RESEARCH ARTICLE

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Risk Factors of Gastric Cancer in High-Risk Region of China: A Population-Based Case-control Study

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Abstract

Background: The reason for the high incidence of gastric cancer (GC) in Xianyou County of China was largely unknown. We aimed to explore the potential sociodemographic risk factors and their associations to GC. **Methods:** A population-based case-control study was conducted during March 2013 and April 2016 in Xianyou County. All newly diagnosed patients of GC were recruited as cases, while controls were selected by matching for cases' sex, age (± 3 years) and the place of residence. **Results:** A total of 523 GC cases and 523 matched healthy controls were included in the final analysis with mean age of 66.27±8.81 years for cases and 66.31±8.83 years for controls, respectively. Participants with low socioeconomic status were observed with higher GC risk compared to those in high socioeconomic status (adjusted OR=2.10, 95% CI: 1.13-3.89). Compared to those regularly drink green tea, patients did not have this dietary habit had nearly 3-fold increased GC risk (adjusted OR=2.91, 95% CI: 1.38-6.13). Other dietary habit, including consumption of hard food, omission of breakfast, consumption of pickled vegetables 30 years ago, overeating were all associated with increased risk of GC. Interaction effect were found. Patients in low socioeconomic status and skipped breakfast had 10-fold higher risk of GC compared to reference group in high socioeconomic status and eat breakfast regularly (OR=10.71, 95% CI: 5.19-22.10). Furthermore, patients in low socioeconomic status and consumed pickled vegetable 30 years ago had 6-fold higher risk of GC compared to those in high socioeconomic status but did not intake pickled vegetables 30 years ago (OR=6.11, 95% CI: 3.87-9.66). **Conclusion:** High incidence of GC risk in Xianyou County might be partly attributed to various sociodemographic factors. Specific prevention effort could be target on population in low socioeconomic status combined with habit of breakfast omission or intake of pickled vegetables.

Keywords: Stomach cancer- risk factors- case-control study- interaction

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Introduction

Background

Gastric cancer (GC) is one of the most common malignant tumors in the world, although the incidence of GC showed a significant decreasing trend in the past few decades (Pisani et al., 1999). A large number of clinical studies showed that five-year survival rate of patients with advanced GC were generally less than 20%, while the five-year survival rate for early GC is more than 90% (La Torre et al., 2011). Therefore, early prevention of GC is valuable to improve the prognosis of GC, especially in areas with high incidence of GC.

GC is a multifactorial disease, and both environmental (68%) and genetic factors (22%) have a role in its etiology (Kelley and Duggan, 2003). The established risk factor of GC, most notably H.pylori infection could not fully explain the heterogeneity in its distribution (Karimi et al., 2014). Only a small proportion of people who carry H.pylori in their stomachs develop GC, suggesting that other factors, such as sociodemographic and dietary factors, may be responsible in cocarcinogenesis (Peek and Blaser, 2002). Several dietary intakes and dietary habits have been widely observed associated with increased risk of GC, including smoking, alcohol drinking, and intake of salty food.

Xianyou County locates on the southeast coast of China. According to our earlier study during 2011 and 2012, GC was the leading cause of death in this area (Li et al., 2017). The mortality rate of GC was 49.47/100,000 in Xianyou County, which was two times higher than the Chinese national average level (21.9/100,000) (Li et al., 2017). H.pylori infection cannot fully explain the high incidence of GC in Xianyou. Sociodemographic factors and life styles were suggested to associate with high incidence of GC in Xianyou County but evidence is lack. Similar to many other high-risk areas of China,

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pickled vegetables were commonly consumed in Xianyou County as an important part of family diet. A recent meta-analysis study had proved that high consumption of pickled vegetables indeed increase the GC risk in China (OR=1.86, 95% CI 1.61–2.15) (Ren et al., 2012). On the other hand, green tea is also commonly consumed by residents in Xianyou County. Many epidemiological studies on the correlation between green tea and the risk of GC have been reported, but their results are inconsistent (Setiawan et al., 2001; Mao et al., 2011; Wang et al., 2015b). Other sociodemographic factors such as low socioeconomic status might also contribute to high incidence of GC. However, the potential role of various sociodemographic factors is still largely unknown in Xianyou County.

