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Dietary Protective and Risk Factors for Esophageal and Stomach Cancers in a Low-epidemic Area for Stomach Cancer in Jiangsu Province, China: Comparison with Those in a High-epidemic Area

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Comparative epidemiological studies with ecological and case-control approaches in high- and low-epidemic areas of China have provided us with much evidence with regard to risk and benefit in the environment. To clarify how dietary factors are involved in esophageal and stomach cancer development, we performed a case-control study in a low-epidemic area, and compared the findings with those obtained earlier for a high-epidemic area for stomach cancer in the same Jiangsu Province, China. We recruited 199 and 187 cases with esophageal and stomach cancers, respectively, and 333 population-based common controls. Odds ratios (ORs) for esophageal and stomach cancers were calculated with adjustment for potential confounding factors, using an unconditional logistic model. Current and former smoking elevated the OR for esophageal cancer, along with high intake of pickled vegetables and broiled meat, while decreased ORs were observed for frequently consumed raw vegetables and garlic. With regard to stomach cancer, ORs were increased with frequent consumption of salty fish, leftover gruel, and broiled meat, and lowered by snap bean consumption. The present risk factors were common to the previously obtained results in the high-epidemic area, and similarly distributed in each general population. While more protective factors were observed in the high-epidemic area, their penetrance was much greater in the low-epidemic area. The present study thus suggests that frequent vegetable and garlic consumption contributes to low mortality rates for esophageal and stomach cancers in a low-epidemic area, counteracting similar exposure levels for risk factors as in the high-epidemic area.

Key words: Dietary factors — Stomach cancer — Esophageal cancer

East Asia is a region of the world where stomach cancer is epidemic[1)] but there is considerable geographical variation and mortality rates also differ greatly at the provincial level in China.[2)] Dietary factors are considered to be major contributors in this respect and previous studies have shown a positive association between increased risk for stomach cancer, and income, occupation, smoking, mental injury, overeating, high consumption of salt, dietary carbohydrates, sweet potatoes, sour pancakes, salted and fermented soya paste, fermented staple, leftover gruel and pickled vegetables, and low consumption of animal protein in China.[3–10)] Decreased risk has been reported with frequent consumption of allium and other vegetables.[4, 9, 11)] Most of these risk and protective factors appear to act in common for esophageal cancer,[9, 12)] and geographical variation in high-epidemic areas in China is also similar for neoplasms of both these organ sites.[2)]

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Comparative ecological studies between high- and low-epidemic regions can yield valuable information, especially when the level of exposure to specific environmental factors is common to people living in one area and very different from that in the other. We have found such high- and low-epidemic areas for stomach cancer in Jiangsu Province, China,[13)] and shown that people living in the low-epidemic area have a diet unusually rich in allium and other vegetables. Our comparative study, however, had the limitations associated with the so-called "ecological fallacy" and for clarification, further comparative case-control or cohort studies are required. We are aware of no report on such a comprehensive investigation for upper gastrointestinal (GI)-tract cancer, although Buiatti *et al.* conducted a comparative case-control study on stomach cancer in Italy.[14)]

We have already conducted a case-control study in the high-epidemic area and observed risk reduction for both esophageal and gastric cancers with frequent consumption of garlic and vegetables.[9)] To clarify how dietary factors are involved in esophageal and stomach cancer development in the low-epidemic area, we performed an identical case-control study for the two types of cancers, and compared the findings with those obtained earlier.

MATERIALS AND METHODS

Study area Pizhou City, with a population of around 1.46 million, is located inland in the north of Jiangsu Province. The major industry of Pizhou is agriculture, notably garlic production. A nationwide survey in 1990 and 1992 showed the age-adjusted mortality rate (AMR) per 100 000 for stomach cancer in Pizhou (28.2 in males and 12.6 in females) to be half of the mean of the AMR for all rural areas (46.4 in males and 23.9 in females) of Jiangsu Province. In contrast, the AMR for esophageal cancer (39.5 in males and 18.2 in females) did not greatly differ from the mean AMR for rural areas (43.7 in males and 28.1 in females) of the province, although it was much lower than that in a high-epidemic area, Yangzhong (104.3 in males and 88.3 in females).[13)]

