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Dietary Factors and Gastric Intestinal Metaplasia Risk Among US Veterans

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Abstract

Background—Studies on diet and gastric intestinal metaplasia (GIM) risk are lacking in US populations.

Aim—To determine the associations of dietary factors and risk of GIM among a US population with typical American diet.

Methods—We analyzed data from a cross-sectional study of veterans attending primary care and endoscopy clinics at the Houston VA Medical Center. Patients completed a 110-item Block Food Frequency Questionnaire then underwent upper endoscopy with gastric mapping biopsies. We compared cases defined by GIM on ≥ 1 non-cardia gastric biopsy to controls without GIM. Associations of dietary factors and GIM were estimated using logistic regression models as odds ratios (OR) and 95% confidence intervals (CI).

Results—Among 423 GIM cases and 1796 controls, cases were older (62.1 vs. 59.9 years) and more likely to be male (97.2% vs. 90.8%) and non-White (58.6% vs. 39.0%). GIM cases had

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Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

lower fat intake (percent kcal from fat tertile 1: 43.6% vs. 33.4%) and higher carbohydrate intake (percent kcal from carbohydrate T3: 41.8% vs. 33.3%) than controls. Adjusting for age, gender, race, smoking, and *Helicobacter* pylori, percent kcal from carbohydrates (T3 vs. T1: OR 1.35, 95% CI 1.08–1.67), fruit intake (T3 vs. T1: OR 1.28, 95% CI 1.02–1.61), and fiber intake (T3 vs. T1: OR 1.37, 95% CI 1.04–1.80) were associated with GIM. In subgroup analyses, these associations were primarily seen in non-White patients.

Conclusions—Few dietary factors, including high carbohydrate intake, are associated with increased risk of GIM in US populations, independent of *H. pylori* or smoking.

Keywords

Diet; Dietary factors; Nutrition; Gastric intestinal metaplasia; Gastric cancer

Introduction

Non-cardia gastric adenocarcinoma (gastric cancer) is the fifth-leading cause of cancer-related death worldwide [1]. Despite a decreasing overall incidence of gastric cancer in the USA [2], the incidence rates are increasing among adults < 50 years [3]. The majority of gastric cancer occurs in the setting of mucosal inflammation and is preceded by the development of gastric intestinal metaplasia (GIM) and atrophy. In the US population, *Helicobacter pylori* infection [4–8], smoking [8], and family history of gastric cancer [7, 9–12] have been described as independent risk factors for GIM.

There has been much interest in identifying potentially modifiable dietary factors and determining the role that diet and food preparation may have in the development of GIM and gastric cancer. In countries with high gastric cancer rates (e.g., Asia, Central/South America), spicy foods, salt, nitrite-rich foods, and low intake of fruits and vegetables have been associated with increased risk of GIM [5, 6, 13, 14]. However, few studies have focused on dietary factors in countries with Western diets (e.g., USA), and these studies produced conflicting results on the effect of salt, fruits, vegetables, and high fat foods on the risk of GIM [10, 15, 16].

The few previous US studies of diet and gastric cancer primarily consisted of populations with high numbers of immigrants, who usually maintain similar diets as their home country [17–19], and have focused on gastric cancer [20] rather than GIM, the precancerous stage with greatest potential benefit from dietary modification. Additionally, few studies on Western dietary factors have adjusted for the presence of *H. pylori* infection, which is the strongest risk factor for gastric cancer. The purpose of this study was to examine dietary factors associated with the development of GIM among a US veteran population with diets representative of typical American diets.

Methods

Study Design

We used data from a previously completed cross-sectional study of patients attending primary care and endoscopy clinics at the Michael E. DeBakey Veterans Affairs Medical

