RESEARCH COMMUNICATION

Residential Environment, Diet and Risk of Stomach Cancer: a Case-control Study in Linzhou, China.

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Abstract

A case-control study was conducted to investigate risk factors for stomach cancer in a rural population in China. Linzhou Cancer Registry was used to identify cases of stomach cancer, aged between 30 and 75 years, diagnosed between January 1998 and April 1999. Three neighbourhood controls were selected for each case, matched according to age, sex and village of residence. A total of 210 cases and 630 controls were interviewed. Conditional logistic regression was used to estimate odds ratios (OR) for factors associated with the risk of cancer. Among characteristics of the residential environment, significantly increased risk was found for: frequent irritation on eyes or throat by soot (OR 5.54, 95% CI 1.42-21.65, p for trend <0.01). This effect was particularly strong in women (OR 19.5, 95% CI 1.28-297.09, p for trend =0.01). Dietary factors that were significantly associated with an increased risk were food grains other than rice, wheat and maize (OR 2.93, 95% 1.16-7.38), pickled or salted vegetables (OR 3.99, 95% CI 1.63-9.75) and preference for a high salt diet (OR 2.58, 95% CI 1.56-4.26). The consumption of vegetables showed a protective effect with an odds ratio of 0.27 (95% CI 0.11-0.61). It follows that a developing economy and improvement in living standards, with associated increased intake of fruit and vegetables and reduced consumption of salt, can contribute to a reduction in the incidence of stomach cancer in the Linzhou population.

Introduction

Incidence and mortality rates of gastric cancer in Asia remain the highest in the world (Parkin et al., 1997). In Linzhou, gastric cancer is the second most common cancer in terms of both incidence and mortality. Linzhou City (formerly LinXian County) is situated in the northwest of Henan province in the Taihang mountain area, China. Linzhou is a rural area with a total population of 1.06 million, 90% of who work in agriculture. The climate is dry with little rainfall and the main crops are wheat, maize and other cereals.

According to the Linzhou Cancer Registry, the annual average age-standardised (world standard population) incidence of stomach cancer in the period from 1993 to 1997 was 124/100,000 for men and 57/100,000 for women, respectively. During the same period, the annual average age-standardised mortality rate of this cancer was 97/100,000 for men and 48/100,000 for women.

A case-control study was conducted to investigate potential risk factors for stomach cancer in Linzhou City, China between August 1999 and June 2000.

Materials and Methods

Linzhou Cancer Registry is a population-based registry system, which collects data on all cancers in residents of the Linzhou City area. In the beginning of 1959 the registry only collected incident data on oesophageal cancer and cancers of the gastric cardia. Data collection was extended to all cancers in 1987.

In the present study, we used the Linzhou Cancer Registry to identify cases of stomach cancer, aged between 30 and 75 years, which were diagnosed in the period from 1 January 1998 to 30 April 1999. Cases were only included if they were alive at the time of inquiry, August 1999 to June 2000, and if the diagnosis was confirmed by histopathology. A total of 210 incident cases of stomach cancer were

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identified during the study period.

Three neighbourhood controls were selected for each case, matched by sex and age (within 5 years) and residing in the same village. The controls were selected by choosing the fifth residence along from the residence of the index case, in three different directions. A requirement of the study was that both cases and controls must have lived in the Linzhou area for the last 10 years. Controls were excluded if they had been diagnosed with any cancer before 30th April 1999.

Trained village doctors visited the residence of a case or control and invited them to respond to a questionnaire, enquiring about factors such as socio-economic characteristics and dietary habits. For cases, the relevant time of exposure was taken to be ten years prior to the diagnosis of stomach cancer and the same time points were defined for the matched controls.

Some continuous variables, such as consumption of rice, were grouped into categories by combining the frequency and amount consumed. Using a conditional logistic regression model, the odds ratio associated with a given risk factor or level of categorical variable was estimated, along with its 95% confidence interval (CI). The group with no exposure or the group with the lowest level of exposure, or an intermediate group with high prevalence, was used as the baseline group.

