Dietary glycemic load and risk of colorectal cancer in Chinese women[1–3]

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ABSTRACT

Background: Mixed results have been reported in recent epidemiologic studies in Western populations that have investigated the hypothesis that high glycemic load may increase the risk of colorectal cancer. This association has not been prospectively evaluated in other populations.

Objective: We examined the association of overall glycemic index and glycemic load with colorectal cancer risk in a prospective cohort of Chinese women.

Design: A total of 73,061 women aged 40–70 y and free of cancer at enrollment were included in this analysis. Usual dietary intake was assessed at baseline (1997–2000) and reassessed during the first follow-up (2000–2002) through in-person interviews by using a validated food-frequency questionnaire.

Results: During an average follow-up of 9.1 y, 475 incident colorectal cancer cases were identified. Glycemic load was not associated with colorectal cancer risk (*P* for trend = 0.84). The multivariable hazard ratio for the highest compared with the lowest quintile of glycemic load was 0.94 (95% CI: 0.71, 1.24). Similar results were also observed for associations with dietary glycemic index and total carbohydrate intake, and results did not vary by excluding individuals with a history of diabetes from the analysis.

Conclusion: This prospective study, conducted in a population with a high intake of carbohydrates, provides no evidence that a high–glycemic index diet or high glycemic load is associated with an increased risk of colorectal cancer. *Am J Clin Nutr* 2011;93:101–7.

INTRODUCTION

Colorectal cancer is the third most common cancer in women worldwide (1) and the third leading cause of cancer mortality in the United States (2). In urban Shanghai, China, the incidence rate of colon cancer over the past 3 decades has doubled in both men and women (3, 4). Lifestyle and dietary factors are believed to play a significant role in disease risk (5, 6).

Epidemiologic and clinical observations have shown an increased risk of colorectal cancer in patients with type 2 diabetes, suggesting that elevated circulating insulin may play a role in colorectal carcinogenesis (7–9). Many of the established risk factors for colorectal cancer, including obesity and physical inactivity, may directly influence circulating insulin (7, 10). Carbohydrates are the main dietary component affecting insulin secretion and postprandial glycemia (11). High-carbohydrate diets cause a rapid elevation in blood glucose and may promote weight gain over time (12). Chronic hyperglycemia and obesity-induced insulin resistance result in hyperinsulinemia. Hyperinsulinemia is suggested to stimulate proliferation and promote metastasis of malignant colonic epithelial cells by elevating the bioactivity of insulin-like growth factor (IGF) I and reducing IGF-binding protein-3 (13–15).

The ability of carbohydrates to influence blood glucose and insulin concentrations varies substantially and depends largely on both the amount and type of carbohydrates consumed (16, 17). Measures that quantify such variation are useful in assessing the health effects of different dietary carbohydrates, given the importance of postprandial glucose metabolism and insulin response in human health (8, 16, 18–20). The glycemic index is a ranking of carbohydrate-containing foods on the basis of their postprandial blood glucose response; the higher the glycemic index, the greater the postprandial glucose and insulin responses (16, 17, 19). Glycemic load incorporates both the quality, measured by using the glycemic index, and the quantity of carbohydrates (17–19). Glycemic load is often used in epidemiologic studies to evaluate the effect of carbohydrate intake on the risk of obesity, diabetes, and cardiovascular diseases (8, 18, 20–23). With the increasing recognition that abnormal glucose metabolism and hyperinsulinemia may play a role in the etiology of certain cancers, including colorectal cancer, there is also a growing interest in the association between dietary glycemic load and cancer risk (24).

The association between overall dietary glycemic index, glycemic load, and colorectal cancer risk was evaluated in several case-control and prospective cohort studies, and results have been mixed (25). All of the cohort studies were conducted in Western societies, with dietary patterns that differ substantially from a traditional Chinese diet. In this study, we prospectively evaluated the association between overall glycemic index, glycemic load, and colorectal cancer risk in the Shanghai Women's Health Study (SWHS), a large cohort study of Chinese women who habitually consume a large amount of carbohydrates.

