

## RESEARCH COMMUNICATION

# Green Tea Drinking Habits and Esophageal Cancer in Southern China: A Case- Control Study

Zuhui Chen<sup>1,2\*</sup>, Qing Chen<sup>1</sup>, Haiyan Xia<sup>2</sup>, Jinrong Lin<sup>1</sup>

### Abstract

**Aim:** To investigate effects of green tea drinking and its temperature on esophageal cancer development. **Methods:** A 1:2 matched hospital-based case-control study including 150 cases and 300 controls was conducted in southern area of China from June 2004 to May 2010. A self-designed questionnaire was used to collect information on possible risk factors of esophageal cancer, and to assess the tea drinking habit and temperature. Conditional logistic regression was used to calculate odds ratios (ORs) and corresponding 95% confidence intervals (CIs). **Results:** We find a significant protective effect of high consumption of green tea on esophageal cancer with low temperature tea (OR=0.79, 95% CI=0.29-0.97). However, drinking tea at a temperature of 70-79°C and above 80°C was related to greatly elevated risk of esophageal cancer with ORs of 2.21 (1.57-5.53) and 4.74 (2.67-10.51). An agreement was found between reported tea temperature and measured temperature (correlation coefficient =0.62). Further analysis indicated hot tea temperature to be associated with heavy risk of esophageal cancer in former and current smokers and current drinkers (former and current smokers: OR=8.91(1.91-16.77) and 7.33(2.23-12.46), respectively; former and current drinkers: OR=7.58(0.83-9.53) and 6.93(2.01-10.65)). **Conclusion:** In the South China context, drinking tea at high temperature significantly increases risk of esophageal cancer, especially in drinkers and smokers.

**Keywords:** Green tea - tea drinking temperature - esophageal cancer

*Asian Pacific J Cancer Prev*, 12, 229-233

### Introduction

Oesophageal cancer is a global health problem, ranking eighth in terms of incidence and sixth in terms of mortality in 2002 (Parkin et al., 2005). Its incidence and mortality rates showed a wide geographic variation at an international level, and there are marked differences between high-risk and low-risk areas (Parkin et al., 2005). The mortality of esophageal cancer has substantially decreased in the past fifty years in China, but still the fourth leading cause of cancer death in China, and almost of 50% esophageal cancer death occurred in China. It is estimated that the incidence and mortality in China of 2002 are 27.4 and 21.6 for men and 12.0 and 9.6 for women, respectively (Cai et al., 2008).

Dietary habit and lifestyle habits play a role in the development of esophageal cancer by epidemiologic studies (Hu et al., 1994; Castellsague et al., 1999). Green tea contains polyphenolic antioxidants, such as epigallocatechin gallate, is regarded as a protective factor for esophageal cancer by a number of studies (Graham, 1992; Ahmad et al., 1997; Yang et al., 1998). Previous studies evaluated the association between the green tea and esophageal cancer, and some studies indicated the

polyphenolic antioxidants in green tea contribute to cancer prevention, but the results are conflicting (Gao et al., 1994; Mu et al., 2003; Ishikawa et al., 2006; Wang et al., 2007). A large case-control study indicated the green tea showed protective effect on esophageal cancer (Gao et al., 1994). While an ecological study showed that people in the high incidence area tend to have more consumption of tea at a higher temperature than those in the low incidence area (Ghadirian, 1987), and another case-control study indicated that people who frequently drank hot tea showed a two fold increase in the risk of esophageal cancer compared with lukewarm or warm tea (Cook-Mozaffari et al., 1979).

Green tea is one of the most popular beverages in Asia countries, especially in China, and its consumption is about 120 ml brewed tea per capital per day, and is usually starts at an early age and continues for life in China (McKay and Blumberg, 2002). Therefore, drinking hot tea may be a potential risk factor for esophageal cancer. We conducted a case-control study in Guangdong province, China. In our analysis, we measured association of tea drinking habits and the temperature when drinking with the esophageal cancer, and provide information on the risk factor on development of esophageal cancer.

