

## A case-control study on the relationship between salt intake and salty taste and risk of gastric cancer

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### Abstract

**AIM:** To investigate the relationship between salt intake and salty taste and risk of gastric cancer.

**METHODS:** A 1:2 matched hospital based case-control study including 300 patients with gastric cancer and 600 cancer-free subjects as controls. Subjects were interviewed with a structured questionnaire containing 80 items, which elicited information on dietary, lifestyle habits, smoking and drinking histories. Subjects were tested for salt taste sensitivity threshold (STST) using

concentrated saline solutions (0.22-58.4 g/L). Conditional logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (95% CI).

**RESULTS:** Alcohol and tobacco consumption increased the risk of gastric cancer [OR (95% CI) was 2.27 (1.27-4.04) for alcohol and 2.41 (1.51-3.87) for tobacco]. A protective effect was observed in frequent consumption of fresh vegetable and fruit [OR (95% CI) was 0.92 (0.58-0.98) for fresh vegetable and 0.87 (0.67-0.93) for fruit]. Strong association was found between STST  $\geq 5$  and gastric cancer [OR = 5.71 (3.18-6.72)]. Increased STST score was significantly associated with salted food intake and salty taste preference ( $P < 0.05$ ).

**CONCLUSION:** A high STST score is strongly associated with gastric cancer risk. STST can be used to evaluate an inherited characteristic of salt preference, and it is a simple index to verify the salt intake in clinic.

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**Key words:** Gastric cancer; Salt taste sensitivity threshold; Salt taste preference

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### INTRODUCTION

Gastric cancer is the fourth most common cancer in the world, and is the second most common cause of death

from cancer<sup>[1]</sup>. Its incidence shows wide geographical variation, but almost two-thirds of the cases are from developing countries, including 42% from China. Although gastric cancer is decreasing in most populations, the absolute number of cases is predicted to increase up to the year 2050 due to the aging of the population<sup>[2]</sup>. In China, gastric cancer is the third most common cancer, with an age-standardized incidence of 37.1 and 17.4 cases per 100000 person-years in men and women, respectively<sup>[3]</sup>. Therefore, prevention of gastric cancer is one of the most important cancer control strategies both in China and around the world.

High intake of salt is hypothesized to be a cause of cancer and an important cause of gastric cancer<sup>[4,5]</sup>. Evidence has proved that a high salt intake damages the gastric mucosa producing atrophy and intestinal metaplasia<sup>[6,7]</sup>. In addition, a high salt diet has been shown to have a synergistic interaction with gastric carcinogens<sup>[8,9]</sup>. In animal experiments, the co-administration of a high dietary salt intake enhances both the initiation and promotion of gastric cancer induced by carcinogenic N-nitroso compounds<sup>[10]</sup>. It has been shown that a high intake of salted food is associated with increased risk for gastric cancer. But a recent meta-analysis showed a weak association between salt and gastric cancer<sup>[4]</sup>, and the relationship between quantity of salt intake and gastric cancer is hard to estimate. Most studies evaluated the salt preference only by the subjective feeling of subjects, and salty taste sensitivity test has the capacity to identify the flavor of salt, and its threshold can influence salt appetite or salt food preference<sup>[11]</sup>. This method can be used to assess the association between salt preference and gastric cancer. The purpose of this study was to analyze the relationship between salt intake, salty taste and risk of gastric cancer.

## MATERIALS AND METHODS

A hospital-based case-control study was carried out in the Shanyin People's Hospital in Shanyin of Shanxi. The study included 300 patients aged 40-75 years who had histologically confirmed diagnosis of gastric cancer from January 2006 to July 2010. Hospital-based controls were individually matched to cases by gender and age ( $\pm 5$  years). Controls were patients selected from the Surgical Department, Plastic Surgery Department, ENT Department and Department of Gynecology. Ratio of cases to controls was 1:2. Totally, there were 600 controls who were non-cancer or cancer-free subjects.

