Journal of Multidisciplinary Healthcare

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ORIGINAL RESEARCH

Pro-Inflammatory Diet as a Risk Factor for Stomach Cancer: Findings from a Multicenter Study in Central and Western China

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Purpose: We conducted a multicenter cross-sectional study in central and western China to explore the association between inflammatory diet and stomach cancer odds.

Patients and Methods: Participants from five hospitals in the central and western regions were collected. All participants completed the questionnaire we provided before the gastroscopy examination, which includes inquiries about risk factors for stomach cancer and food frequency. All participants underwent gastroscopy, and a mucosal biopsy was confirmed pathologically. Pathological findings were classified as chronic gastritis group, precancerous lesions group and stomach cancer group. Dietary Inflammatory Index (DII) scores were calculated based on the frequency of food occurrences in the questionnaire, and finally SPSS was used to calculate the correlation between variables.

Results: A total of 1162 patients were included in this study, including 668 cases of chronic gastritis, 411 cases of precancerous lesions, and 83 cases of cancer. A single factor analysis was conducted to examine the risk factors of stomach cancer, revealing a significant association between a pro-inflammatory diet and the stomach cancer odds (p value < 0.05). The results of binary classification analysis further confirmed that a pro-inflammatory diet is a risk factor for stomach cancer 【odds ratio (OR) =7.400)】. Moreover, correlation analysis demonstrated a positive correlation between the severity of gastric mucosal diseases and an inflammatory diet (including anti-inflammatory and pro-inflammatory diets) (r_s=0.274, p-value < 0.001).

Conclusion: Pro-Inflammatory diet is a risk factor for stomach cancer, and may accelerate the progression of stomach mucosal disease.

Keywords: stomach cancer, chronic gastritis, precancerous lesions, dietary inflammatory index, pro-inflammatory diet

Introduction

In 2020, there were an estimated 1,089,103 new cases of stomach cancer (5.6%) and almost 768,793 deaths (7.7%) worldwide. Stomach cancer ranks 5th in terms of morbidity and 4th in terms of mortality among malignant tumors globally.[1] While the incidence of stomach cancer has declined in recent years,[2] more than 70% of cases still occur in developing countries.[1] Eastern countries like Japan and China have particularly high incidence rates of stomach cancer.[1] In fact, stomach cancer was one of the most common malignant tumors in China in 2015.[3] The incidence of stomach cancer varies significantly among different regions, with higher rates in rural areas compared to cities, and higher rates in the north compared to the south.[4]

The occurrence of stomach cancer was a multistep and multifactorial process. According to the sequence of stomach cancer described by Correa, stomach cancer gradually develops from chronic gastritis-atrophic gastritis-atrophic gastritis

Received: 22 November 2023
Accepted: 23 February 2024
Published: 2 March 2024

with intestinal metaplasia—dysplasia.[5] The etiology of stomach cancer is multifactorial, involving both genetic and environmental factors.[6] Among these factors, dietary factors have been found to play a critical role,[7] with alcohol consumption, pickled vegetables, and smoking increasing the risk of stomach cancer, while fruit and vegetable consumption has been associated with a substantial reduction in risk.[6] Although previous studies have explored the impact of specific dietary patterns on the onset of stomach cancer,[8–11] it is important to note that humans, as true omnivores, require a balanced nutritional intake and cannot rely on a single diet.

The Dietary Inflammation Index (DII) was developed by the University of South Carolina to comprehensively measure the inflammatory effect of an individual's diet. It is based on 45 dietary factors, including macronutrients, vitamins, minerals, flavonoids, spices, and herbs. The DII has been associated with inflammatory cytokines such as C-reactive protein (CRP), interleukin (IL), and tumor necrosis factor-α (TNF-α).[12] A case-control study from Italy indicated that participants following an anti-inflammatory diet had a higher risk of developing stomach cancer compared to those not following the diet.[13] Similarly, a case-control study conducted in Iran found that participants with a DII score greater than −1.77 were nearly 3.5 times more likely to develop stomach cancer than those with a DII score of −1.77 or lower.[14] However, it is yet to be verified whether this conclusion holds true among the Chinese population. Therefore, we conducted the first study in China to examine the correlation between DII score and stomach cancer. This study aims to contribute to the international consensus that a pro-inflammatory diet is indeed a risk factor for cancer, further strengthening its credibility.

Participants and Methods

Participant Population

We conducted a cross-sectional and multi-center study from June 3 to October 18, 2019 in five hospitals in China. The hospitals included the First Affiliated Hospital of Zhengzhou University (Zhengzhou, Henan Province), the Affiliated Hospital of Qinghai University (Xining, Qinghai Province), Mianyang Central Hospital (Mianyang, Sichuan Province), Shaanxi Traditional Chinese Medicine Hospital (Xi'an, Shaanxi Province), and Xijing Hospital (Xi'an, Shaanxi Province). To ensure ethical principles are followed and the rights and safety of participant are safeguarded, our study underwent review and approval by the Ethics Committee of the First Affiliated Hospital of the Fourth Military Medical University (Approval No. KY20192026-F-1). The study was conducted in accordance with the Helsinki Declaration (2000 edition). Written informed consent (no. KY20192026-F-1) was obtained from each participant prior to enrollment in the clinical trial.

