GASTRO-OESOPHAGEAL REFLUX

Dietary intake and the risk of gastro-oesophageal reflux disease: a cross sectional study in volunteers

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Background: Although diet has been associated with gastro-oesophageal reflux disease (GORD), the role of dietary components (total energy, macro and micronutrients) is unknown. We examined associations of GORD symptoms with intakes of specific dietary components.

Methods: We conducted a cross sectional study in a sample of employees (non-patients) at the Houston VAMC. The Gastro Esophageal Reflux Questionnaire was used to identify the onset, frequency, and severity of GORD symptoms. Dietary intake (usual frequency of consumption of various foods and portion sizes) over the preceding year was assessed using the Block 98 food frequency questionnaire. Upper endoscopy was offered to all participants and oesophageal erosions recorded according to the LA classification. We compared the dietary intake (macronutrients, micronutrients, food groups) of participants with or without GORD symptoms, or erosive oesophagitis. Stepwise multiple logistic regression analyses were used to examine associations between nutrients and GORD symptoms or oesophageal erosions, adjusting for demographic characteristics, body mass index (BMI), and total energy intake.

Results: A total of 371 of 915 respondents (41%) had complete and interpretable answers to both heartburn and regurgitation questions and met validity criteria for the Block 98 FFQ. Mean age was 43 years, 260 (70%) were women, and 103 (28%) reported at least weekly occurrences of heartburn or regurgitation. Of the 164 respondents on whom endoscopies were performed, erosive oesophagitis was detected in 40 (24%). Compared to participants without GORD symptoms, daily intakes of total fat, saturated fat, cholesterol, percentage of energy from dietary fat, and average fat servings were significantly higher in participants with GORD symptoms. In addition, there was a dose-response relationship between GORD and saturated fat and cholesterol. The effect of dietary fat became non-significant when adjusted for BMI. However, high saturated fat, cholesterol, or fat servings were associated with GORD symptoms only in participants with a BMI >25 kg/m^2 (effect modification). Fibre intake remained inversely associated with the risk of GORD symptoms in adjusted full models. Participants with erosive oesophagitis had significantly higher daily intakes of total fat and protein than those without it ($p<0.05$).

Conclusions: In this cross sectional study, high dietary fat intake was associated with an increased risk of GORD symptoms and erosive oesophagitis while high fibre intake correlated with a reduced risk of GORD symptoms. It is unclear if the effects of dietary fat are independent of obesity.

It is estimated that 15–20% of persons in the general population exhibit symptoms suggestive of gastro-oesophageal reflux disease (GORD), such as heartburn and acid regurgitation.[1–3] These symptoms can be present with no visible damage to the oesophageal mucosa or they could be associated with erosive oesophagitis, oesophageal stricture, Barrett's oesophagus, or oesophageal adenocarcinoma.

Given the relatively high prevalence of GORD symptoms and the rapidly rising incidence of oesophageal adenocarcinoma in the USA,[4] it is important to identify potentially modifiable risk factors for GORD. One such risk factor may be diet, as some food types have been associated with an increased risk for GORD.[5] Specifically, physiological studies have shown a decrease in lower oesophageal pressure and an increase in oesophageal acid exposure in response to ingestion of a variety of food items, such as those rich in fat, chocolate, and carminatives (for example, spearmint).[6–9] In addition, patients with GORD symptoms often associate the occurrence of these symptoms with ingestion of certain types of foods. For example, in a survey of 1004 respondents in the general population, chocolate precipitated symptoms in 40% and fatty foods in 70%.[3] However, this study did not have controls, and it also did not quantify the intake of dietary items.

Few studies have examined the associations of GORD with dietary composition, and those that have been published were conducted in patients with the most severe forms of GORD, specifically hospitalised patients with oesophagitis and those with oesophageal adenocarcinoma.[10 11] One study that evaluated data from the NHANES I Epidemiologic Follow-up found no association between dietary fat intake and erosive oesophagitis.[10] In a recent population based epidemiological studies in the USA, the authors reported a significant increase in the risk of oesophageal adenocarcinoma with increased dietary fat intake.[11] To our knowledge, no study has examined associations between GORD symptoms and specific amounts of dietary components.

Given this deficit of information about possible diet-GORD relationships, the objective of this report was to elucidate associations of various nutrients (total energy, macronutrients, and micronutrients) with the risk for GORD in a large well characterised cohort of volunteers.

