Dietary Factors and the Risk of Gastric Cancer in Hanzhong Area of China

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Abstract

Background: Dietary factors play an important role in gastric cancer risk. They have not been investigated extensively in Hanzhong area, China.

Methods: We conducted a population-based case-control study of gastric cancer in Hanzhong area, China in 2018-2020. A total of 121 patients with historically confirmed gastric adenocarcinomas were interviewed. Controls were an age-stratified random sample of residents of Hanzhong area. The dietary questionnaire was a 70-item semiquantitative food frequency adapted for the Hanzhong diet. Odds ratios were calculated for quartiles of consumption of food groups and were adjusted for age, gender, calories, chili pepper intake, cigarette smoking, socioeconomic status, added salt, and history of peptic ulcer disease.

Results: There was approximately a threefold increased risk of gastric cancer for frequent consumption (highest quartile) of both fresh meat (odds ratio (OR) = 3.0) and processed meat (OR = 3.3). Odds ratios were also significantly elevated for frequent consumption of dairy products (OR = 3.1) and fish (OR = 3.1). The authors observed a decreasing gradient of risk with increasing frequency of vegetable consumption due to a significant inverse trend for the yellow and orange vegetables.

Conclusion: High intake of citrus fruits showed a slight inverse association. These findings are consistent with many studies around the world that indicate important roles for salt, processed meats, and vegetable consumption in gastric cancer risk.

Keywords: Dietary; Gastric cancer; China

Introduction

Gastric cancer is the second highest cause of cancer-related deaths in China. In 2015, 498,000 Chinese people died from gastric cancer, which accounted for 17.7% of all cancer related deaths (1). Although *Helicobacter pylori* has been acknowledged as the most important carcinogen in the stomach, it is regarded as the initial factor for progression to gastric cancer. When the gastric mucosa is in a state of atrophy, *H. pylori* eradication cannot prevent gastric cancer. Moreover, *H. pylori* is less abundant or absent in later steps of gastric carcinogenesis (2). However, *H. pylori* in-

fection may not be sufficient to cause this cancer because only a small%age of those infected develop this disease.

Dietary factors are thought to play a role as cofactors in the progression from gastritis to gastric cancer (3). Low consumption of vegetables and fruits and high consumption of meat (4) and pickled foods (5) may also play important etiological roles in the pathogenesis of gastric cancer (6). However, few epidemiological studies have investigated the interaction between consumption of vegetables, fruit, soya bean products, pickled food, and meat with respect to risk of gastric cancer in Hanzhong area of China.

Here we report on the association of the intake of meat and other foods and gastric cancer risk.

Materials and Methods

Briefly, 167 newly diagnosed cases of gastric cancer in patients aged 20 years and older were identified through the tumor reporting system of Hanzhong Municipal Health Commission between September 17, 2018, and June 30, 2020, in 15 metropolitan area hospitals in Hanzhong City, China. These cases represented approximately 80% of those reported to the Hanzhong Cancer Registry in the same period. Twenty (12%) of the identified cases were unavailable for interview. A further 21 cases (12.6%) were excluded because the pathology material could not be obtained, and five cases (3%) were excluded because their tumors were not adenocarcinomas of the stomach, leaving 121 cases confirmed as gastric adenocarcinomas.

This study was approved by the Ethics Committee of the Hanzhong Central Hospital (2019), Ethics Committee Review No. 1.

Information was obtained either from the cases themselves (78%) or from a proxy (22%) if the cases were too ill to give the interview. The mean time between diagnosis and interview was 22 days. Controls were an age-stratified random sample of Hanzhong area selected from the 2018-2020 household sampling frame of the Hanzhong Health Survey. A total of 144 controls

were interviewed, with a response rate of 95%. A random sample of 7% of the controls was selected for surrogate interviews. The dietary questionnaire was a 70-item semiquantitative food frequency based on the methodology developed by Wu et al. (16) and adapted for the Hanzhong diet. A validation study was performed in a Hanzhong population with good results. Dietary information was assessed for the period 1 year before onset of symptoms for cases and 1 year before the interview for controls. We assessed intake of fresh meats, including beef, pork, liver, and chicken, and processed meats containing nitrite or nitrate (bacon, sausage). Dairy products included milk, yogurt, and cheese. The intake of 13 vegetables and 17 fruits was ascertained. Dark green vegetables, yellow/orange vegetables, and high nitrate vegetables were evaluated as separate groups. Beans were evaluated separately due to their frequent intake by this population. Fruit intake was evaluated separately for citrus fruits and other fruits. For each food group, consumption categories were created by dividing the frequency distribution for the control group into approximate quartiles. For food groups that showed an association with risk, we evaluated the individual foods in the group separately. For individual food items, intake was usually not distributed normally because the responses were precoded into categories. Therefore, categories were based on cutpoints around categories that contained at least 30 controls.

