

RESEARCH COMMUNICATION

Green Tea Drinking Habits and Gastric Cancer in Southwest China

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Abstract

Aim: The purpose of this study was to investigate relationships between green tea consumption and gastric cancer development. **Methods:** A population-based case-control study including 200 cases and 200 controls was conducted in the southwest area of China from May 2010 to February 2011. A self-designed questionnaire was used to collect data on factors influencing gastric cancer development, including tea drinking, conditional logistic regression being used to calculate odds ratios (ORs) and corresponding 95% confidence intervals (95% CIs). **Results:** Cases with higher economic status had a reduced risk of gastric cancer, while those with cancer family history, drinking and smoking showed increased risk. Hot and very hot tea temperature was significantly related to high risk of gastric cancer with ORs (95% CI) of 1.82 (1.03-3.52) and 3.07 (1.78-7.36), respectively. Further analysis indicated elevated risk of gastric cancer in former drinkers, former smokers and current drinkers when the measured tea temperature was hot. **Conclusion:** Drinking tea at high temperature increases the gastric cancer risk, especially in drinkers and smokers.

Keywords: Green tea - tea drinking temperature - case-control study - gastric cancer - South-west China

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Introduction

Gastric cancer is a global health problem, ranking the second in terms of mortality and the fourth in terms of morbidity in 2008 (Ferlay et al., 2008). The mortality of gastric cancer has substantially decreased in the past fifty years in China, but still the second leading cause of cancer death in China, and almost of 50% gastric cancer death occurred in China. It is estimated the absolute number of gastric cancer cases would increase up to the middle of 21 century due to population increasing and aging. It is estimated that the incidence and mortality in China of 2002 are 23 per 10⁵ for males and 17 per 10⁵ for females, respectively (Cai et al., 2008).

Tea is currently grown in at least 30 countries, and it is the most frequently consumed beverage worldwide after water, especially in Asian countries such as China, Japan and India (Mukhtar and Ahmad, 1999). The per capita worldwide consumption of tea is estimated to be 120 ml brewed tea per day⁴. Tea could be classified into 3 major types, including green tea (non-fermented), oolong tea (half-fermented) and black tea (fermented). Catechism, the main constituents of green tea extracts, has anti carcinogenic, anti mutagenic and antioxidant activity in experimental studies by using in vivo animal models (Yang et al., 1997; Khan et al., 1998; Mukhtar

and Ahmad, 1999). It has been considered the green tea consumption has a protective effect against the development of gastric cancer which is still prevalent in several Asian countries, including Korea, Japan and China. Since 1985, many epidemiological studies have addressed the association between green tea and gastric cancer, but results remain inconclusive. Previous studies reported a inverse association between green tea consumption and the risk of gastric cancer (Kono et al., 1988; Kato et al., 1990; Lee et al., 1990; Hoshiyama and Sasa, 1992; Yu et al., 1995; Inoue et al., 1998). Several prospective cohort studies reported no significant association was found between green tea consumption and gastric cancer risk (Galanis et al., 1998; Nagano et al., 2001; Tsubono et al., 2001; Hoshiyama et al., 2002). But a meta-analysis with cohort study reported highest green tea consumption was shown to significantly increase gastric cancer (Myung et al., 2009).

The controversial results might be that many studies did not consider the role of tea temperature in the development of esophageal cancer and may bias the their conclusions. A previous study suggested the high-temperature drinks are associated with gastric cancer (Silvia et al., 2010). Moreover, green tea drinking is often accompanied by tobacco smoking and alcohol drinking among Chinese population, people who frequently drink

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high concentration of green tea are often heavy smokers or alcohol drinkers (Sun et al., 2002). The smoking and drinking habit may offset the protective effect of green tea drinking or increase the risk of hot tea drinking for esophageal cancer (Mu et al., 2005).

Drinking green tea may showed protective affect on gastric cancer, but the hot temperature may be a potential risk factor. Therefore, we conducted a case-control study in Yunnan province, southwest of China. In our analysis, we measured the association of green tea drinking habits and its temperature with the gastric cancer, and provide information on the prevention of gastric cancer.