Therefore, the aim of the current study was to investigate the associations between potential sociodemographic factors and GC risk in Xianyou County of Southeastern China.

Materials and Methods

Study design and study population

A population-based case-control study of GC was conducted in Xianyou County between March 2013 and April 2016. All newly diagnosed cases of GC that were aged ≥18 years and have been lived in Xianyou for at least 10 years were eligible. Patients who had history of cancer, mental illness, and those unable to complete the questionnaire were excluded. Control subjects were individually selected from the same residence town of matched case patient or from the town with similar incidence of GC , matching for sex and age (±3 years). We divided Xianyou County into three groups of region (high, middle, and low incidence area) based on the standardized mortality rate of GC that was reported in our previously study (Huang et al., 2016). Eligible controls must have also been resided in Xianyou County for at least 10 years and haven't been diagnosed with GC.

Data collection

All cases and controls were personally interviewed by strictly trained research nurses from Xianyou hospital. A structured questionnaire consisted of 337 items under 8 categories was used for the data collection. For case group, cancer related diagnosis and treatment i.e., surgery, chemotherapy, radiotherapy were obtained from medical record.

During the interview, participants were asked about their 1) general demographic information, including age (years), height (meter), weight (kg), marital status (yes, no), education level (formal or primary education), monthly income (<600, ≥600 RMB); 2) occupational history, including profession type (farmer, not farmer), pesticide exposure at work (yes, no); 3) lifetime smoking habits (yes, no), lifetime use of alcohol (yes, no), and tea consumption (yes, no); 4) dietary habit; 5) drinking water and living condition; 6) medical history including personal disease record, medication, and family history of cancer) and 7) mental health.

Regarding dietary habit, participants were asked if they have changed their dietary habit in the past 5 years. If the dietary habit has not been changed in the past 5 years, participants were required to answer the questionnaire mainly based on their dietary habit in the past 1-2 year. If the dietary habit has been changed, participants were requested to report their dietary habit one year before the dietary habit change. Given that the dietary change has occurred more than 5 years, participants were still asked to report their dietary habit in the recent 1-2 years. It should be noted that, few questions concerning dietary habits at 10 years before the interview were also asked. In addition to the main questionnaire, a supplementary questionnaire concerning consumption of pickle vegetables was also used, in which participants were asked their consumption of pickle vegetables 30 years and 15 years before interview. It is generally believed that atypical hyperplasia evolved into GC for about 3-5 years, while intestinal metaplasia evolving into GC about 10-20 years. Therefore, our study investigated the effects of factors on GC over the past thirty years, in order to provide intervention for GC on time window. Patient consents were obtained from all participants at the beginning of study enrollment. Smokers were confirmed if at least one cigarette per day were consumed and lasted for at least half year. Drinking tea was defined as yes if at least one cup of tea per week was consumed, lasting for at least half year.

Statistical analysis

Socioeconomic status was classified into two categories (high and low) based on the monthly income. The income cut-points were 3,000 RMB and 2,000 RMB for socioeconomic status at investigation and in 10 years ago, respectively. Body mass index was classified into four groups: <18.5, 18.5-24, 24-28 and ≥ 28 kg/m^2.

T-test was used to compare continuous valuables, while χ^2 test was used to compare the discrete variables. To assess the relative risk between demographic and dietary factors and GC, unconditional logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI). All reported p-values were two-tailed, and those $p<0.05$ were considered statistically significant. The SPSS 20.0 software was used for all analyses. This study was approved by Ethics Committee of Fujian Medical University.