Data collection We recruited patients aged 40–79 years who visited Pizhou City Municipal Hospital and were histopathologically diagnosed as having a primary esophageal or stomach cancer in 1996–2000. Cases living outside of Pizhou were excluded from the present study. We earlier conducted a population-based ecological study in 1995–1996, recruiting 215 male and 210 female healthy residents who were 30–79 years old and randomly selected according to the age distribution of the population in Pizhou. They were also interviewed, using the same questionnaire as for the present case-control study. We used these residents as pooled controls, after adjustment for sex, ethnicity and age within 2 years of each case. We collected 143 male and 43 female cases, and 96 male and 42 female controls in 1995–1998. Since a sufficient number of male controls could not be obtained, because the mean ages of the candidates were younger than those of the cases, new controls were recruited from the general population from the middle of 1998. These were randomly selected, using registered records of the local government in the same area of each case, after adjustment as detailed above. We collected a further 144 male and 56 female cases, and 139 male and 56 female controls in 1998–2000. Physicians at the hospital asked eligible cases to participate in our study, and doctors or nurses performed interviews after obtaining oral informed consent. Doctors of public health centers also asked eligible residents for their participation, and conducted interviews in the same way. A few patients and residents refused to take part, although exact participation rates were not recorded.

Data analysis We used the same questionnaire as that for our previous ecological and case-control study in the high-epidemic area.[9, 13)] The questionnaire included 152 items, covering demographics, water supply, dietary habits, food consumption frequency (at the time of the interview and 10 years previously), smoking, alcohol drinking, and tea consumption. The items on smoking habit included smoking status (current and former, or never), age started smoking, age quit smoking, and number of cigarettes per day. Drinking habits included frequency, kinds of alcohol (beers, hard liquors, medium liquors, and fruit liquors) and total amount of alcohol consumption. Tea consumption was rated according to the average number of grams consumed per month.

The consumption frequencies of selected foods and cooking styles were rated in four or six categories and divided into three or four groups to give almost equal distributions of intake amount and frequency in controls. Grouping into three categories was applied for foods with relatively low intake frequencies. Consumption of pickled vegetables was rated according to the average number of kilograms consumed per year.

Comparison with previous findings We summarized our present and previous results,[9, 13)] to compare the selected risk and protective factors for esophageal and stomach cancers and the prevalence of these factors in a general population between high- and low-epidemic areas. We selected factors for which: 1) odds ratios (ORs) were estimated in both case-control studies; 2) decrease or increase in ORs with statistical significance was evident in either case-control study; 3) prevalence in both areas was estimated in the ecological study. As regards prevalence of each factor, weighted mean percentage of the distribution was calculated, using the distribution by gender.

Statistical analysis For data analyses, ORs and their 95% confidence intervals (CIs) of all items for cases and controls were calculated, using the unconditional logistic regression model.[15)] *P* values for OR trend were generated by the χ^2 test after making continuous dummy variables. To control for the effects of potential confounding factors, ORs were calculated after adjustment for age (continuous), sex, smoking status (never; current and former [<20 cigarettes/day]; or current and former [≥20 cigarettes/day]) and drinking habits (<2 times/week, 2–4 times/week, everyday). The procedure LOGISTIC from the statistical package SAS, version 6.12 (SAS Institute, Cary, NC) was used for the calculations.

RESULTS

The age distributions of controls and cases with esophageal or stomach cancers were similar, with mean values of 62.0, 59.9 and 62.5 years for males, and 60.9, 61.9 and 62.6 years for females, respectively (Table I). Most of the study subjects were farmers, and occupation, education, and income were also similarly distributed in cases and controls.