Materials and Methods

A case-control study was conducted from May 2010 to February 2011 in the Kunming General Hospital of Chinese PLA and the First People's Hospital of Yunnan Province. A total of 200 patients diagnosed with histological confirmed gastric cancer in the Kunming General Hospital of Chinese PLA and the First People's Hospital of Yunnan Province were collected. After selecting one case, we selected one health control visiting in the First Affiliated Hospital of Jinan University for routine physical examination, and matched the case with sex and age (± 5 years). A total of 200 control subjects (one control/ One case) who did not have a malignancy were selected and matched to cases.

The ethics committee of Kunming General Hospital of Chinese PLA and the First People's Hospital of Yunnan Province reviewed and approved the study, and informed consent was obtained from all participants.

Face to face interview was performed for all subjects.

Table 1. Characteristics of Gastric Cancer Cases and Matched Controls

Variables	Cases (%)	Controls (%)	OR (95% CI)
Mean age (years)	51.5 \pm 7	52.3 \pm 6	0.89
Sex			
Men	139(70)	139(70)	-
Women	61(30)	61(30)	
Education level			
Illiteracy	124(62)	102(51)	0.03
Literacy	76(38)	98(49)	0.64(0.42-0.97)
Income five years age (RMB)			
<1,000	46(23)	34(17)	0.009
1000-3000	90(45)	72(16)	0.92(0.52-1.64)
>3000	64(32)	94(47)	0.50(0.28-0.90)
Body Mass Index (BMI) ³			
Mean \pm SD	20.3 \pm 5.4	22.8 \pm 6.2	1.0 (reference)
<18.5	44(22)	17 (8)	<0.01
18.5-23.9	117(59)	119(60)	0.61 (0.31-0.92)
24-27.9	22(11)	41(21)	0.75 (0.42-1.07)
\geq 28	17 (8)	23(11)	0.92 (0.63-1.41)
Cancer family history (First degree relatives)			
No	126(63)	141(71)	0.14
Yes	74(37)	59(29)	1.40(0.90-2.10)
Smoking status			
Never	98(49)	144(72)	<0.001
Former	24(12)	12 (6)	2.94(1.33-6.75)
Current	78(39)	64(32)	1.79(1.15-2.78)
Alcohol drinking status			
Never	76(38)	112(56)	<0.001
Former	22(11)	10 (5)	3.24(1.37-8.08)
Current	102(51)	78(39)	1.93(1.25-2.98)

Two interviewers were trained and were not aware of the study hypothesis. Cancer patients were asked to refer about dietary habit a year before diagnosis. A structured questionnaire was specifically designed for this study, including demographic information, lifestyle habit [tobacco and all types of alcoholic beverages (beer, wine and distilled spirit)] and consumption of green tea, green tea drinking habit and disease history.

In the analysis, green tea drinking habits were categorized into former, never and current green tea drinking. Ever green tea drinking was defined as drinking at least one cup of green tea per week for more than 6 months. Individuals who quit drinking but quit in less than 1 year at the time of interview were considered current tea drinkers. Water temperature of green tea drinking was divided into cool, warm, hot or very hot. Alcohol drinking was categorized into former, never and current drinking. Individuals who quit drinking more than one year were considered as former drinkers, and individuals who drank more than 200 ml beers, 125 wine ml and 50 ml white spirit per month and continued for 6 months were regarded as current drinkers.

Tobacco smoking was categorized into former, never and current drinking. Individuals who quit smoking more than one year were considered as former smokers, while individuals who smoked more than 20 packets of cigarettes per year, or who smoked more than one cigarette per day and continued for 6 months were regarded as current smokers.