The effect of foods on gastric cancer risk was quantified by odds ratios. Odds ratios and 95% confidence intervals were calculated by unconditional logistic regression analysis (17, 18). The logistic regression models were adjusted for age, gender, and total calorie intake. All models included the following factors associated with gastric cancer risk in this study population (13): frequency of consumption of chili peppers, cigarette smoking, history of peptic ulcer disease, adding salt after tasting food, and socioeconomic status (SES). After adjustment for calories and the above-specified gastric cancer risk factors, the food groups were also adjusted for the effects of other food groups by including them individually

in the logistic models. We stratified the food group analyses by SES to evaluate possible differences in risk across groups.

To test for trend, we included an ordinal score for the food group categories as a continuous variable in the logistic model. Chi-square test was used for comparison between groups. Measurement data were expressed as X±S, independent *t* test was used between groups, and paired *t* test was used within groups.

Results

Demographic Data

Results of this study were available for 358 people (121 patients as case and 137 healthy people as control group). There was significant difference between ages in case and control groups ($P<0.001$). Male patients accounted for 76.03% of the total number of patients, compared with 52.55% in the control group, which was statistically significant ($P<0.001$). About 47 and 43% of patients and controls used cigarette, respectively, and there was non-significant difference in the smoking status. Table 1 manifested the demographic characteristics of people that participated in both groups.

Table 1: The demographic characteristics of people that participated in both groups

Characteristics	Patient group (n=121)	Control group (n=137)	P-value
Gender, n (%)			$P<0.001$
Male	92 (76.03)	72(52.55)	
Female	29 (23.97)	65(47.45)	
Age (y)	58.63±5.29	51.92±10.19	$P<0.001$
Current smoking, n (%)	57(47.11)	59(43.07)	$P>0.05$

P values comparing within-group changes were calculated using paired two-tailed Student's t test.
Plus-minus values are means ± SD rounded to the nearest tenth

Meat and other animal products

A high intake of fresh meat was associated with an approximately threefold increased risk of gastric cancer after controlling for total calorie intake and other gastric cancer risk factors (Table 2). Among the fresh meats, risks were elevated for beef and liver (highest quartile of beef (four or more times/week): odds ratio (OR) = 1.8, 95% confidence interval (CI) 0.9-4.7; liver (two or more times/week): OR = 1.5, 95% CI 0.9-2.7. Chicken and pork intakes were not associated with risk.

Increasing processed meat consumption was associated with a significant increased risk of gastric cancer (OR for highest quartile =3.1). Risks were elevated for some of the most frequently eaten processed meats (highest quartile of two or more

times per week): bacon (a pork is smoked with salt and seasoning), sausage and other salted dried meat. Adjusted odds ratios were 1.3 for bacon (95% CI 0.7-2.7), 1.5 for sausage (95% CI 0.9-2.8), and 1.2 for other salted dried meat (95% CI 0.5-2.7).

We observed an increasing gradient in risk with increasing dairy products intake; the risk was 2.5-fold for the highest quartile of consumption. Individual dairy products associated with risk (highest vs. lowest quartile) was milk (greater than once/day vs. less than once/week, OR = 2.1, 95% Cl 1.1-3.5). Consumption of yogurt and cheese was infrequent, and they were not associated with risk.

For high intake of fish , there was associated with an approximately twofold increased risk of gastric cancer. This was due mainly to the consumption of fresh fish (two or more times per week vs. never: OR = 2.7, 95% Cl 1.3-4.5).