Abbreviations: GORD, gastro-oesophageal reflux disease; GERQ, Gastro Esophageal Reflux Questionnaire; BMI, body mass index; FFQ, food frequency questionnaire

METHODS

Study design

A cross sectional survey followed by endoscopy.

Study population

We targeted a sample of 1000 employees at the Houston VA Medical Center (VAMC) between 2000 and 2001. Of the 3095 total Houston VAMC employees, 1424 (46%) were African American of whom 954 (67%) were women; 1114 (36%) were Caucasian of whom 635 (57%) were women. Mean age was 45 years (range 18–70). Every employee belonged to one of 19 hospital services, an arrangement that facilitated organised and comprehensive distribution of the study questionnaires. Our sampling frame comprised employees who belonged to 12 selected services within the hospital; these services were specifically chosen to represent the professional spectrum of employees. These services include nurses, physicians, administrators, researchers, as well as labourers in building maintenance. The 1000 employees targeted in the study were randomly chosen from lists of employees in these 12 services. The study was approved by the Institutional Review Board for Human Subject Research at Baylor College of Medicine. The study questionnaires were either dropped in mailboxes or given in person to those who did not have a mailbox. Questionnaires were distributed a second time to those who did not respond initially.

Questionnaire

The Gastro Esophageal Reflux Questionnaire (GERQ) is a self report instrument containing 32 questions that examine symptoms of heartburn and acid regurgitation in detail. The questionnaire identifies the onset of GORD symptoms (heartburn, acid regurgitation) and grades the frequency and severity of symptoms experienced over the previous year.[12] Symptom frequency over the past year is measured on the following scale: 1, less than once a month; 2, about once a month; 3, about once a week; 4, several times a week; and 5, daily. Previous testing has shown this instrument to be reliable on test-retest, with a median Kappa statistic for the symptom items of 0.71 (interquartile range 0.63–0.81). In comparison with a physician interview, the questionnaire was also found to be a valid measure of symptoms (median kappa 0.62 (interquartile range 0.49–0.74)).[12] Additional clinical and demographic information was collected and analysed, including smoking, alcohol consumption, body mass index (BMI), level of education, family history of GORD, physician visits for GORD, and use of the following medications: aspirin or non-steroidal anti-inflammatory drugs, histamine 2 receptor antagonist, proton pump inhibitor, and over the counter GORD therapy.

Dietary questionnaires

Dietary intake was assessed using the 100 item Block food frequency questionnaire (FFQ) (Block 98). The Block FFQ is a self administered instrument that takes 30–40 minutes to complete and has been extensively used and validated in several population groups.[13 14] The 1998 version was developed from foods reported in NHANES 3, which included several sites in Texas with a high representation of African Americans and Caucasians.

Participants were asked to estimate their usual frequency of consumption of various foods and typical portion sizes over the previous year. The one year period was chosen to account for seasonal variations in dietary intake. Each food item had nine options for frequency (ranging from ''never or less than once per month'' to ''2+ times per day'') and three options for portion size. Nutrient intake was calculated by an analysis program at the National Cancer Institute that incorporates the nutrient content of each food item, consumption frequency, and a portion size based on age, and employs several checks for completeness and internal validity.[12] For these analyses, we examined intakes of total energy, macronutrients (carbohydrates, protein, and fat), and micronutrients (vitamins and minerals). Participants with reported energy intakes <800 kcal and >5000 kcal for men ($n = 10$) and <600 kcal and >4000 kcal for women ($n = 22$) were excluded because their FFQs were considered to be unreliable.[15]

The Block FFQ was also used to ascertain the use of vitamin and minerals supplements over the previous year.

Endoscopy

Upper endoscopy was offered to all participants who responded to the survey. Standardised non-sedated endoscopic examination of the oesophagus, stomach, and duodenum was performed. One endoscopist (HBE-S) who was blinded to the results of the questionnaire performed all procedures. The severity of erosive oesophagitis seen on endoscopy was graded from A to D according to the LA classification.[16] The presence of oesophageal stricture or areas suspicious for Barrett's oesophagus was also recorded. Gastric mucosal biopsies were taken (two from the antrum, two from the corpus, and one from the incisura angularis). Four quadrant biopsies were also taken at 2 cm intervals from any visible length of columnar lined oesophagus to assess the presence of Barrett's metaplastic epithelium.