Statistical analysis

Data were entered into the computer by Epidata 3.0, and analyzed by STATA 9.0 software program. The age of patients and controls were compared by t-test, and the education level, income, BMI, cancer family history,

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

Variables	Cases (%)	Controls (%)	Crude OR (95% CI)	Adjusted OR (95% CI) [†]
Green tea drinking status				
Never	66 (33)	64(32)	1.0 (reference)	1.0 (reference)
Former	2(1)	3(2)	0.55(0.44-4.96)	0.58(0.46-5.03)
Current	132 (66)	133(66)	0.96(0.62-1.50)	1.02(0.70-1.64)
Investigated tea temperature				
Never	66(33)	64(32)	1.0 (reference)	1.0 (reference)
Cool	18(9)	26(13)	0.67(0.31-1.42)	0.85(0.54-1.72)
Warm	34(17)	62(31)	0.53(0.30-0.95)	0.81(0.58-0.97)
Hot	38(19)	28(14)	1.31(0.69-2.50)	1.82(1.03-3.52)
Very hot	44(22)	20(10)	2.13(1.09-4.25)	3.07(1.78-7.36)
Monthly consumption of green tea (g/month)				
Never	66(33)	64(32)	1.0 (reference)	1.0 (reference)
<150	54(37)	80(40)	0.65(0.39-1.10)	0.88(0.57-1.36)
150~	42(21)	40(20)	1.02(0.56-1.84)	1.15(0.76-2.35)
>250	18(9)	16(8)	1.09(0.49-2.50)	1.13(0.52-2.67)
Green tea concentration				
Never	66(33)	64(32)	1.0(reference)	1.0(reference)
Low	64(32)	90(45)	0.69(0.42-1.13)	0.65(0.38-1.03)
Moderate	48(24)	36(18)	1.29(0.72-2.33)	1.46(0.84-2.79)
High	22(11)	10(5)	2.13(0.88-5.44)	2.59(1.02-6.32)

[†]Adjusted for age, sex, education level, BMI, annual income, cancer family history, smoking and drinking status.

Table 3. The Effects of Green Tea Temperature on Gastric Cancer in Individuals with a Different Smoking and Drinking Status

Variables		Measured tea temperature				P for interaction
		Never	Warm	Hot	Very hot	
Smoking status	Never	1.0 (reference)	0.87(0.58-1.03)	1.21(0.79-2.16)	1.57(1.03-4.64)	0.24
	Former	2.76(1.21-6.43)	2.11(1.03-4.73)	3.96(1.29-6.35)	5.41(2.02-9.32)	
	Current	1.68(1.08-2.64)	1.19(0.83-1.96)	2.38(1.28-4.85)	3.43(1.85-5.98)	
Alcohol drinking	Never	1.0 (reference)	0.92(0.61-1.16)	1.34(1.03-2.67)	2.19(1.17-4.75)	0.37
	Former	3.17(1.26-7.04)	1.26(0.97-2.43)	3.98(1.68-4.82)	5.77(2.47-8.95)	
	Current	1.72(1.19-2.66)	1.15(0.85-1.94)	2.76(1.44-4.86)	3.06(1.95-5.92)	

Crude odds ratio (95% CI), adjusted for age, sex, education level, BMI, annual income and cancer family history

smoking and alcohol status, and green tea drinking status were compared by chi-square statistics, and we estimated the odds ratios (OR), and corresponding 95% confidence intervals (CI) by single factor analysis. The conditional logistic regression was used to OR and 95% (CI) for gastric cancer in relation to exposure of interest. Two models, a) none adjusted b) age, sex, education level, BMI, annual income, cancer family history status were examined. Dose-response relationship of green tea drinking habits was analyzed by chi-squared test for trend. Effect modification of smoking and drinking on green tea drinking habits was analyzed by stratification. All reported trend test significance levels (p-values) were two-sided (Castellsague et al., 1999). The chi-square test was used in analyzing the difference between groups. The significant level was set at 5%.