Table 2: Consumption of meat, dairy and fish

Food group	Odds ratio (95% confidence interval)	P-value
Fresh meats	3.0 (1.5, 6.3)	P=0.002
Beef	1.8 (0.9, 4.7)	P=0.045
Liver	1.5 (0.9, 2.7)	P=0.033
Chicken	1.0 (0.5, 1.6)	P=0.889
Pork	1.0 (0.5, 1.9)	P=0.919
Processed meats	3.1 (1.7, 5.5)	P=0.003
Bacon	1.3 (0.7, 2.7)	P=0.026
Sausage	1.5 (0.9, 2.8)	P=0.047
Other salted dried meat	1.2 (0.5, 2.7)	P=0.035
Dairy products	2.5 (1.4, 4.3)	P<0.001
Milk	2.1 (1.1, 3.5)	P<0.001
Yogurt	1.1 (0.8, 2.3)	P=0.153
Cheese	1.2 (0.6, 1.7)	P=0.581
Fish	2.7(1.3, 4.5)	P<0.001

Adjusted for age, gender, and total calorie intake

Vegetables and fruits

Vegetable consumption was high in this study population (Table 3). A high intake of vegetable consumption was inversely associated with risk. This was due to a highly significant inverse trend for the yellow and orange vegetables, which constituted the majority of vegetables consumed. Consumption of dark green vegetables was not related to risk. Increasing intake of vegetables with high nitrate levels, to which spinach and lettuce were the major contributors, was associated with modest increases in risk, but the trend was not significant.

Table 3: Consumption of vegetable

Food group	Odds ratio (95% confidence interval)	P-value
Vegetable	0.8 (0.7, 1.0)	P<0.001
Yellow and orange vegetables	0.5 (0.3, 0.9)	P<0.001
Dark green vegetables	1.0 (0.8, 2.0)	P=0.384
Vegetables with high nitrate levels	1.1 (0.5, 2.7)	P=0.047
Beans	0.3 (0.2, 0.6)	P<0.001
Fruit	1.0 (0.6, 1.7)	P=0.882
Citrus fruits	0.7 (0.5, 1.0)	P<0.001
Other fruits	1.0 (0.7, 1.6)	P=0.753

Adjusted for age, gender, and total calorie intake

We observed a decreasing gradient of risk with increasing frequency of beans (one or more times per day vs. once a week or less; OR = 0.3) consumption.

Fruit intake was also high in this population, ranging from less than two per day for the lowest quartile to five or more times/day for the highest quartile. Fruit intake overall was not associated with risk. Frequent intake of citrus fruits was associated with a nonsignificant decreased risk (OR = 0.7), and the trend with intake was not signifi-

cant. Intake of other fruits showed no relation to risk of gastric cancer.

Rice and sweets

Consumption of rice, cereals, and grains was not associated with risk (Table 4). High intake of sweets (15 or more times per week vs. less than six times per week) was associated with a 75% statistically nonsignificant increased risk of gastric cancer, but there was no trend with increasing intake.

Table 4: Consumption of rice, cereals, and grains

Food group	Odds ratio (95% confidence interval)	P-value
Rice, cereals and grains	1.0 (0.5, 2.4)	P=0.913
Sweets	1.0 (0.6, 1.6)	P=0.920

Adjusted for age, gender, and total calorie intake

Discussion

Cancer is an excessive and uncontrolled proliferation of the body cells without obvious physiological demands of organs (7). Occupational factors including toxic element smoking, physical inactivity, and unhealthy dietary habits were offered as the most serious environmental risk factors that cause GI tract cancer (8, 9).

This study provides further evidence that high intakes of processed meats, salty foods are risk factors for gastric cancer, and that a high intake of vegetables is probably protective. The association for vegetables was due to a strong decreasing trend in risk with increasing intake of yellow and orange vegetables. Frequent consumption of beans was also strongly inversely associated with risk. We also found that frequent consumption of fresh meats, dairy products, and fresh fish was a risk factor. Frequent consumption of citrus fruits was slightly inversely associated with risk, whereas frequent consumption of sweets was associated with a 75% increased risk of gastric cancer.Bacon, sausage and other salted dried meat

accounted for the elevated risk we observed for processed meats. Methods of curing meats include the use of salt and nitrite, both of which have been linked to gastric cancer in animal and human studies (10). Salt is not a directly acting carcinogen, but it is thought to increase the risk of gastric cancer through direct damage to the gastric mucosa, which results in gastritis, increased DNA synthesis, and cell proliferation (11). Superficial gastritis can lead to chronic atrophic gastritis, which is a precursor lesion in the development of gastric cancer (12). Nitrite reacts with amines and amides found in meats and other proteins to form N-nitroso compounds, which are animal carcinogens and possible human carcinogens (13). Because both salt and nitrite are added to most types of processed meats, it is difficult to separate these as risk factors for gastric cancer. Our findings suggest that cured meats also contribute toward gastric cancer risk in the Hanzhong population. Hanzhong city, located in the Qinba Mountains, prefers salted pork and preserved meat, which has been proved

to contain too much nitrite. Nitrite and barbecue cooking are risk factors for stomach cancer.