Our questionnaire consisted of two parts. The first part was a survey on risk factors for stomach cancer conducted by Professor Shi's research group in 2014 which included 39 items.[15] This survey was guided by epidemiological and statistical experts and aimed to investigate risk factors for gastric mucosal intestinal metaplasia in Northwest China. The second part was a food frequency questionnaire (FFQ). We used the FFQ from the China Health and Nutrition Survey (CHNS), which included 118 items and was suitable for Chinese individuals aged 6 and above.[16]

The Inclusion Criteria for the Study Were

1. Both genders, aged between 18 and 75 years.
2. Participants with recurrent upper gastrointestinal symptoms and indications for upper endoscopy.
3. Participants who willingness to participate in the study.

The Exclusion Criteria for the Study Were

1. Participants who had undergone upper gastrointestinal surgery.
2. Participants with a previous diagnosis of esophageal cancer.
3. Participants with a previously diagnosed gastric cancer.
4. Pregnant and lactating women.
5. Mentally handicapped individuals.
6. Individuals refusing to sign informed consent.

A total of 1229 participants were included in this study, while 67 participants were excluded based on the exclusion criteria. The exclusion criteria included 14 cases of previously diagnosed esophageal cancer, 45 cases of previously performed upper gastrointestinal surgery, and 8 cases of previously diagnosed stomach cancer.

Diagnosis and Grouping

All participants underwent pathological biopsy. In cases where there are significant abnormalities in the gastric mucosa, physicians choose abnormal tissues based on the location and severity of the patient's lesions. However, for participants with no obvious abnormalities, five samples are taken from the entire stomach following the Sydney criteria for chronic gastritis. These samples include two from the large and small bends of the gastric antrum, one from the gastric angle, and two from the large and small bends of the gastric body.[17] Before commencing this study, a research group WeChat group was established. Remote meetings were conducted within the group to provide unified training for experts from each hospital. In case of unexpected or uncertain situations, communication was conducted in the WeChat group. The final diagnosis depended on the results of the pathological examination, which significantly reduced the possibility of errors. Based on the Histopathology, the participants were divided into the following three groups:

1. Chronic gastritis group (chronic gastritis and atrophic gastritis);
2. The precancerous lesions group (atrophic gastritis with intestinal metaplasia and dysplasia);
3. Stomach cancer group.

Assessment of Dietary Intake

Dietary intake depends on our second part FFQ. The specific collection process is as follows:

1. Assessing the amount of food consumed: the average amount of food consumed per serving can be estimated using the international unit "g". This calculation is based on the raw weight of the food before any processing takes place.
2. As part of the evaluation process, the patients were asked to provide information on their food consumption frequency using the Food Guide Pagoda for Chinese Residents.[18] This information was recorded in a table by converting the frequency (daily, weekly, or monthly) of each food into daily intake. If the patient consumes rice twice a day and eats 75 g each time, the corresponding food eating frequency column in the table will record "2" in the "every day" cell and "75" in the corresponding cell.
3. Seasonal food consumption can be converted from an annual frequency to a monthly frequency. For instance, if a patient consumes watermelon 3 times a week during the months of July and August every year, the total frequency of eating watermelon, which is 24 times a year, can be converted to 2 times a month.

The Calculation of DII

According to the China Food Composition (2016 Edition),[18] the nutrient content of each food was calculated. After calculation, this study included 25 nutrients from the original 45 ingredients of DII. The 25 nutrients consist of 7 pro-inflammatory dietary ingredients 【carbohydrates, cholesterol, energy, total fat, Ferrum (Fe), saturated fat, protein】 and 18 anti-inflammatory dietary ingredients 【caffeine, alcohol, eugenol, garlic, ginger, onion, fiber, saffron, monosaturated fat acids (MUFAs), niacin, polyunsaturated fat acids (PUFAs), pepper, vitamin A, vitamin C, Amin D, vitamin E, Rosemary, Green/black tea】. This proportion is similar to previous studies.[19–21] Individual DII scores were calculated using the following formula: Z score = (daily intake of the dietary ingredient or nutrient - mean of global per capita daily intake of the dietary ingredient or nutrient) / standard deviation of global per capita daily intake of the dietary ingredient or nutrient × This dietary component or nutrient inflammatory effect index.[12] The z-scores were then transformed into a percentile scale, doubling each percentile, and subtracting 1 to achieve a symmetrical distribution (ranging from −1 to +1, centered at 0). The total score for dietary inflammation was defined as the sum of the DII scores for all food parameters. A positive score implies a pro-inflammatory diet, while a negative score indicates an anti-inflammatory diet.