Statistical analyses

Among the total number of respondents with complete answers to questions about GORD symptoms and dietary intake, we calculated the proportion of persons reporting at least weekly heartburn and/or regurgitation. We also calculated the proportion of persons with erosive oesophagitis among the total number of participants who underwent upper endoscopy.

In univariate analyses, we compared the demographic characteristics, health related habits, and dietary intake among participants categorised according to the presence or absence of GORD symptoms or erosive oesophagitis. Demographic characteristics included age, sex, ethnicity (Caucasian, African American, other), and education level (less than college, college and above). Health related habits included tobacco smoking (past, current, none) and an approximate marker for physical activity (active: watching less than three hours of TV or inactive). Dietary intake (from the Block 98 FFQ) included average daily intakes of total energy (calories), macronutrients and several micronutrients, food items, and vitamin/mineral supplements. We analysed micronutrients derived from the diet alone as well as total intake from diet plus supplements.

The χ^2 tests were used to test for statistical significance for categorical variables, t tests for parametric continuous variables, and Wilcoxon's test for non-parametric continuous variables. The Cochrane-Armitage test was used to examine possible dose-response relationships of dietary intake (in tertiles) with GORD symptoms and erosive oesophagitis.

Multiple stepwise logistic regression models were constructed to examine two separate outcome variables (weekly heartburn or acid regurgitation, erosive oesophagitis). The main predictors in the model were the dietary variables examined as continuous variables. Odds ratios were scaled based on the interquartile range for each nutrient and thus show risk comparing the 75th centile of intake for each nutrient with the 25th centile. We controlled for several covariates including age, sex, race, BMI, energy intake, physical activity, smoking, and alcohol consumption. Only variables with $p>0.1$ were kept in the model. For all models, the number of covariates examined was determined by the

Table 1 Baseline characteristics of participants who completed a gastro-oesophageal reflux disease (GORD) and dietary questionnaires (total = 371) shown as a comparison between those with at least weekly GORD symptoms and the rest of participants with no or infrequent GORD symptoms

	Frequent GORD (%) (n = 103)	Rest (%) (n = 268)	p Value	Any oesophageal erosion (%) (n = 40)	No oesophageal erosion (%) (n = 124)	p Value
Age (y)						
Mean (SD)	44.5 (11.3)	44 (10.5)	0.600	46.5 (10.8)	44 (10.0)	0.164
<35	19 (18.4)	60 (22.4)	0.904	4 (10.0)	30 (24.2)	0.173
35–44	29 (28.2)	78 (29.1)		13 (32.5)	31 (25.0)	
45–54	30 (29.1)	84 (31.3)		11 (27.5)	44 (35.5)	
⩾55	18 (17.5)	43 (16.0)		10 (25.0)	17 (13.7)	
Unknown	7 (6.8)	3 (1.1)		2 (5.0)	2 (1.6)	
Sex						
Men	27 (26.2)	84 (31.3)	0.376	14 (35.0)	44 (35.5)	
Women	76 (73.8)	184 (68.7)		26 (65.0)	80 (64.5)	
Race/ethnicity						
Asian	8 (7.8)	37 (13.8)	0.602	1 (2.5)	15 (12.1)	0.034
African American	47 (45.6)	112 (41.8)		15 (37.5)	64 (51.6)	
Hispanic	9 (8.7)	21 (7.8)		3 (7.5)	7 (5.6)	
White	36 (35.0)	91 (34.0)		20 (50.0)	32 (25.9)	
Other	3 (2.9)	7 (2.6)		7 (17.5)	6 (4.8)	
Tobacco smoking						
Never smoker	87 (84.5)	224 (83.6)	0.739	31 (77.5)	108 (87.1)	0.242
Current smoker	13 (12.6)	40 (14.9)		2 (5.0)	13 (10.5)	
Unknown	3 (2.9)	4 (1.5)		7 (17.5)	3 (2.4)	
Education						
High school	7 (6.8)	13 (4.9)	0.173	1 (2.5)	6 (4.8)	0.333
Some college	25 (24.3)	93 (34.7)		12 (30.0)	44 (35.5)	
College	27 (26.2)	126 (47.0)		12 (30.0)	46 (37.1)	
Unknown	44 (42.7)	36 (13.4)		15 (37.5)	28 (22.6)	
Physical activity*						
Active	15 (14.6)	32 (11.9)	0.409	5 (12.5)	19 (15.3)	0.800
Inactive	88 (85.4)	236 (88.1)		35 (87.5)	105 (84.7)	
Vitamin/mineral supplement use†						
Yes	64 (62.1)	150 (56.0)	0.293	26 (65.0)	71 (57.3)	0.461
No	39 (37.9)	118 (44.0)		14 (35.0)	53 (42.7)	

*Defined as watching TV less than three hours a day.
†Defined as the use of any vitamin or mineral supplement at least once a week over the past one year.

number of outcome events with 10 events required for one covariate.[17] A p value of <0.05 was considered statistically significant.