Results

Demographic characteristics of the subjects

A total of 523 GC cases and 523 matched controls were included in the final analysis from low (18.7%), medium (33.3%) and high (48%) incidence areas. The mean age was 66.27±8.81 years for cases and 66.31±8.83 years for controls, respectively (Table 1). There was no statistically significant difference in age and family GC history ($p>0.05$). The distribution of BMI, H. Pylori infection was statistically significant between case and control groups (both $p <0.05$). Higher prevalence of chronic atrophic gastritis was observed in cases (10.33%) in compared to controls (5.54%). Controls tend to have more education, married or lived with partner, had higher socioeconomic

Table 1. Baseline Characteristics of Gastric Cancer Cases and Controls in a Chinese Population-based Case-control Study

Characteristics	Control Number (%)	Case Number (%)	p value
Sex			-
Male	392 (74.95)	392 (74.95)	
Female	131 (25.05)	131 (25.05)	
Age (year)			0.62
< 60	120 (22.94)	126 (24.09)	
60-65	118 (22.56)	101 (19.31)	
65-70	140 (26.77)	149 (28.49)	
≥70	145 (27.72)	147 (28.11)	
Age (year) (mean±SD)[1]	66.31±8.83	66.27±8.81	
BMI (kg/m^2)[2]			< 0.001
< 18.5	47 (8.99)	97 (18.55)	
18.5-24	341 (65.20)	370 (70.75)	
24-28	116 (22.18)	53 (10.13)	
≥ 28	19 (3.63)	3 (0.57)	
H. Pylori infection			< 0.001
Yes	36 (6.88)	56 (10.71)	
No	138 (26.39)	398 (76.10)	
Unknown	349 (66.73)	69 (13.19)	
Family history of gastric cancer			0.3
Yes	111 (21.22)	125 (23.90)	
No	412 (78.78)	398 (76.10)	
Chronic atrophic gastritis			0.004
Yes	29 (5.54)	54 (10.33)	
No	494 (94.46)	469 (89.64)	
Tumor location			
Cardia	NA	35 (6.69)	
Non-cardia	NA	488 (93.31)	
Formal or primary education			0.004
Yes	157 (30.02)	116 (22.18)	
No	366 (69.98)	407 (77.82)	
Farmer			0.45
Yes	386 (73.80)	375 (71.70)	
No	137 (26.20)	148 (28.30)	
Married or living with a partner			< 0.001
Yes	489 (93.50)	455 (87.00)	
No	34 (6.50)	68 (13.00)	
Socioeconomic status of now			< 0.001
High	376 (71.89)	277 (52.96)	
Low	147 (28.11)	246 (47.04)	
Socioeconomic status 10 years ago			< 0.001
High	282 (53.92)	143 (27.34)	
Low	241 (46.08)	380 (72.66)	
Smoking			< 0.001
Yes	265 (50.67)	308 (58.89)	
No	258 (49.33)	215 (41.11)	
Alcohol intake			0.11
Yes	94 (17.97)	75 (14.34)	
No	429 (82.03)	448 (85.66)	
Consumption of green tea			< 0.001
Yes	148 (28.30)	75 (14.34)	
No	375 (71.70)	448 (85.66)	
Eating quickly			< 0.001
Yes	430 (82.22)	485 (92.73)	
No	93 (17.78)	38 (7.27)	
Irregular eating habit			0.4
Yes	395 (75.53)	383 (73.23)	
No	128 (24.47)	140 (26.77)	
Consumption of very hot food			0.02
Yes	475 (90.82)	495 (94.65)	
No	48 (9.18)	28 (5.35)	
Consumption of very hard food			< 0.001
Yes	414 (79.16)	483 (92.35)	
No	109 (20.84)	40 (7.65)	
Consumption of very salty food			< 0.001
Yes	159 (30.40)	213 (40.73)	
No	364 (69.60)	309 (59.08)	
Consumption of very spicy food			0.13
Yes	148 (28.30)	126 (24.09)	
No	374 (71.51)	395 (75.53)	
Consumption of vinegar			< 0.001
Yes	217 (41.49)	135 (25.81)	
No	305 (58.32)	388 (74.19)	
Omission of breakfast			< 0.001
Yes	216 (41.30)	382 (73.04)	
No	307 (58.70)	141 (26.96)	
Consumption of pickled vegetable 30 years ago			< 0.001
Yes	171 (32.70)	270 (51.63)	
No	352 (67.30)	253 (48.37)	
Overeating			< 0.001
Yes	151 (28.87)	210 (40.15)	
No	368 (70.36)	310 (59.27)	
Working after eating immediately			0.1
Yes	331 (63.29)	356 (68.07)	
No	192 (36.71)	167 (31.93)	
Family disharmony			< 0.001
Yes	67 (12.81)	207 (39.58)	
No	456 (87.19)	316 (60.42)	
Mental stimulation or trauma			0.001
Yes	472 (90.25)	500 (95.60)	
No	51 (9.75)	23 (4.40)	

