RESEARCH COMMUNICATION

Population-based Case-control Study on Risk Factors for Esophageal Cancer in Five High-risk Areas in China

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Abstract

Objective: To study major etiological factors for esophageal cancer in upper gastrointestinal cancer high risk areas in China. Methods: Five areas with high incidences of esophageal and gastric cancer with good quality cancer registration data were selected for the study: Cixian, Shexian from Hebei Province, Linxian from Henan Province, Feicheng from Shandong Province and Zhuanghe from Liaoning Province. A total of 250 cases were randomly recruited from the cancer registration database diagnosed as arising in the lower esophageal segment since January 1, 2009. Three controls were identified and matched with each case as having similar characteristics, such as gender, sex and residency. Questionnaires were applied by face to face interview with trained staff, and data entry was conducted using EPIDATA software. Conditional logistic models were employed for univariate and multivariate analyses to evaluate odd ratios and 95% confident intervals, with SPSS 13.0 statistic software. Results: In single variable analysis, gastrointestinal history, GERD, smoking, passive smoking, alcohol drinking, hot food, pickled food, overnight vegetable, dried food, no breakfast, false dining posture were found to be risk factors of esophageal cancer. Eating more fresh vegetables and high BMI were protective factors. Gastrointestinal history (OR=12.658), not taking regular meals (3.465), overnight vegetables (OR=3.296), GERD (OR=3.044), hot food (OR=2.510), passive smoking (OR=2.423), pickled food (OR=2.273), alcohol drinking (OR=2.074), seldom eating breakfast(OR=1.987), and false dining posture (OR=1.977) increased the risk of esophageal cancer on multivariate logistic analysis, and fresh vegetables (OR=0.279) and BMI≥25 (OR=0.528) continued to be protective. Conclusions: Esophageal cancer could be caused by genetics acting in synergy with environmental factors. Health education for the general population in high risk areas should be strengthened, with intervention programs of nutrition and lifestyle focusing on effective prevention and control for upper gastrointestinal cancer.

Keywords: Esophageal cancer - high risk regions of China - case-control study - risk factor

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Introduction

Esophageal cancer occurs in esophageal epithelium, is a common digestive system malignant tumor with a high incidence in developing country. It ranked the eighth in incidence in the world, and had 460 000 new cases per year (Kamangar et al., 2006). With a poor prognosis, about 400 000 persons per year died because of esophageal cancer (World Cancer Research Fund/American Institute for Cancer Research, 2007), which threatened seriously the health of human beings. China is one of the countries with highest incidence rate and mortality rate of esophageal cancer. The incidence cases and deaths reached to 52.8% and 49.3% in total worldwide, respectively (Parkin et al., 2005). In China, the incidence rate and mortality rate of esophageal cancer were 195.5 per million and 152.1 per million according to the cancer registration data, and ranked the sixth and the fourth, respectively (Chen et al., 2008; Zhao and Chen, 2008). The incidence of esophageal cancer in our country shows distinct regional difference. The first national death cause investigation preliminarily surveyed the epidemical status of esophageal cancer in our country, also found some areas with high incidence of esophageal cancer, but the exact reason was not clear. In our study, main risk factors for esophageal cancer in upper gastrointestinal cancer high risk areas in China were studied, in order to offer a theoretical basis for cancer prevention.

Materials and Methods

Study population

Five areas with high incidence of esophageal cancer and gastric cancer with good quality of cancer registration data were selected for the study, including Cixian, Shexian from Hebei Province, Linxian from Henan Province,

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Feicheng from Shandong Province and Zhuanghe from Liaoning Province. Totally 50 cases were randomly recruited from each cancer registration database diagnosed as cancers in lower segment of esophagus since January 1st, 2009. Case information and pathology diagnosis should be clear. Efforts were made to 1:3 individual-matching the cases and controls by several factors, including same gender, age with 2-year intervals and same village. Also, controls should have no history of malignancy and no family history of upper gastrointestinal cancer. At last, a total of 250 cases and 750 controls comprised the subjects in this analysis ultimately.