RESULTS

Study population

Of 915 employees who were verified to have received the study questionnaires, 496 (54.2%) returned either the GORD or dietary questionnaire, 421 returned the dietary questionnaires, and 371 (40.5%) had complete and interpretable answers to both heartburn and regurgitation questions and met the minimum required internal validity criteria for the Block 98 FFQ. Among the 371 respondents included in this analysis, mean age was 44.0 years (SD 10.7, range 18–71) and 260 (70.1%) were women. There were no significant differences in age (44 *v* 46 years) or ethnicity (43% *v* 45% Blacks) between participants and non-participants; however, significantly more participants were female (68% *v* 57%). There were also no significant differences between participants with (n = 371) or without (n = 125) complete dietary data with regard to age (44 *v* 45 years), sex (70% *v* 61% women; p = 0.06), race (43% *v* 42% Blacks), or education (37.2% *v* 32.8% with no or incomplete college education).

Of 371 participants who completed both the GERQ and dietary questionnaires, 103 (27.8%) reported at least weekly occurrence of heartburn or regurgitation, and the rest (72.2%) had either no or less frequent GORD symptoms. There were no significant differences in age, sex, or race between the two groups with or without GORD symptoms (table 1). Similarly, respondents with and without symptoms did not differ significantly in terms of smoking, physical activity, or use of vitamin and mineral supplements (table 1).

Endoscopy

Upper endoscopy was performed on 164/371 (39.4%) persons, of whom 79 (48.2%) were African American and 106 (64.6%) were women. Persons of ethnicity other than African American or Caucasian were less likely to undergo endoscopy. A significantly greater proportion of those who underwent endoscopy had weekly heartburn or regurgitation or used proton pump inhibitor, histamine 2 receptor antagonist, or over the counter GORD medications than those who did not have endoscopy. In a logistic regression model (data not shown), only the presence of weekly heartburn or regurgitation was found to be an independent predictor of upper endoscopy.

Oesophageal erosions were detected in 40/164 (24.4%) patients who underwent endoscopy, and in most (90%) oesophagitis was classified as grade A. Oesophageal erosions were significantly less frequent in African Americans than Caucasians (table 1). Participants with oesophageal erosions were not different from those without erosions with regard to age, sex, smoking, education level, physical activity, or supplement use (table 1).

Diet and GORD symptoms

Intakes of various nutrients in participants with and without weekly GORD symptoms are given in table 2. Compared with those who did not report weekly GORD symptoms, daily intakes of total fat and saturated fat were statistically

Table 2 Comparison of dietary intake (measured by Block food frequency questionnaire 98) between participants with and without gastro-oesophageal reflux disease (GORD) symptoms defined as at least weekly heartburn or regurgitation (n = 371), and between participants with and without erosive oesophagitis (n = 164)