Results

A total of 200 cases and 200 controls were recruited into study. Cases with higher economic status reduced the risk of gastric cancer (annual income > 3000 RMB, OR=0.50, 95% CI=0.28-0.90) (Table 1). Cancer family history in first degree relatives significantly increased the risk of gastric cancer (OR=1.40, 95% CI=0.90-2.10). A heavy risk of gastric cancer was found in former smokers and drinkers (former smokers: OR=2.94, 95% CI=1.33-6.75; former drinkers: OR=3.24, 95% CI=1.37-8.08), a moderate risk in current drinkers (OR=1.93, 95% CI=1.25-2.98), and a light risk in current smokers (OR=1.79, 95% CI=1.15-2.78).

The relationship between green tea drinking habits and gastric cancer was showed in table 2. After adjusting the potential confounding factors, the hot and very hot green tea temperature were significantly related to high risk of gastric cancer with ORs (95% CIs) of 1.82(1.03-3.52) and 3.07(1.78-7.36) compared with never green tea drinking, respectively. The high concentration of green tea was showed, the high risk of gastric cancer was observed. No association was found between the monthly consumption of green tea and gastric cancer.

The alcohol drinking and smoking showed increased risk of esophageal cancer, so further analysis on the modification of green tea drinking by alcohol drinking and smoking were conducted in our study (Table 3). Additive effect was observed between hot green tea temperature and smoking or drinking. When the temperature was hot, a moderate risk of gastric cancer was observed in former smokers and drinkers, and a light risk in current smokers

and drinkers. When measured green tea temperature was very hot, a heavy risk of gastric cancer was found in former drinkers and smokers, and current drinkers.

Discussion

This population-based study found there was relationship between the green tea intake and gastric cancer, the warm tea presented protective effect on gastric cancer, while the hot and very hot tea showed a heavy risk of gastric cancer. The drinkers and smokers revealed heavy gastric cancer risk when drinking high temperature tea.

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 (Ahmad et al., 1997; Graham, 1992; Yang, 1998). Green tea was shown to have a preventive effect on gastric cancer by a meta-analysis with pooling case-control studies (Myung, 2009). But a significantly increased gastric cancer risk was found in cohort studies (Myung, 2009). The tea temperature might be a plausible modification for the conflicting relationship between them. Therefore, our study analyzed the association between tea temperature and gastric cancer, and showed the tea temperature is a great modification on the risk of gastric cancer.

Previous study indicated hot food could increase the risk of gastric cancer. The explanation might be that hot food could cause chronic thermal injury to the upper digestive tract and therefore make it more susceptible to carcinogenesis. Some studies indicated the inflammatory induced by hot food processes associated with chronic irritation of the gastric 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 found intake of hot temperature tea was positive associated with the risk of gastric cancer. It is in line with the previous study, which indicated the hot tea intake was associated with gastric cancer risk, while lukewarm was negative related to the gastric cancer risk (Li et al., 2003).

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 heavy cancer risk in drinkers and smokers could be explained by the green tea drinkers usually together with tobacco and alcohol, which may increase the risk of gastric

cancer (Silvia et al., 2010; Sun et al., 2002). Additional, we found hot tea drinking had heavy cancer risk in former drinkers and smokers. This explanation may be individuals quitting drinking or smoking may be due to 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 detect the it in cases and controls in our study, and this may induce information bias. However, the H.pylori infection rate is above 50% (Li et al., 2003) in Chinese general population and is also about 50%-70% in gastric cancer patients (Wang and Wang, 2003), which suggested the environmental factors may play a important role in gastric cancer development rather than H.pylori. Therefore, the H.pylori may not be greatly influence the results. Secondly, there might be recall bias in our study. But recall bias exists in all case-control studies. We reminded cases the green tea drinking habit should be one year refer to cancer diagnosis, and this minimized the recall bias in our study. Thirdly, potential selection bias and information bias may exist in our study. But 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. Finally, the small number of subjects may lower the statistical power to find the relationship between green tea consumption and gastric cancer, so a large scale study is warranted.

To summarize, warm tea showed a protective effect on gastric cancer, while a heavy risk of gastric cancer was found in very hot tea drinking, and modified by drinking and smoking. The findings broaden the effect of green tea on gastric cancer and may provide a new strategic approach to the prevention of gastric cancer.

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