Data collection

Considering of influencing factors of esophageal cancer, a structured questionnaire was designed by experts' repeated argument. It was interviewed face-to-face by trained professionals, and it included general information, drinking water sources, smoking, alcohol drinking, tea drinking, regular meals, dining posture, taste, breakfast eating, refrigerator using; overnight vegetable eating, fresh vegetable, fresh fruits, meat and eggs, milk, beans, garlic, rice and flour, dried foods, pickled food, fried foods, hot foods, moldy foods, history of digestive diseases, body mass index (BMI), gastroesophageal reflux disease, and so on.

Quality control

①All cases were diagnosed by pathological data, and signed by attending physician. ②In order to decrease the memory bias, the interviewee should be patients himself or his closest relative. ③The interviewers should be trained professionally, understand content of the questionnaire and natives living habits, know some of the common idiom, and also should learn to communicate with the local residents. ④After every day investigation, the interviewers should summarize the problem occurred in the investigation and solve promptly. The questionnaire with poor quality must be investigated once again.

Statistical analysis

EPI-DATA was used for data entry and SPSS 13.0 for data analysis. Table 1 showed the items of questionnaire and their values. Conditional logistic model was used for univariate and multivariate analysis to evaluate the association between exposure factors and esophageal cancer risk. At last, the odd ratios (OR) and 95% confident interval (CI) of risk factors were calculated by multivariate logistic analysis.

Results

General information

Totals of 250 esophageal cancer cases and 750 controls were collected in our study. Of 250 cases, the male was 180 cases, while the female was 70 cases. The average age of case group and control group was 61.21±8.946 years and 60.8±8.898 years, respectively. No significant difference existed in age, marriage status, ethnic and job occupation between case group and control group (Table 2).

Table 1. Variables in the Questionnaire

Variables		Value
Demographic features	Sex	1=male 2=female
	Age	Continuous
	Marital status	0=unmarried 1=married 2=divorced 3=widowed
	Job occupation	1=peasant 2=worker 3=other
	Ethnic group	1=han 2=hui 3=other
Lifestyle	Drinking water sources	1=running water 2=cellar water, pool water, surface well water, river water, lake water 3=deep well water
	Smoking	0=no 1=yes
	Alcohol drinking	0=no 1=yes
	Tea drinking	0=no 1=yes
	Regular of meal	0=no 1=almost 2=yes
	Dining posture	0=false 1=true
	Taste	0=heavy 1=light 2=right
	Breakfast	0=eat everyday 1=sometimes
	Refrigerator	0=yes 1=no
	Overnight vegetables	0=no 1=yes
Diet	Fresh vegetable	1=everyday 2=sometimes
	Fresh fruit	1=everyday or often 2=sometimes or never
	Meat and eggs	1=everyday 2=always 3=sometimes
	Milk	1=always 2=sometimes 3=never
	Beans	1=always 2=sometimes 3=never
	Garlic	1=always 2=sometimes 3=never
	Rice and flour	1=everyday 2=often
	Dried foods	1=often 2=sometimes 3=never
	Pickled food	1=often 2=sometimes or never
	Fried foods	1=often 2=sometimes 3=never
	Hot foods	1=often 2=sometimes
	Moldy foods	1=never 2=sometimes
History of digestive diseases		0=no 1=yes
GERD		0=no 1=yes
BMI		1= (>=25) 2= (<25)

Lifestyles and esophageal cancer risk

Smoking, passive smoking and alcohol drinking increased the risk of esophageal cancer. The ORs were 2.055, 1.957 and 1.941, respectively. There was a dose-response relationship between smoking amount and esophageal cancer risk. The risk increased significantly while the smoking amount was more than 30 cigarettes per day (OR=3.027). No significant association existed between drinking water sources and esophageal cancer risk.

Not regular meal, overnight vegetables, seldom eating breakfast and false dining posture could increase the risk of esophageal cancer (Table 3).

Diet factors and esophageal cancer risk

Often eating pickled food, fried foods and hot foods could increase the risk of esophageal cancer, while eating vegetables and fruits could decrease the risk of esophageal cancer (Table 4).