Table I. Background Information for Population-based Controls and Esophagus and Stomach Cancer Cases by Sex (Pizhou, China)

	No. (%) of									
	Males					Females				
	Controls N=235	Esophageal cancer		Stomach cancer		Controls N=98	Esophageal cancer		Stomach cancer	
		N=150	P value	N=137	P value		N=49	P value	N=50	P value
Age in years										
40–49	31 (13.2)	16 (10.7)		13 (9.5)		8 (8.2)	2 (4.1)		4 (8.0)	
50–59	84 (35.7)	41 (27.3)		32 (23.4)		28 (28.6)	19 (38.8)		12 (24.0)	
60–69	74 (31.5)	54 (36.0)		52 (38.0)		47 (48.0)	20 (40.8)		22 (44.0)	
70–79	46 (19.6)	39 (26.0)		40 (29.2)		15 (15.3)	8 (16.3)		12 (24.0)	
Occupation[a)]										
Farmers	182 (77.4)	119 (79.3)		99 (72.3)		92 (93.9)	45 (91.8)		46 (92.0)	
Others	50 (21.3)	30 (20.0)	0.740	35 (25.5)	0.319	3 (3.1)	2 (4.1)	0.738	3 (6.0)	0.399
Education[b)]										
No	88 (37.4)	63 (42.0)		53 (38.7)		79 (80.6)	36 (73.5)		41 (82.0)	
Elementary school or more	146 (62.1)	87 (58.0)	0.390	83 (60.6)	0.795	19 (19.4)	13 (26.5)	0.323	8 (16.0)	0.651
Income[c)]										
<200 yuan/month	185 (78.7)	123 (82.0)		102 (74.5)		82 (83.7)	41 (83.7)		41 (82.0)	
≥200 yuan/month	49 (20.9)	27 (18.0)	0.480	35 (25.5)	0.306	15 (15.3)	8 (16.3)	0.893	9 (18.0)	0.693

a) Information was not obtained for three male and three female controls, one male and two female cases with esophageal cancer, and three male and one female cases with stomach cancer.
b) Information was not obtained for one male control, and one male and one female case with stomach cancer.
c) Information was not obtained for one male and one female control.

Table II. Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for Esophageal and Stomach Cancers According to Smoking and Drinking Habits, and Tea Consumption

	Esophagus			Stomach		
	Ca/ctrl	OR[a)]	(95%CI)	Ca/ctrl	OR[a)]	(95%CI)
Smoking						
Never	44/120	1.00		58/120	1.00	
Current and former (<20 cigarettes/day)	81/95	2.47	(1.43–4.26)	63/95	1.28	(0.75–2.20)
Current and former (≥20 cigarettes/day)	72/118	1.85	(1.03–3.31)	66/118	1.18	(0.67–2.08)
Drinking						
<2 times/week	116/201	1.00		111/201	1.00	
2–4 times/week	35/42	1.23	(0.71–2.13)	32/42	1.23	(0.70–2.17)
Everyday	45/88	0.75	(0.46–1.21)	41/88	0.83	(0.51–1.36)
Tea consumption						
Never	141/222	1.00		130/222	1.00	
1–149 g/month	33/60	0.73	(0.44–1.22)	31/60	0.79	(0.47–1.33)
≥150 g/month	21/49	0.64	(0.36–1.15)	23/49	0.83	(0.47–1.48)

Ca, cases; ctrl, controls.
a) Adjusted for age (continuous), sex, smoking and drinking habits, except for each independent variable.

Current and former smoking elevated the OR for esophageal cancer, but no dose-response relationship with number of cigarettes smoked was apparent (Table II). Increased ORs were not observed for a drinking habit alone and esophageal cancer or smoking and drinking together and stomach cancer. The OR for esophageal cancer with tea consumption showed a tendency for decrease, with no statistical significance.

Consumption of pickled vegetables, deep fried foods and broiled meat increased the ORs for esophageal cancer, and this was statistically significant (Table III). Decreased ORs for esophageal cancer were observed for frequently

Table III. Estimated Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for Patients with Esophageal Cancer According to Selected Food Consumption and Cooking Styles