A self-administered structured questionnaire consisting of 80 items was used in the study. It included questions about demographic information, dietary and lifestyle habits, smoking and drinking history and so on. Face to face interview was made for all subjects by trained interviewers. A completed questionnaire was obtained from 900 subjects. Cancer patients were asked of habits a year before the disease diagnosed. After interviewing for questionnaires, the salt taste sensitivity test was performed in all the subjects. The salt taste sensitivity threshold (STST) was measured using NaCl solutions on the tip of the tongue with

Table 1 Concentration of sodium chloride *n* (%)

STST score	NaCl concentration		Cases ( <i>n</i> = 300)	Controls ( <i>n</i> = 600)
	g/L	mol/L		
1	0.22	0.004	5 (2)	12 (2)
2	0.45	0.008	7 (2)	48 (8)
3	0.90	0.015	24 (8)	108 (18)
4	1.80	0.030	43 (14)	174 (29)
5	3.60	0.060	57 (19)	132 (22)
6	7.30	0.120	76 (25)	60 (10)
7	14.60	0.150	54 (18)	42 (7)
8	29.20	0.500	31 (10)	18 (3)
9	58.40	1	3 (1)	6 (1)

STST: Salt taste sensitivity threshold.

a dropper. Five drops of the test solution were dripped on the tongue. Ten seconds after closing the mouth, the cases and controls who tasted the usual food were perceived. The solutions were offered in increasing concentrations. Between the tests, the subjects were asked to wash their mouths with distilled water at a 30-s interval during the 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 recognition in normal individuals was 0.015 mol/L of NaCl (0.9 g/L) (Table 1).

Questions included the frequency of intake of various food. For diet preference, the subjects chose one of the following frequencies: < 3 times/wk and  $\geq 3$  times/wk. Salty food preference was classified into not salty, medium, and salty. Cigarette smoking was measured in pack-years (number of cigarette smoking per day/20  $\times$  smoking time in years) and divided into two categories: smokers who consumed < 40 packs/year and  $\geq 40$  packs/year or more; alcohol consumption was calculated according to the amount of alcohol consumed per day in grams. The subjects were classified into two categories: drinkers who consumed less than 22.8 g alcohol per day and  $\geq 22.8$  alcohol per day.

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

### Statistical analysis

The conditional logistic regression was used to calculate odds ratios (ORs), and corresponding 95% confidence intervals (CI) for gastric cancer in relation to exposure of interest. Two models were examined: (1) none-adjusted; (2) age, sex, smoking, drinking, fresh fruit and fresh vegetables adjusted. 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<sup>[12]</sup>. The relationship between STST score and lifestyle and dietary factors was evaluated by Chi-square test. The coherence of STST score with salty taste preference was detected by Anova test. All the calculations were performed by statistical package version 9, STATA 9, College Station, TX.

Table 2 Odds ratio and 95% CIs for lifestyle- and diet-related factors and gastric cancer *n* (%)

Characteristics	Cases ( <i>n</i> = 300)	Controls ( <i>n</i> = 600)	OR (95% CI)	<i>P</i> value
Age (yr)	52.1 ± 5.4	52.4 ± 4.9		> 0.05
Male	214 (23.7)	428 (71.3)		
Education				0.12
Literate	96 (32.0)	162 (27.0)	0.79 (0.59-1.06)	
Smoking	156 (52.0)	276 (46.0)	2.27 (1.27-4.04)	< 0.001
Drinking	72 (24.0)	134 (22.3)	2.41 (1.51-3.87)	< 0.001
Fresh vegetable				
< 3 times/wk	99 (33.0)	282 (47.0)	-	< 0.001
≥ 3 times/wk	201 (67.0)	318 (53.0)	0.92 (0.58-0.98)	
Fresh fruit				
< 3 times/wk	144 (48.0)	219 (36.5)	-	< 0.001
≥ 3 times/wk	156 (52.0)	381 (63.5)	0.87 (0.67-0.93)	
Salted food(meat and fishes, pickled vegetable)				
< 3 times/wk	120 (40.0)	298 (49.7)	-	
≥ 3 times/wk	180 (60.0)	302 (50.3)	1.54 (1.15-2.93)	< 0.05
STST score	5.52 ± 1.26	4.4 ± 0.91	1.66 (1.48-1.85)	< 0.001

STST: Salt taste sensitivity threshold. OR: Odds ratio.

Table 3 Relationship between salt taste sensitivity threshold score and lifestyle factors

	<i>n</i> (%)	STST score (mean ± SD)	<i>P</i>
Age (yr)			
< 50	224 (24.9)	4.79 ± 1.25	0.76
50-64	543 (60.3)	5.10 ± 0.83	
≥ 65	133 (14.8)	5.08 ± 1.56	
Smoking (packs/yr)			
< 40	660 (73.3)	4.88 ± 1.02	0.93
≥ 40	240 (26.7)	5.24 ± 1.51	
Drinking (g/d)			
< 22.8	517 (57.4)	5.10 ± 1.02	0.10
≥ 22.8	383 (42.6)	5.19 ± 1.12	
Fresh vegetable(times/wk)			
< 3	241 (26.8)	5.14 ± 1.08	0.18
≥ 3	659 (73.2)	5.07 ± 0.97	
Fresh fruit (times/wk)			
< 3	363 (40.3)	5.18 ± 1.41	0.11
≥ 3	537 (59.7)	5.07 ± 1.15	
Salted food intake (times/wk)			
< 3	418 (46.4)	4.68 ± 1.32	
≥ 3	482 (53.6)	5.47 ± 0.98	< 0.001

STST: Salt taste sensitivity threshold.