1. SD, standard deviation; 2. BMI, body mass index.

status, or drink green tea (all p<0.05) than cases. Cases consumed more hot food, hard food, salty food, vinegar, pickled vegetables, and tend to eat quickly, skip breakfast, eat too much in contrast to controls (all p<0.05).

Logistic regression analysis for risk factors of GC

Participants with low socioeconomic status 30 years ago were observed with higher GC risk compared to those in high socioeconomic status (adjusted OR=2.10, 95% CI: 1.13-3.89) (Table 2). Non-smokers had reduced risk of GC compared to smokers (adjusted OR=0.51, 95% CI: 0.25-1.01). Compared to those regularly drink green tea, patients did not have this dietary habit had nearly 3-fold increased GC risk (adjusted OR=2.91, 95% CI:

Table 2. Association between Sociodemographic Characteristics and Risk of Gastric Cancer

Variables	OR[1] (95% CI)	p value	OR[2] (95% CI)	p value
Formal or primary education				0.54
Yes	1.00		1.00	
No	1.70 (1.13-2.58)	0.01	0.80 (0.38-1.65)	
Farmer				0.87
Yes	1.00		1.00	
No	0.99 (0.66-1.50)	0.97	0.95 (0.49-1.82)	
Married or living with a partner				0.15
Yes	1.00		1.00	
No	2.41 (1.28-4.54)	0.006	1.98 (0.78-5.05)	
Socioeconomic status of now				0.14
High	1.00		1.00	
Low	2.56 (1.71-3.83)	< 0.001	1.73 (0.84-3.59)	
Socioeconomic status 10 years ago				0.02
High	1.00		1.00	
Low	2.89 (1.99-4.19)	< 0.001	2.10 (1.13-3.89)	
Smoking				0.05
Yes	1.00		1.00	
No	0.60 (0.38-0.94)	0.03	0.51 (0.25-1.01)	
Alcohol intake				0.91
Yes	1.00		1.00	
No	0.85 (0.51-1.40)	0.51	0.96 (0.45-2.05)	
Green tea intake				0.005
Yes	1.00		1.00	
No	2.67 (1.63-4.37)	< 0.001	2.91 (1.38-6.13)	
Eating quickly				0.57
Yes	1.00		1.00	
No	0.44 (0.26-0.75)	0.003	0.57 (0.24-1.34)	
Irregular eating habit				0.62
Yes	1.00		1.00	
No	0.99 (0.66-1.47)	0.95	0.85 (0.46-1.59)	
Consumption of hot food				0.62
Yes	1.00		1.00	
No	0.58 (0.30-1.11)	0.10	0.79 (0.31-2.02)	
Consumption of hard food				0.04
Yes	1.00		1.00	
No	0.26 (0.15-0.45)	< 0.001	0.45 (0.21-0.98)	
Consumption of salty food				0.56
Yes	1.00		1.00	
No	0.62 (0.43-0.89)	0.01	0.85 (0.48-1.49)	
Consumption of spicy food				0.61
Yes	1.00		1.00	
No	0.99 (0.66-1.48)	0.95	0.83 (0.42-1.67)	
Consumption of vinegar				0.06
Yes	1.00		1.00	
No	1.75 (1.20-2.57)	0.004	1.85 (0.98-3.47)	
Omission of breakfast				< 0.001
Yes	1.00		1.00	
No	0.21 (0.14-0.32)	< 0.001	0.33 (0.19-0.58)	
Consumption of pickled vegetable 30 years ago				< 0.001
Yes	1.00		1.00	
No	0.45 (0.32-0.64)	< 0.001	0.35 (0.20-0.63)	
Overeating				0.04
Yes	1.00		1.00	
No	0.63 (0.43-0.93)	0.02	0.54 (0.30-0.97)	
Working after eating immediately				0.16
Yes	1.00		1.00	
No	0.54 (0.36-0.81)	0.003	0.63 (0.33-1.20)	
Family disharmony				< 0.001
Yes	1.00		1.00	
No	0.14 (0.08-0.24)	< 0.001	0.25 (0.12-0.51)	
Mental stimulation or trauma				0.04
Yes	1.00		1.00	
No	0.27 (0.12-0.58)	0.001	0.27 (0.08-0.93)	