Center (MEDVAMC) in Houston, Texas, from February 2008 to August 2013 [21]. Study participants were selected and recruited to undergo study esophagogastroduodenoscopy (EGD) from 2 sources: (1) randomly selected patients eligible for screening colonoscopy from 1 of 7 primary care facilities and also agreed to undergo an EGD for the research study, and (2) consecutive patients previously scheduled to undergo EGD for any indication and agreed to research study enrollment. The first group of patients were patients eligible for colon cancer screening colonoscopy and who consented to additional EGD with gastric biopsies at the time of their colonoscopy; the second group of patients were ones already scheduled for EGD due to gastrointestinal symptoms and who consented to additional gastric biopsies as part of the research study. Inclusion criteria included any patient between 40 and 80 years old (50–80 years among the patients recruited from primary care clinics given colonoscopy recommendation starting at age 50). Exclusion criteria included: (1) previous gastroesophageal surgery; (2) previous cancer; (3) the use of anticoagulants; (4) platelet counts < 70,000, ascites, or gastroesophageal varices; or (5) history of major stroke or mental condition inhibiting interview ability. All participants provided written informed consent to take part in the study. The study was approved by the Institutional Review Board for Human Subjects Research for Baylor College of Medicine and the VA Research and Development Committee of the MEDVAMC.

All study participants answered questionnaires administered by trained research assistants reporting demographics (age, sex, race/ethnicity), lifestyle factors (alcohol, smoking), and medical history, including the use of medications (proton-pump inhibitor [PPI], histamine-2 receptor antagonist [H2RA], aspirin, and non-steroidal anti-inflammatory drug [NSAID]). Each individual had measurements of height, weight, and waist and hip circumference to calculate body mass index (BMI) and waist-to-hip ratio (WHR).

Dietary Questionnaire and Endoscopy

All subjects completed a 110-item Block Food Frequency Questionnaire (FFQ) version 2005 which ascertained dietary intake in the past year. The Block FFQ has previously been used and validated to estimate absolute intake [22]. The Block FFQ takes about 40–50 min to complete, and subjects who did not complete it at the endoscopy visit were asked to complete the questionnaire after the visit. The Block FFQ includes estimations of frequency (“never or less than once per month” to “2 + times per day”) and portion sizes (“small”, “medium”, “large”) for various types of food. Pictures were provided to help approximate portion size. All raw food items data from the Block FFQ were analyzed by NutritionQuest (Nutrition Data Systems for Research database version 2005, Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN, 2005) software. The amount consumed for each FFQ food item in the Nutrition Data Systems for Research was translated to cup or ounce equivalents.

Upper endoscopy with gastric mapping biopsies (at least 10 total biopsies from 5 to 7 biopsy sites) from the antrum (both greater and lesser curvature), corpus (distal greater curvature, distal lesser curvature, proximal greater curvature, and proximal lesser curvature), and cardia was performed on all study participants. The presence of GIM and *H. pylori* was determined according to updated Sydney classification [23] by two independent

gastrointestinal pathologists, blinded to dietary data and endoscopic findings. A third gastrointestinal pathologist determined the readings in cases where there were discrepancies. *H. pylori* positivity was determined as *H. pylori* bacteria seen on histopathology of any gastric biopsy site (using hematoxylin and eosin, alcian blue at pH 2.5, a modified silver stain, or alcian blue–periodic acid Schiff stain) or positive *H. pylori* culture of gastric biopsy tissue. We have previously described the details of gastric tissue processing and storage for *H. pylori* culture [24].

Definition of Cases and Controls

Cases were defined as those patients with evidence of GIM on histopathology of ≥ 1 non-cardia gastric biopsy obtained during the study endoscopy. Cases were compared to controls without GIM present on histopathology of any non-cardia gastric biopsy.

Statistical Analysis

We compared characteristics between cases and controls using Chi-square for categorical variables and Student's *t* test for continuous variables. Tertiles for each dietary factor were generated based on distribution of intake in the control group (3 highest to 1 lowest). Odds ratios (OR) and 95% confidence intervals (95% CI) were estimated for associations of dietary factors with risk of GIM using multivariable logistic regression models adjusted for age, gender, race/ethnicity, smoking, alcohol use, BMI, *H. pylori* infection, and total energy intake. Percent of daily kcal intake from fat, protein, carbohydrates, and sweets was ascertained, and associations of each factor with risk of GIM were estimated from multivariable models without a term for total energy intake.

All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC), and a 2-tailed *p* value of < 0.05 was considered statistically significant.