Results

A total of 210 cases and 630 controls were included in this study. The general characteristics of cases and controls are shown in Table 1. Men accounted for 67.6% of the total (142 cases and 426 controls) and women accounted for 32.4% (68 cases and 204 controls). The mean age was 59.8 years for cases and 59.5 years for controls. The majority of cases (82.4%) and controls (84.3%) were married. The majority of cases and controls (94.8% and 92.4%, respectively) were farmers.

The results of the conditional logistic regression analysis of factors relating to socio-economic status are shown in Table 2. Univariate analysis gave odds ratios for increasing per capita income 10 years ago of 0.88, 0.68, and 0.61 (p for trend=0.05), using less than 38 yuan/month as the baseline. After adjusting for age and other socio-economic factors, the trend in risk with increasing income was attenuated. For residential space, people with 10-20 square metres had an adjusted odds ratio of 0.61 and those with more than 20 square metres had an adjusted odds ratio of 0.75, compared with people with residential space below 10 square metres (p for trend=0.39). The adjusted odds ratio of the group with the highest education level versus the group without any education was 0.54 (95% CI 0.29-1.04). Using a refrigerator was significantly associated with a decreased risk of stomach cancer (OR 0.11, 95% CI 0.02-0.86).

Table 3 shows the results of analysis for stomach cancer in relation to residential environmental risk factors. The

feeling of irritation in the eyes or throat by soot was found to be strongly and positively associated with the risk of stomach cancer. The adjusted odds ratio was 5.54 for the group with a frequent feeling of irritation in the eyes or throat (95% CI 1.42-21.65) relative to those without the feeling of irritation; the test for trend was statistically significant (p for trend <0.01). Stratifying by sex the effect was only particularly strong in women, with odds ratios of 3.07, 6.59 and 19.49 in the groups with increasing frequency of a feeling of irritation, relative to those without (p for trend =0.01). In men these odds ratios were 1.15, 1.60 and 4.15, and the trend was not statistically significant (p=0.10). The presence of soot at home when cooking was significantly associated with an increased risk of stomach cancer in univariate analysis, but this association was slightly attenuated after adjusting for age, income, residential space, educational level and using a refrigerator.

The main type of drinking water and most common fuel used ten years ago were not significantly associated with risk of stomach cancer. Adjusted odds ratios were 1.50 (95% CI 0.34-6.64) for using firewood as the most common fuel and 1.56 (95% CI 0.64-3.81) for having a drinking water source other than tap water (such as well, surface and cellar water).

Table 4 shows the summary analysis of dietary characteristics. A high intake of rice was associated with an increased risk (OR=2.16) but this association was not statistically significant and the trend with intake was not significant. Intake of wheat and maize showed no relation to the risk of stomach cancer. No association was found between consumption of animal proteins (pork, egg and milk) or oils (animal oil and vegetable oil) ten years previously and the risk of stomach cancer. Intake of beans or bean products, vinegar, deep-fried food and spring onion

Table 1. General Characteristics of Cases and Control

Variable	210 Cases %	630 Controls %
Sex		
Male	67.6	67.6
Female	32.4	32.4
Agegroup		
<40	4.3	5.6
45-49	10.0	9.8
50-54	16.2	16.2
55-59	12.4	13.6
60-64	24.7	23.0
65-69	16.2	18.1
70+	16.2	13.7
Marriage		
Married	82.4	84.3
Divorce	0.0	0.3
Widow or widower	15.2	14.8
Never married	2.4	0.6