<sup>1</sup>School of Public Health and Tropical Medicine, Southern Medical University, <sup>2</sup>College of Clinical Medicine, Jinan University, China \*For correspondence : chenzuhui0808@126.com

## Materials and Methods

### Participants

A case-control study was conducted in June 2004 from May 2010 in the First Affiliated Hospital of Ji'nan University. All subjects were restricted to local inhabitants who have lived in either area for at least 5 years. A total of 150 patients diagnosed with histologically confirmed squamous cell esophageal carcinoma in the First Affiliated Hospital of Jinan University. A total of 300 control subjects (Two controls/ One case), who did not have a malignancy were selected from health individuals visiting Hospital for routine physical examination. Control subjects were case-matched with respect to the sex and age ( $\pm 3$  years).

**Table 1. Characteristics of Patients with Esophageal Cancer and Matched Controls**

Characteristic	Cases (%) n=150	Controls (%) n=300	OR (95% CI)	P value
Mean age (years)	54.5 $\pm$ 6	54.0 $\pm$ 7	-	-
Sex				
Men	102 (68)	204 (68)	-	-
Women	48 (32)	96 (32)		
Education level				
Illiteracy	92 (61)	156 (52)	1.0(reference)	0.06
Literacy	58 (39)	144 (48)	0.68(0.45-1.04)	
Income five years age (RMB)				
<1,000	36 (21)	54 (18)	1.0(reference)	0.006
1000-3000	63 (42)	96 (32)	0.98(0.56-1.73)	
>3000	51 (34)	150 (50)	0.51(0.29-0.90)	
Cancer Family history (First degree relatives)				
No	108 (72)	243 (81)	1.0(reference)	0.03
Yes	42 (28)	57 (19)	1.66(1.02-2.68)	
Smoking status				
Never	78 (52)	198 (66)	1.0(reference)	0.015
Former	12 (8)	15 (5)	2.03(0.83-4.87)	
Current	60 (40)	87 (29)	1.75(1.12-2.72)	
Alcohol drinking status				
Never	48 (32)	135 (45)	1.0(reference)	0.03
Former	15 (10)	24 (8)	1.75(0.79-3.83)	
Current	87 (58)	141 (47)	1.74(1.11-2.72)	

**Table 2. Tea Drinking Habits and Odds Ratios (95% CIs) among Cases with Esophageal Cancer and Matched Controls**

Variables	Cases (%) n=150	Controls (%) n=300	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI) <sup>1</sup>	Contingency coefficient (P value)
Investigated tea temperature					
Never	63 (42)	120 (40)	1.0(reference)	1.0(reference)	0.235 (<0.001)
Warm	33 (22)	126 (42)	0.52(0.27-0.98)	0.76(0.36-1.32)	
Hot	24 (16)	30 (10)	1.52(0.78-2.95)	2.41(1.53-4.17)	
Very hot	30 (20)	24 (8)	2.38(1.23-4.63)	3.69(2.56-6.73)	
Measured tea temperature (°C)					
Never	63 (42)	120 (40)	1.0(reference)	1.0(reference)	0.167 (0.024)
$\geq 80$	12 (8)	9 (3)	2.54(0.92-7.19)	4.74(2.67-10.51)	
70-79	18 (12)	24 (8)	1.43(0.67-2.98)	2.21(1.57-5.53)	
60-69	30 (20)	57 (19)	1.0(0.56-1.77)	1.53(0.91-2.14)	
50-59	15 (10)	45 (15)	0.63(0.30-1.27)	0.87(0.54-1.55)	
<50	12 (8)	45 (15)	0.51(0.23-1.07)	0.75(0.48-1.39)	
Monthly consumption of green tea (g/month)					
Never	63 (42)	120 (40)	1.0(reference)	1.0(reference)	0.047 (0.8)
<100	54 (26)	102 (33)	1.01(0.63-1.62)	1.27(0.72-1.89)	
100-250	24 (22)	54 (18)	0.85(0.46-1.55)	0.97(0.59-2.56)	
>250	9 (10)	24 (9)	0.71(0.28-1.71)	0.92(0.49-2.32)	

Adjusted for age, sex, education level, annual income, cancer family history, smoking and drinking status

The ethics committee of each collaborating institution reviewed and approved the study, and informed consent was obtained from all participants.