Results

A total of 564 patients were recruited from primary care clinics, and 1655 patients were recruited from endoscopy clinic. We analyzed 423 cases with GIM and 1796 controls without GIM. The overall prevalence of GIM was 19.1% in this cohort, ranging from 18.3% among asymptomatic patients recruited from primary care clinics to 21.3% among symptomatic patients recruited from endoscopy clinic. Of the control group, 21.9% had *H. pylori* infection, 22.0% had active gastritis, and 43.6% had chronic gastritis. Cases were older on average (mean age 62.1 years, SD 7.4 years) than controls (59.9 years, SD 8.2 years) and more likely to be male (97.2% vs. 90.8%), non-White ethnicity/race (58.6% vs. 39.0%), and ever smokers (76.4% vs. 66.3%) (Table 1). Of 40 patients with other/unknown race, 29 were of Asian ancestry (5 cases, 24 controls). Due to the small numbers, we were unable to examine associations between dietary factors and GIM among Asian race subgroup.

Cases with GIM had a median dietary energy consumption of 1683.5 kcal (25–75 percentile: 1161.2–2317.0 kcal) which was not different from controls (1613.5 kcal; 25–75 percentile: 1159.3–2161.4 kcal) (Table 2). A greater proportion of GIM cases than controls were in the lowest tertile of percent kcal from fat (tertile 1: 43.6% vs. 33.4%). However, higher

proportions of GIM cases than controls were in the highest tertile of percent kcal from carbohydrates (tertile 3: 41.8% vs. 33.3%). Total fruit intake was the only dietary factor positively associated with GIM on unadjusted analysis (tertile 3 vs. 1: OR 1.51, 95% CI 1.04–2.18) (Table 3). There were no significant differences between cases and controls in the distribution of dietary consumption of total vegetables, dietary fiber, dietary fat, saturated fat, monounsaturated fat, polyunsaturated fat, cholesterol, trans fat, omega 3 fatty acids, sodium, or vitamin C. Similarly, the distribution of serving frequency of grains, meat, dairy, fat, and whole grains was not different between cases and controls.

After adjusting for age, gender, race/ethnicity, smoking, alcohol, BMI, *H. pylori*, and total energy intake, percent kcal from carbohydrates (OR 1.35, 95% CI 1.08–1.67) showed a positive association with GIM but also total fruit intake (tertile 3 vs. 1: OR 1.28, 95% CI 1.02–1.61) and total fiber intake (OR 1.37, 95% CI 1.04–1.80). Examining these associations among race/ethnic subgroups, the point estimates were generally higher and only statistically significant among non-Whites; however, the CIs overlapped with those for associations among Whites (Supplementary Table 1).

Discussion

Total fruit intake was the dietary factor consistently associated with GIM in this study of a non-immigrant US population. High carbohydrate intake but also fiber was associated with GIM on adjusted analysis. Otherwise, there were no significant associations between the presence of GIM and other self-reported dietary factors, including intake of vegetables, fat (including saturated, monounsaturated, polyunsaturated, cholesterol, trans fat, omega 3 fatty acids), sodium, vitamin C, grains, meat, dairy, and whole grains. The results from our stratified analyses suggest that these dietary associations may be strongest among non-Whites. However, we caution about drawing strong inferences from these small stratified analyses.

Several Western dietary studies found a significant relationship between high consumption levels of refined carbohydrates specifically and risk of gastric cancer [25–27]. One meta-analysis included 4 previous studies on carbohydrates and found a non-significant trend toward increased risk of gastric cancer with carbohydrate intake (RR 1.17, 95% CI 0.92–1.49) [28]. However, to our knowledge our study is the first to have described an association between carbohydrate consumption and development of GIM. High carbohydrate foods, such as rice, bread, and potatoes, often have a high glycemic index and are low in antioxidants [29] that may protect against gastric carcinogenesis. In mouse models, excess carbohydrates when combined with salt caused hypertrophy of the forestomach to digest carbohydrates with compensatory atrophic changes in the glandular stomach [30].