Statistical Analysis

All statistical analyses were conducted using SPSS Statistics 23.0 (IBM, Armonk, NY). For the description and statistics of baseline characteristics, the appropriate description and detection methods were selected based on the different characteristics of the variables (such as continuous variables, categorical variables, normal distribution, non-normal distribution) and the number of groups (two or more groups). Non-normal distribution of continuous variables was described as "median, interquartile range (IQR)" 【eg, age, body mass index (BMI), DII score】, and the Kruskal–Wallis test was used for comparisons involving more than two groups (Supplementary Table 1 and Table 1), while the Wilcoxon rank test was used for two-group comparisons (Supplementary Table 2). Categorical variables were described using "frequency (percent)", and the chi-square test was used to assess balance between groups. The chi-square test was used for statistical description and single-factor analysis of cancer risk factors, and a binary logistic regression model was used for multi-factor analysis. Rank correlation was employed to analyze the correlation between the severity of gastric mucosal disease and the degree of inflammatory diet. The specific process is shown in Figure 1.

Table 1 Comparison of General Clinical Data of Participants with Gastric Mucosal Diseases

Variable	Chronic Gastritis Group (n=668)	Precancerous Lesions Group (n=411)	Stomach Cancer Group (n=83)	χ^2	p-value
Sociodemographic characteristics					
Age, (Q2 〔Q1, Q3〕)	48〔39, 56〕	54〔46, 59〕	60〔53, 68〕	100.081	< 0.001
BMI, (Q2 〔Q1, Q3〕)	22.41〔20.20, 24.83〕	22.65〔20.20, 25.10〕	21.88〔19.59, 23.67〕	5.816	0.055
Female, n (%)	336 (50.3)	166 (40.4)	28 (33.7)	15.155	0.001
Race, n (%)				4.935	0.085
Han	617 (92.4)	393 (95.6)	76 (91.6)		
Others	51 (7.6)	18 (4.4)	7 (8.4)		
Residence, n (%)				36.750	< 0.001
City	387 (57.9)	248 (60.3)	24 (28.9)		
Township	98 (14.7)	58 (14.1)	12 (14.5)		
Rural	183 (27.4)	104 (25.3)	47 (56.6)		
Character, n (%)				13.178	0.010
Introverted	222 (33.2)	162 (39.4)	37 (44.6)		
Intermediate	292 (43.7)	158 (38.4)	21 (25.3)		
Extrovert	154 (23.1)	91 (22.2)	25 (30.1)		
Education, n (%)				54.193	< 0.001
Primary School	136 (20.4)	99 (24.1)	42 (50.6)		
Middle School	273 (40.9)	189 (46.0)	35 (42.2)		
University and Above	259 (38.8)	123 (29.9)	6 (7.2)		
Blood Type, n (%)				18.262	0.019
A	81 (12.1)	59 (14.3)	6 (7.2)		
B	112 (16.8)	57 (13.9)	7 (8.4)		
O	109 (16.3)	79 (19.2)	17 (20.5)		
AB	45 (6.7)	33 (8.0)	5 (6.0)		
Unknown	321 (47.5)	183 (44.0)	48 (57.8)		
Profession, n (%)				27.790	< 0.001
Farmers	196 (29.4)	155 (37.7)	47 (56.6)		
Others	472 (61.8)	256 (33.5)	36 (4.7)		
Income (RMB), n (%)				22.479	< 0.001
Lower (< 5000)	187 (28.0)	145 (35.3)	42 (50.6)		
Middle (5000–10,000)	427 (63.9)	235 (57.2)	40 (48.2)		
Higher (> 10,000)	54 (8.1)	31 (7.5)	1 (1.2)		

(*Continued*)

Table 1 (Continued).

Variable	Chronic Gastritis Group (n=668)	Precancerous Lesions Group (n=411)	Stomach Cancer Group (n=83)	χ^2	p-value
Main Drinking Water, n (%)				47.316	< 0.001
Tap Water	597 (89.4)	332 (80.1)	55 (66.3)		
Well Water	61 (9.1)	56 (13.6)	25 (30.1)		
Rivers and Lakes	10 (1.5)	23 (5.6)	3 (3.6)		
Clinical features					
Disease history, n (%)					
Hypertension	57 (8.5)	44 (10.7)	11(13.3)	2.720	0.257
Diabetes	23 (3.4)	15 (3.6)	3 (3.6)	0.034	0.983
Immune diseases	8 (1.2)	6 (1.5)	3 (3.6)	2.991	0.326
Medical history, n (%)					
NSAIDS	12 (1.8)	4 (1.0)	1 (1.2)	1.237	0.523
Aspirin	8 (1.2)	3 (0.7)	2 (2.4)	1.850	0.445
Metformin	16 (2.4)	11 (2.7)	2 (2.4)	0.085	0.959
Statin	3 (1.2)	5 (1.2)	1 (0.4)	2.165	0.342
Daily habit					
High Salt Diet, n (%)	156 (23.4)	113 (27.5)	36 (43.4)	15.796	< 0.001
Smoking status, n (%)				27.201	< 0.001
Never smoker	467 (69.9)	245 (59.6)	37 (44.6)		
Past smoker or Current smoker	201 (30.1)	166 (40.4)	46 (55.4)		
Family History of Stomach Cancer, n (%)	58 (8.7)	66 (16.1)	15 (18.1)	15.599	< 0.001
***Hp* infection, n (%)**	310 (46.4)	232 (56.4)	37 (44.6)	11.246	0.004
DII score, (Q2 〔Q1, Q3〕)	0.030 (−0.840, 0.705)	0.200 (−0.920, 0.460)	0.030 (−0.92, 0.46)	9.945	0.007