SUBJECTS AND METHODS

Study participants

The SWHS, initiated in March 1997, is a population-based, prospective cohort study. The study was approved by the relevant institutional review boards for human research (Vanderbilt University; Shanghai Cancer Institute, China; and the National Cancer Institute), and the details of the study design have been described elsewhere (26, 27). Briefly, 81,170 women aged 40–70 y who resided in 7 geographically defined communities in urban Shanghai were approached to participate in this study, and 75,221 women enrolled (response rate: 92.7%). After excluding from the cohort 279 women who were later found to be younger than 40 y or older than 70 y at the time of the baseline interview, the remaining 74,942 women constituted the cohort.

In-person interviews were conducted by trained interviewers who were retired medical professionals. The questionnaire included questions on sociodemographic factors, dietary and life-style habits, physical activity, menstrual and reproductive history, hormone use, medical history, and occupational history. Anthropometric measurements, including current weight, height, and circumferences of the waist and hip, were taken at baseline according to a standard protocol (28).

The cohort was followed for occurrence of cancer and other chronic diseases by a combination of active surveys conducted every 2–3 y and annual record linkage of the cohort to the population-based Shanghai Cancer Registry and the Shanghai Municipal Vital Statistics Registry. The response rates for the first (2000–2002), second (2002–2004), and third (2004–2007) in-person follow-up surveys were 99.8%, 98.7%, and 96.7%, respectively. All possible incident cancer cases were verified through home visits. Medical charts were reviewed to verify cancer diagnoses and to collect detailed diagnostic information.

Dietary assessment

A quantitative food-frequency questionnaire (FFQ) was used to assess usual dietary intake at the baseline survey and again at the first follow-up survey 2–3 y after the baseline assessment. The FFQ was validated against the mean of 24 d of 24-h dietary recalls (the recalls were conducted twice per month over a 12-mo period). The correlation coefficients between the FFQ and dietary recalls for estimates of carbohydrates and rice (the major contributor to glycemic load in this population) were both 0.66 (27). The FFQ comprised 71 food items and food groups that covered >90% of foods commonly consumed in urban Shanghai (27). During the in-person interviews, each participant was first asked, on average, how often she had consumed a specific food or food group during the past 12 mo (the possible responses were daily, weekly, monthly, yearly, or never) and then how much she consumed in *liang* (1 liang = 50 g) per unit of time. Nutrient intakes for each food were calculated by multiplying the amount of food consumed by the nutrient content per gram of the food, as obtained from the Chinese Food Composition Tables (29). The total dietary intake of each nutrient was calculated by summing the nutrient in all food items of the FFQ.

The glycemic index ranks foods on the basis of the relative postprandial blood glucose response per gram of carbohydrate. The glycemic index values of major carbohydrate-contributing foods (92.4% of total carbohydrates) were obtained from the Chinese Food Composition Tables and supplemented by other published data including the International Table of Glycemic Index and Glycemic Load Values, 2002 version (17, 30). A food's glycemic load was calculated by multiplying the amount of carbohydrates consumed from the food by its glycemic index value. Dietary glycemic load for a participant was calculated by summing the values of glycemic load for all food items. Overall dietary glycemic index for a participant was derived by dividing glycemic load by the amount of carbohydrates consumed.

To better estimate usual dietary intake, we used the average intake of the first FFQ at baseline and the second FFQ conducted 2–3 y after the baseline survey. For individuals who provided no second FFQ data or who reported having diabetes, cardiovascular disease, or cancer diagnosed between the 2 FFQ surveys (*n* = 8654, 11.8%), only the baseline dietary intake was used as the exposure.

Statistical analysis

We excluded participants who reported a history of cancer (*n* = 1,576) or familial adenomatous polyposis at baseline (*n* = 86), participants who were lost to follow-up after enrollment (*n* = 7), and self-reported cases whose diagnosis of cancer could not be confirmed (*n* = 177, including 8 self-reported cases of colorectal cancer). After the additional exclusion of those with extreme total energy intake (<500 or >3500 kcal/d, *n* = 42), the study cohort for our analyses consisted of 73,061 women.