We could not replicate most of the positive findings shown in previous studies from countries with high prevalence of gastric cancer. In these studies, dietary factors associated with GIM included excessive consumption of spicy foods, salt, and nitrite-rich proteins, such as canned or smoked meat or fish, and low consumption of fruits and vegetables [5, 6, 13, 14]. In a study of Japanese immigrants living in Hawaii, nitrite-rich salty foods (cured meats) were associated with GIM, while vitamin C consumption was not [31]. However,

in studies on Western diets, there have been conflicting data on the benefit of fruits and vegetables and harm of salt and high fat foods (e.g., butter, milk) on GIM risk. One Italian study compared *H. pylori*-positive patients with GIM to *H. pylori*-positive patients without GIM and found that butter was a risk factor for GIM development [10]. Similar to our findings, this study did not find a significant association between consumption of vegetables, milk, and processed meat and risk of GIM. Similar to our study, another Brazilian study found no association with salt intake but found fruit and vegetable intake to be inversely associated with GIM, while canned and smoked foods were associated with increased risk [14]. A US study found that higher milk consumption was associated with increased risk for GIM but inconsistent findings with fruit, vegetable, and vitamin C consumption [16]. One meta-analysis of 17 studies (that included 10 Western studies) found a trend toward increased risk of GIM with higher intake of salt and salted meats (combined OR 1.68, 95% CI 0.98–2.90) [15]. These studies, however, did not consistently control for important demographic and clinical risk factors in GIM (e.g., age, smoking, race, and *H. pylori* infection). Our study controlled for these demographic and clinical risk factors of GIM in addition to total energy intake and represents a more comprehensive risk assessment for GIM.

Recent studies have examined the interactions of diet, *H. pylori*, and the gastric microbiome on gastric cancer and GIM risk. Gastric atrophy and resulting hypochlorhydria due to *H. pylori* infection result in increased colonization by acid-intolerant bacteria [32, 33] and increased carcinogen production by ingested foods and nitrates [34–36]. Additionally, dietary factors (e.g., high salt) may increase the virulence of *H. pylori* organisms [37, 38]. Intake of starchy vegetables and fiber has been shown to increase precancerous gastric lesions in a Venezuelan study [39]. Although one study found high fiber intake increases mucosal cell apoptosis in rats treated with carcinogen [40], fiber has not conclusively been associated with gastric cancer risk [41]. Intake of antioxidants, such as vitamin E, C, beta-carotene found in fruits and vegetables, can promote apoptosis of cancerous cells in people with normal levels of reactive oxygen species. However, excessive consumption of these antioxidants could overly suppress reactive oxygen species and allow proliferation of cancerous cells, especially in those with low baseline levels of reactive oxygen species [42]. Vitamin E, contained in some nuts, vegetables, and fruits, may inhibit apoptosis and accelerate carcinogenesis [42] and has been shown to increase risk of gastric cancer [43].

Given the inconsistent and generally weak associations of dietary factors with GIM in this and other studies conducted in Western countries, there may not be an important role for diet in GIM development. Demographic and clinical risk factors (i.e., *H. pylori*, race/ethnicity, smoking) have been extensively described in GIM [8] and remain the strongest risk factors in GIM development. Diet may play a bigger role in neoplastic progression after GIM development. A subset of patients with GIM who continue to consume high-risk foods (nitrite, salty, low intake of fruits, vegetables, vitamin C) may progress to gastric cancer as there are stronger associations of dietary factors with gastric cancer than with GIM. Our findings should be replicated in future studies before recommending to decrease carbohydrate, fruit, and fiber consumption to attenuate the risk of GIM, especially as fruits and fiber may be beneficial to other conditions, such as cardiovascular disease and colon cancer [44–46]. Modifiable risk factors, such as smoking and *H. pylori*, that have shown

consistent associations with GIM should be primarily targeted rather than diet for gastric cancer prevention.

Strengths of this study include the use of prospective subject enrollment and the use of the FFQ to gather dietary data prior to participants and study team knowing GIM case–control status. Patients were recruited from both an asymptomatic primary care clinic population and from those scheduled for upper endoscopy for gastrointestinal complaints and thus are representative of the overall VA population. Our high-risk cohort (GIM prevalence 19.1%) adequately allowed examination of significant dietary factors. Previous US studies that included only symptomatic patients undergoing biopsies in the setting of abnormal endoscopic findings estimated GIM prevalence to be 3.1–15.0% [47–49]. However, these studies did not perform systematic biopsies and may have under-reported true prevalence of GIM as GIM detection using white-light endoscopy is poor (51.0–71.2%) [50–52]. A previous US study performed systematic biopsies in symptomatic patients and found prevalence of GIM to be 11% among those who underwent 2 gastric biopsies and 25% among those who underwent 4 gastric biopsies [53]. Our cohort underwent systematic gastric mapping biopsies irrespective of symptoms or endoscopic findings, therefore minimizing bias by indication for endoscopy and abnormal endoscopic findings. Additionally, we systematically gathered *H. pylori* data on all patients and adjusted for multiple important risk factors for GIM risk (age, gender, race/ethnicity, smoking, and alcohol use).