### Date collection

Face to face interview was performed for all subjects. Two interviewers were trained and were not aware of the study hypothesis. Cancer patients were asked to refer about dietary habit a year before the disease diagnosed.

A self-designed structured questionnaire was used in the study, including demographic information, consumption of green tea, salted food, preserved/picked food, spicy food, fruit, vegetable, tobacco, all types of alcoholic beverages (beer, wine and distilled spirit), and disease history. Ever drinking green tea was defined as drinking at least one cup of green tea per week for more than 6 months. We collected lifetime general consumption of green tea drinking, and the tea drinking habits include drinking status (former, never and current tea drinking), years of tea drinking, monthly consumption of tea, and water temperature of tea drinking (warm, hot or very hot). In order to validate the water temperature above, we prepared a fresh cup of tea for each participant and measured the temperature of the tea using a digital thermometer. When the temperature was 80°C we asked the participants to sip the tea and verify whether it was the temperature they used to drink. If not, the tea was allowed to cool with 10°C intervals of the above temperature. We recorded the water temperature of tea they were used to drunk.

### Statistical analysis

Data was analyzed by using STATA 9 software program. In the analysis, drinking status was categorized into former, never and current drinkers. Individual who quit drinking less than one year were considered as current drinkers. Smoking status was also categorized into former, never and current drinkers. The conditional logistic regression was used to calculate odds ratios

**Table 3. Relationship between Questionnaire Data on Tea Temperature and Measured Tea Temperature**

Measured tea temperature(°C)	Investigated tea temperature			Total	Correlation coefficient (P value)
	Very hot	Hot	Warm		
≥80	17	4	0	21	0.62
70-79	19	21	2	42	(<0.001)
60-69	12	17	58	87	
50-59	5	9	46	60	
<50	1	3	53	57	
Total	54	54	159	267	

(OR), and corresponding 95% confidence intervals (CI) for gastric cancer in relation to exposure of interest. Two models, a) none adjusted b) age, sex, family history, smoking, drinking, salted food, preserved/picked food, spicy food, fruit and vegetables adjusted, were examined. Dose-response relationship of tea drinking habits was analyzed by chi-squared test for trend. The agreement between measured tea temperature and investigated tea temperature were tested by Spearman's rank correlation coefficients. All reported trend test significance levels (p-values) were two-sided. The chi-square test was used in analyze the difference between groups. The significance level was set at 5%.

## Results

A total of 150 cases and 300 controls were recruited into study. The age, sex, education level related variable of the cases and controls presented to be similar ( $P>0.05$ , Table 1). Cases with higher economic status presented lower risk of esophageal cancer (annual income>3000 RMB, OR=0.51, 95% CI=0.29-0.90). Cases with cancer family history in first degree relatives was observed significantly increased risk of esophageal cancer (OR=1.66, 95% CI=1.02-2.68). An increased risk of esophageal cancer was found in former and current smokers (former smokers, OR=2.03, 95% CI=0.83-4.87; current smokers, OR=1.75, 95% CI=1.12-2.72), and also found in former and current drinkers (former drinkers, OR=1.75, 95% CI=0.79-3.83; current drinkers, OR=1.74, 95% CI=1.11-2.72).

The relationship between tea drinking habits and esophageal cancer was showed in Table 2. After adjusting

for potential confounding factors, including age, gender, education level and drinking and smoking, the hot and very hot tea temperature was significantly increase the risk of esophageal cancer with OR (95% CIs) of 2.41 (1.53-4.17) and 3.69 (2.56-6.73) compared with never drink, respectively. When the tea temperature was 70-79°C, the adjusted OR(95% CI) of tea temperature for esophageal cancer was 2.21 (1.57-5.53), and the risk of esophageal cancer revealed to be high when temperature above 80°C (OR=4.74, 95% CI=2.67-10.51). The more consumption of green tea was showed, the low risk of esophageal cancer was observed. Positive dose-response relationship for esophageal cancer risk was found in investigated tea temperature ( $p<0.001$ ) and measured tea temperature ( $p<0.024$ ).