Notes: statistical analyses were performed on the age, BMI and DII score variables using the Kruskal Wallis H-rank sum test, while the other variables were tested using the chi-square test. A statistically significant difference was defined as p-value < 0.05. The chronic gastritis group includes chronic gastritis and atrophic gastritis; The precancerous lesions group includes atrophic gastritis with intestinal metaplasia and dysplasia.
Abbreviations: Q1, First quartile; Q2, Second quartile; Q3, Third quartile; BMI, body mass index; RMB, Rén mín bì'; *HP, Helicobacter pylori*; DII, Dietary Inflammatory Index.

Results

Baseline Information

Comparison of General Data of Participants by the IQR of DII Score

The study included a total of 1162 participants, consisting of 632 males and 530 females. The participants had a median age of 51 years and a median BMI of 22.49. The maximum DII score recorded was 2.64, while the minimum value was −2.43. The DII score quartiles were as follows: first quartile (Q1): −0.433, second quartile (Q2): −0.190, third quartile (Q3): 0.609. Supplementary Table 1 provides a summary of the basic characteristics of participants within the IQR of DII scores. Among these characteristics, gender, residence, character, profession, *Helicobacter pylori* (*Hp*), and smoking status showed statistical significance (p-value < 0.05) in relation to the IQR of DII scores of participants.

Comparison of General Clinical Data Between Anti-Inflammatory Group and Pro-Inflammatory Group

In the anti-inflammatory group, there were 761 individuals, while the pro-inflammatory group consisted of 401 individuals. Statistical differences were observed in BMI, residence, personality, residence, and family history of stomach cancer between the two groups (p-value <0.05) (Supplementary Table 2).

Comparison of General Data of Participants with Gastric Mucosal Diseases

A total of 668, 411, and 83 participants were observed in the chronic gastritis, precancerous lesions, and stomach cancer groups, respectively. The median age for chronic gastritis, precancerous lesions, and stomach cancer were 48, 54, and 60, respectively. The median BMI values were 22.41, 22.65, and 21.88 for chronic gastritis, precancerous lesions, and