	GORD symptoms (n = 103)		No GORD symptoms (n = 268)			Oesophageal erosion (n = 40)		No erosion (n = 124)		
Variable	Mean	SD	Mean	SD	p Value	Mean	SD	Mean	SD	p Value
Total energy (kcal/day)	1937	834	1770	786	0.072	2023	922	1745	680	0.042
Macronutrients										
Total carbohydrates	245	105	226	104	0.123	241	101	222	91	0.263
Total protein (g/day)	67	31	63	32	0.201	73	33	61	28	0.027
Total alcohol (g/day)	9	20	12	24	0.372	15	35	11	22	0.342
Total fat (g/day)	77	40	68	36	0.038	84	48	68	31	0.017
Total saturated fat (g/day)	23	12	20	11	0.017	24	14	20	10	0.065
Cholesterol (mg/day)	231	132	202	131	0.097	234	136	216	132	0.326
% Energy from carbohydrates	50	8.0	50	10	0.585	49	9.0	51	8.0	0.112
% Energy from protein	10	3.0	10	3.0	0.744	15	3.0	14	3.0	0.161
% Energy from fat	40	7.0	30	8.0	0.033	36	7.0	35	7.0	0.377
Total fibre (g/1000 kcal)	8.5	3.2	9.2	4.0	0.097	9.0	3.1	9.0	4.0	0.962
Micronutrients (without supplements)										
Beta-carotene (μg/day)	3619	3754	3566	3394	0.897	3811	2995	3388	3930	0.533
Lutein (mg/day)	1840	1979	1988	2326	0.569	1987	1246	1909	2477	0.848
Vitamin C (mg/day)	125	75	122	86	0.721	120	65	125	89	0.741
Vitamin E (mg/day)	10	4	9	5	0.369	10	5	9	4	0.191
Folate (μg/day)	375	169	357	178	0.387	403	187	347	164	0.071
Iron (mg/day)	13	6	13	7	0.573	14	7	12	6	0.189
Sodium (mg/day)	2457	1154	2280	1161	0.188	2721	1395	2252	1020	0.023
Calcium (mg/day)	735	387	681	393	0.232	718	312	672	372	0.483
Micronutrients (with supplements)										
Beta-carotene (μg/day)	4450	4236	4930	6426	0.484	5217	5361	4708	7230	0.683
Lutein (mg/day)	1840	1979	1988	2326	0.569	1987	1246	1909	2477	0.848
Vitamin C (mg/day)	329	369	263	307	0.083	408	404	258	307	0.014
Vitamin E (mg/day)	67	100	81	145	0.393	107	146	75	146	0.235
Folate (μg/day)	583	298	528	305	0.116	700	363	521	314	0.003
Iron (mg/day)	23	16	23	20	0.850	23	15	23	21	0.925
Sodium (mg/day)	2457	1154	2280	1161	0.188	2721	1395	2252	1020	0.023
Calcium (mg/day)	920	517	871	563	0.447	968	509	835	554	0.181
Food groups										
Fruits (servings/day)	1.3	0.9	1.4	1.0	0.336	1.4	0.93	1.2	1.0	0.546
Vegetables (servings/day)	3.0	2.0	3.0	2.3	0.597	3.4	2.5	3.0	2.4	0.206
Meat (servings/day)	2.0	1.0	2.0	1.2	0.577	2.4	1.3	2.0	1.1	0.012
Dairy (servings/day)	1.0	1.0	1.0	0.9	0.189	1.0	0.87	1.0	1.0	0.830
Grains (servings/day)	5.0	3.0	4.0	2.5	0.237	5.0	3.3	4.0	2.3	0.104

p Values are based on *t* tests.

significantly higher in respondents with GORD symptoms. There was a non-significant trend for higher total caloric (energy) intake and lower fibre intake among persons with GORD symptoms. Similarly, the percentage of energy from dietary fat and average number of fat servings (data not shown) were significantly higher in participants with compared with those without GORD symptoms. There were no significant differences in intakes of carbohydrate, protein, micronutrients, and other food groups between respondents with and without GORD symptoms. Given the largely non-significant associations, correction for multiple comparisons was not employed.

There was a dose-response relationship between GORD and total energy (calories) ($p = 0.06$), saturated fat ($p = 0.04$), cholesterol ($p = 0.03$), and fat servings ($p = 0.06$) (Cochran Armitage test conducted to compare tertiles); specifically, saturated fat intake was positively associated with an increased risk of GORD symptoms. There were no significant differences in the reported intake of the other dietary variables.

In multiple logistic regression models (table 3), the observed effect of fats was reduced and became statistically non-significant when BMI was examined in the same model. There was a significant correlation between fat intake and BMI. Pearson's r was 0.21 ($p = 0.008$), 0.21 (0.006), 0.23 ($p = 0.003$) for total fat, total saturated fat, and cholesterol, respectively. However, in addition to confounding (statistical collinearity), there was evidence for an interaction between BMI and dietary fat intake. Table 4 shows the distribution of dietary intake of total fat, saturated fat, cholesterol, and fat servings among participants with and without GORD symptoms across two strata of BMI (<25 and >25). Among persons with a BMI <25, there were no significant differences in intake of these items between participants with or without GORD symptoms. On the other hand, among those with BMI >25, there was a significant increase in intake of saturated fat, cholesterol, and number of fat servings among participants with GORD symptoms compared with those without symptoms. These interactions between fat intake of fat and BMI were not significant in predicting oesophageal erosions.

