RESEARCH COMMUNICATION

Salt Taste Sensitivity, Physical Activity and Gastric Cancer

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Abstract

Background: Gastric cancer is one of the main health issues in China. The risk factors of the disease are related to nutrition and environment. Salt taste sensitivity is the capacity to identify the flavor of salt. Salt taste sensitivity threshold (STST) can influence salt appetite, and it is assumed to have association with gastric cancer. Methods: A 1:2 matched hospital based case-control study including 300 cases with newly histological confirmed diagnosis of gastric cancer and 600 controls that were cancer and gastric diseases free were used. A self-designed questionnaire was used to collect information dietary and lifestyle habit, and physical activity, and salt taste sensitivity test was used to measure the STST for all subjects. Conditional logistic regression was used to calculated Odds Ratios (ORs) and 95% confidence intervals (95% CI). Results: An increased risk of gastric cancer is related to the consumption of smoking, drinking, family history of cancer and salted food. Walking and sports activity [adjust OR=0.69(0.51-0.99) for ≥4 times/week] presented protective effect for gastric cancer. There is a significant positive association between increased STST and gastric cancer, and the adjusted OR was 2.05(1.68-2.5). When we used STST≥5 as a cut point, people with STST≥5 were at 5.71 times greater risk of gastric cancer than those with STST<5. STST showed moderate association with physical activity (Correlation coefficient =0.22). Cut point of STST ≥5 had a best sensitivity and specificity for predicting gastric cancer risk detection (sensitivity for 73.67%, specificity for 57%). Conclusion:Salt and salted food intake is association with gastric cancer, while physical activity showed protective effect. A high STST is strong association with gastric cancer risk.

Keywords: Salt taste sensitivity threshold - physical activity - gastric cancer

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Introduction

Gastric cancer is the fourth most common cancer world, and is the second most common cause of death from cancer (Stewart and Kleihues, 2003). Its incidence shows wide geographical variation, and almost two-thirds of the cases occur in developing countries and 42% of them in China alone. Although the incidence and mortality rates of gastric cancer, the absolute number of cases is predicted to increased up to the year 2050 (Forman and Burley, 2006). In China, gastric cancer ranked the third among the most common cancer, with an age-standardized incidence of 37.1 and 17.4 cases per 100,000 person-years for men and women, respectively, according to the 2005 national cancer statistics (Yang, 2006). Therefore, prevention of gastric cancer is one of the most important cancer control strategies both in China and around the world.

Salt is usually used for improve the taste of food, and it has been hypothesized to be a cause of cancer and an important cause for gastric cancer (WCRF/AICR, 2006; WCRF/AICR,2007). High dietary salt intake may potentiate the colonization of *H pylori* through the increase of surface mucous cell mucin and decrease of gland mucous cell mucin (Fox et al., 1999; Kato et al., 2006). At the molecular level, high dietary salt intake may potentiate CagA (*H pylori* gene) expression and enhance the ability of CagA to translocate into gastric epithelial cells and enhance the ability of *H pylori* to alter gastric epithelial cell function (Loh et al., 2007). Lots of population-based studies and experimental studies showed that high intake of salted food may be a risk factor for the development of gastric cancer (WCRF/AICR, 2006). But the quantity of salt intake is hard to measure. Usually, 24 urinary was used to accurate detect salt intake, but this method is complicated, and cannot be used in case-control study. Salt taste sensitivity is the capacity to identify the flavor of salt, salt taste sensitivity threshold can influence salt appetite or salt food preference (Nilsson et al., 1979), and this test is simple for patients and investigator. Therefore, it is possible that the high salt taste sensitivity could be associated with the development of gastric cancer. Physical activity is regarded as a protective factor for gastric cancer, it is associated with higher levels of physical functioning and cardiorespiratory fitness, reduced feelings of fatigue, and improved health-related quality of life in cancer patients (Yancik et al., 2000). But heavy and frequently physical activity may related to large loss of sweat salt, it may increase the salt intake and influencing the salt taste. This study aimed to analyze the relationships among salt taste sensitivity threshold, physical activity and gastric

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cancer. We are not aware of any previous study examining such relationship.

Materials and Methods

A hospital-based case-control study has been carried out in the Shayin People's Hospital in Shayin County of Shanxi Province. The study included 300 patients aged 40-75 years who had histological confirmed diagnosis of gastric cancer from January 2008 to July 2010. Hospital-based controls were individually matched to case-patients by gender and age (±5 years). Controls were patients selected from Surgical Department, Plastic Surgery Department, ENT Department and Department of Gynecology. Ratio of cases to controls was 1:2. Totally, we selected 600 controls that were malignant tumors or digestive tract disorders free.