We found an increased risk of gastric cancer with frequent intake of fresh meat that was due to elevated risks for high intakes of beef and liver. A few case-control studies found elevated risks for high consumption of all meats, beef, or pork, but most found no association with intake of fresh meats (14). The elevated risk we observed for fish overall was due to fresh fish intake. High intake of salted or smoked fish has been associated with an increased risk of gastric cancer (15), but not of fresh fish (16). Frequent intake of meats and fish that have been cooked at high temperatures (grilled, broiled, or fried) has generally been associated with elevated risks of gastric cancer. We had no information on usual cooking method for meats or fish, but frying is the major mode of preparing fish, while meats are prepared by a variety of means. We found an increased risk with frequent consumption of dairy products. High intake of milk was considered a potential risk factor in an early review (17), but later studies generally have found no association or weak associations with milk or dairy products as a group (18). Our data suggest that frequent consumption of animal products increases the risk of gastric cancer. However, evidence from previous studies indicates that it is more likely that a specific aspect of animal protein intake, such as additives used in processing or the cooking method, may account for the excess risk.

Frequent consumption of sweets was associated with a 75% increased risk of gastric cancer. High intake of sweets (usually including cakes and candy) has been associated with slightly elevated risks of gastric cancer risk in several case-control studies (19). Sweets contain high levels of vegetable fats, sugar, and simple carbohydrates, but there is little evidence that these dietary factors are associated with gastric cancer risk. Rather, a high intake of sweets may indicate a diet low in fruits, vegetables, and whole grains, which have been consistently shown to reduce gastric cancer risk (20). We found a strong inverse association between vegetable consumption and gastric cancer risk that was mainly due to the yellow and orange vegetables, which included corn, cauliflower, carrots, and tomatoes. Frequent intake of beans, a staple food in the Hanzhong diet, was also associated with a reduced gastric cancer risk. The relation with frequent intake of citrus fruit was inverse. Vegetables and fruits contain many compounds with anticarcinogenic properties, including carotenoids, vitamin C, folate, vitamin E, and selenium. The yellow and orange vegetables are particularly high in carotenoids. More than 30 case control studies and six prospective studies in many countries with diverse dietary habits have reported on vegetable and fruit intake and gastric cancer (20), and almost all found a statistically significant protective effect for either vegetables or fruit or both. The protective effect that we found for yellow and orange vegetables was greater than in most previous studies and may be due to the high level of consumption in this population. Similarly, our finding of a protective effect for daily or more frequent intake of beans was stronger than that for most studies reporting on the intake of legumes (including soybeans) and gastric cancer (6). Aside from soybeans, intakes of beans in other study populations have been lower, and this may explain the weaker associations observed.

Limitations of the study include the fact that the dietary information we collected was about adult diet 1 year before the diagnosis or interview. Recent diet may not reflect past diet, which may be more important to the risk of gastric cancer. Further, we had no information on infection with *H. pylori*. Dietary risk factors such as high intake of salt or low intake of vegetables may act as cofactors with *H. pylori* infection to increase the risk of gastric cancer (4). If risks are higher in the infected subgroup of the population, lack of knowledge about infection status may cause associations to be missed.

Conclusion

We observed an increased risk of gastric cancer with frequent consumption of cured meats and salty foods and a decreased risk with frequent

consumption of vegetables in our study population from the Hanzhong area. These findings are consistent with data from other countries around the world. We also found elevated risk types of fresh meat and fish that may be due to the use of high-temperature cooking methods, but this could not be evaluated directly. Future research into dietary risk factors in Mexico should evaluate cooking methods to explore further the associations with consumption of animal products. Furthermore, *H. pylori* infection status should be determined to evaluate possible interactions with dietary factors.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interest.

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