Fibre intake remained inversely associated with the risk of GORD symptoms in fully adjusted models while associations between the other nutrients and GORD symptoms were not altered in direction or magnitude after adjusting for BMI, energy, or demographic features. There were no significant independent associations between any macronutrients, micronutrients, or food groups with either GORD symptoms or oesophageal erosions.

Diet and erosive oesophagitis

The calculated amounts of dietary items were compared between participants with and without erosive oesophagitis. In unadjusted comparisons, participants with erosive

Table 3 Risk of gastro-oesophageal reflux disease (GORD) symptoms with selected dietary items (measured by Block food frequency questionnaire 98)

Daily intake	OR	95% CI	p Value
Macronutrients			
Total carbohydrates (g/day)			
Unadjusted	1.24	0.94–1.64	0.12
Adjusted			
BMI	1.14	0.86–1.52	0.37
BMI, energy, demographics	0.76	0.34–1.69	0.50
Total protein (g/day)			
Unadjusted	1.19	0.91–1.57	0.20
Adjusted			
BMI	1.12	0.85–1.48	0.43
BMI, energy, demographics	0.87	0.48–1.57	0.65
Alcohol (% of calories)			
Unadjusted	0.95	0.86–1.06	0.37
Adjusted			
BMI	0.98	0.89–1.09	0.73
BMI, energy, demographics	0.99	0.88–1.10	0.82
Total fat (g/day)			
Unadjusted	1.33	1.01–1.74	0.04
Adjusted			
BMI	1.20	0.91–1.58	0.20
BMI, energy, demographics	1.09	0.89–1.37	0.41
Saturated fat (g/day)			
Unadjusted	1.37	1.07–1.75	0.01
Adjusted			
BMI	1.97	0.23–6.19	0.21
BMI, energy, demographics	1.71	0.92–3.17	0.09
Cholesterol (mg/day)			
Unadjusted	1.34	1.02–1.76	0.03
Adjusted			
BMI	1.22	0.92–1.61	0.18
BMI, energy, demographics	1.34	1.02–1.76	0.28
Total fibre (g/day)			
Unadjusted	0.80	0.61–1.03	0.09
Adjusted			
BMI	0.81	0.62–1.07	0.13
BMI, energy, demographics	0.72	0.53–0.99	0.04
Micronutrients			
Beta-carotene (mcg/day)			
Unadjusted	1.01	0.84–1.22	0.90
Adjusted			
BMI	0.97	0.80–1.19	0.75
BMI, energy, demographics	0.86	0.67–1.11	0.26
Vitamin C (mg/day)			
Unadjusted	1.04	0.82–1.32	0.72
Adjusted			
BMI	1.00	0.79–1.27	0.99
BMI, energy, demographics	0.87	0.65–1.16	0.33
Vitamin E (IU)			
Unadjusted	1.13	0.86–1.49	0.37
Adjusted			
BMI	1.05	0.79–1.40	0.72
BMI, energy, demographics	0.77	0.47–1.26	0.30
Folate (μg/day)			
Unadjusted	1.12	0.87–1.45	0.39
Adjusted			
BMI	1.07	0.82–1.40	0.60
BMI, energy, demographics	0.84	0.54–1.30	0.44
Sodium (mg/day)			
Unadjusted	1.20	0.92–1. 57	0.19
Adjusted			
BMI	1.10	0.84–1.46	0.48
BMI, energy, demographics	0.76	0.38–1.52	0.44
Calcium (mg/day)			
Unadjusted	1.18	0.90–1. 54	0.23
Adjusted			
BMI	1.19	0.91–1.57	0.20
BMI, energy, demographics	0.96	0.65–1.42	0.85
Food groups			
Servings of fruit (No/day)			
Unadjusted	0.85	0.62–1.18	0.34
Adjusted			
BMI	0.90	0.64–1.24	0.51
BMI, energy, demographics	0.77	0.54–1.10	0.14
Servings of vegetables (No/day)			
Unadjusted	1.07	0.84–1.35	0.60
Adjusted			
BMI	1.01	0.79–1.30	0.91
BMI, energy, demographics	0.90	0.67–1.20	0.47
Servings of meat (No/day)			
Unadjusted	1.08	0.82–1.42	0.58
Adjusted			
BMI	0.98	0.74–1.31	0.92
BMI, energy, demographics	0.80	0.51–1.25	0.33
Servings of dairy (g/day)			
Unadjusted	1.19	0.92–1.55	0.19
Adjusted			
BMI	1.26	0.96–1.65	0.10
BMI, energy, demographics	1.09	0.79–1.51	0.58
Servings of grain (g/day)			
Unadjusted	1.17	0.90–1.52	0.24
Adjusted			
BMI	1.14	0.88–1.48	0.35
BMI, energy, demographics	1.05	0.70–1.57	0.82
Fat servings (No/day)			
Unadjusted	1.46	1.09–1.97	0.01
Adjusted			
BMI	1.41	1.04–1.91	0.03
BMI, energy, demographics	1.18	0.98–1.42	0.08