## RESULTS

The characteristics of the subjects are listed in Table 2. Among the 300 cases and 600 controls, 71% were males, and their mean age was 52.1 and 52.4 years, respectively. There was a significant difference in educational level between cases and controls. Smokers and drinkers showed an increased risk of developing gastric cancer with OR (95% CI) = 2.27 (1.27-4.04) and 2.41 (1.51-3.87), respectively. In contrast, consumed protective effect was found in those who took 3 times/wk of fresh vegetable and fruit, OR (95% CI) = 0.92 (0.58-0.98) and 0.87 (0.67-0.93), respectively. The mean STST score of cases was significantly higher than that of controls.

We analyzed the association between STST score and other risk factors. The results showed that STST score was increased with age and duration of smoking and drinking, but no significant association was found (Table 3). STST score was significantly increased with a higher salted food intake.

The mean STST score of all subjects was  $4.8 \pm 1.1$ , 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 (Table 2). There were more patients with STST ≥ 5 than the controls (Table 4). We defined the STST cut-point as 5 (3.6 g/L or 0.06 mol/L). Subjects with STST ≥ 5 had 5.71 times greater risk of gastric cancer than those with STST < 5 (Table 4).

The relationship between the salty taste preference and STST score indicated that the salty taste preference was significantly associated with STST score ( $P < 0.001$ ) (Table 5), which means that the subjects with a higher STST score was more likely to prefer a salty taste.

## DISCUSSION

The present hospital based case-control study indicated that high consumption of smoking, drinking and salty taste preference elevated the risk of gastric cancer, and that the gastric cancer was associated with a higher STST score. The STST score of 3.6 g/L (0.03 mol/L) was independently associated with a high risk of gastric cancer with the OR (95% CI) of 5.71 (3.18-6.72).

STST is a personal characteristic of an individual and is a useful index to evaluate the salty preference<sup>[13]</sup>. STST test was used for predicting hypertension in previous studies<sup>[14,15]</sup>, and it indicated that hypertensive individuals were more salt sensitive than the normal individuals<sup>[16]</sup>. Our study proved that subjects with a higher STST score were more likely to have salty taste preference and a high intake of salty food (Table 4), and it further indicated that STST is a helpful test to evaluate the salty taste preference and

**Table 4 Odds ratio and 95% CIs for salt-related factors and gastric cancer *n* (%)**

Salt factors	Cases	Controls	OR1 (95% CI)	<i>P</i>	OR2 (95% CI)	<i>P</i> value
Salted taste preference						
Not salty	118 (39.3)	301 (50.2)	-	-	-	-
Medium	162 (54)	265 (44.2)	1.12 (0.79-1.89)	<i>P</i> = 0.45	1.34 (0.92-2.67)	<i>P</i> = 0.08
Salty	20 (6.6)	34 (5.7)	1.33 (1.02-1.75)	< 0.05	1.94 (1.37-4.76)	< 0.05
STST ≥ 5	221 (73.7)	258 (43)	4.03 (2.87-5.65)	< 0.001	5.71 (3.18-6.72)	< 0.001

OR1 for salt related factors and gastric cancer was none-adjusted; OR2 was adjusted for age, sex, smoking, drinking, fresh fruit and fresh vegetables; STST: Salt taste sensitivity threshold. OR: Odds ratio.