One of the limitations of this study is the use of the Block FFQ, which requires participants to recall their dietary habits within the last 12 months. This may present recall bias associated with survey data, although any bias is unlikely to be differential between cases and controls as participants completed the FFQ prior to the study EGD. Furthermore, the median total calories are low in our study population (1683 kcal), possibly due to missing/not accounted for dietary components in the FFQ that are relevant to a veteran population. To our knowledge, the Block FFQ has not been validated in a veteran population. Nonetheless, this would not have impacted the study findings as reporting was consistent between cases and controls. The Block FFQ was not able to quantify nitrite-rich and processed foods, which have been associated with GIM and gastric cancer carcinogenesis. However, measurement of nitrites using FFQ is prone to errors as nitrite intake is difficult to directly quantify. Most nitrite exposure occurs when ingested nitrate is excreted in saliva and reduced to nitrite by oral bacteria and re-ingested [54]. Although we adjusted for several important risk factors (i.e., age, gender, race/ethnicity, smoking, alcohol, *H. pylori*), we were not able to adjust for all risk factors (e.g., family history of gastric cancer) which were not reliably available. As such, we cannot completely exclude residual confounding by these factors. Due to the observational, cross-sectional design of this study, there may be remaining bias due to unmeasured confounders, and the associations found in our study may not explain a causal relationship between diet and GIM risk. Additionally, we excluded certain populations from our recruitment (e.g., patients with cirrhosis and stroke) which introduces a selection bias, but these excluded populations with significant co-morbid conditions would have little benefit from reducing risk of GIM. The generalizability of our findings may be limited to older men as our population was a US veteran population. But

given the high prevalence of GIM found in our cohort, our findings may apply to high-risk populations in the USA (e.g., immigrant, Hispanic).

We found higher intake of carbohydrates but also fruits and fiber were associated with GIM, but did not find an association for vegetable, fat, sodium, vitamin C, grain, meat, or dairy intake in a US population with primarily Western diets. The main actionable risk factors remain *H. pylori* and smoking, and these need to be targeted to reduce gastric cancer risk in US populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Demographic and clinical characteristics of 423 cases with gastric intestinal metaplasia and 1796 controls at the Michael E. DeBakey VA Medical Center who answered dietary questionnaires then underwent gastric mapping biopsies

	Cases (*n* = 423)	Controls (*n* = 1796)	*p* value
Recruitment source			0.121
Endoscopy	303 (71.63)	1352 (75.28)	
Primary care	120 (28.37)	444 (24.72)	
Age			
< 60	138 (32.62)	761 (42.37)	< 0.001
60-69	218 (51.54)	842 (46.88)	
≥ 70	67 (15.84)	193 (10.75)	
Sex			< 0.001
Male	411 (97.16)	1630 (90.76)	
Female	12 (2.84)	166 (9.24)	
Race/ethnicity			< .0001
White	175 (41.37)	1095 (60.97)	
Hispanic	62 (14.66)	148 (8.24)	
Black	178 (42.08)	521 (29.01)	
Other/unknown	8 (1.89)	32 (1.78)	
BMI (kg/m^2)			0.080
< 25	89 (21.04)	318 (17.71)	
25-29	163 (38.53)	634 (35.03)	
≥ 30	171 (40.43)	840 (46.77)	
Unknown/missing	0 (0.00)	4 (0.22)	
Waist-to-hip ratio			
Low	60 (14.18)	248 (13.81)	0.712
High	349 (82.51)	1501 (83.57)	
Unknown/missing	14 (3.31)	47 (2.62)	
Smoking status			< 0.001
Never smoked	82 (19.39)	501 (27.90)	
Current smoker	138 (32.62)	473 (26.34)	
Former smoker	185 (43.74)	718 (39.98)	
Unknown/missing	18 (4.26)	104 (5.79)	
Alcohol status			0.169
Never drinker	26 (6.15)	151 (8.41)	
Current drinker	211 (49.88)	891 (49.61)	
Former drinker	166 (39.24)	639 (35.58)	
Unknown/missing	20 (4.73)	115 (6.40)	
GERD symptoms			0.047
No	224 (52.96)	832 (46.33)	
Yes	180 (42.55)	865 (48.16)	