Results of logistic regression analyses for the outcome of having at least weekly heartburn or regurgitation among all participants (n = 371). Adjusted odds ratios were derived from logistic regression models. Odds ratios were scaled based on the interquartile range for each nutrient and thus show risk comparing the 75th centile of intake for each nutrient with the 25th centile.
OR, odds ratio; CI, confidence interval; BMI, body mass index.

oesophagitis had significantly greater daily intakes of total fat and protein than those without erosive oesophagitis (table 2). In addition, non-significant trends were observed for higher intakes of saturated fat, total energy, and sodium with high erosive oesophagitis. In addition, there was a non-significant trend towards greater daily intake of total calories and sodium. Of food types, the number of meat servings was significantly greater in participants with erosive oesophagitis than those without oesophagitis. No significant dose-response relationship was observed when the dietary items were examined in tertiles of daily intake. In multiple logistic regression analysis (not shown), associations between erosive oesophagitis and nutrients described above were attenuated after adjusting for either BMI or hiatus hernia and were no longer significant after adjustment for demographic characteristics and total energy intake.

DISCUSSION

To our knowledge, this is the first study that has quantified intakes of specific dietary nutrients (total energy, macronutrients, micronutrients, and food groups) in persons with and without GORD. We found that high dietary fat intake, particularly saturated fat, was associated with an increased risk of GORD symptoms and erosive oesophagitis. These associations are independent of energy intake and therefore do not reflect a mere increase in total dietary intake. However, the effects were not completely independent of body mass index and were statistically significant only in overweight individuals. Other findings included a possible protective effect for high fibre intake relative to GORD symptoms and a non-significant unfavourable trend for total energy intake.

An important role for dietary fat is supported by previous physiological and epidemiological studies. There is consistent evidence to support the role of dietary fat in causing temporary episodes of reflux. Several physiological studies of human volunteers have shown increased frequency of transient lower oesophageal sphincter relaxation and increased oesophageal acid exposure with high fat consumption. These studies examined both healthy volunteers[6 7] as well as patients with GORD.[8 9] Several food items have been

Table 4 Interaction between body mass index (BMI) and dietary fat intake in subjects with and without frequent gastro-oesophageal reflux disease (GORD) symptoms

	Frequent GORD symptoms			No GORD symptoms			
	No	Mean	SD	No	Mean	SD	p Value
Total fat							
BMI<25	26	66.5	29.3	115	63.0	31.8	0.607
BMI≥25	77	81.0	42.0	153	72.5	37.8	0.125
Saturated fat							
BMI<25	26	19.6	9.6	115	18.0	9.4	0.436
BMI≥25	77	24.4	13.07	153	21.3	11.6	0.062
Cholesterol							
BMI<25	26	168.0	72.3	115	185.6	130.3	0.508
BMI≥25	77	252.4	141.3	153	210.1	119.7	0.018
Fat servings							
BMI<25	26	3.2	1.5	115	3.0	1.5	0.374
BMI≥25	77	3.6	1.7	153	3.1	1.6	0.029

Frequent GORD symptoms implies at least weekly heartburn or acid regurgitation.

associated with precipitating reflux symptoms in cross sectional surveys.[3] Previous case control studies reported a significant positive effect for fat on oesophageal adenocarcinoma.[11 18 19] However, of ''refluxegenic'' food items, high fat food is more likely to be consumed with significant frequency and amount, to account for rising rates of GORD and oesophageal adenocarcinoma in the general population. The fat content of the US food supply has increased 38% between 1909 and 1988.[20] These secular trends are consistent with the notion that high fat intake may be at least partially responsible for rising rates of oesophageal adenocarcinoma, which were first observed in the late 1970s. The absence of significant associations between GORD and other dietary items in the current study could at least in some instances represent a type II error due to the relatively small sample size although the study had sufficient power to detect a 10% difference in total fat intake between those with and without GORD symptoms.