**Table 5 Relationship between salt taste sensitivity threshold score and salt intake *n* (%)**

Salty taste preference	STST score						<i>P</i>
	1-2	3-4	5-6	7-8	9	Total	
Dislike	60 (6.7)	233 (25.9)	98 (10.9)	26 (2.9)	2 (0.2)	419 (46.6)	$\chi^2 = 220.1$ <i>P</i> < 0.001
Not prefer	11 (1.2)	104 (11.6)	206 (22.9)	104 (11.6)	2 (0.2)	427 (47.4)	
Like	1 (0.1)	12 (1.3)	21 (2.3)	15 (1.7)	5 (0.6)	54 (6.0)	
Total	72 (8.0)	349 (38.8)	325 (36.1)	145 (16.1)	9 (1.0)	900 (100)	

STST: Salt taste sensitivity threshold.

salt intake. The 24 h urinary excretion of salt was used previously as an objective method for salt intake measurement<sup>[17,18]</sup>, and epidemiologic studies indicated that gastric cancer mortality is weakly or non-significantly correlated with dietary salt measured by the 24 h urinary salt excretion. This method is impracticable for a large-scale population study and case-control study because it can only reflect the situation of 24 h salt intake. However, STST test is simpler, cheaper and more acceptable than the 24 h urinary salt excretion, and patients can identify the taste before diagnosis.

In our study, significantly increased risk for gastric cancer was observed among those with a high STST score. Age, histories of smoking and drinking, and consumption of fruit and vegetables did not show any significant interactions with STST for gastric cancer. STST ≥ 5 showed a higher risk for gastric cancer in our study, and the possible explanation may be that the high STST is associated with a high intake of salty food such as salted meat or fish (Table 3). Previous studies indicated that ingestion of salt could induce gastritis and co-administration with N-methyl-N-nitro-N-nitrosoguanidine could enhance the effect of gastric carcinogens<sup>[9,19]</sup>, and high intragastric salt concentration could destroy the mucosal barrier, leading to inflammation and damage such as diffuse erosion and degeneration. The induced proliferous change might enhance the effect of food-derived carcinogens.

There are various methods for measuring salt intake and salt preference. Most studies only use the frequency of salt consumption and self-reported salty taste preference, but these methods could not objectively reflect the real situation of the subjects. The mean salt intake varies among different populations, and salt consumption levels which were considered high in one study might be considered low in another one<sup>[19]</sup>. Salt can be derived from different food species, so it is difficult to calculate the total salt consumption from all food. Self-reported salty taste preference is a method often biased

by subject's feelings. Therefore, the methods of measuring salt intake from food consumption and self-reported salty taste preference could induce measurement bias and confounding bias. In contrast, STST test is a simple method which is related to salt intake and consumption, and it could indirectly reflect the objective salty preference and avoid the measurement bias.

Several limitations of this study should be considered. Firstly, the STST test was not conducted before the cancer occurred, and the patients may change their salt preference after clinical symptom appearance, so there is recall bias in our study. But as the recall bias could not be avoided in every case-control study, we used the method of STST and the habits were defined to a year before the disease was diagnosed. Secondly, the cases and controls were selected from a hospital, which may have selection bias. We selected controls from the Surgical Department, Plastic Surgery Department, ENT Department and Department of Gynecology. Thirdly, we did not detect the *Helicobacter pylori* (*H. pylori*) infection in both the cases and controls, and *H. pylori* could bias the effect of STST score in gastric cancer, but the *H. pylori* could not reverse the result of STST score in gastric cancer due to the high OR. We will detect the *H. pylori* infection in the future studies. Fourthly, the objective method of measuring salt intake is the 24 h urinary salt excretion, but we did not use it to verify STST in our study. Because 24 h urinary salt excretion could not reflect the previous salt habit, we could only used salt preference questionnaire to verify it. Further cohort studies on the relationship between STST and 24 h urinary salt excretion are needed. Finally, there may be variability in the taste of each subject, and it may induce measurement bias. In order to avoid the bias, we offered the same concentration of NaCl solution to subjects after they chose the usual taste concentration.

To summarize, this study suggests that a high STST score is strongly associated with gastric cancer risk. STST

may be used as a test to evaluate an inherited characteristic of salt preference, and a useful index to verify the salt intake in clinic. However, the role of STST has to be further studied to answer the questions raised from the present study.

## COMMENTS

### Background

A high intake of salt is hypothesized to be a cause of cancer and an important cause of gastric cancer. But the salt intake and salt preference are hard to measure. salt taste sensitivity threshold (STST) test was once used to predict hypertension, and this study used it to measure the salt intake in an attempt to explore its association with gastric cancer.

### Research frontiers

Salt taste sensitivity is independently associated with gastric cancer, and it is proved to be a better index to reflect the salt preference in this study. This method could help identify the risk population of gastric cancer.

### Innovations and breakthroughs

This study for the first time explored the relationship between salt taste sensitivity and risk of gastric cancer. A high STST score was found to be strongly associated with gastric cancer risk, and STST score could also reflect the salt preference and salt intake of the subjects, and it may be used for predicting the risk population of gastric cancer.