Hazard ratios (HRs) of developing colorectal cancer and their 95% CIs were estimated by using the Cox proportional hazards regression model, with age as the time scale. Entry time was defined as age at enrollment, and exit time was defined as age at colorectal cancer diagnosis or censoring (either 31 December 2007 or the date of death), whichever came first.

Carbohydrate intake, glycemic index, and glycemic load were adjusted for total energy intake with the logarithmically transformed regression residual method (31). Energy-adjusted dietary intakes were categorized into quintiles and analyzed as continuous variables to evaluate linear trends. The interaction of continuous dietary variables with other risk factors for colorectal cancer was evaluated with a likelihood ratio test by comparing the Cox models with and without the interaction term. Information on menopausal status was updated at follow-up interviews and treated as a time-varying covariate in the model. In addition to total energy intake (continuous) and age at baseline (continuous), education (4 categories), household income (3 categories), body mass index (BMI; calculated as weight in kilograms divided by height in meters squared, continuous), colorectal cancer history in first-degree relatives (yes or no), physical activity [measured

by metabolic equivalent task hours per week per year (28), continuous], and use of hormone replacement therapy (yes or no) were adjusted for in the analysis. Because dietary patterns may be a better predictor of health outcomes than any single nutrient (32), we also evaluated 3 major dietary patterns as potential confounders or effect modifiers in multivariate analyses. As described in detail elsewhere (33), dietary patterns were derived by using principal components analysis, with all individual food variables adjusted for energy intake using the residual approach. Additional adjustments for use of nonsteroidal antiinflammatory drugs, cigarette smoking, and other dietary factors, such as intakes of fruit and vegetables, red meat, dietary fiber, calcium, and folic acid, did not appreciably alter the results; these variables were therefore not included in the final model. We also conducted sensitivity analyses excluding cases diagnosed during the first year of follow-up to address the potential influence of prediagnosed diseases on risk estimates.

Statistical analyses were carried out by using SAS version 9.2 (SAS Institute, Cary, NC). All P values are based on 2-sided tests.

RESULTS

Baseline characteristics of the study population according to quintiles of energy-adjusted glycemic load are presented in **Table 1**. In general, women with a higher glycemic load—that is, women who consumed greater amounts of carbohydrates with a higher glycemic index—were older, were likely to be less educated, had a slightly higher BMI, and were physically more active. They were also likely to have lower intakes of red meat, fruit, and vegetables and were less likely to use postmenopausal

hormones regularly or to have a prior history of diabetes or a family history of colorectal cancer at baseline. Few women in this cohort ever smoked cigarettes (2.8%) or consumed alcoholic beverages regularly (2.2%).

During an average follow-up of 9.1 y, 475 incident cases of colorectal cancer, including 287 cases of colon cancer and 188 cases of rectal cancer, were documented after the baseline recruitment. Overall, there was no association between glycemic load or glycemic index and colorectal cancer risk (**Table 2**). In analyses adjusted for age and total energy intake, the HRs (95% CIs) of colorectal cancer across the lowest to the highest quintiles of glycemic load were 1 (reference), 0.74 (0.55, 1.00), 0.69 (0.51, 0.94), 0.72 (0.54, 0.97), and 0.95 (0.73, 1.24), respectively (P for trend = 0.97). The corresponding HRs (95% CIs) for overall glycemic index were 1 (reference), 1.14 (0.85, 1.53), 0.87 (0.64, 1.19), 1.00 (0.74, 1.34), and 1.10 (0.83, 1.46) (P for trend = 0.78). Similar results were also observed for total carbohydrate intake. Further adjustment for lifestyle and other dietary factors did not appreciably alter the risk estimates. The risk estimates did not differ in analyses stratified by anatomic sites (colon compared with rectum; Table 2).

We also conducted analyses excluding colorectal cancer cases that occurred within the first year after the baseline interview to minimize the possible effect of dietary changes related to subclinical disease. Results were similar to those observed in the entire study population. The HR for the highest quintile compared with the lowest quintile of glycemic load was 1.06 (95% CI: 0.79, 1.41).