Our study found a statistically significant positive association between fat intake and GORD. Individuals with GORD in this study may have avoided ingesting certain foods associated with precipitating symptoms or may have increased their intake of other foods (such as dairy products) that ameliorate these symptoms. Neither the degree nor the pattern of dietary change is known in this study. This potential bias is likely to have lowered the observed significant association between high dietary fat intake and GORD as it is highly unlikely that high fat foods were used to ameliorate GORD related symptoms; for example dairy product intake was not different between the groups with and without GORD. However, dietary avoidance could have resulted in us missing important associations between GORD and other dietary items. Although an observed increase in any particular dietary item may reflect a higher overall caloric intake, effects for dietary fat were independent of the total caloric intake. Lastly, physical activity could confound the observed associations between dietary intake and GORD. For example, individuals who consume a large amount of fat are likely to lead a sedentary life style while those with high fibre intake might represent a more active athletic sector of the community. Our adjustment for physical activity was rather crude in this study. However, it remains unknown whether physical activity or other behaviours associated with patterns of eating have an impact on the development and maintenance of GORD.

These results indicate that BMI is an important confounder as well as an effect modifier of the relation between dietary fat and GORD. High fat intake is positively associated with obesity because fat is more energy dense (9 kcal/g) than carbohydrate or protein (4 kcal/g). Adjustment for BMI reduced the observed effect of fat intake to a large extent. However, there was a strong correlation between fat intake and BMI, and therefore the reduction of effect could represent an over adjustment. In addition, there was a significant interaction between these two variables where high fat intake increased the risk of GORD only in individuals who were overweight. We conclude that there is probably an independent role for dietary fat, especially in obese individuals. However, given the cross sectional design, the putative confounding and modifying effects of BMI should be interpreted with caution.

To our knowledge this is the first study to indicate a protective effect of dietary fibre on GORD although it was not clear that the protective effect of fibre intake was not independent of BMI. Several case control studies[23–28] reported a consistent significant inverse association between high dietary fibre intake and reduced risk of oesophageal adenocarcinoma, including large well designed studies in the USA[24] and Sweden.[28] The mechanism(s) for such a protective effect is not known. One study that used geographic surveys suggested that dietary deficiency of fibre increases the risk of hiatus hernia.[29 30]

We chose hospital employees as our sampling frame because it offers a large accessible ethnically diverse sample of the general population, which generally obviates bias related to differential access to healthcare facilities based on race or ethnicity. We also used a single endoscopist blinded to the results of the questionnaire and a single pathologist blinded to results of endoscopy. Moreover, the fact that more than 70% were first time participants in endoscopy is an indication that most participants were neither previous patients nor ''career'' volunteers for medical studies.

Several possible limitations of this study also warrant consideration. Firstly, the moderate response rate to the questionnaire may have resulted in a selection bias with persons with GORD symptoms being more likely to participate in the study. Therefore, the reported GORD symptom prevalence rates may be an overestimate compared with the general population. As with other survey studies, participants may differ from non-participants with regards to important characteristics. Endoscopy was offered to all participants and this could have contributed to the lower participation rate although it was made clear in the invitation letter that completing the questionnaire was a separate phase of the study that was not contingent upon endoscopy. In this case, age and ethnicity did not differ between participants and non-participants; however, we have no information on the prevalence of heartburn or regurgitation among non-participants. Selection bias may have also affected the endoscopy phase of the study resulting in an overestimate of the

prevalence of erosive oesophagitis. Secondly, estimates of nutrient intakes from an FFQ are not precise and there is always the potential for measurement error[21]; however, the Block 98 FFQ is one of the most well validated and commonly used food frequency questionnaires.[22] In addition, measurement of physical activity was only approximated and detailed validated questionnaires were not used. Finally, our cross sectional design did not permit definitive conclusions about causality. However, dietary intake and GORD symptoms were measured in this study within the past one year while erosive oesophagitis was evaluated during the study. Most individuals maintain a relatively constant pattern of dietary intake over time[15 31] and therefore the assessment performed in this study can conceivably reflect dietary patterns preceding the development of GORD.

In conclusion, this study indicates a statistically significant association between high dietary fat intake and the presence of GORD symptoms and erosive oesophagitis. This finding can at least partly explain the rising rates of GORD in the USA. It remains unclear however whether this effect is completely independent of BMI. Further studies should attempt to disentangle the effect of these important variables.

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