Table 2. Distribution of Influencing Factors on Case and Control

Variables	Case		Control		X^2	P
	N	%	N	%		
Sex						
Male	180	72.00	540	72.00	1.000	0.500
Female	70	28.00	210	28.00		
Marital status						
Unmarried	3	1.20	21	2.80	4.023	0.259
Married	227	90.80	647	86.30		
Divorced	1	0.40	4	0.50		
Widowed	19	7.60	78	10.40		
Job occupation						
Worker	12	4.80	19	2.50	3.605	0.188
Peasant	226	90.40	686	91.50		
Other	12	4.80	45	6.00		
Ethnic group						
Han	248	99.20	745	99.30	2.334	0.311
Hui	0	0.00	3	0.40		
Other	2	0.80	2	0.30		
Age	250	61.21±8.946	750	60.84±8.898	0.570*	0.569

*: t value

Table 3. Univariate Analysis of Lifestyles and Esophageal Cancer Risk

Factors	Case		Control		OR	95% CI		P_{Trend}
	n	%	n	%		low	upper	
Drinking water sources								
Running water	16	6.40	54	7.20	1.000			
Deep well	129	51.60	420	56.00	0.967	0.372	2.514	
Shallow well	105	42.00	276	36.80	2.081	0.778	5.567	0.04
Smoking								
No	129	51.60	470	62.70	1.000			
Yes	121	48.40	280	37.30	2.055	1.411	2.994	
Number of cigarettes per day								
<10	149	59.60	497	66.30				
10--19	25	10.00	80	10.70	1.122	0.652	1.933	
20--29	51	20.40	140	18.70	1.411	0.920	2.162	
>=30	25	10.00	33	4.40	3.027	1.645	5.570	0.005
Passive smoking								
No	177	70.80	588	78.40				
Yes	73	29.20	162	21.60	1.957	1.286	2.977	
Drinking								
No	170	68.00	572	76.30				
Yes	80	32.00	178	23.70	1.941	1.290	2.921	
Green Tea								
No	221	88.4	666	88.80				
Yes	29	11.6	84	11.20	1.067	0.601	1.894	
Regular of meal								
Yes	68	27.20	259	34.50				
Almost	151	60.40	462	61.60	1.393	0.939	2.066	
No	31	12.40	29	3.90	4.800	2.561	8.996	0.000
Dining posture								
True	144	57.60	510	68.00				
False	106	42.40	240	32.00	2.373	1.563	3.604	
Taste								
Right	143	57.20	430	57.30				
Light	30	12.00	137	18.30	0.633	0.399	1.004	
Heavy	77	30.80	183	24.40	1.353	0.937	1.951	0.015
Breakfast								
Eat everyday	189	75.60	627	83.60				
Sometime	61	24.40	123	16.40	2.102	1.369	3.226	
Refrigerator								
Yes	50	20.00	143	19.10				
No	200	80.00	607	80.90	1.084	0.714	1.645	
Overnight vegetable								
No	83	33.20	348	46.40				
Yes	167	66.80	402	53.60	3.967	2.653	5.932	

Table 4. Univariate Analysis of Diet Factors and Esophageal Cancer Risk

Factors	Case		Control		OR	95% CI		P_{Trend}
	n	%	n	%		low	upper	
Vegetables								
Sometimes	132	52.80	316	42.10				
Everyday	118	47.20	434	57.90	0.390	0.254	0.599	
Fruits								
Sometime	182	72.80	495	66.00				
Always	68	27.20	222	34.00	0.652	0.451	0.942	
Meat and Eggs								
Sometime	130	52.00	402	53.60				
Always	99	39.60	282	37.60	0.989	0.531	1.840	
Everyday	21	8.40	66	8.80	1.108	0.617	1.990	0.420
Milk								
Never	71	28.40	213	28.40				
Sometime	138	55.20	424	56.50	1.120	0.664	1.889	
Always	41	16.40	113	15.10	0.970	0.659	1.427	0.363
Beans								
Never	15	6.00	45	6.00				
Sometime	152	60.80	458	61.10	1.012	0.506	2.023	
Always	83	33.20	247	32.90	0.995	0.518	1.911	0.008
Garlic								
Never	29	11.60	129	17.20				
Sometimes	142	56.80	388	51.70	0.615	0.363	1.041	
Often	79	31.60	233	31.10	1.127	0.770	1.649	0.058
Rice and flour								
Often	24	9.60	90	12.00				
Everyday	226	90.40	660	88.00	1.493	0.813	2.741	
Dried foods								
Never	49	19.60	181	24.10				
Sometimes	171	68.40	493	65.70	1.416	0.924	2.170	
Often	30	12.00	76	10.10	1.712	0.908	3.225	0.172
Pickled food								
Sometimes	168	67.20	595	79.30				
Often	82	32.80	155	20.70	2.347	1.602	3.438	
Fried foods								
Never	19	7.60	136	18.10				
Sometimes	208	83.20	545	72.70	3.940	2.195	7.073	
Often	23	9.20	69	9.20	3.244	1.521	6.918	0.000
Hot foods								
Sometimes	141	56.40	577	76.90				
Often	109	43.60	173	23.10	4.107	2.777	6.073	
Moldy foods								
Never	236	94.40	703	93.70				
Sometimes	14	5.60	47	5.83	0.855	0.423	1.729	