Consumption of	Categories of consumption frequency							P for trend
	1 (lowest)	2		3		4 (highest)		
	OR[a)]	OR[a)]	(95%CI)	OR[a)]	(95%CI)	OR[a)]	(95%CI)	
Consumption of meat, fish and poultry								
Meat[b)]	1.00	0.78	(0.51–1.20)	1.33	(0.79–2.22)	1.31	(0.60–2.85)	0.258
Fish[b)]	1.00	1.02	(0.66–1.57)	1.49	(0.88–2.53)	1.42	(0.67–3.04)	0.135
Poultry[b)]	1.00	1.24	(0.80–1.94)	2.71	(1.55–4.73)	1.42	(0.62–3.25)	0.005
Egg[c)]	1.00	1.44	(0.89–2.33)	1.24	(0.77–1.99)	1.55	(0.86–2.79)	0.193
Consumption of salted and preserved foods								
Pickled vegetables[d)]	1.00	0.98	(0.48–1.98)	2.16	(1.12–4.18)	2.36	(1.20–4.65)	<0.001
Salted meat[e)]	1.00	1.34	(0.72–2.48)	0.93	(0.38–2.29)	—		0.708
Salted fish[e)]	1.00	1.16	(0.71–1.90)	1.78	(0.96–3.30)	—		0.074
Leftover gruel[f)]	1.00	1.35	(0.91–2.01)	1.31	(0.76–2.28)	—		0.186
Fermented foods[c)]	1.00	2.11	(1.30–3.45)	0.75	(0.45–1.24)	0.76	(0.43–1.34)	0.155
Consumption of beans								
Soybean products[c)]	1.00	1.07	(0.65–1.76)	0.74	(0.46–1.20)	0.46	(0.23–0.91)	0.015
Snap beans[c)]	1.00	0.99	(0.63–1.57)	0.79	(0.49–1.25)	0.51	(0.25–1.00)	0.052
Consumption of vegetables and fruit								
Vegetables[c)]	1.00	2.56	(1.36–4.79)	1.93	(1.09–3.40)	0.81	(0.46–1.44)	0.068
Raw vegetables[f)]	1.00	0.40	(0.19–0.83)	0.30	(0.15–0.61)	—		0.001
Tomatoes[c)]	1.00	1.21	(0.78–1.89)	0.72	(0.44–1.20)	0.83	(0.41–1.68)	0.313
Fruit[c)]	1.00	0.81	(0.50–1.29)	0.98	(0.62–1.56)	0.91	(0.48–1.73)	0.866
Consumption of allium vegetables								
Garlic[c)]	1.00	1.49	(0.86–2.59)	0.67	(0.40–1.15)	0.37	(0.20–0.68)	<0.001
Welsh onion[c)]	1.00	2.31	(1.04–5.14)	1.34	(0.69–2.62)	0.57	(0.31–1.07)	<0.001
Onion[b)]	1.00	0.96	(0.59–1.54)	1.42	(0.85–2.37)	1.26	(0.72–2.21)	0.218
Leek[b)]	1.00	1.06	(0.65–1.73)	0.95	(0.59–1.53)	1.00	(0.57–1.77)	0.879
Cooking styles								
Deep fried foods[e)]	1.00	1.18	(0.75–1.86)	1.79	(1.12–2.86)	—		0.018
Broiled meat[e)]	1.00	2.73	(1.32–5.63)	5.57	(2.10–14.8)	—		<0.001

a) Adjusted for age (continuous), sex, and smoking (never, <20 cigarettes/day and ≥20 cigarettes/day) and drinking (<2 times/week, 2–4 times/week, everyday) habits.
Categories for quartiles and tertile are *b*) <1 time/month, 1–3 times/month, 1–2 times/week and ≥3 times/week; *c*) <1 time/week, 1–2 times/week, 3–5 times/week and everyday; *d*) almost never, 0.5–4.0 kg/year, 4.5–10.0 kg/year and >10.0 kg/year; *e*) <1 time/month, 1–3 times/month and ≥1 time/week; *f*) almost never, occasionally and frequently.

consumed soybean products, raw vegetables and garlic. A similar trend was noted for Welsh onions, in spite of an increased OR with the second lowest level of consumption. Moderate consumption of poultry increased the OR for esophageal cancer, but this was not the case with the highest consumption.