	Cases (*n* = 423)	Controls (*n* = 1796)	*p* value
Unknown/missing	19 (4.49)	99 (5.51)	
Helicobacter pylori			< 0.001
No	199 (47.04)	1377 (76.67)	
Yes	219 (51.77)	394 (21.94)	
Unknown/missing	5 (1.18)	25 (1.39)	
Active gastritis			< 0.001
No	193 (45.63)	1395 (77.67)	
Yes	225 (53.19)	395 (21.99)	
Missing	5 (1.18)	6 (0.33)	
Chronic gastritis			< 0.001
No	77 (18.20)	1011 (56.29)	
Yes	344 (81.32)	783 (43.60)	
Missing	2 (0.47)	2 (0.11)	
PPI/H2RA use			0.076
No	180 (42.55)	659 (36.69)	
Yes	218 (51.54)	1010 (56.24)	
Unknown/missing	25 (5.91)	127 (7.07)	
NSAID use			0.267
No	153 (36.17)	717 (39.92)	
Less than daily	18 (4.26)	83 (4.62)	
At least daily	188 (44.44)	704 (39.20)	
Unknown/missing	64 (15.13)	292 (16.26)	

BMI body mass index, *GERD* gastroesophageal reflux disease, *PPI* proton-pump inhibitor, *H2RA* histamine-2 receptor antagonist, *NSAID* non-steroidal anti-inflammatory drug

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Table 2

Comparison of dietary intake between 423 cases with and 1796 controls without gastric intestinal metaplasia who answered dietary questionnaires then underwent gastric mapping biopsies

	Cases (*n* = 423)	**Controls (*n* = 1796)**	***p* value**
Dietary kcal (kcal), median (P25–P75)	1683.45 (1161.22–2317.01)	1613.5 (1159.31–2161.35)	0.221
Dietary protein (gm), median (P25–P75)	62.41 (42.46–88.64)	60.8 (43.31–84.48)	0.441
Dietary carbohydrate (gm), median (P25–P75)	192.42 (130.81–269.69)	180.36 (127.29–257.22)	0.283
Total fruit			0.087
Tertile 1	59 (26.82)	291 (34.11)	
Tertile 2	74 (33.64)	278 (32.59)	
Tertile 3	87 (39.55)	284 (33.29)	
Total vegetables			0.487
Tertile 1	71 (32.42)	286 (33.53)	
Tertile 2	66 (30.14)	283 (33.18)	
Tertile 3	82 (37.44)	284 (33.29)	
Fiber			0.151
Tertile 1	59 (26.94)	284 (33.29)	
Tertile 2	75 (34.25)	285 (33.41)	
Tertile 3	85 (38.81)	284 (33.29)	
Fat			0.511
Tertile 1	74 (34.10)	284 (33.29)	
Tertile 2	64 (29.49)	285 (33.41)	
Tertile 3	79 (36.41)	284 (33.29)	
Saturated fat			0.385
Tertile 1	73 (33.64)	283 (33.18)	
Tertile 2	63 (29.03)	286 (33.53)	
Tertile 3	81 (37.33)	284 (33.29)	
Monounsaturated fat			0.607
Tertile 1	71 (32.57)	284 (33.29)	
Tertile 2	67 (30.73)	285 (33.41)	
Tertile 3	80 (36.70)	284 (33.29)	