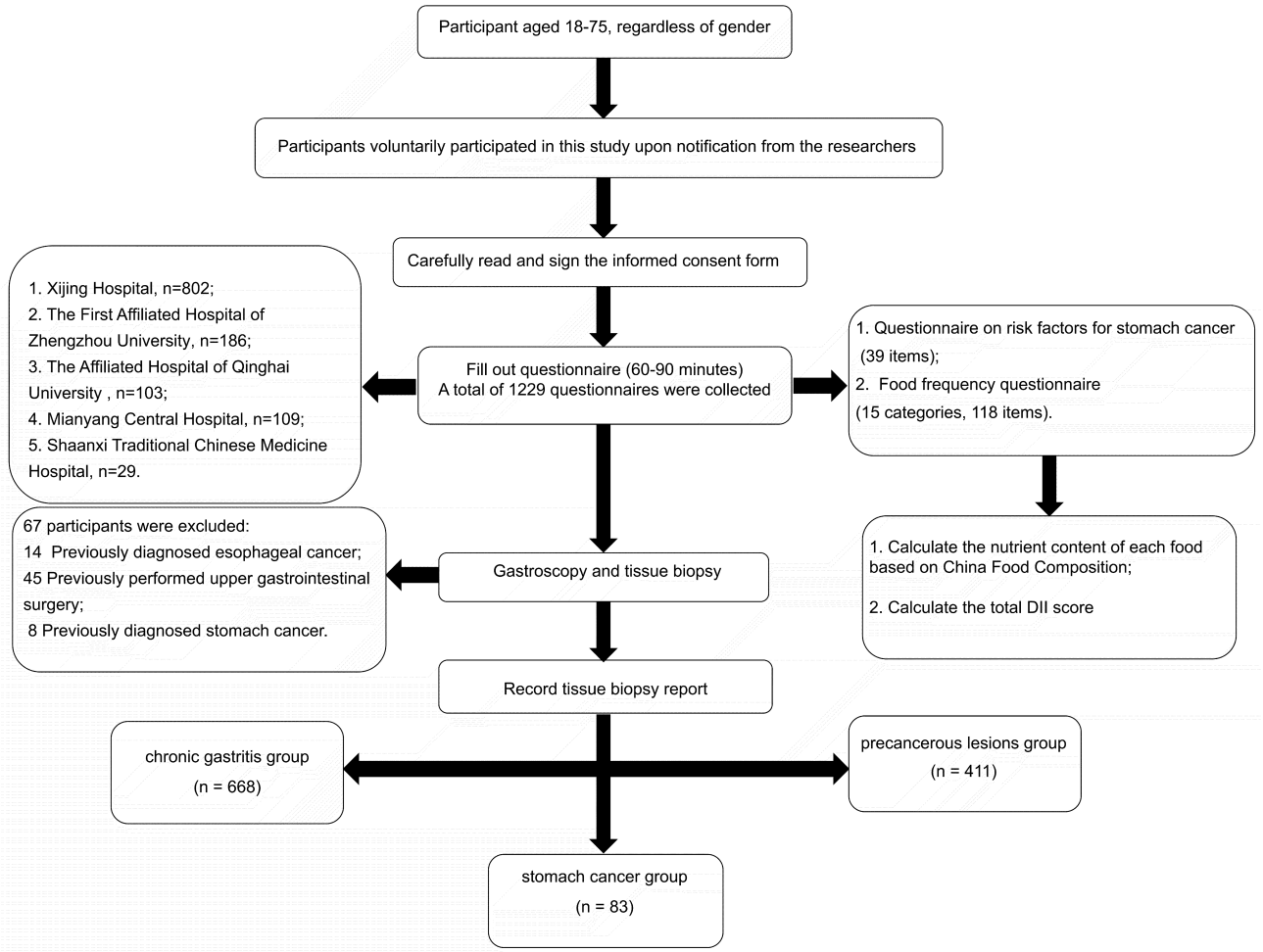

Figure 1 Research flowchart.

stomach cancer, respectively. Table 1 presents the clinical characteristics of the participants in each group. The influence of age, gender, character, residence, education, blood type, profession, income, main drinking water, high salt diet, family history of gastric cancer, smoking status, *Hp* infection and DII score on gastric mucosal disease was statistically significant (p-value <0.05).

Risk Factors and Symptoms of Stomach Cancer

Univariate Analysis of Risk Factors for Stomach Cancer

A total of 1079 cases of non-stomach cancer and 83 cases of stomach cancer were observed. In the univariate analysis, several independent variables showed statistically significant differences (p-value < 0.05) between the stomach cancer group and the non-stomach cancer group. These variables included age, gender, character, residence, education, blood type, profession, income, main drinking water, high salt diet, family history of stomach cancer, smoking status, and pro-inflammatory diet (Table 2).

Multivariate Analysis of Risk Factors for Stomach Cancer

The study found that patients with higher educational levels had a lower likelihood of suffering from stomach cancer compared to patients with lower educational levels (*OR*=0.385). The regression analysis showed that the median age, place of residence, smoking status, and inflammatory diet were all associated with an increased risk of stomach cancer. Specifically, individuals older than 52 years had a higher likelihood of developing stomach cancer compared to those

Table 2 Single-Factor Analysis of Risk Factors for Stomach Cancer

Variable	Non-Stomach Cancer Group (n=1079)	Stomach Cancer Group (n=83)	χ^2	p-value
Age (years old)			34.347	<0.001
18–51	581 (53.8)	17 (20.5)		
52–75	498	66		
Gender, Men, n (%)	577 (53.5)	55(66.5)	5.082	0.024
Residence, n (%)			36.432	<0.001
City	635 (58.9)	24 (28.9)		
Township	156 (14.5)	12 (14.5)		
Rural	288 (26.7)	47 (56.6)		
Character, n(%)			8.789	0.032
Introverted	384 (35.6)	37 (44.6)		
Intermediate	450 (41.7)	21 (25.3)		
Extrovert	244 (22.7)	25 (30.1)		
Education, n(%)			45.189	<0.001
Primary School	235 (21.8)	42 (50.6)		
Middle School	462 (42.8)	35 (42.2)		
University and Above	382 (35.4)	6 (7.2)		
Blood Type, n(%)			7.974	0.537
A	139 (12.9)	6 (7.2)		
B	169 (15.7)	7 (8.4)		
O	188 (17.4)	17 (20.5)		
AB	78 (7.2)	5 (6)		
Unknown	505 (46.9)	48 (57.8)		
Profession n(%)			19.872	<0.001
Farmers	357 (32.5)	47 (56.6)		
Others	728 (67.5)	36 (43.4)		
Income (RMB), n (%)			16.266	<0.001
Lower (< 5000)	332 (30.8)	42 (50.6)		
Middle (5000–10,000)	662 (61.4)	40 (48.2)		
Higher (> 10,000)	85 (7.9)	1 (1.2)_		
Main Drinking Water, n (%)			27.094	<0.001
Tap Water	929 (86.1)	55 (66.3)		
Well Water	117 (10.8)	25 (30.1)		
Rivers and Lakes	33 (3.1)	3 (3.6)		
High Salt Diet, n(%)	269 (24.9)	36 (43.4)	13.679	0.003
Family History of Stomach Cancer, n(%)	124 (11.5)	15 (18.1)	3.503	0.623
Hp infection, n(%)	542 (50.2)	37 (44.6)	1.363	0.506
Smoking status, n(%)			16.132	0.003
Never smoker	711 (65.9)	37 (44.6)		
Past smoker or Current smoker	114 (10.6)	12 (41)		
Pro-inflammatory diet, n(%)	342 (31.7)	59 (71.1)	52.907	<0.001