### Applications

STST test is a cheap and fast examination to evaluate an inherited characteristic of salt preference, and it is a simple method to verify the salt intake in clinic.

### Peer review

This is an interesting study, and the data suggest that STST may be a potentially useful tool to screen patients at risk of developing gastric cancer.

## REFERENCES

- 1 **Stewart BW**, Kleihues P. World Cancer Report. Lyon: IARC Press, 2003
- 2 **Forman D**, Burley VJ. Gastric cancer: global pattern of the disease and an overview of environmental risk factors. *Best Pract Res Clin Gastroenterol* 2006; **20**: 633-649
- 3 **Yang L**. Incidence and mortality of gastric cancer in China. *World J Gastroenterol* 2006; **12**: 17-20
- 4 **World Cancer Research Fund/American Institute for Cancer Research**. The associations between food, nutrition and physical activity and the risk of stomach cancer and underlying mechanisms. Leed, UK: University of Leed, 2006: 8
- 5 **World Cancer Research Fund/American Institute for Cancer Research**. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. 2nd ed. Washington DC: World Cancer Research Fund/American Institute for Cancer Research, 2007: 10
- 6 **Fox JG**, Dangler CA, Taylor NS, King A, Koh TJ, Wang TC. High-salt diet induces gastric epithelial hyperplasia and parietal cell loss, and enhances *Helicobacter pylori* colonization in C57BL/6 mice. *Cancer Res* 1999; **59**: 4823-4828
- 7 **Kato S**, Tsukamoto T, Mizoshita T, Tanaka H, Kumagai T, Ota H, Katsuyama T, Asaka M, Tatematsu M. High salt diets dose-dependently promote gastric chemical carcinogenesis in *Helicobacter pylori*-infected Mongolian gerbils associated with a shift in mucin production from glandular to surface mucous cells. *Int J Cancer* 2006; **119**: 1558-1566
- 8 **Loh JT**, Torres VJ, Cover TL. Regulation of *Helicobacter pylori* cagA expression in response to salt. *Cancer Res* 2007; **67**: 4709-4715
- 9 **Nilsson B**. Taste acuity of the human palate. III. Studies with taste solutions on subjects in different age groups. *Acta Odontol Scand* 1979; **37**: 235-252
- 10 **Woodward M**. Case-control studies. Epidemiology study design and data analysis. New York: Chapman&Hall/CRC, 1999: 20
- 11 **Spritzer N**. [Salt taste threshold in hypertensive patients]. *Arq Bras Cardiol* 1985; **44**: 151-155
- 12 **Campepe VM**. Salt sensitivity in hypertension. Renal and cardiovascular implications. *Hypertension* 1994; **23**: 531-550
- 13 **Weinberger MH**, Miller JZ, Luft FC, Grim CE, Fineberg NS. Definitions and characteristics of sodium sensitivity and blood pressure resistance. *Hypertension* 1986; **8**: II127-II134
- 14 **Weinberger MH**. Salt sensitivity of blood pressure in humans. *Hypertension* 1996; **27**: 481-490
- 15 **Tsugane S**, Gey F, Ichinowatari Y, Miyajima Y, Ishibashi T, Matsushima S, Hirota Y, Inami T, Yamaguchi M, Karita K. Cross-sectional epidemiologic study for assessing cancer risks at the population level. I. Study design and participation rate. *J Epidemiol* 1992; **30**: 75-81
- 16 **Montes G**, Cuello C, Correa P, Zarama G, Liuzza G, Zavala D, de Marin E, Haenszel W. Sodium intake and gastric cancer. *J Cancer Res Clin Oncol* 1985; **109**: 42-45
- 17 **Tatematsu M**, Takahashi M, Fukushima S, Hananouchi M, Shirai T. Effects in rats of sodium chloride on experimental gastric cancers induced by N-methyl-N-nitro-N-nitrosoguanidine or 4-nitroquinoline-1-oxide. *J Natl Cancer Inst* 1975; **55**: 101-106
- 18 **Takahashi M**, Hasegawa R. Enhancing effects of dietary salt on both initiation and promotion stages of rat gastric carcinogenesis. *Princess Takamatsu Symp* 1985; **16**: 169-182
- 19 **Kato I**, Tominaga S, Ito Y, Kobayashi S, Yoshii Y, Matsuura A, Kameya A, Kano T. A comparative case-control analysis of stomach cancer and atrophic gastritis. *Cancer Res* 1990; **50**: 6559-6564

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