Table 2. Risk of Stomach Cancer in Relation to Socio-economic Status

Risk factors	Distribution of Cases %	Univariate OR (95%CI)	Multivariate* OR (95%CI)
Per capita income at 10 Year ago (yuan/month)			
<38	25.7	1.00	1.00
38-69	28.6	0.88 (0.54-1.43)	0.93 (0.56-1.55)
70-123	24.3	0.68 (0.40-1.14)	0.73 (0.43-1.24)
124+	21.4	0.61 (0.34-1.07)	0.73 (0.40-1.33)
Trend		P=0.05	P=0.21
Per capita residential space 10 years ago (square metres)			
<10	30.5	1.00	1.00
10-20	32.9	0.58 (0.35-0.95)	0.61 (0.36-1.01)
20+	36.7	0.67 (0.38-1.18)	0.75 (0.42-1.36)
Trend		P=0.20	P=0.39
Educational level			
No education	28.6	1.00	1.00
Primary	52.4	0.74 (0.45-1.20)	0.81 (0.49-1.34)
Middle or higher	19.0	0.44 (0.23-0.83)	0.54 (0.29-1.04)
Trend		P=0.01	P=0.06
Using refrigerator			
No	99.5	1.00	1.00
Yes	0.5	0.10 (0.01-0.76)	0.11 (0.02-0.86)

* Mutually adjusted and adjusted for age

Table 3. Risk of Stomach Cancer in Relation to Residential Environment (at 10 years ago)

Risk factors	Distribution of Cases %	Univariate OR (95% CI)	Multivariate* OR (95% CI)
Main type of drinking water			
Tap water	34.8	1.00	1.00
Other water source	65.2	1.94 (0.82-4.61)	1.56 (0.64-3.81)
Most common used fuel			
Coal	93.3	1.00	1.00
Firewood	6.7	1.91 (0.53-6.83)	1.56 (0.34-6.64)
The generation of soot at home when cooking			
No	18.1	1.00	1.00
A little	60.5	1.16 (0.60-2.25)	1.12 (0.54-2.34)
More	21.4	2.66 (1.21-5.86)	2.30 (0.96-5.52)
Trend		P<0.01	P=0.02
Irritation on eyes or throat by soot			
No	17.6	1.00	1.00
Occasionally	47.6	1.34 (0.66-2.71)	1.28 (0.61-2.68)
Sometimes	29.5	2.27 (1.05-4.29)	2.02 (0.89-4.57)
Often	5.2	6.23 (1.69-22.9)	5.54 (1.42-21.6)
Trend		P<0.01	P<0.01

* Mutually adjusted and adjusted for age, income, resident space, using refrigerator and educational level

or garlic, and fruit were not associated with risk of stomach cancer. The results were similar for univariate and multivariate analysis.

Table 5 shows the detailed results for dietary factors that were statistically significantly associated with the risk of stomach cancer. We observed an increasing gradient in risk with increasing intake of other food grains; the risk was three-fold for the highest group of consumption (95% CI 1.16-7.38) and the trend for level of intake was significant (p=0.02). A similar result was observed for the intake of pickled or salted vegetables (40 gram/week vs. zero: OR = 3.99; 95% CI 1.63-9.75; p for trend < 0.01). Fresh vegetables were found to be protective with a decreasing gradient of risk of stomach cancer with increasing intake. The risk of stomach cancer in the group with the highest vegetable intake (1400gram per week vs. 700gram/week) decreased to 0.27 (95% CI 0.11-0.61). A preference for hot flavoured food was inversely associated with risk (OR=0.47). A preference for very salty food was associated with an increased risk (OR=2.58), compared with a preference for a moderate amount of salt in the diet. Conversely, a preference for a low salt diet was also associated with an increased risk (OR=1.89).

Discussion

A large number of studies have indicated that there is an association between the risk of stomach cancer, socio-economic status and diet (Howson et al., 1986; Kono and Hirohata, 1996; Gammon et al., 1997). Being of low socio-economic status increases the risk of stomach cancer. This

study provides further evidence that the use of refrigeration is a protective factor for stomach cancer (World Cancer Research Fund, 1997).

We found an increased risk of gastric cancer associated with frequent feeling of irritation in the eyes or throat by soot, particularly in women. Because men generally spend less time cooking and have less exposure to indoor air pollution than women in this area, the differential effect (in men and women) may point to a role of air-borne carcinogen, rather than an effect of ingested pollutants in the prepared food. A number of studies have found an elevated risk of long cancer with indoor air pollution (Liu et al., 1993; Lan et al., 1993), but few studies report a relationship between the risk of stomach cancer and indoor air pollution (Sun et al., 2000). The question of whether indoor air pollution plays a role in the aetiology of stomach cancer for female in this area, and if confirmed, the biological mechanisms involved, warrant further investigation.