Because the value for average dietary intake for 11.8% of participants was based on the baseline FFQ only, we further

TABLE 1
Baseline characteristics of study participants according to quintiles (Q) of dietary glycemic load: the Shanghai Women's Health Study, 1996–2007[1]

	Glycemic load				
	Q1	Q2	Q3	Q4	Q5
No. of individuals	14,612	14,612	14,612	14,612	14,613
Age (y)[2]	50.4 ± 8.44	51.2 ± 8.66	51.8 ± 8.83	53.1 ± 9.07	55.9 ± 9.22
Daily intake[3,4]					
Total energy (kcal)	1644 ± 2.88	1664 ± 2.87	1641 ± 2.87	1616 ± 2.87	1651 ± 2.91
Glycemic load (g)	155.9 ± 0.08	179.4 ± 0.08	192.7 ± 0.08	206.1 ± 0.08	229.0 ± 0.08
GIycemic index	64.6 ± 0.02	68.6 ± 0.02	70.7 ± 0.02	72.6 ± 0.02	75.6 ± 0.02
Carbohydrates (g)	241.2 ± 0.10	261.7 ± 0.10	272.8 ± 0.10	284.0 ± 0.10	302.7 ± 0.10
Red meat (g)	58.6 ± 0.18	49.8 ± 0.18	45.4 ± 0.18	40.9 ± 0.18	33.0 ± 0.18
Vegetables (g)	368.4 ± 1.03	319.3 ± 1.02	292.6 ± 1.02	268.2 ± 1.02	227.8 ± 1.04
Fruit (g)	311.2 ± 1.09	263.5 ± 1.09	239.4 ± 1.09	216.2 ± 1.09	167.2 ± 1.10
Education, high school and above (%)	55.0	48.9	43.2	36.4	24.8
Ever smoker (%)	2.9	2.3	2.5	2.4	3.4
Ever drinker (%)	3.8	2.1	1.8	1.7	1.7
Diabetes (%)	6.9	5.0	4.5	3.8	2.7
Hormone replacement therapy (%)[5]	10.6	10.7	8.0	6.7	2.8
Family history of colorectal cancer (%)	2.6	2.3	2.4	2.1	1.8
Physical activity (MET-h · wk^{-1} · y^{-1})[3]	103.5 ± 0.38	105.0 ± 0.37	106.8 ± 0.37	108.0 ± 0.37	109.6 ± 0.38
BMI (kg/m^2)[3]	23.7 ± 0.03	23.8 ± 0.03	23.9 ± 0.03	24.0 ± 0.03	24.6 ± 0.03

[1] MET-h, metabolic equivalent task hours. All variables were standardized to the age distribution at baseline. All tests for trend were significant ($P <$ 0.05); the general linear model for continuous variables and Cochran-Mantel-Haenszel statistics for categorical variables were used.

[2] Values are means ± SDs.

[3] Values are means ± SEs.

[4] Represents average intake according to the baseline and second food-frequency questionnaires. Values for dietary intakes (except for total energy) were energy-adjusted by a nutrient logarithmically transformed residual model.

[5] Among postmenopausal women.

TABLE 2
Multivariate hazard ratios (HRs; 95% CIs) for colorectal cancer associated with dietary glycemic load, glycemic index, and intake of carbohydrates: the Shanghai Women's Health Study, 1996–2007[1]