1, Crude odd ratio; 2, Adjusted to body mass index, H, Pylori infection, family history of gastric cancer, and chronic atrophic gastritis.

1.38-6.13). Other dietary habit, including consumption of hard food, omission of breakfast, consumption of pickled vegetables 30 years ago, overeating were all associated with risk of GC. Compared to those having dietary habit of consuming very hard food, pickled vegetable 30 years ago, overeating, patients did not have these dietary habit were all observed with 50% decreased risk of GC. Family disharmony and mental stimulation or trauma was also associated with increased risk of GC. Compared to those experienced family disharmony, patient in harmony family had OR of 0.25 (95% CI: 0.12-0.51). Patients without metal stimulation or trauma had only 27% of GC risk compared to those had these psychological stress (adjusted OR=0.27, 95% CI: 0.08-0.93).

Interaction analysis

The GMDR model was introduced to investigate the interaction of sociodemographic characteristics -dietary factors- behavioral habits-psychological interaction on the GC risk. The results obtained from GMDR analysis for factors interactions were summarized in Table 3.We found the optimal model was socioeconomic status 10 years ago-omission of breakfast- consumption of pickled vegetable 30 years ago, which showed the best cross-validation consistency (10/10), and the highest testing accuracy (0.828). Furthermore, the interaction between this model had a statistically significant effect on GC (p=0.001).

Table 4 displayed the conjoint analysis to further illustrate the interaction correlation between the detected three factors in GMDR model. In participants with high socioeconomic status, omission of breakfast increased the risk of GC (OR=2.20, 95% CI: 1.31-3.68). Patients in low socioeconomic status and skip breakfast had 10-fold higher risk of GC compared to reference group with high socioeconomic status and eat breakfast regularly (OR=10.71, 95% CI: 5.19-22.10). Furthermore, patients in low socioeconomic status and consumed pickled vegetable in 30 years ago had 6-fold higher risk of GC compared to those in high socioeconomic status but did not intake pickled vegetables (OR=6.11, 95% CI: 3.87-9.66). Interestingly, among patients without intake habit of

Table 3. GMDR Analysis on the Best Interaction Models

Best combination	Testing accuracy	Cross-validation accuracy	p value
1	0.815	10/1	0.001
1, 2	0.815	9/1	0.001
1, 2, 3	0.828	10/1	0.001
1, 2, 3, 4	0.819	6/1	0.001
1, 2, 3, 5, 6	0.825	7/1	0.001

1, Represents socioeconomic status in 10 years ago; 2, Represents omission of breakfast; 3, Represents consumption of pickled vegetable 30 years ago; 4, Represents smoking; 5, Represents overeating; 6, Represents working after eating immediately.