The measured and investigated hot tea temperature was significantly associated with esophageal cancer, and we explored the correlation between measured and investigated tea temperature. The spearman's rank correlation coefficient for agreement between the two variables was 0.62 ( $p<0.001$ ) (Table 3).

Stratified analysis was conducted to explore the modification effect of smoking status and alcohol drinking status on measured tea temperature (Table 4). The additive effect was observed between hot tea temperature and smoking or drinking. When the temperature at 60-69°C, the significant moderate risk of esophageal cancer was observed in current smokers and drinkers. When measured tea temperature above 70°C, the significantly highest risk of esophageal cancer was found in former and current smokers, and current drinkers. The high consumption of green tea was observed protective effect for gastric cancer in low temperature tea (OR=0.79, 95%CI=0.29-0.97).

## Discussion

This population-based case-control study conducted in south of China to explore the association between green tea habit and esophageal cancer. In our study, we did find significant protective effect of high consumption of green tea on esophageal cancer in low temperature tea, and we found drinking hot tea temperature was significantly related to esophageal cancer risk. Heavy risk of esophageal

**Table 4. The Effect of Green Tea Temperature on Esophageal Cancer in Different Smoking and Drinking Status**

	Crude odds ratio (95% CI) <sup>1</sup>				P for interaction
	Measured tea temperature(°C)				
	Never	<60	60-69	≥70	
Smoking status					
Never	1.0(reference)	0.79(0.49-0.98)	1.69(1.07-3.98)	3.53(1.70-8.45)	0.08
Former	4.23(1.15-9.52)	1.58(0.81-5.96)	6.98(0.89-15.99)	8.91(1.91-16.77)	
Current	2.98(1.32-3.26)	1.07(0.63-3.34)	3.87(1.32-6.58)	7.33(2.23-12.46)	
Alcohol drinking status					
Never	1.0(reference)	0.68(0.50-0.96)	1.68(1.14-3.76)	3.25(1.62-7.63)	0.15
Former	2.44(0.91-5.89)	1.07(0.78-3.11)	4.09(0.73-6.36)	7.58(0.83-9.53)	
Current	1.90(1.35-3.43)	0.92(0.54-3.05)	3.31(1.98-5.53)	6.93(2.01-10.65)	
Monthly consumption of green tea (g/month)					
Never	1.0(reference)	-	-	-	0.32
<100	-	1.27(0.72-1.89)	1.53(0.77-2.38)	1.74(0.92-2.99)	
100-250	-	0.85(0.37-1.43)	1.04(0.68-1.63)	1.42(0.75-1.92)	
>250	-	0.79(0.29-0.97)	0.89(0.49-1.21)	1.25(0.61-1.69)	

Adjusted for age, gender, education level, income and cancer family history

cancer risk for hot tea temperature was observed in drinkers and smokers.

Experimental and epidemiological studies indicated green tea possessed antimicrobial, immunostimulant, anti-oxidant and anti-inflammatory effects (Dufresne and Farnworth, 2001; Lambert and Yang, 2003), and this properties made green tea as a potential cancer preventive agent on the basis of numerous in vitro and in vivo (Graham, 1992; Ahmad et al., 1997; Yang et al., 1998). A study conducted in Shanghai indicated the gastric cancer risk decreased with the increased of green tea consumption (Gao et al., 1994), another study conducted in Jiangsu found a protective effect of green tea in women. In our study, the more consumption of green tea had, the lower risk of esophageal cancer was found, which is in line with the previous study. But our study did not find no relationship was found between high intake of green tea and gastric cancer risk, this may be the modification effect of the temperature of green tea. Therefore, in the further analysis of association between tea consumption and temperature, we observed the cancer risk of esophageal cancer was significantly reduced as the tea consumption rose in the low temperature.