A self-designed structured questionnaire was used in the study, including demographic information, family history, lifestyle habits, and dietary habits, diet and lifetime consumptions of all types of alcoholic beverages (beer, wine and distilled spirit) as well as physical activity.

Face to face interview was performed for all subjects by two trained interviewer. Cancer patients were asked to refer about some lifestyle habits (diet and physical activity) a year before the disease diagnosed. After interviewing for questionnaires, the salt taste sensitivity test was performed to all the subjects. The STST was measured by using NaCl solutions on the tip of the tongue with a dropper. Five drops of the test solution were placed on the tongue. After 10 s closing the mouth, the cases and controls mentioned which taste of usually food was perceived. The solutions were offered in increasing concentrations. Between the tests, the mouth will be washed with distilled water, with 30s intervals among successive tests. The concentrations of each test NaCl solution were classified into ten grades from 0.22 g/L to 58.4 g/L, and the STST value for salt recognizing in normal individuals was 0.015mol/L of NaCl (0.9g/L) (Table 1).

Questions on dietary habits, a main variable of interest, pertained to the following: meal regularity(regular, medium, and irregular), salt food preference(not salty, medium, and salty), and diet preference was classified into three categories: never, ≤3 times/ week and ≥4 times/week. Physical activity was classified into three categories: never, ≤3 times/ week and ≥4 times/week. Cigarette smoking was measured in pack-years(number of cigarettes smoked per day/20×smoking time(in years)), and divided into three categories: non-smokers;smokers who consumed less than 41 pack/year, and 41pack/year or more; Alcohol consumption was calculated from the amount of alcohol consumed per day in grams. The subjects were classified into four categories: nondrinkers,drinkers who consumed less than 22.8g alcohol per day, 22.8-45.5g alcohol per day and 45.6 g or more alcohol per day.

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

Statistical analysis

The conditional logistic regression was used to calculate odds ratios (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, fresh fruit and fresh vegetables adjusted, were examined. Tests for trend were computed by fitting conditional logistic regression model to ordinal values representing levels of exposure. All reported trend test significance levels(p-values) were two-sided (Woodward, 1999). The association between STST and physical activity was tested by Spearman's rank correlation coefficients. The chi-square test was used in analyze the difference between groups. The significant level was set at 5%. All the calculations were performed with the STATA 9 software program.

Results

All the patients finished questionnaires and STST. The mean NaCl concentration in patients was 3.6 g/L with the 95% CI of 1.8 to 7.3, and in controls was 1.8 g/L with the 95% CI of 0.9 to 3.6. The NaCl concentration of patients was significantly higher than that in controls (t=14.67, p<0.001) (Table 1). The general variables and proportion of selected risk factors among cases and controls was shown in Table 2. Of 300 cases and 600 controls, 71% of them were males and 29% of them were females. About 66% cases were at the age of 50 to 64 years old. Cases had lower education level compared with controls. A positive association was found between family history and gastric cancer (2.07 (1.46-2.95)). The alcohol consumption and tobacco consumption also were significantly association

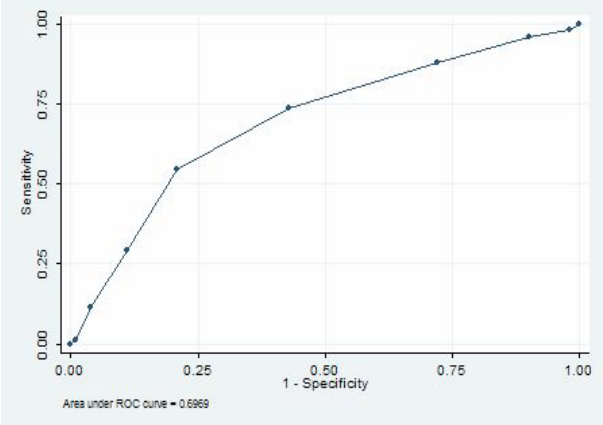

Figure 1. ROC Plot of STST for Gastric Cancer Risk

Table 1. Concentration of Sodium Chloride in All Bottles

STST Score	NaCl Concentration		Patients	Controls
	g/L	Mol/L	n=300	N=600
1	0.22	0.004	5 (2%)	12 (2%)
2	0.45	0.008	7 (2%)	48 (8%)
3	0.9	0.015	24 (8%)	108(18%)
4	1.8	0.030	43(14%)	174(29%)
5	3.6	0.060	57(19%)	132(22%)
6	7.3	0.120	76(25%)	60(10%)
7	14.6	0.150	54(18%)	42 (7%)
8	29.2	0.500	31(10%)	18 (3%)
9	58.4	1	3 (1%)	6 (1%)