Table 4. Conjoint Analysis for Socioeconomic Status 10 Years ago, Omission of Breakfast and Consumption of Pickled Vegetable 30 Years ago Using Logistic Regression

Variables		Case	Control	OR1 (95%CI)	p value
Socioeconomic status in 10 years ago	Omission of breakfast				
High	No	204	351	1.00	
High	Yes	37	29	2.20 (1.31-3.68)	0.003
Low	No	226	134	2.90 (2.21-3.82)	< 0.001
Low	Yes	56	9	10.71 (5.19-22.10)	< 0.001
Socioeconomic status 10 years ago	Consumption of pickled vegetable 30 years ago				
High	No	50	114	1.00	
High	Yes	191	266	1.64 (1.12-2.40)	0.011
Low	No	142	53	2.12 (1.47-3.05)	< 0.001
Low	Yes	331	356	6.11 (3.87-9.66)	< 0.001
Consumption of pickled vegetable 30 years ago	Omission of breakfast				
No	No	144	158	1.00	
Yes	No	286	327	0.96 (0.73-1.27)	0.77
No	Yes	48	9	5.85 (2.77-12.35)	< 0.001
Yes	Yes	45	29	1.70 (1.01-2.86)	0.04

1. Adjust for body mass index, H. Pylori infection, family history of gastric cancer, and chronic atrophic gastritis.

pickled vegetables 30 years ago, those skipped breakfast had OR of 5.85 (95% CI: 2.77-12.35) in compared to those did not skip breakfast. In the additive interaction analysis, highest RERI was observed in the interaction between socioeconomic status in 10 years ago and omission of breakfast (RERI=6.61, 95% CI: -1.09-14.31), followed by socioeconomic status in 10 years ago and pickled vegetables consumption 30 years ago (RERI=3.35, 95% CI: 1.23-5.48) (Table 5).

Disscussion

In the current study, we found that socioeconomic status 10 years ago, smoking, consumption of green tea, consumption of very hard food, omission of breakfast, consumption of pickled vegetables 30 years ago, overeating, family disharmony and psychological trauma were associated with the risk of GC in Xianyou County. The effect of low socioeconomic status 10 years ago on the development of GC was exacerbated by omission of breakfast, as well as the consumption of pickled vegetables 30 years ago.

Our study confirmed that GC was associated with low socioeconomic status, which is in line with previous studies (Khatami and Karbakhsh, 2015).A recent meta-analysis also observed an increased risk of GC among the lowest education (OR=2.97, 95% CI: 1.923-4.58), occupation (OR=2.64, 95% CI: 2.57-7.29) and overall socioeconomic status (OR=2.64, 95% CI: 1.05-6.63) (Khatami and Karbakhsh, 2015). As lower socioeconomic status was associated with GC risk factors including H. pylori infection, genetic inheritance and lifestyle factors, the effect of lower socioeconomic status might therefore be mediated partly through these risk factors (Khatami and Karbakhsh, 2015).

A bordering statistically significant association was observed between smoking and risk of GC in the current study. Although the causing role of smoking

Table 5. Add Interaction Analysis for Socioeconomic Status 10 Years ago, Breakfast and Consumption of Pickled Vegetable in 30 Years ago