We observed an elevated risk with increasing consumption of food grain other than rice, wheat and maize. This is consistent with the concept that a more diversified and richer diet is a relevant underlying correlate of the decline in gastric cancer rate (La Vecchia et al., 1997). In this population, other food grain are principally sorghum and millet which are deficient in nutrient elements.

We found a strong inverse association between fresh vegetable consumption and stomach cancer risk. Vegetables and fruits are the main source of dietary ascorbic acid and β–carotene as well as many other substances with antioxidant properties. Antioxidants have the potential to neutralise DNA-free radicals and might therefore lower the risk of

Table 4. Risk of Stomach Cancer in Relation to Diet (consumption each week 10 years ago)

Risk factors	Distribution of cases % low-high intake	Multivariate * Odds Ratio	P trend
Rice	11, 16, 28, 45	1.00, 1.37, 1.60, 2.16	0.08
Wheat flour	18, 17, 45, 20	1.00, 1.54, 1.56, 1.14	0.82
Maize	17, 31, 24, 28	1.00, 2.05, 1.46, 2.10	0.21
Other food grain	8, 30, 23, 39	1.00, 1.81, 2.72, 2.93	0.02
Bean or bean's products	30, 14, 28, 28	1.00, 1.17, 1.16, 0.90	0.80
Vegetable	12, 39, 22, 26	1.00, 0.52, 0.48, 0.27	<0.01
Pickled or salted vegetable	60, 6, 15, 19	1.00, 1.21, 2.87, 3.99	<0.01
Fruit	37, 19, 18, 26	1.00, 0.85, 1.25, 1.24	0.44
Spring onion or garlic	15, 16, 28, 41	1.00, 1.37, 0.88, 0.73	0.35
Pork	24, 32, 28, 16	1.00, 1.48, 1.82, 0.88	0.95
Eggs	51, 11, 12, 26	1.00, 1.13, 0.61, 0.69	0.19
Milk	91, 9	1.00, 2.02	_
Animal oil	92, 8	1.00, 0.83	_
Vegetable oil	47, 22, 13, 18	1.00, 1.11, 0.60, 1.71	0.54
Deep-fry food	19, 14, 35, 32	1.00, 1.00, 0.91, 1.10	0.81
Hot flavour food	83, 17	1.00, 0.47	_
Vinegar	15, 12, 31, 42	1.00, 0.57, 0.72, 1.00	0.77
Salt preference	18, 56, 26	1.89, 1.00, 2.58	<0.01

* Mutually adjusted and adjusted for age, income, resident space, using refrigerator and educational level

Table 5. Risk of Stomach Cancer in Relation to Diet (consumption each week 10 years ago)

Risk factors	211 Cases %	Univariate OR (95%CI)	Multivariate* OR (95%CI)
Other food grains			
<100 grams	8.1	1.00	1.00
100-449	29.5	2.30 (1.07-4.94)	1.81 (0.76-4.33)
450-809	22.9	2.59 (1.15-5.83)	2.72 (1.08-6.94)
810+	39.5	3.32 (1.47-7.52)	2.93 (1.16-7.38)
Trend		P<0.01	P=0.02
Vegetables			
<700 grams	11.9	1.00	1.00
700-799	39.5	0.56 (0.31-1.01)	0.52 (0.26-1.06)
800-1399	22.9	0.47 (0.25-0.88)	0.48 (0.23-1.03)
1400+	25.7	0.34 (0.17-0.67)	0.27 (0.11-0.61)
Trend		P<0.01	P<0.01
Pickled or salted Vegetables			
No	60.0	1.00	1.00
<10 grams	5.7	1.29 (0.58-2.91)	1.21 (0.46-3.17)
10-39	14.8	2.06 (1.07-3.88)	2.87 (1.25-6.61)
40+	19.5	3.35 (1.67-6.72)	3.99 (1.63-9.75)
Trend		P<0.01	P<0.01
Hot flavour food			
No	82.9	1.00	1.00
Yes	17.1	0.64 (0.38-1.08)	0.47 (0.24-0.92)
Salt preference			
Low	18.1	1.64 (1.03-2.60)	1.89 (1.09-3.29)
Moderate	55.7	1.00	1.00
High	26.2	2.35 (1.55-3.55)	2.58 (1.56-4.26)
Trend		P<0.01	P<0.01