Table 2. OR and 95% CIs for Lifestyle and Dietary Related Factors and GC

Characteristics	Patients N=300	Controls N=600	OR (95% CI)	P[1]
Age (yr)				
<50	41 (14%)	101 (17%)	-	>0.05
50-64	189 (63%)	396 (66%)	-	
≥65	70 (23%)	103 (17%)	-	
Mean age (SD)	58.9(0.48)	57.7(0.33)		
Sex				
Male	214 (71%)	428 (71%)		
Female	86 (29%)	172 (29%)		
Education				0.12
Illiterate	96 (42%)	162 (27%)		
Literate	204 (58%)	438 (73%)	0.79(0.59-1.06)	
BMI, kg/m2				
<25	169 (56%)	282 (47%)	Reference	<0.001
25-29.9	72 (24%)	162 (27%)	0.74(0.52-1.05)	
≥30	59 (20%)	156 (26%)	0.63(0.43-0.91)	
Smoking (pack-years)				
None-smokers	66 (22%)	162 (27%)	-	<0.001
<41	156 (52%)	276 (46%)	2.27(1.27-4.04)	
≥41	78 (26%)	162 (27%)	2.08(1.07-4.05)	
Drinking (g/day)				
None-drinkers	60 (20%)	197 (33%)	-	<0.001
<41	72 (24%)	134 (22%)	2.41(1.51-3.87)	
≥41	105 (35%)	177 (30%)	3.24(1.97-5.35)	
≥45.6	63 (21%)	92 (15%)	3.96(2.25-6.96)	
Family history of cancer				
No	227 (76%)	521 (87%)	Reference	<0.001
Yes	73 (24%)	79 (13%)	2.07 (1.46-2.95)	
Fresh vegetable				
never	27 (9%)	42 (7%)	Reference	<0.001
≤3 times/ week	201 (67%)	318 (53%)	0.97(0.58-1.67)	
≥4 times/week	72 (24%)	240 (40%)	0.67(0.36-0.92)	
Fresh fruit				
never	144 (48%)	180 (30%)	Reference	<0.001
≤3 times/ week	120 (40%)	282 (47%)	0.72(0.47-0.93)	
≥4 times/week	36 (12%)	138 (23%)	0.52(0.33-0.69)	

Table 3. OR and 95% CIs for Salt Related Factors and GC

	Cases	Controls	OR[1](95%CI)	P	OR[2](95%CI)	P
Domestic activity						
never	234(78%)	449(75%)	Reference	-	-	-
≤3 times/ week	37(12%)	85(14%)	0.82(0.52-1.26)	0.34	0.95(0.74-1.67)	0.78
≥4 times/week	29(10%)	76(13%)	0.72(0.44-1.15)	0.15	0.83(0.57-1.44)	0.31
Walking and sports activity						
never	135(45%)	231(39%)	Reference	-	-	-
≤3 times/ week	89(30%)	179(30%)	0.73(0.52-1.03)	0.06	0.77(0.61-1.23)	0.09
≥4 times/week	76(25%)	190(31%)	0.68(0.48-0.98)	0.03	0.69(0.51-0.99)	0.04

OR[1] for salt related factors and GC were none adjusted. OR[2] were adjusted for age, sex, BMI, family history, smoking, drinking, fresh fruit and fresh vegetables.

with gastric cancer, and we observed a dose-dependent increased risk of gastric cancer with the consumption of alcohol consumption (p for trend <0.001). In contrast, intake of fresh vegetable and fruit were protective against gastric cancer. Those who consumed fresh vegetable and fruit more than 4 times per week was associated with a significantly lower risk compared with never consumption [OR=0.67(0.36-0.92) for fresh vegetables, p for trend <0.001; OR=0.52(0.33-0.69) for fresh fruit, p for trend <0.001].

Table 3 showed the relationship between the physical activity and gastric cancer. Domestic activity showed light protective effect on the gastric cancer, but no significant difference was found. Frequently walking and sports activity could play an protective effect on gastric cancer with adjusted OR(95%CI) of 0.69 (0.51-0.99).