	Quintile category					
	1	2	3	4	5	P for trend
Glycemic load						
Median (g/d)	159.7	179.6	192.7	205.9	225.9	
Person-years	132,319	133,177	133,439	133,323	131,905	
Colorectal cancer						
No. of cases	97	78	76	86	138	
HR[2]	1.00	0.74 (0.55, 1.00)	0.69 (0.51, 0.94)	0.72 (0.54, 0.97)	0.95 (0.73, 1.24)	0.97
HR[3]	1.00	0.74 (0.55, 1.00)	0.69 (0.51, 0.93)	0.71 (0.53, 0.96)	0.94 (0.71, 1.24)	0.84
Colon cancer						
No. of cases	56	55	44	50	82	
HR[2]	1.00	0.90 (0.62, 1.31)	0.68 (0.46, 1.02)	0.71 (0.49, 1.03)	0.93 (0.66, 1.31)	0.52
HR[3]	1.00	0.90 (0.62, 1.30)	0.68 (0.45, 1.01)	0.69 (0.47, 1.02)	0.92 (0.64, 1.32)	0.45
Rectal cancer						
No. of cases	41	23	32	36	56	
HR[2]	1.00	0.53 (0.32, 0.88)	0.71 (0.45, 1.13)	0.75 (0.48, 1.18)	1.00 (0.66, 1.51)	0.46
HR[3]	1.00	0.53 (0.32, 0.88)	0.70 (0.44, 1.12)	0.74 (0.47, 1.17)	0.99 (0.64, 1.52)	0.55
Glycemic index						
Median	64.4	68.4	70.8	73.1	76.0	
Person-years	132,796	133,192	133,277	133,203	131,695	
Colorectal cancer						
No. of cases	80	95	78	97	125	
HR[2]	1.00	1.14 (0.85, 1.53)	0.87 (0.64, 1.19)	1.00 (0.74, 1.34)	1.10 (0.83, 1.46)	0.78
HR[3]	1.00	1.13 (0.84, 1.53)	0.86 (0.63, 1.18)	0.99 (0.73, 1.34)	1.09 (0.81, 1.46)	0.86
Colon cancer						
No. of cases	47	62	45	59	74	
HR[2]	1.00	1.26 (0.86, 1.83)	0.84 (0.56, 1.26)	1.01 (0.69, 1.48)	1.06 (0.73, 1.53)	0.82
HR[3]	1.00	1.25 (0.85, 1.82)	0.83 (0.55, 1.26)	0.99 (0.67, 1.47)	1.05 (0.71, 1.54)	0.77
Rectal cancer						
No. of cases	33	33	33	38	51	
HR[2]	1.00	0.97 (0.60, 1.57)	0.92 (0.56, 1.48)	0.99 (0.62, 1.58)	1.17 (0.75, 1.82)	0.46
HR[3]	1.00	0.97 (0.60, 1.57)	0.91 (0.56, 1.48)	0.98 (0.61, 1.57)	1.16 (0.73, 1.84)	0.53
Carbohydrates						
Median (g/d)	242.2	261.1	273.3	285.3	302.3	
Person-years	132,252	133,085	133,409	133,331	132,087	
Colorectal cancer						
No. of cases	100	85	69	92	129	
HR[2]	1.00	0.80 (0.60, 1.07)	0.63 (0.46, 0.85)	0.77 (0.58, 1.02)	0.89 (0.69, 1.17)	0.54
HR[3]	1.00	0.80 (0.60, 1.06)	0.62 (0.46, 0.84)	0.75 (0.57, 1.01)	0.87 (0.66, 1.15)	0.41
Colon cancer						
No. of cases	62	53	41	55	76	
HR[2]	1.00	0.80 (0.56, 1.16)	0.59 (0.40, 0.88)	0.72 (0.50, 1.04)	0.81 (0.58, 1.13)	0.25
HR[3]	1.00	0.79 (0.55, 1.15)	0.58 (0.39, 0.87)	0.71 (0.49, 1.02)	0.79 (0.55, 1.12)	0.20
Rectal cancer						
No. of cases	38	32	28	37	53	
HR[2]	1.00	0.81 (0.50, 1.29)	0.69 (0.42, 1.12)	0.85 (0.54, 1.34)	1.05 (0.69, 1.60)	0.65
HR[3]	1.00	0.80 (0.50, 1.28)	0.68 (0.54, 1.11)	0.84 (0.53, 1.32)	1.02 (0.66, 1.59)	0.76

[1] Energy-adjusted glycemic load, glycemic index, and carbohydrates were determined by the logarithmically transformed residual method. Quintile cutoffs for glycemic load were 171.4, 186.3, 199.1, and 214.1 g/d; for glycemic index were 66.80, 69.69, 71.93, and 74.32; and for carbohydrate intake were 253.4, 267.4, 279.1, and 292.4 g/d.
[2] Adjusted for age and total energy intake by using a Cox model with age as the time scale and stratified by birth year.
[3] Adjusted for age, education, income, BMI, physical activity, family history of colorectal cancer, total energy intake, and hormone replacement therapy use by using a Cox model with age as the time scale and stratified by birth year.