Table 5. Univariate Analysis of Healthy Status and Esophageal Cancer Risk

Factors	Case		Control		OR	95% CI	
	n	%	n	%		low	upper
History of digestive diseases							
No	164	65.60	706	94.10			
Yes	86	34.40	44	5.90	8.011	5.241	12.245
GERD							
<8	148	59.20	596	79.50			
>=8	102	40.80	154	20.50	3.429	2.391	4.919
BMI							
<25	213	85.20	555	74.00			
>=25	37	14.80	195	26.00	0.452	0.30	0.681

History of digestive diseases, gastroesophageal reflux disease, BMI and esophageal cancer risk

Table 5 showed that history of digestive diseases and gastroesophageal reflux disease were risk factors of esophageal cancer, the ORs were 8.01 and 3.43, respectively. BMI>=25 was protective factor, and the OR was 0.42.

Multivariate analysis

Variables with statistical significance entered into the multivariate logistic regression model. The results showed that gastrointestinal history (OR=12.658), not regular meal (OR=3.465), overnight vegetables (OR=3.296), gastroesophageal reflux disease (OR=3.044), hot food (OR=2.510), passive smoking (OR=2.423), pickled food

Table 6. Multivariate Analysis of Influencing Factors and Esophageal Cancer Risk

Factors	B	SE	Wald	Sig.	Exp(B)	95% CI	
						Lower	Upper
Passive smoking	0.885	0.295	9.015	0.003	2.423	1.360	4.317
Drinking	0.730	0.283	6.624	0.010	2.074	1.190	3.616
Regular of meal			7.875	0.019			
Regular of meal (1)	0.318	0.262	1.475	0.225	1.375	0.823	2.298
Regular of meal (2)	1.243	0.443	7.875	0.005	3.465	1.455	8.253
Dining posture	0.682	0.267	6.505	0.011	1.977	1.171	3.338
Breakfast	0.686	0.307	4.995	0.025	1.987	1.088	3.627
Overnight vegetable	1.193	0.268	19.771	0.000	3.296	1.948	5.576
Vegetables	-1.276	0.304	17.565	0.000	0.279	0.154	0.507
Pickled food	0.821	0.266	9.532	0.002	2.273	1.350	3.828
Hot foods	0.920	0.260	12.562	0.000	2.510	1.509	4.176
History of digestive diseases	2.538	0.290	76.760	0.000	12.658	7.174	22.335
BMI	-0.639	0.270	5.598	0.018	0.528	0.311	0.896
GERD	1.113	0.246	20.481	0.000	3.044	1.880	4.930

(OR=2.273), alcohol drinking (OR=2.074), seldom eating breakfast (OR=1.987), false dining posture (OR=1.977) could increase the risk of esophageal cancer, and fresh vegetables(OR=0.279), BMI>=25 (OR=0.528) were protective factors (Table 6).

Discussion

Esophageal cancer is the result of both effect of environmental factors and genetic susceptibility, and the way of living and behaving is one of the most important influencing factors. However, the exact mechanism is still not clear. Thus, association study of influencing factors and esophageal cancer risk is still a topic to be concerned. The risk factors of esophageal cancer are discrepant in different countries and regions. For example, in developed country smoking, alcohol drinking and Barrett esophagitis are main risk factors, and in developing country nitrosamine, mold pollution, lack of vitamin, unhealthy lifestyles and smoking are main risk factors. There are many case control studies on influencing factors and esophageal cancer risk, but the results are inconsistent. Thus, we conducted a population-based, multi-centers case control study in five areas with high incidence of esophageal cancer and gastric cancer, in order to assess the risk factor of esophageal cancer.