	Cases (n = 423)	Controls (n = 1796)	p value
Polyunsaturated fat			0.684
Tertile 1	68 (31.78)	284 (33.29)	
Tertile 2	68 (31.78)	285 (33.41)	
Tertile 3	78 (36.45)	284 (33.29)	
Cholesterol			0.639
Tertile 1	67 (30.59)	284 (33.29)	
Tertile 2	80 (36.53)	285 (33.41)	
Tertile 3	72 (32.88)	284 (33.29)	
Trans fat			0.363
Tertile 1	72 (32.88)	284 (33.29)	
Tertile 2	64 (29.22)	285 (33.41)	
Tertile 3	83 (37.90)	284 (33.29)	
Omega 3 fatty acids			0.53
Tertile 1	66 (30.41)	284 (33.29)	
Tertile 2	70 (32.26)	284 (33.29)	
Tertile 3	81 (37.33)	285 (33.41)	
Sodium			0.629
Tertile 1	67 (31.16)	284 (33.29)	
Tertile 2	69 (32.09)	285 (33.41)	
Tertile 3	79 (36.74)	284 (33.29)	
Vitamin C			0.413
Tertile 1	64 (29.09)	284 (33.29)	
Tertile 2	74 (33.64)	285 (33.41)	
Tertile 3	82 (37.27)	284 (33.29)	
Grain servings			0.87
Tertile 1			0.87
Tertile 2	74 (33.79)	285 (33.41)	
Tertile 3	76 (34.70)	284 (33.29)	
Meat servings			0.745
Tertile 1	79 (35.91)	283 (33.18)	
Tertile 2	70 (31.82)	285 (33.41)	

	Cases (*n* = 423)	Controls (*n* = 1796)	*p* value
Tertile 3	71 (32.27)	285 (33.41)	
Dairy servings			0.296
Tertile 1	81 (36.99)	285 (33.41)	0.296
Tertile 2	61 (27.85)	284 (33.29)	
Tertile 3	77 (35.16)	284 (33.29)	
Fat servings			0.282
Tertile 1	76 (34.70)	284 (33.29)	
Tertile 2	61 (27.85)	284 (33.29)	
Tertile 3	82 (37.44)	285 (33.41)	
Whole grain servings			0.609
Tertile 1	70 (31.96)	287 (33.65)	
Tertile 2	68 (31.05)	281 (32.94)	
Tertile 3	81 (36.99)	285 (33.41)	
Percent kcal from fat			**0.003**
Tertile 1	95 (43.58)	285 (33.41)	
Tertile 2	49 (22.48)	284 (33.29)	
Tertile 3	74 (33.94)	284 (33.29)	
Percent kcal from protein			0.502
Tertile 1	80 (36.87)	285 (33.41)	
Tertile 2	73 (33.64)	284 (33.29)	
Tertile 3	64 (29.49)	284 (33.29)	
Percent kcal from carbohydrates			**0.004**
Tertile 1	79 (35.91)	284 (33.29)	
Tertile 2	49 (22.27)	285 (33.41)	
Tertile 3	92 (41.82)	284 (33.29)	
Percent kcal from sweets			0.412
Tertile 1	63 (28.64)	284 (33.29)	
Tertile 2	80 (36.36)	285 (33.41)	
Tertile 3	77 (35.00)	284 (33.29)	