The Mean STST score was 4.8±1.1, and the median NaCl concentration was 3.6 g/L(3.6-7.3) or 0.06(0.06-0.12) Mol/L corresponding to a score of 5(5-6). Then we defined the STST cut point to be 5 score (3.6g/L or 0.06 Mol/L). The Mean STST score for cases and controls were 5.52±1.26 and 4.4±0.91, respectively (Table 4). There was a significant positive association between increased STST and gastric cancer, and the adjusted OR was 2.05(1.68-

Table 4. OR and 95% CIs for Salt Related Factors and GC

Salted factors	Cases	Controls	OR[1](95%CI)	P	OR[2](95%CI)	P
Salted and preserved meat						
never	45 (15%)	91 (15%)	Reference		Reference	
≤3 times/ week	99 (32%)	241 (40%)	1.54(1.15-2.93)	0.01	2.01(1.71-3.67)	<0.001
≥4 times/week	156 (52%)	268 (45%)	1.94(1.44-3.82)	<0.001	2.55(1.37-4.76)	<0.001
Pickled vegetables						
never	120 (40%)	298 (50%)	Reference		Reference	-
≤3 times/ week	97 (32%)	219 (37%)	1.11(0.81-1.53)	0.52	1.23(0.59-1.76)	<0.001
≥4 times/week	83 (28%)	83(13.8%)	1.69(1.14-2.17)	<0.001	2.13(1.74-4.33)	<0.001
Salted fish						
never	99 (33%)	201 (35%)	Reference		Reference	
≤3 times/ week	126 (45%)	282 (47%)	0.87(0.67-1.21)	0.34	0.93(0.57-1.35)	0.56
≥4 times/week	75 (22%)	108 (18%)	1.21(0.92-1.68)	0.07	1.46(0.98-1.97)	0.06
STST score	5.52±1.26	4.4±0.91	1.66(1.48-1.85)	<0.001	2.05 (1.68-2.5)	<0.001
STST≥5	221(73.7%)	258 (43%)	4.03(2.87-5.65)	<0.001	5.71(3.18-6.72)	<0.001

OR[1] for salt related factors and GC were none adjusted. OR[2] were adjusted for age, sex, BMI, family history, smoking, drinking, fresh fruit and fresh vegetables.

Table 5. Accuracy of STST for Predicting Gastric Cancer Risk

STST Score	Sensitivity	Specificity
1	100.00%	0.00%
2	98.33%	2.00%
3	96.00%	10.00%
4	88.00%	28.00%
5	73.67%	57.00%
6	54.67%	79.00%
7	29.33%	89.00%
8	11.33%	96.00%
9	1.00%	99.00%

2.5). When we use STST≥5 as a cut point, people with STST≥5 were at 5.71 times greater risk of gastric cancer than those with STST<5 (OR=5.71(3.18-6.72)). Also, the pickled vegetables and salted meat intake presented significant association with gastric cancer ($p<0.05$), and a significant dose-response increased risk of gastric cancer was found in salted meat and pickled vegetables (p for trend <0.001).

The frequently activity may cause the loss of sweat salt, thus may induce the frequently high consumption of salt, and we explored the correlation between the relationship between the physical activity and STST. The spearman's rank correlation coefficient for agreement between the two variables was 0.22 ($p<0.001$).

The accurate of STST for predicting gastric cancer risk was showed in Table 4. The ROC curve (Figure 1) presented A STST≥5 had a best sensitivity and specificity for gastric cancer risk detection compared with other threshold (sensitivity for 73.7%, specificity for 57.0%).

Discussion

The present hospital based case-control study has demonstrated an increased risk of gastric cancer related to the consumption of smoking, drinking, family history of cancer and salted food, also a dose-dependent increased risk of gastric cancer was found for smoking, drinking and salted food. Patients with frequently walking and sports activity presented protective effect on gastric cancer, and showed a light correlation with STST (correlation coefficient=0.22). Patients with gastric cancer have a higher mean STST than controls, and that a STST of 3.6g/L (0.03Mol/L) was associated with a strong risk of gastric cancer. A STST of 3.6g/L (0.03Mol/L) had a best sensitivity and specificity to predicting gastric cancer risk compared with other salt concentration. compared with other salt concentration.