restricted analyses to participants (*n* = 64,407) who completed both the first and second FFQs. The multivariable-adjusted HR for the comparison of extreme quintiles was 1.06 (95% CI: 0.77, 1.47). Likewise, a null association was observed when only the baseline intake was analyzed for the entire cohort, with a corresponding HR of 0.96 (95% CI: 0.72, 1.26).

There was no evidence that the effect of glycemic load on colorectal cancer was modified by traditional risk factors for colorectal cancer, including BMI, physical activity, and 3 major dietary patterns (**Table 3**), or other dietary factors such as intakes of red meat, fruit, and vegetables (data not shown). We also conducted analyses excluding individuals who reported

TABLE 3
Association of dietary glycemic load with colorectal cancer risk by BMI, physical activity, and dietary patterns: the Shanghai Women's Health Study, 1996–2007[1]

	Q1	Q2	Q3	Q4	Q5	P for trend	P for interaction
BMI							
<25 kg/m^2	1.00	0.82 (0.57, 1.20)	0.65 (0.44, 0.97)	0.80 (0.55, 1.16)	1.08 (0.75, 1.55)	0.73	0.19
≥25 kg/m^2	1.00	0.62 (0.37, 1.02)	0.73 (0.46, 1.17)	0.60 (0.37, 0.97)	0.79 (0.51, 1.21)	0.49	
Physical activity (MET-h · wk^{-1} · y^{-1})							
<100.45 (median)	1.00	0.73 (0.47, 1.14)	0.75 (0.48, 1.16)	0.77 (0.49, 1.18)	1.08 (0.72, 1.63)	0.58	0.15
≥100.45	1.00	0.75 (0.50, 1.12)	0.64 (0.42, 0.97)	0.66 (0.44, 0.99)	0.83 (0.57, 1.22)	0.41	
Dietary pattern							
Factor 1 (vegetable-rich diet)							
<0.175 (median)	1.00	0.98 (0.58, 1.65)	0.87 (0.51, 1.49)	1.00 (0.59, 1.71)	1.46 (0.85, 2.52)	0.10	0.09
≥0.175	1.00	0.67 (0.46, 0.99)	0.66 (0.44, 0.98)	0.65 (0.43, 0.98)	0.86 (0.56, 1.31)	0.40	
Factor 2 (fruit-rich diet)							
<0.129 (median)	1.00	0.71 (0.46, 1.10)	0.48 (0.30, 0.77)	0.62 (0.41, 0.95)	0.77 (0.50, 1.17)	0.49	0.09
≥0.129	1.00	0.80 (0.52, 1.23)	1.02 (0.66, 1.57)	0.85 (0.52, 1.38)	1.46 (0.88, 2.44)	0.24	
Factor 3 (meat-rich diet)							
<0.082 (median)	1.00	0.67 (0.40, 1.14)	0.85 (0.52, 1.37)	0.67 (0.41, 1.10)	1.15 (0.72, 1.83)	0.15	0.12
≥0.082	1.00	0.81 (0.56, 1.18)	0.58 (0.37, 0.90)	0.90 (0.58, 1.40)	0.74 (0.41, 1.32)	0.28	

[1] Values are hazard ratios (95% CIs) by quintile (Q) of glycemic load. MET-h, metabolic equivalent task hours. Multivariate hazard ratios were adjusted for age, education, income, BMI, physical activity, family history of colorectal cancer, total energy intake, and hormone replacement therapy use by using a Cox model with age as the time scale and stratified by birth year.

a history of diabetes at baseline and censored the observation at the diagnosis of diabetes during follow-up. No material changes in risk estimates for colorectal cancer were observed (HR for the highest compared with the lowest quintile of glycemic load: 1.06; 95% CI: 0.78, 1.43; *P* for trend = 0.40).