Smoking is the main influencing factor of esophageal cancer in developed countries (Ishikawa et al., 2006; Freedman et al., 2007), but it is inconsistent in our country. Liu et al. (2006) conducted a widespread case control study in 103 regions of China, containing 20,000 esophageal cancer cases and 30,000 and 100,000 healthy controls, respectively, in order to assess the association between smoking and esophageal cancer risk. He found that smoking was an important risk factor of esophageal cancer, and the attributable risk proportion (ARP) was 13.4%~21.1% in rural areas, and 27.6%~31.3% in urban areas. Liao and Tian, 2009 carried out a meta analysis on smoking and esophageal cancer risk, and the OR ratio was 1.81 (95%CI: 1.47~2.24).

However, some studies found no association, and even an inverse relationship (Xie et al., 2005). In our study, no association was found between smoking and esophageal cancer risk, although passive smoking could increase the risk of esophageal cancer significantly. The real reason is not clear, which needs to be studied further. In addition, we also found that alcohol drinking increased the esophageal cancer risk. Alcohol, a solvent for carcinogens, can promote carcinogen access to the esophageal mucosa, which can enhance the effect of damage effects, especially for the individuals who are both smoking and drinking.

Seldom eating breakfast and long-term irregular diet will lead to esophageal campaign and coordinate obstacles, and will result in the damage of esophagus. A Meta analysis indicated that irregular diet could increase the risk of esophageal cancer, the OR was 2.76 (95%CI: 2.42~3.14) (Wang et al., 2007). Residents in high incidence area are accustomed to having a meal crouching, which greatly increases the burden of the digestive system and the chance of occurring chronic esophagus injuries. It is consistent with the Chen et al. (2004) report.

Great quantity of researches confirm that excess intake of pickled food can increase the esophageal cancer risk. Residents in high incidence area are fond of sour cabbage, in which trace benzopyrene, nitrosamine and Roussin 's methyl ester can be detected. Roussin 's methyl ester can supply secondary amine with NO to form nitrosamine, which is a recognized strong carcinogen. According to the studies on nitrosamine and its precursor in vivo and in vitro of residents in high incidence area of esophageal cancer, nitrosamine is strongly associated with the risk of esophageal cancer. Thus, Chinese sour cabbage has been defined as human carcinogenic substances (2B) by IARC (International Agency for Research on Cancer, 1993). The salt in overnight vegetable can translate to nitrates and trace nitrite, which is also one of the carcinogens. It is consistent with our result that eating overnight vegetable is a risk factor of esophageal cancer. Moreover, it is said that hot foods can increase esophageal cancer risk, maybe because high temperature can injury esophageal mucosa or increase the sensitivity of risk factors. Hot food more than 70°C can effect the growth cycle of esophageal mucosa epithelial cells, and create conditions to cancerous change (De Jong et al., 1972). Recently there were plenty of studies on the association between hot foods and esophageal cancer risk, including 50 case control studies and 2 cohort studies, much of which showed that eating hot foods could increase the risk of esophageal cancer

(Farin et al., 2009).

Regardless of univariate or multivariate analysis, vegetables still is a protective factor of esophageal cancer. Scientific research has shown that the fresh vegetables contain abundant anticancer substance and various minor elements. Fresh vegetables are rich in vitamin C, which can avoid cell mutation, reduce cell genetic damage caused by poisonous substance, and also can decrease the formation of nitrosamine, so it has good ability of preventing cancer. Besides, fresh vegetables are rich in cellulose that supposed to prevent cancer. Vegetables also contain carotenoid and tocopherol, which can boost human immunity. Chlorophyll in vegetables helps to prevent cancer and reduce chance of cancer for the individual smoking or drinking. Green broccoli is rich in sulforaphane, while mushroom is rich in purine bases, vitamin B and so on. In a word, intake of fruits or vegetables (>50g/day) can reduce 20% risk of esophageal cancer (World Cancer Research Fund/American Institute for Cancer Research, 2007).