Variables		RERI (95%CI)	AP (95%CI)	S (95%CI)
Socioeconomic status 10 years ago	Breakfast	6.61 (-1.09-14.31)	0.62 (0.32-0.91)	3.13 (1.30-7.54)
Socioeconomic status 10 years ago	Pickled vegetable intake 30 years ago	3.35 (1.23-5.48)	0.55 (0.38-0.72)	2.91 (1.68-5.04)
Pickled vegetable intake 30 years ago	Breakfast	-4.19 (-8.60-0.21)	-2.46 (-5.40-0.48)	0.14 (0.03-0.60)

was well established in many other cancers , it was not until 2002 that the International Agency for Research on Cancer concluded that there was "sufficient" evidence of causality between smoking and GC (Humans, 2010). A recent meta-analysis of cohort studies reported that GC was increased by only 60% (RR: 1.6) in male smokers and 20% (RR: 1.2) in female smokers compared with never smokers, and the associations were even weaker in former smokers (Ladeiras-Lopes et al., 2008). Although the results are inconsistent, overall the accumulated data suggest that smoking is a risk factor for both cardia and noncardia GC (Freedman et al., 2007; Ladeiras-Lopes et al., 2008; Cook et al., 2010). Previous experiments demonstrated that the poly- phenols in green tea had antioxidant effects and could suppress the occurrence and development of cancer (Srivastava et al., 2013; Wang et al., 2015a). The inverse association between green tea consumption and risk of GC has been frequently reported in Chinese population as early as year 1996 and in the recent decades (Ji et al., 1996; Setiawan et al., 2001; Nechuta et al., 2012; Wang et al., 2015b). However, many cohort studied in Japanese population did not found such an association (Galanis et al., 1998; Tsubono et al., 2001). The dose of green tea and duration of tea intake habit were believed to explain the differences. When the green tea exposure consumed in a low dose ($\leq$ 4 cups/day), the protective effect on gastric cancer might not be strong (Huang et al., 2017). In contrast, when green tea was consumed $\geq$ 5 cups/day, GC risk was decreased (Tsubono et al., 2001; Huang et al., 2017). It however shall be noted that, hot and very hot tea temperature was significantly related to high risk of GC (Mao et al., 2011). The explanation might be that hot food could cause chronic thermal injury to the upper digestive tract and therefore make it more susceptible to carcinogenesis. Furthermore, we also observed that dietary habit of hard food could also increase the risk of GC, which might be due to the chronic injury to gastric mucosa. Pickled vegetables were eaten 9 to 12 months a year in high-risk area of China (Yang, 1980). High concentration of carcinogenic compounds such as N-nitroso compounds and mycotoxins were the toxic effect of pickled vegetables (Yang, 1980; Cheng et al., 1981; Zhang et al., 1983; Ren et al., 2012). A recent meta-analysis study analyzing 60 English and Chinese studies reported an overall OR of 1.52 (95% CI: 1.37-1.68) (Ren et al., 2012), which was in line to another meta-analysis focusing on 14 Japanese and Korean studies (OR=1.28, 95% CI: 1.05-1.53) (Kim et al., 2010).

We observed that low socioeconomic status 10 years ago combined with breakfast omission have the highest GC risk, compared to high socioeconomic status 10 years ago with having breakfast, which indicated a strong interaction effect between low socioeconomic status and omission of breakfast. The omission of breakfast might be more common in patients in lower social class or low level education.

Our study has several strengths, including large sample size, matching for age, sex and region individually and availability of H. pylori infection. All cases were diagnosed using uniform criteria. However, similar to other case-control studies, our study is also limited by recall bias when answering questionnaire and selection bias (Moradzadeh et al., 2015; Moradzadeh et al., 2018).

In conclusion, socioeconomic status 10 years ago, smoking, consumption of green tea, consumption of very hard food, omission of breakfast, consumption of pickled vegetables 30 years ago, overeating, family disharmony and psychological trauma were associated with the risk of GC in Xianyou County. Specific prevention effort could be focused on population with habit of skipping breakfast combined with low socioeconomic status or intake of pickled vegetables.

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Authors' contributions

The authors' contributions to this study were as follow: study design, PC, YLL, KCZ,CCW, BYL, WY and YHC; data collection, PC, CCW, BYL, WY and YHC; statistical analysis PC and YLL; manuscript writing by all authors.

Conflicts of Interest

None of authors had a personal or financial conflict of interest.

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