Previous study indicated hot food could increase the risk of esophageal cancer. The explanation might be that hot food could cause chronic thermal injury to the upper digestive tract and gastric mucosa and therefore make it more susceptible to carcinogenesis. Some studies indicated the inflammatory induced by hot food processes associated with chronic irritation of the esophageal mucosa by local hyperthermia might stimulate the endogenous formation of reactive nitrogen species, and which may direct or indirect induce the carcinogenesis (Mirvish, 1995). Our study indicated the hot tea drinking could cause risk of esophageal cancer (OR=2.41, 95%CI=1.53-4.17), and heavy risk when taking very hot tea (OR=3.69, 95%CI=2.56-6.73). Previous case-control study reported the hot green tea had 3.1 fold elevated risk of esophageal cancer in Jiangsu compared with warm temperature tea (Wu et al., 2009), and a meta-analysis with cohort studies showed the green tea was significantly increase gastric cancer risk, but the adjusted results of case control studies showed reduced risk (Myung et al., 2009). The tea temperature might be a plausible modification for the conflicting relationship between them.

Our study indicated that tea temperature at 70°C and above was observed the increased cancer risk as the temperature raised, and a significant dose-response relationship was found between them (p=0.024). An previous experimental study reported the hot water administered by installation in the upper section of esophagus, more tumors showed with the temperature increased, and the size of esophagus papillomas rapidly increased when the temperature at 70°C and above (Li et al., 2003). A study reported a significantly higher tea drinking temperature (mean 62°C, range 53-73°C) among esophageal disorders cases than that among health controls (mean 56°C, range 47.5-65°C) (Pearson and McCloy, 1989). The threshold temperature suggested the threshold of epithelial barrier impaired of esophagus. Once exceed this temperature, the epithelial barrier impaired

rapidly with the exposure times.

Our study also proved the modification of alcohol and tobacco on hot green tea, and an addictive effect was found between green tea and alcohol or tobacco. The addictive effect was also reported by a study conducted in Jiangsu, it showed the smokers or drinkers had highest odds ratio of esophageal cancer when drinking hot green tea, and was in line with our study (Wu et al., 2009). The heavy cancer risk in drinkers and smokers could be explained by the tea drinkers usually together with tobacco and alcohol used, which may increase the risk of esophageal cancer (Sun et al., 2002). But we did not find a significant interaction effect, the mainly reason might be the small sample size. Additional, we found hot tea drinking had heavy cancer risk in former drinkers and smokers. This explanation may be the reason of quitting drinking or smoking for cases because of the clinical manifestation of digestive tract or other chronic disease, and these cases may have been long term use of tobacco or alcohol.

Several limitations should be considered in our study. Firstly, we did not finish the temperature measurement before the cancer happened, and there might be recall bias in our study. But we emphasized to the investigated cases the tea drinking habit should be one year age before cancer diagnosis. Secondly, potential selection bias and information bias may be exist in our study, and we selected the controls from the health individuals visiting Hospital for routine physical examination, and a sex and age matched method was used. These may minimize selection bias. We used well trained investigators in data collection to avoid information bias. Finally, the small number of subjects may be another potential bias for us to find the relationship between green tea consumption and esophageal cancer, so further studies in a large scale appear warranted.

To summarize, high consumption of green tea drinking showed protective effect for esophageal cancer in warm tea. But hot tea drinking possessed a significant strong risk of esophageal cancer, and modified by drinking and smoking. When tea temperature at 70°C and above, a rapidly increased risk of esophageal cancer was observed. The findings broaden the effect of green tea on esophageal cancer and may provide a new strategic approach to the prevention of esophageal cancer.

## Acknowledgments

We thank the Medical Science fund of Guangdong Province (B2008094) for financial support.