* Mutually adjusted and adjusted for age, income, resident space, using refrigerator and educational level

stomach cancer (Shklar et al., 1998). The anticarcinogenic properties of antioxidants and protective effect of vegetables in relation to stomach cancer have been shown by many studies in many countries (Gonzalez et al., 1994; Steinmetz and Potter, 1996; Harrison et al., 1997; Ji et al., 1998; Ward and Lopez-Carrillo, 1999; Ekstrâm et al., 2000; Palli et al., 2001). In this rural area fruit was very rarely consumed ten years ago. The main source of some vitamins were the vegetables that farmers produced themselves. This may explain why there is a protective effect of vegetables, but not of fruit consumption in this population.

In the present data an unexpected decreased risk with intake of hot flavoured food was observed. Laboratory studies have indicated that capsaicin may be carcinogenic and Lopez-Carrillo et al (Lpez-Carrillo et al., 1994) reported that chilli pepper consumption was a strong risk factor for gastric cancer in Mexico. In South India (Mathew et al., 2000) the result of a case-control study showed that high consumption of chilli peppers was an independent risk factor for stomach cancer. In the present study, only a small proportion of the population reported a preference for hot food. It is possible that this was lower in the cases because the symptoms of superficial or atrophic gastritis, a precursor lesion of stomach cancer, may deter an individual from consuming stimulant food such as hot pepper.

Epidemiological evidence has supported an association between the risk of developing gastric cancer and the intake of salt and salt-preserved foods (Riboli and Norat, 2001; Tuyns, 1988). Salt is not a directly acting carcinogen, but a high-salt diet in human and experimental animals is known to cause gastritis and may promote the effect of gastric carcinogens (Fox et al., 1999). Superficial gastritis can led to chronic atrophic gastritis, which is a precancerous lesion (Correa, 1988). Pickled or salted vegetables, which were commonly consumed 20 years ago in this area, contain nitrosamines and their precursors (Lu et al., 1981; Correa P, 1992). Our data suggest that a high intake of pickled or salted vegetables and preference for a high salt diet are strongly associated with increased risk of stomach cancer in Linzhou population. The most likely explanation for the association

between a preference for a low salt diet and increased risk of stomach cancer is that the disease or its precursor stages changes the dietary preferences of the person.

In conclusion, a high intake of pickled or salted vegetables and preference for a high salt diet were associated with an increased risk of stomach cancer and a higher intake of vegetables was associated with a decreased risk. These findings are consistent with previous studies in other places in China and in other countries around the world. We also found an elevated risk for indoor air pollution, particularly in women.

A developing economy and improvement in living standards for local people, with associated increased intake of fruit and vegetables and reduced consumption of salt, may contribute to further reduction of the incidence of stomach cancer in the Linzhou population.

References

Correa P (1988). A human model of gastric carcinogenesis. *Cancer Res, 48*, 3554-60.

Correa P (1992). Human gastric carcinogenesis: a multistep and multifactorial process. *Cancer Res, 52*, 6735-40.

Ekstrâm AM, Serafini M, Nyrân O, et al (2000). Dietary antioxidant intake and the risk of cardia and noncardia cancer of the intestinal and diffuse types: A population-based case-control study in Sweden. *Int J Cancer, 87*, 133-40.