p values < 0.05 are in bold

Kcal kilocalorie; P25–P75: 25–75 percentile; *gm* grams

Table 3

Associations of dietary factors with risk of gastric intestinal metaplasia

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Total fruit		
Tertile 2 versus 1	1.31 (0.90–1.92)	0.96 (0.76–1.20)
Tertile 3 versus 1	**1.51 (1.04–2.18)**	**1.28 (1.02–1.61)**
Total vegetables		
Tertile 2 versus 1	0.94 (0.65–1.36)	0.89 (0.71–1.12)
Tertile 3 versus 1	1.16 (0.81–1.66)	1.19 (0.93–1.51)
Fiber		
Tertile 2 versus 1	1.27 (0.87–1.85)	0.99 (0.79–1.25)
Tertile 3 versus 1	1.44 (0.99–2.09)	**1.37 (1.04–1.80)**
Fat		
Tertile 2 versus 1	0.86 (0.59–1.25)	0.91 (0.72–1.16)
Tertile 3 versus 1	1.07 (0.75–1.53)	1.00 (0.74–1.36)
Saturated fat		
Tertile 2 versus 1	0.85 (0.59–1.24)	0.84 (0.67–1.07)
Tertile 3 versus 1	1.11 (0.77–1.58)	1.11 (0.82–1.50)
Monounsaturated fat		
Tertile 2 versus 1	0.94 (0.65–1.36)	0.96 (0.76–1.20)
Tertile 3 versus 1	1.13 (0.79–1.61)	1.06 (0.78–1.44)
Polyunsaturated fat		
Tertile 2 versus 1	1.00 (0.69–1.45)	0.96 (0.76–1.21)
Tertile 3 versus 1	1.15 (0.80–1.65)	1.06 (0.79–1.43)
Cholesterol		
Tertile 2 versus 1	1.19 (0.83–1.71)	1.10 (0.88–1.37)
Tertile 3 versus 1	1.07 (0.74–1.56)	0.88 (0.67–1.16)
Trans fat		
Tertile 2 versus 1	0.89 (0.61–1.29)	0.85 (0.67–1.07)
Tertile 3 versus 1	1.15 (0.81–1.65)	1.17 (0.88–1.56)
Omega 3 fatty acids		

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Tertile 2 versus 1	1.06 (0.73–1.54)	0.99 (0.79–1.25)
Tertile 3 versus 1	1.22 (0.85–1.76)	1.09 (0.82–1.44)
Sodium		
Tertile 2 versus 1	1.03 (0.71–1.49)	0.99 (0.78–1.24)
Tertile 3 versus 1	1.18 (0.82–1.70)	1.09 (0.80–1.48)
Vitamin C		
Tertile 2 versus 1	1.15 (0.79–1.67)	1.08 (0.86–1.35)
Tertile 3 versus 1	1.28 (0.89–1.85)	1.11 (0.87–1.42)
Grain servings		
Tertile 2 versus 1	1.07 (0.74–1.54)	0.99 (0.79–1.24)
Tertile 3 versus 1	1.10 (0.76–1.59)	1.04 (0.79–1.37)
Meat servings		
Tertile 2 versus 1	0.88 (0.61–1.26)	0.96 (0.77–1.21)
Tertile 3 versus 1	0.89 (0.62–1.28)	0.82 (0.62–1.10)
Dairy servings		
Tertile 2 versus 1	0.76 (0.52–1.09)	0.82 (0.65–1.03)
Tertile 3 versus 1	0.95 (0.67–1.36)	1.04 (0.82–1.32)
Fat servings		
Tertile 2 versus 1	0.80 (0.55–1.17)	0.83 (0.65–1.05)
Tertile 3 versus 1	1.08 (0.76–1.53)	1.03 (0.80–1.33)
Whole grain servings		
Tertile 2 versus 1	0.99 (0.68–1.44)	0.93 (0.74–1.17)
Tertile 3 versus 1	1.17 (0.81–1.67)	1.16 (0.92–1.47)
Percent kcal from fat [a]		
Tertile 2 versus 1	0.52 (0.35–0.76)	0.68 (0.53–0.87)
Tertile 3 versus 1	0.78 (0.55–1.10)	1.05 (0.83–1.31)
Percent kcal from protein [a]		
Tertile 2 versus 1	0.92 (0.64–1.31)	1.03 (0.82–1.29)
Tertile 3 versus 1	0.80 (0.56–1.16)	0.88 (0.70–1.11)
Percent kcal from carbohydrates [a]		

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Tertile 2 versus 1	0.62 (0.42–0.92)	0.68 (0.53–0.87)
Tertile 3 versus 1	1.16 (0.83–1.64)	**1.35 (1.08–1.67)**
Percent kcal from sweets [a]		
Tertile 2 versus 1	1.27 (0.88–1.83)	1.12 (0.90–1.40)
Tertile 3 versus 1	1.22 (0.84–1.77)	0.98 (0.79–1.23)

Dietary factors that demonstrate statistically significant associations with GIM are in bold

Models adjusted for age, gender, race/ethnicity, smoking status, alcohol status, body mass index, *H. pylori* infection, and total energy intake

OR odds ratio, *CI* confidence interval, *Kcal* kilocalorie

[a] adjusted without total energy intake