Intake of salted meat, salted fish, leftover gruel, deep fried foods and broiled meat elevated the ORs for stomach cancer, with statistical significance (Table IV). In contrast, snap bean and vegetable consumption lowered the ORs, with a tendency for decrease with tomato consumption. Moderate but not the highest consumption of fish, poultry and onion increased the ORs. Garlic tended to lower the OR, but without statistical significance.

DISCUSSION

The present study demonstrated several risk and protective factors for esophageal and stomach cancers in a low-epidemic area of Jiangsu Province, China, pointing to a particularly important role for vegetable consumption in defining a low incidence population.

Smoking and drinking habits did not influence the risk, except for the increased OR observed for esophageal cancer with smoking. This might be considered surprising given the numerous investigations in Western countries[16, 17] and Japan[18, 19] that have repeatedly pointed to a strong link between smoking and drinking habits and esophageal cancer risk. Such positive associations have

Table IV. Estimated Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for Patients with Stomach Cancer According to Selected Food Consumption and Cooking Styles

Consumption of	Categories of consumption frequency							P for trend
	1 (lowest)	2		3		4 (highest)		
	OR[a]	OR[a]	(95%CI)	OR[a]	(95%CI)	OR[a]	(95%CI)	
Consumption of meat, fish and poultry								
Meat[b]	1.00	0.70	(0.44–1.10)	1.53	(0.92–2.54)	1.56	(0.73–3.31)	0.057
Fish[b]	1.00	0.71	(0.45–1.13)	2.11	(1.28–3.48)	1.35	(0.64–2.85)	0.015
Poultry[b]	1.00	1.09	(0.69–1.71)	3.12	(1.82–5.36)	1.54	(0.68–3.52)	0.001
Egg[c]	1.00	1.37	(0.85–2.21)	1.10	(0.68–1.78)	1.33	(0.73–2.43)	0.488
Consumption of salted and preserved foods								
Pickled vegetables[d]	1.00	1.72	(0.88–3.37)	1.64	(0.84–3.20)	1.62	(0.82–3.20)	0.399
Salted meat[e]	1.00	3.82	(2.24–6.50)	2.36	(1.08–5.14)	—		<0.001
Salted fish[e]	1.00	1.72	(1.07–2.77)	3.44	(1.94–6.09)	—		<0.001
Leftover gruel[f]	1.00	1.50	(0.99–2.27)	2.10	(1.25–3.54)	—		0.004
Fermented foods[c]	1.00	1.43	(0.84–2.42)	1.12	(0.70–1.80)	1.22	(0.72–2.07)	0.491
Consumption of beans								
Soybean products[c]	1.00	1.06	(0.63–1.79)	0.93	(0.57–1.52)	0.85	(0.45–1.61)	0.542
Snap beans[c]	1.00	1.02	(0.65–1.58)	0.53	(0.32–0.86)	0.28	(0.13–0.64)	<0.001
Consumption of vegetables and fruit								
Vegetables[c]	1.00	1.80	(0.99–3.28)	1.33	(0.77–2.27)	0.50	(0.29–0.87)	0.002
Raw vegetables[f]	1.00	0.75	(0.33–1.72)	0.63	(0.29–1.38)		0.183	
Tomatoes[c]	1.00	1.33	(0.86–2.04)	0.45	(0.25–0.79)	0.58	(0.27–1.26)	0.020
Fruit[c]	1.00	1.06	(0.68–1.66)	0.63	(0.38–1.04)	0.62	(0.30–1.25)	0.047
Consumption of allium vegetables								
Garlic[c]	1.00	1.00	(0.56–1.81)	0.72	(0.42–1.24)	0.66	(0.37–1.17)	0.077
Welsh onion[c]	1.00	1.70	(0.73–3.98)	1.42	(0.71–2.86)	0.70	(0.36–1.34)	0.014
Onion[b]	1.00	1.40	(0.87–2.24)	1.84	(1.11–3.05)	1.48	(0.83–2.62)	0.035
Leek[b]	1.00	0.78	(0.46–1.30)	1.03	(0.64–1.65)	0.89	(0.50–1.58)	0.961
Cooking styles								
Deep fried foods[e]	1.00	1.34	(0.85–2.11)	2.11	(1.32–3.37)	—		0.002
Broiled meat[e]	1.00	5.18	(2.65–10.1)	6.47	(2.45–17.1)	—		<0.001