Because rice contributed 69% of total carbohydrate intake in this study population, we also analyzed its association with colorectal cancer risk. There was no apparent association observed for rice intake. Women in the highest quintile compared with the lowest quintile of intake had an HR of 1.17 (95% CI: 0.87, 1.57; *P* for trend = 0.67). Similar results were also observed for total intake of major starch-rich foods, including rice, noodle, cake, bread, and other wheat products (corresponding HR = 0.91; 95% CI: 0.69, 1.20; *P* for trend = 0.52).

DISCUSSION

In this population-based prospective study, we observed no association of overall dietary glycemic index, glycemic load, or carbohydrate intake with colorectal cancer risk, either overall or by subsite of the colon compared with the rectum. Excluding women with diabetes from the analysis yielded similar results. Furthermore, risk estimates associated with glycemic load, glycemic index, and carbohydrate intake were neither confounded nor modified by traditional risk factors for colorectal cancer or by other dietary factors, such as intakes of calcium, fiber, and folic acid and 3 major dietary patterns.

Several case-control studies evaluated the association of colorectal cancer with dietary glycemic load and glycemic index. Results have been mixed but generally point toward a positive association (34–36), with odds ratios for colorectal cancer ranging from 1.59 to 1.82. However, such an increased risk was not observed in recent prospective cohort studies conducted in the United States and in European countries (37–43). One exception was the Women's Health Study (44), which showed an increased

risk of colorectal cancer in women with elevated glycemic load; however, the analysis was based on a small number of cases (*n* = 174). A recent meta-analysis of 8 cohort studies (25) found that, compared with the lowest category of glycemic load, people with the highest category of glycemic load had a pooled relative risk of 1.06 (95% CI: 0.96, 1.17; *P* for heterogeneity = 0.25), which is similar to the findings observed in our study.

Interestingly, an inverse association between glycemic load and colorectal cancer risk was suggested in a recent analysis of the Multiethnic Cohort Study, which showed an HR for the highest compared with the lowest quintile of 0.75 (95% CI: 0.57, 0.97; *P* for trend = 0.02) (45). Rice is an important staple of that study population, contributing 4–33% of glycemic load in the various ethnic groups of the study (45). The authors speculated that rice-based diets may not provide as robust a measure of a physiologic response to glycemic load as do bread and potatoes. In our cohort, rice was the single largest contributor to carbohydrate and glycemic load, contributing 69% of total carbohydrates and 80% of total glycemic load. Consistent with the findings for total carbohydrates and glycemic load, no significant association was observed for rice intake in our study.

The primary strengths of this study include its large sample size, prospective cohort design, and extraordinarily high participation rate (92.7%) at baseline and follow-up (>95% for active, in-person follow-up). This study also has several limitations. As with any epidemiologic study using an FFQ, a potential limitation is that the assessment of dietary intake is prone to measurement errors. However, the SWHS's FFQ has been previously evaluated as compared with intake assessed by 24 d (2 d each month) of 24-h dietary recalls and showed good validity for the measurement of intakes of commonly consumed food groups and most nutrients (27). In addition, dietary intake was measured twice, first at the baseline enrollment and 2–3 y after the baseline survey. We analyzed dietary intakes from different measurements and observed similar results when

dietary intakes from only the baseline interview or the average of 2 dietary surveys were considered. This may alleviate some concerns about dietary measurement error. Because of the observational design, we cannot completely rule out confounding from unmeasured factors, despite having carefully adjusted for a range of potential confounders, including both dietary and nondietary factors. Another limitation of this study was that we were not able to analyze the effect of specific types of carbohydrates, such as fructose, on the basis of nutrient variables derived from the Chinese Food Composition Tables. Some studies have suggested that a high intake of fructose may increase the risk of colorectal cancer (44). Finally, results from this study of women may not be necessarily applicable to men, and further research in men is warranted.

In conclusion, this large cohort study in Chinese women suggests no association of a diet characterized by high glycemic index or glycemic load or by a high intake of carbohydrates with the risk of colorectal cancer. Our findings are in agreement with most previous cohort studies conducted in Western populations.

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