## References

- Ahmad N, Feyes DK, Nieminen AL, et al (1997). Green tea constituent epigallocatechin-3-gallate and induction of apoptosis and cell cycle arrest in human carcinoma cells. *J Natl Cancer Inst*, **89**, 1881-6.
- Cai L, Parkin DM, Zhang ZF (2008). Cancer burden and preventive strategy in Eastern Asia. *Tumor*, **28**, 410-4.
- Gao YT, McLaughlin JK, Blot WJ, et al (1994). Reduced risk of esophageal cancer associated with green tea consumption. *J Natl Cancer Inst*, **86**, 855-88.

- Castellsagué X, Muñoz N, De Stefani E, et al (1999). Independent and joint effects of tobacco smoking and alcohol drinking on the risk of esophageal cancer in men and women. *Int J Cancer*, **82**, 657-64.
- Cook-Mozaffari PJ, Azordegan F, Day NE, et al (1979). Oesophageal cancer studies in the Caspian Littoral of Iran: results of a case-control study. *Br J Cancer*, **39**, 293-309.
- Dufresne CJ, Farnworth ER (2001). A review of latest research findings on the health promotion properties of tea. *J Nutr Biochem*, **12**, 404-21.
- Ghadirian P (1987). Thermal irritation and esophageal cancer in northern Iran. *Cancer*, **59**, 1909-14.
- Graham HN (1992). Green tea composition, consumption, and polyphenol chemistry. *Prev Med*, **21**, 334-50.
- Parkin DM, Ferlay J, Pisani P (2005). Global cancer statistics, 2002. *Cancer J Clin*, **55**, 74-108.
- Hu J, Nyrén O, Wolk A, et al (1994). Risk factors for oesophageal cancer in northeast China. *Int J Cancer*, **57**, 38-46.
- Ishikawa A, Kuriyama S, Tsubono Y, et al (2006). Smoking, alcohol drinking, green tea consumption and the risk of esophageal cancer in Japanese men. *J Epidemiol*, **16**, 185-92.
- Lambert JD, Yang CS (2003). Mechanisms of cancer prevention by tea constituents. *J Nutr*, **133**, S3262-7.
- Li ZG, Shimada Y, Sato F, et al (2003). Promotion effects of hot water on N-nitrosomethylbenzylamine-induced esophageal tumorigenesis in F344 rats. *Oncol Rep*, **10**, 421-6.
- McKay DL, Blumberg JB (2002). The role of tea in human health: an update. *J Am Coll Nutr*, **21**, 1-13.
- Mirvish SS (1995). Role of N-nitroso compounds (NOC) and N-nitrosation in etiology of gastric, esophageal, nasopharyngeal and bladder cancer and contribution to cancer of known exposures to NOC. *Cancer Lett*, **93**, 17-48.
- Mu LN, Zhou XF, Ding BG, et al (2003). Study on the protective effect of green tea on gastric, liver and esophageal cancers. *Zhonghua Yufang Yixue Zazhi*, **37**, 171-3.
- Myung SK, Bae WK, Oh SM, et al (2009). Green tea consumption and risk of stomach cancer: a meta-analysis of epidemiologic studies. *Int J Cancer*, **124**, 670-7.
- Pearson RC, McCloy RF (1989). Preference for hot drinks is associated with peptic disease. *Gut*, **30**, 1201-5.
- Sun CL, Yuan JM, Lee MJ, et al (2002). Urinary tea polyphenols in relation to gastric and esophageal cancers: a prospective study of men in Shanghai, China. *Carcinogenesis*, **23**, 1497-1503.
- Wang JM, Xu B, Rao JY, et al (2007). Diet habits, alcohol drinking, tobacco smoking, green tea drinking, and the risk of esophageal squamous cell carcinoma in the Chinese population. *Eur J Gastroenterol Hepatol*, **19**, 171-6.
- Wu M, Liu AM, Kampman E, et al (2009). Green tea drinking, high tea temperature and esophageal cancer in high- and low-risk areas of Jiangsu Province, China: a population-based case-control study. *Int J Cancer*, **124**, 1907-13.
- Yang GY, Liao J, Kim K, et al (1998). Inhibition of growth and induction of apoptosis in human cancer cell lines by tea polyphenols. *Carcinogenesis*, **19**, 611-6.