Notes: Statistical single factor analysis of stomach cancer risk factors using chi square test. A statistically significant difference was defined as p-value < 0.05. The non-stomach cancer group includes chronic gastritis group and precancerous lesions group.
Abbreviations: RMB, Rén mín bì'; *HP, Helicobacter pylori.*

aged 51 years or younger (*OR*=3.763). Living in rural areas was also associated with a higher risk of stomach cancer compared to city areas (*OR*=1.699). Additionally, being a smoker or former smoker increased the likelihood of developing stomach cancer compared to never smokers (*OR*=4.433). Finally, consuming a pro-inflammatory diet was found to be associated with a higher risk of stomach cancer compared to an anti-inflammatory diet (*OR*=7.400) (Table 3).

Table 3 Multivariate Analysis of Risk Factors for Stomach Cancer

Variable	β	SE	Wald χ^2	OR (95% CI)	p-value
Age, (ref: ≤51 years old)	1.325	0.298	19.715	3.763 (2.096–6.754)	< 0.001
Residence, (ref: city)	0.530	0.150	12.418	1.699 (1.265–2.282)	< 0.001
Education level, (ref: primary school)	−0.954	0.216	19.544	0.385 (0.259–0.606)	< 0.001
Smoking status, (ref: never smoker)	0.889	0.274	12.069	2.433 (1.473–4.019)	0.001
Pro-inflammatory diet: (ref: anti-inflammatory diet)	2.002	0.274	53.370	7.400 (4.4326–12.661)	< 0.001
Constant	−6.377	0.877	52.823	0.002	< 0.001

Notes: Binary Logistic analysis, forwardL: LR method is used to screen independent variables, αin=0.05, αout=0.10.
Abbreviations: β, regression coefficient; SE, Standard Error; OR, Odds Ratio; CI, Confidence Intervals.

Stomach Cancer and Gastrointestinal Symptoms

Participants with stomach cancer exhibit a higher incidence of abdominal distension, anorexia, vomiting, and blood in the stool compared to patients without gastric cancer (p-value <0.05). Conversely, symptoms of acid reflux and heartburn are less commonly observed in patients with stomach cancer. This is depicted in Figure 2.

Correlation Analysis Between Gastric Mucosal Diseases and Inflammatory Diet

Rank correlation analysis was performed to examine the relationship between the severity of gastric mucosal diseases (including normal gastric mucosa, atrophic gastritis, intestinal metaplasia, atypical hyperplasia, and stomach cancer) and the level of inflammatory diet (including anti-inflammatory and pro-inflammatory diets) among the participants. The findings revealed a significant positive correlation between the degree of gastric mucosal inflammation and the level of inflammatory diet (r_s=0.274, p value<0.001). Grouping analysis of male and female groups showed a significant positive correlation between the degree of gastric mucosal inflammation and the level of inflammatory diet, both in the male group (rs=0.252, p value<0.001) and in the female group (rs=0.305, p value<0.001) (refer to Figure 3).