It is reported that individuals with history of the digestive system diseases (including gastroduodenal ulcer, esophagitis, atrophic gastritis, hepatitis, cirrhosis, and so on) increased the risk of esophageal cancer, and the OR value was high. Stomach content thing caused by gastroesophageal reflux disease can return to the esophagus, and injury mucosa, which may lead to inflammation, erosion, and even ulcer, bleeding. If not control, it will result in esophageal stricture and the change of cell types in diseased area (squamous epithelial cell to columnar epithelial cell), and eventually lead to Barrett esophagitis that generally considered the precancerous lesion of esophageal cancer. In our study, we also found high BMI (>=25) was a protective factor of esophageal cancer, which was conflicting with results of western country, maybe because of the different pathologic types. One population-based cohort study in China followed 22 000 healthy individuals (40~79 years old) 10 years, and found BMI was correlated negatively with mortality of esophageal cancer if BMI>18.5. The mortality decreased 25% when BMI increased 5kg/m^2. High BMI was a protective factor of esophageal cancer (Smith et al., 2008), which was consistent with our study.

This being said, esophageal cancer is the result of both effect of environmental factors and genetic susceptibility. If the genetic background can't be changed, change the bad dietary habits and behavior patterns are the most effective prevention of esophageal cancer. Consequently, we should carry out health education in population in the long run, and appeal keeping away from the risk factors of esophageal cancer, and actively take part in endoscopic examination of the people in high risk area in order to find, diagnosis and treatment as early as possible, eventually to reduce the incidence and mortality of esophageal cancer in high risk areas.

References

Chen WQ, Zhang SW, Kong LZ, et al (2008). Death analysis of malignant neoplasms in 2004 by cancer registry. *China Cancer*, **17**, 913-6.

Chen ZY, Li YC, Zhu XP, et al (2004). Case control study of diet factors and esophageal cancer risk in Rugao City. *China Cancer*, **13**, 506-8.

De Jong UW, Day NE, Mounier-Kuhn PL, et al (1972). The relationship between the ingestion of hot coffee and intraoesophageal temperature. *Gut*, **13**, 24-30.

Freedman ND, Abnet CC, Leitzmann MF, et al (2007). A prospective study of tobacco, alcohol, and the risk of esophageal and gastric cancer subtypes. *Am J Epidemiol*, **165**, 1424-33.

International Agency for Research on Cancer. Pickled vegetables (1993). *IARC Monogr Eval Carcinog Risks Hum*, **56**, 83-113.

Ishikawa A, Kuriyama S, Tsubono Y, et al (2006). Smoking, alcohol drinking, green tea consumption and the risk of esophageal cancer in Japanese men. *J Epidemio*, **16**, 185-92.

Kamangar F, Chow W-H, Christian C, et al (2009). Environmental causes of esophageal cancer. *Gastroenterol Clin N Am*, **38**, 27-57.

Kamangar F, Dores GM, Anderson WF (2006). Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. *J Clin Oncol*, **24**, 2137-50.

Liao ZH, Tian J (2009). Meta analysis on smoking and esophageal cancer risk. *J Med Chem*, **6**.

Liu BQ, Jiang JM, Chen ZM, et al (2006). Study of smoking and esophageal cancer risk in 103 regions of China. *J Chinese Med*, **6**, 380-5.

Parkin DM, Bray F, Ferlay J, et al (2005). Global Cancer Statistics, 2002. *CA Cancer J Clin*, **55**, 74-108.

Smith M, Zhou M, Whitlock G, et al (2008). Esophageal cancer and body mass index: results from a prospective study of 220,000 men in China and a meta-analysis of published studies. *Int J Cancer*, **122**, 1604-10.

Wang MY, Li MX, Jiang YZ, et al (1983). Study of Roussin methyl ester isolated from pickled Chinese cabbage and secondary amines translating to carcinogen. *Cancer Prev Treatment Study*, **3**, 145-7.

Wang QZ, Zhou XB, Teng HS (2007). Meta analysis on diet factors and esophageal cancer risk in Chinese. *China Cancer*, **1**, 3-6.

World Cancer Research Fund/American Institute for Cancer Research (2007). Food nutrition, physical activity, and the prevention of cancer: a global perspective [M].Washington DC: American Institute for Cancer Research, 253.

Xie Y, Sun GJ, Hu Xu, et al (2005). Case control study of diet, behavior factors and esophageal cancer risk in residents of Huaian Chuzhou. *Hlth Study*, **34**, 479-80.

Zhao P, Chen WQ (2009). (Annual report of China cancer in 2008). Military Medical Sciences Press. (In Chinese)