Fox JG, Dangler CA, Taylor NS, et al (1999). High-salt diet induces gastric epithelial hyperplasia and parietal cell loss, and enhances Helicobacter pylori colonization in C57BL/6 mice. *Cancer Res, 59*, 4823-8.

Gammon MD, Schoenberg JB, Ahsan H, et al (1997). Tobacco, alcohol and socioeconomic status and adenocarcinomas of the oesophagus and gastric cardia. *J Natl Cancer Inst, 89*, 1277-84.

Gonzalez CA, Riboli E, Badosa J, et al (1994). Nutritional factors and gastric cancer in Spain. *Am J Epidemiol, 139*, 466-73.

Harrison LE, Zhang ZF, Karpeh MS, Sun M, Kurtz RC (1997). The role of dietary factors in the intestinal and diffuse histologic subtypes of gastric adenocarcinoma. A case-control study in the U S. *Cancer, 80*, 1021-8.

Howson CP, Hiyama T, Wynder EL (1986). The decline in gastric cancer: epidemiology of an unplanned triumph. *Epidemiol Rev, 8*, 1-27.

Ji BT, Chow WH, Yang G, et al (1998). Dietary habits and stomach cancer in Shanghai, China. *Int J Cancer, 76*, 659-64.

Kono S, Hirohata T (1996). Nutrition and stomach cancer. *Cancer Causes & Control, 7*, 41-56.

Lan Q, Chen W, Chen H, He XZ (1993). Risk factors for lung cancer in non-smokers in Xuanwei County of China. *Biomed Environ Sci, 6*, 112-8.

La Vecchia C, Munoz SE, Braga C, Fernandez E, Decarli A (1997). Diet diversity and gastric cancer. *Int J Cancer, 72*, 255-7.

Liu Q, Sasco AJ, Riboli E, Hu MX (1993). Indoor air pollution and lung cancer in Guangzhou, Peoples Republic of China. *Am J Epidemiol, 15*, 145-54.

Lpez-Carrillo L, Hernndez-Avila M, Dubrow R (1994). Chili pepper consumption and gastric cancer in Mexico: a case-control study. *Am J Epidemiol, 139*, 263-7.

Lu SH, Camus AM, Tomatis L, Bartsch H (1981). Mutagenicity of extracts of pickled vegetables collected in Linhsien County, a high-incidence area for esophageal cancer in Northern China. *J Natl Cancer Inst, 66*, 33-6.

Mathew A, Gangadharan P, Varghese C, Nair MK (2000). Diet and stomach cancer: a case-control study in South India. *Eur J Cancer Prev, 9*, 89-97.

Palli D, Russo A, Decarli A (2001). Dietary patterns, nutrient intake and gastric cancer in a high-risk area of Italy. *Cancer Causes Control, 12*, 163-72.

Parkin DM, Whelan SL, Ferlay J, Raymound L, Yong J (1997). Cancer incidence in five continent, IARC Scientific publication, No. 143, Vol., VII: 1240 International Agency for Research on Cancer Lyon, France.

Riboli E, Norat T (2001). Cancer prevention and diet: opportunities in Europe. *Public Health Nutr, 4*, 475-84.

Shklar G (1998). Mechanisms of cancer inhibition by anti-oxidant nutrients. *Oral Oncol, 34*, 24-9.

Steinmetz KA, Potter JD (1996). Vegetables, fruit and cancer prevention: a review. *J Am Diet Assoc, 96*, 1027-39.

Sun Xibin, Lu Jianbang, Dai Dixin (2000). A case-control study on the risk factors of stomach cancer in Linxian, China. *Bulletin of Chinese Cancer, 9*, 86-8.

Tuyns AJ (1988). Salt and gastrointestinal cancer. *Nutr Cancer, 11*, 229-32.

Ward MH and Lopez-Carrillo L (1999). Dietary factors and the risk of gastric cancer in Mexico City. *Am J Epidemiol, 15*, 925-32.

World Cancer Research Fund (1997). Food, nutrition, and the prevention of cancer: a global perspective. Washington, DC; World Cancer Research Fund.