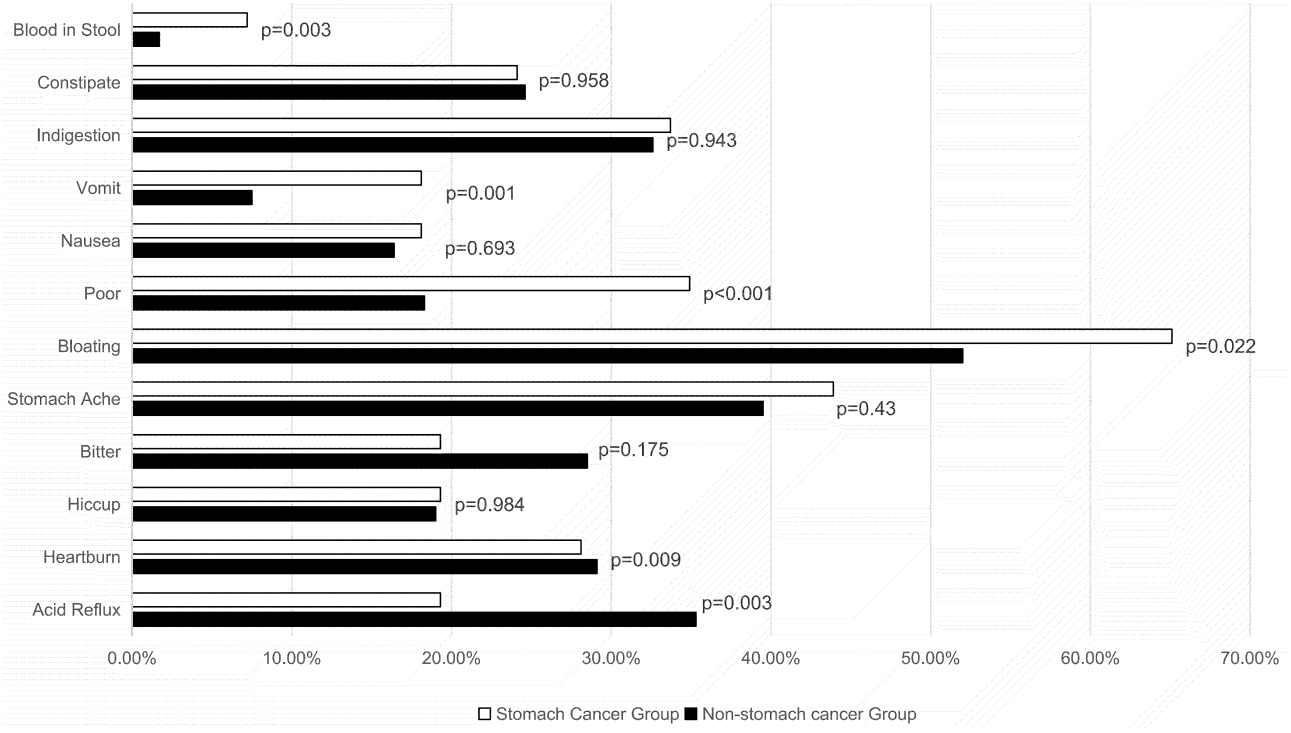

Figure 2 Relationship between stomach cancer and gastrointestinal symptoms.

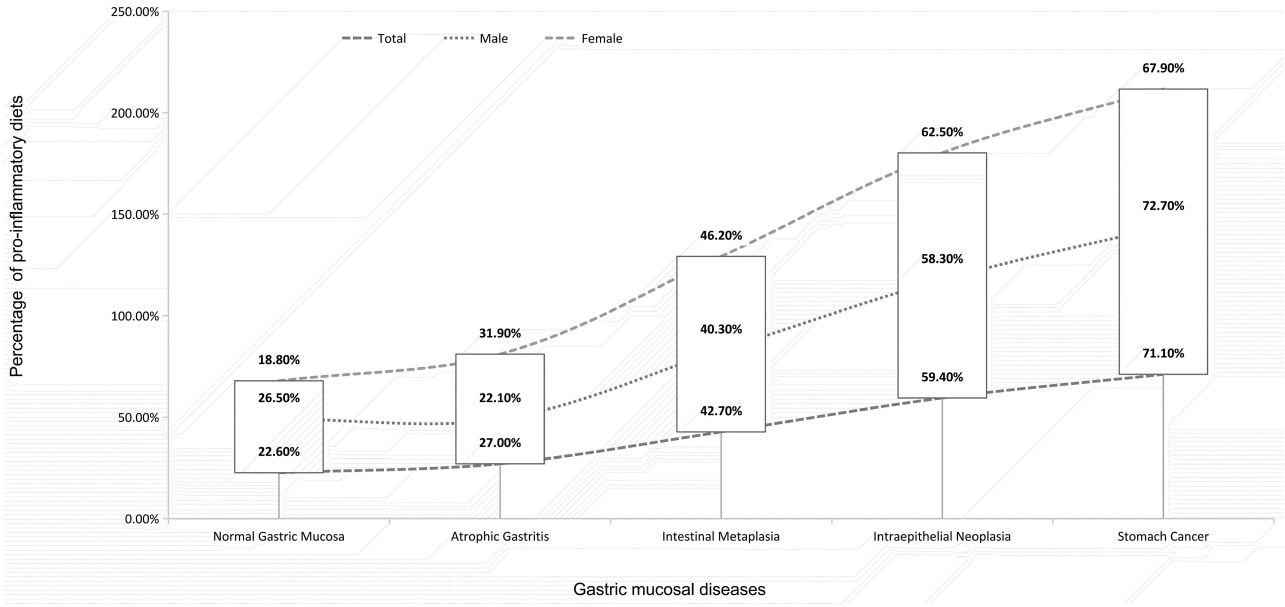

Figure 3 The correlation between pro-inflammatory diet and the severity of gastric mucosal diseases.

Discussion

In this study, we found that a pro-inflammatory diet may increase the odds of stomach cancer in the population of central and western China, and the severity of gastric mucosal disease may be positively correlated with an inflammatory diet.

Previous studies have shown that diet is associated with gastrointestinal tumorigenesis.[20,22,23] It has been demonstrated that specific dietary modifications can act as adjuvant therapies with existing cancer treatments.[24,25] Recent reports have utilized the DII to represent the inflammatory potential of the diet in the study of diseases.[26–29] DII has been found to be particularly relevant to stomach diseases.[30–33] A cohort study in Korea reported that individuals in the highest quartile of DII score showed a 1.22-fold higher risk of incident stomach diseases compared to those in the lowest quartile.[30] Additionally, an Italian case-control study revealed a weak association between a pro-inflammatory diet and an increased risk of stomach cancer, as compared to an anti-inflammatory diet.[31] A previous meta-analysis involving 311 studies also suggested that a potentially inflammatory diet increases the risk of stomach cancer.[32] Furthermore, a case-control study of 1125 people found that the DII was associated with cancer risk, and the impact of DII on stomach cancer risk varied depending on TNF genotype.[33] Our research findings align with the aforementioned results, indicating that a pro-inflammatory diet can be considered a risk factor for stomach cancer.