In our study, the dietary habits were identified as the risk factors for gastric cancer. Smoking plays a role in developing gastric cancer, which is consistent with the recent IRAC report that tobacco smoke has a causal role in gastric cancer development (Secretan et al., 2009). Also, this study showed drinking is positively association with gastric cancer risk, and this association may be due to the biological effect on carcinogenic of alcoholic beverages to humans (Secretan et al., 2009). The protective effect of fresh vegetable and fruit against gastric cancer was found, and it may be dedicated by antio-oxidants such as ascorbic acid (Cai, 2003). Therefore, intake of more fresh vegetable and fruit may significantly lower the risk of gastric cancer, which is consistent with former epidemiologic studies (Hill 1998; Ward et al., 1999; Li et al., 2001; Liu et al., 2001). Family aggregation of the gastric cancer has been confirmed in this study with adjusted OR of 2.07 (1.46-2.95). The reason for the first-degree relatives suggested the inherited genetic susceptibility and shared environmental risk factors might contribute to the gastric cancer development.

Our study observed a lower BMI was related an increased risk of gastric cancer, and the main reason might be the high incidence of gastric cancer usually occurrence in low economic status area, and low economic status is usually related to lower intake of fat and fast food and lower BMI. We further analyzed the association between physical activity and gastric cancer. Frequently physical activity is related a protective effect on gastric cancer, and the main reason might have beneficial impact on reducing the sex hormones or insulin resistance and improving immune system, maintaining a healthy body weight by balancing caloric intake with energy expenditure, these may play an role in cancer prevention (McTiernan et al., 2004). The physical activity also showed a light correlation with STST (correlation coefficient=0.22), this means

heavy and frequently physical activity may associated with high loss of sweat salt, and this may induce the high consumption of salt and influence the salt preference. Their association explanation needs further more studies to prove.

Our study observed a salted meat intake is relatively common, and a high frequent consumption of salted meat increased the OR for gastric cancer, which is in line with other established positive association between salted meat consumption and risk of gastric cancer (Ward et al., 1997; Cai et al., 2003). Elevated risk of the disease might be attributed to enhance the carcinogenic effects of known gastric carcinogens such as N-methyl-N-nitro-Nnitrosoguanidine (Tatamatsu et al., 1975; Takahashi and Hasegawa, 1985), and may also involved the increased cell replication and susceptibility to carcinogenesis from the salt intake. In our study, we did not found a significantly association between salted fish intake and gastric cancer, however, previous studies indicated Chinese-style salted fish could cause the gastric cancer (Secretan et al. 2009). This may be caused by the economic changes of Chinese residents, and a reduction in salted fish intake is seen to be less and a more refrigerators use and fresh fish intake are seen, so the number of high frequent consumption is obviously reduced, and the power is correspondingly lower to detect the risk of salted fish.

STST is a personal characteristic of the individual and may be eventually be a practical way to evaluate who eats more salt and who has the higher preference for salt(Spritzer, 1985). STST test was used to detect hypertension (Weinberger et al., 1986; Campese 1994). But for gastric cancer, there is no study used this method to explore its association with gastric cancer. Previously, 24h urinary excretion of salt was usually used for measuring the salt intake of this kind of people (Montes et al., 1985; Tsugane et al., 1992), and found strong correlation with gastric cancer mortality which showed weak or nonsignificantly correlated in dietary salt. Although 24h urinary collection may be an optimal method and objective in estimating routine salt intake, it is impracticable for a large-scale population study, and is not optimal to be used in case-control study. However, STST test is simpler, cheaper and more acceptable than the STST test. In our study, we could observe a higher STST is significantly association with gastric cancer. The adjusted OR was 2.05(1.68-2.5) compared with the normal STST, which meaned the high STST may associate with high intake of salt to induce high risk of gastric cancer, it is in line with the established positive association between salt intake and gastric cancer by 24h urinary collection. Besides, STST≥5 had a high sensitivity and specificity for gastric cancer risk detection compared with other threshold (sensitivity for 73.67%, specificity for 57%), which gave an clear threshold for people who are more preference to salt and should be give more health education or intervention for salt intake.

Several limitations of this study should be considered. Firstly, the STST test did not finish before the cancer happened, and the patients may change their salt preference after getting cancer, so the recall bias existed. But we analyzed the relationship between the STST score and salt food intake, and positive association was presented, which indicated the STST could correctly reflect the salt preference. Besides, the recall bias could not be partly neglect in every case-control study, so we used method of reminding patients the questions and the STST were their habits and taste a year before the disease diagnosed. Secondly, the small number of subjects is another limitation, and further studies in a large scale appear warranted.

To summarize, it's the first time to explore the association between the STST and gastric cancer, and the study suggests that STST may be a way to evaluate an inherited characteristics of salt preference, a simple way to verify in clinic the STST to salt. The role of STST has to be further studies to answer the questions raised from the present study.

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