decaffeinated green tea was used
Islami, 2009 [22]	Iran	Case-control	300/571	Green tea	OR=0.9 (0.4–2.1)	**2.1 (1.6–3.8), P trend<0.001**	
Increased risk							
Kinjo, 1998 [31]	Japan	Cohort	220272/440	Green tea		**RR=1.5 (1.1–1.9)** hot versus not-hot tea	Only hot tea reported
Zhang 2001 [29]	China	Case-control	240/240	Not specified		**2.3 (1.4–3.7)**	Only over-hot tea reported
Murtaza 2006 [24]	India	Case-control	51/150	Not specified		**Concordance =2.37, at p<0.05**	Only hot salty tea reported
Ren, 1991 [25]	China	Case control	112/112	Not specified	**OR=5.6 (1.7–18.7)**	hot food **OR=2.5 (1.1–5.7)**	Hospital control
Hu, 1994 [21]	China	Case-control	196/392	Not specified	Strong tea **OR=2.5 (1.4–4.3)** high consumption **OR=3.9 (1.7–9.1)**	**OR=5.3 (1.4–20.9)**	
Ishikawa, 2006 [30]	Japan	Cohort	26723/78	Green tea	HR=1.7 (0.9–3.2) **P trend =0.04***		No HR significant

*Case and control numbers in case-control study; total sample size and case numbers in cohort study