a) Adjusted for age (continuous), sex, and smoking (never, <20 cigarettes/day and ≥20 cigarettes/day) and drinking (<2 times/week, 2–4 times/week, everyday) habits.
Categories for quartiles and tertile are *b*) <1 time/month, 1–3 times/month, 1–2 times/week and ≥3 times/week; *c*) <1 time/week, 1–2 times/week, 3–5 times/week and everyday; *d*) almost never, 0.5–4.0 kg/year, 4.5–10.0 kg/year and >10.0 kg/year; *e*) <1 time/month, 1–3 times/month and ≥1 time/week; *f*) almost never, occasionally and frequently.

also been observed in China,[20, 21] albeit not consistently.[9, 22] However, our previous case-control study conducted in a high-epidemic area for esophageal and stomach cancers, Yangzhong, showed no significant link[9] and this might have a bearing on the present findings. Different cumulative exposure levels of tobacco and alcohol, and different dietary habits may contribute to the observed geographical variation. Estimated per capita consumption of cigarettes per adult 15 years and over in China was lower than that in Japan (1900 vs. 3240) in 1990–1992, and this difference was much greater (730 vs. 2950) in 1970–1972.[23] Alcohol consumption per capita in 1993 was also smaller in China than in Japan (3.2 vs. 6.8 liters per capita of 100% alcohol), although earlier data were not available.[24] The present lack of any association with stomach cancer risk was also concordant with our previous and other studies,[9, 14] although several authors have reported a week positive association.[25–27]

The finding that frequent consumption of pickled vegetables increased the OR for esophageal cancer is in line with the established positive association between pickled vegetable consumption and risk of esophageal and stomach cancers, included nitrosamine compounds appearing to be involved as important carcinogens.[28] The increased OR observed for stomach cancer with salty meat and fish consumption is also concordant with the literature.[14, 29] Again, nitrosamine contamination has been reported for salty preserved fish.[30, 31] Furthermore, pickled vegetables and salty fish by definition contain relatively large amounts of salt, and previous studies have revealed a positive association between high salt consumption and stomach cancer risk.[32]

Several studies have revealed a positive association between frequent consumption of broiled meat, and esophageal and stomach cancer risk.[29, 33–35] This was also the case in the present study, increased risk further being evident with frequent consumption of deep fried food. We are only aware of one earlier report of such a link, for stomach cancer in China.[10] In this context it might be of importance that heterocyclic amines, genotoxic carcinogens, are produced during the broiling and frying of creatinine-containing foods such as meats.[36]

The positive association here noted between leftover gruel consumption and stomach cancer was in agreement with our previous study.[9] As this is kept at room temperature and consumed several hours to a whole day after cooking, frequent consumption might increase exposure to bacteria, fungi, and nitrosamines from nitrate. Bacterial colonization of the stomach causes nitrate reduction and formation of N-nitroso compounds.[37, 38]

Decreased ORs for esophageal and stomach cancer with intake of several vegetables were also concordant with previous observations, suggesting protective effects of antioxidants in these foods.[12, 32] The decrease in esophageal cancer with frequent garlic consumption was also expected from our previous study.[9] Garlic is usually consumed in small amounts, which increases the potential for misclassification of consumption. The present study area has advantages in this respect, because garlic intake is high even by Chinese standards.

While poultry, fish and onion were all associated with increased ORs for esophageal or stomach cancer at moderate intake frequencies, this was not the case for the highest intakes. The influence of confounding factors clearly needs to be explored in this context.