The total score of the DII was −8.20 to +6.36 in Korean population cohorts.[30] Median (Standard Deviation, SD) and range of the Energy Adjusted DII (E-DII) in the Mitchelstown cohort were −1.40±0.1 and −5.10 to +3.68.[34] A study from Xiangya Hospital [Xiangya, Hunan Province] calculated that the average E-DII was +0.68± 0.08, and the score ranged from –5.32 to +4.26, but the study population was Americans.[27] However, the total DII scores of 1162 patients in our study ranged from −2.43 to+2.64, with an average score of −0.129 ± 0.032. Although our study has a smaller range of the total score of the DII compared to some studies.[14,35] After our research, we found that some studies were similar to our DII scoring range.[36–39] This indicates that our data results are reasonable. We noted that the range difference might be because diet differed widely among different countries, different areas and different races. The patients in this study were mainly from central and western China, and these four regions mainly rely on wheat as their staple food, which may be the reason for the small range of DII scores.[40]

Compared to individuals in the lowest quartile of DII in this study, those in the highest quartile of DII were more likely to be elderly, male, urban residents, introverted, and civil servants. Furthermore, the pro-inflammatory diet group, when compared to the anti-inflammatory diet group, exhibited a higher likelihood of having a high BMI, being urban residents, being civil servants, and having a family history of stomach cancer. This is inconsistent with some research both domestically and internationally.[27,41,42] Our findings align with previous

studies indicating that patients with higher DII scores tended to be older compared to those with lower DII scores.[43] How often this occurs depends on the investigation method of food frequency. Articles with different results from our study mostly investigated the diet of patients in the past 24 hours, while articles with similar results investigated the diet of patients for most of the time since birth.[44] As we stated earlier, stomach cancer is a gradual process rather than a sudden illness,[5] so our investigation of long-term dietary habits is more reliable.

We found that the greater the age, the greater is the risk of developing stomach cancer, which was consistent with other studies.[45–47] Our finding corroborates those of previous studies that observed higher prevalence of stomach cancer among rural residents than those living in urban areas.[3,4,48,49] A study has shown that high-salt intake could enhance the carcinogenic effect of cagA (+) *Hp* strains.[50] Our research findings indicate that individuals with lower education levels have a higher incidence rate of cancer, which aligns with previous research.[51]

Our study revealed that there was no association between family history and *Hp* infection with the risk of stomach cancer. This could be attributed to the fact that as people's living standards improve, there is a deeper understanding of the disease. It is noteworthy that most patients with *Hp* infection proactively request gastroscopy, leading to a significant increase in the detection rate of *Hp* in the non-stomach cancer population undergoing gastroscopy. This factor becomes important in explaining the lack of correlation between *Hp* infection and the risk of stomach cancer. Similarly, families with a history of tumors tend to be more vigilant about the disease compared to families without such a history. They undergo regular gastroscopy screenings prior to the development of tumors, which renders the family history in this study irrelevant to the risk of stomach cancer.

Our research results indicate that stomach cancer patients exhibit higher symptoms, such as bloody stools, vomiting, loss of appetite, bloating, abdominal pain, heartburn, and reflux, compared to non-stomach cancer patients. These symptoms have not been previously mentioned in studies on risk factors for stomach cancer. Therefore, it is recommended that patients who exhibit the aforementioned symptoms and do not find relief should undergo a gastroscopy examination promptly in order to eliminate the possibility of early stomach cancer.

This study is the first multi-center study conducted in China to investigate the correlation between DII score and stomach cancer. It addresses the gap in international research on this topic and highlights the finding that a pro-inflammatory diet is associated with an increased incidence of stomach cancer. The use of a diet recall questionnaire (FFQ) by participants may introduce some inaccuracies in estimating dietary intake. However, due to the large sample size of our survey population, this method was chosen for its efficiency. It is important to note that our survey was limited to the central and western regions of China and did not cover the entire nation, which may affect comparability with other populations and introduce potential errors and differences in dietary exposure.

Conclusion

The findings of our study demonstrate that the pro-Inflammatory diet is a risk factor for stomach cancer, and may accelerate the progression of stomach mucosal disease. The results of this study are highly significant in terms of providing dietary guidance for high-risk patients with gastric cancer. These patients include those with a family history of stomach cancer, intestinal metaplasia, and atypical hyperplasia.

Acknowledgments

We thank the study participants and the clinical teams. We also thank the Good Clinical Practice (GCP) center at each hospital. We truly appreciate the help provided by members in the endoscopy centers and Department of Pathology from all participating centers.

Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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