In the present study, all cases were histopathologically confirmed and controls were randomly selected from a resident population with high response rates, so selection bias may have been minimized. Furthermore, while variation in socioeconomic backgrounds may potentially lead cancer patients to select different hospitals giving a potential source of error, we did not observe apparent variations in occupation, income and education between cases and controls. It is nevertheless important to bear in mind that previous studies have indicated cases with esophageal and

Table V. Comparison of Ecological Factors in General Population, and Odds Ratios (ORs) of Selected Lifestyles and Age-adjusted Mortality Rates (AMRs) for Esophageal and Stomach Cancers in High-epidemic Area (HEA) and Low-epidemic Area (LEA) in Jiangsu Province, China

	Categories	Ecological study[a]		Case-control study[b]			
		Prevalence (%)		Esophagus		Stomach	
		HEA	LEA	HEA	LEA	HEA	LEA
AMRs[a]	Males			104.3	39.5	147.1	28.2
(per 100 000)	Females			88.3	18.2	80.5	12.6
Smoking	Current and former	34.8	53.2		↑		
Drinking	Everyday	18.4	21.6				
Meat	≥3 times/week	2.4	7.5				
Salted fish	≥3 times/week	0.0	1.6				↑
Leftover gruel	≥3 times/week	8.0	11.1	↑		↑	↑
Pickled vegetables	Frequently	40.3	40.2	↑	↑	↑	
Soybean products	≥3 times/week	4.4	58.6		↓		
Fermented foods	≥3 times/week	0.0	48.7				
Vegetables	≥3 times/week	94.7	80.2				↓
Raw vegetables	Frequently	11.5	79.1	↓	↓	↓	
Tomatoes	≥3 times/week	0.0	44.2	↓		↓	
Snap bean	≥3 times/week	0.5	56.9	↓		↓	↓
Garlic	≥3 times/week	0.5	78.5	↓	↓	↓	
Fruit	≥3 times/week	2.9	41.9				
Tea consumption	≥200 g/month	19.3	8.0	↓		↓	

↑ Increased ORs with statistical significance.
↓ Decreased ORs with statistical significance.
a) Takezaki *et al.*[13]
b) Gao *et al.*[9]

stomach cancers to have a relatively low socioeconomic status.[39, 40]

No validation data to evaluate the reliability of death certificates for esophageal and stomach cancer in the study area are available. However, we obtained the data of cancer mortality from the nationwide survey in 1990–1992.[2] This survey was conducted in all the provinces of China by the central government, using a standardized method. This procedure included not only a passive survey from death certificates, but also an active survey involving direct investigation of medical records in hospitals. Therefore, the present data of cancer mortality should be more reliable than that from death certificate only.

A comparison of prevalence of risk and protective factors for esophageal and stomach cancers in the general population between high- and low-epidemic areas is given in Table V.[9, 13] Risk factors were similarly observed and distributed in the two areas, except for smoking, this habit being more prevalent in the low-epidemic area. Broiled meat and deep fried foods are not frequently consumed in either area[13] and ORs could not be calculated in the high-epidemic area, because of the lack of variation in consumption between cases and controls.[9] The data suggest that the observed risk factors did not contribute in a major way to the geographical variation in mortality from esophageal and stomach cancers. In contrast, raw vegetables, tomatoes, snap bean and garlic were found to be consumed much more often in the low-epidemic area. High exposure to many protective factors in a general population may dilute the effect of each factor and thus make detection difficult in a case-control study, even where appropriate adjustments are made. The combined findings of our ecological and case-control studies, however, provide strong evidence that lower mortality in the low-epidemic area is attributable to frequent consumption of these antioxidant-containing foods. Garlic has not only antioxidant actions, but also may influence the immune system, inhibiting carcinogen-induced DNA binding and adduct formation, with benefits in terms of both initiation and promotion of carcinogenesis.[41] Risk reduction with garlic consumption was more obvious for esophageal cancer than for stomach cancer in the low-epidemic area where raw garlic is frequently eaten. However, garlic may have some toxicity and unwanted side effects.[42] Extremely high intake of raw garlic may increase local irritation, especially in the stomach, where it may be retained.

In conclusion, the present study showed frequent vegetable and garlic consumption to contribute to lower mortality rates from esophageal and stomach cancers in the low-epidemic area, regardless of similar exposure to risk factors as in the high-epidemic area. Thus, the comparative ecological and case-control studies in high- and low-epidemic areas have provided us with confirmative evidence regarding protective factors for esophageal and stomach cancers. The approach adopted, combining case-control and ecological studies, is particularly important since it allows the limitations of analytical studies to be overcome.

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