Dietary glycemic index and load in relation to risk of uterine leiomyomata in the Black Women's Health Study[1–3]

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ABSTRACT

Background: High dietary glycemic index (GI) and glycemic load (GL) may promote tumorigenesis by increasing endogenous concentrations of insulin-like growth factor I (IGF-I) or the bioavailability of estradiol. In vitro studies have shown that uterine leiomyoma (UL) cells proliferate in response to IGF-I and display increased IGF-I gene expression and protein synthesis. Previous epidemiologic studies suggest that a high GL is a risk factor for endometrial and ovarian cancers, which, like UL, are hormone-responsive tumors.

Objective: We investigated the relation of dietary GI and GL with UL risk in the Black Women's Health Study.

Design: In this prospective cohort study, we followed 21,861 premenopausal women for incident UL from 1997 to 2007. Diet was assessed in 1995 and 2001 with food-frequency questionnaires. We used Cox regression to estimate incidence rate ratios (IRRs) and 95% CIs, controlled for potential confounders.

Results: During 162,604 person-years of follow-up, there were 5800 cases of UL diagnosed by ultrasound or surgery. Dietary GI was weakly associated with UL risk overall (IRR for highest compared with lowest quintile: 1.09; 95% CI: 0.99, 1.19; *P* for trend = 0.04). Positive associations were observed between GL and UL in women aged <35 y (IRR for highest compared with lowest quintile: 1.18; 95% CI: 1.02, 1.37; *P* for trend = 0.15) and between GI and UL in college-educated women (IRR for highest compared with lowest quintile: 1.17; 95% CI: 1.03, 1.34; *P* for trend = 0.004).

Conclusions: Our results suggest that high dietary GI and GL may be associated with an increased UL risk in some women. The observed associations warrant investigation in future studies. *Am J Clin Nutr* 2010;91:1281–8.

INTRODUCTION

Uterine leiomyomata (UL), benign neoplasms that develop from uterine smooth muscle cells, are the leading indication for hysterectomy in the United States (1, 2). This condition is particularly burdensome in US black women, for whom the incidence of clinically recognized UL is 2–3 times that of US white women (1, 3–5). Sex steroid hormones are believed to stimulate UL development and growth (6, 7), and studies have consistently identified reproductive and hormonal risk factors for UL (8–14). Identification of modifiable lifestyle risk factors, such as dietary intake, could lead to public health recommendations aimed at prevention of UL.

Long-term consumption of excess simple carbohydrates may lead to hyperinsulinemia, defined as prolonged, elevated blood glucose concentrations and insulin resistance in the liver, muscle, and adipose tissues. Studies of blood samples from nondiabetic adults show that high concentrations of insulin correlate with increased free circulating concentrations of insulin-like growth factor I (IGF-I) (15) and, in females, with decreased sex hormone–binding protein concentrations, thereby increasing bioavailable estradiol (16). In vitro (17, 18) and animal (19, 20) studies have shown that IGF-I has a role in activating mitogenic and anti-apoptotic cell pathways that support tumor growth. IGF-I stimulates UL cell proliferation in culture (21, 22), and studies of human UL cells have found increased IGF-I gene expression (23–26) and protein (27, 28) levels relative to normal myometrial cells. In vitro evidence indicates that up-regulation of IGF-I in UL cells may occur in an estrogen-dependent manner (29, 30). However, a recent cross-sectional epidemiologic study found no association between IGF-I and UL in black women, and a suggestive inverse association in white women (31).

An indicator of a food's insulin demand, glycemic index (GI), quantifies a food's capacity to raise postprandial blood glucose concentrations (32) relative to an equivalent carbohydrate portion of a reference food (glucose or white bread) (33). Glycemic load (GL), the mathematical product of a food's GI multiplied by grams of carbohydrate in a serving, provides a more complete measure of the portion's effect on postprandial blood glucose (34, 35). Results from epidemiologic studies of GI and GL in relation to other hormone-responsive tumors have been mixed, with some studies reporting positive associations for endometrial (36–38) and ovarian (39, 40) cancers and others reporting no association (41, 42). There have been no studies of GI and GL in relation to risk of UL. We prospectively evaluated the association of dietary GI and GL with UL incidence in the Black Women's Health Study (BWHS)—a cohort study of US black women.

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SUBJECTS AND METHODS

Study population

The BWHS is an ongoing prospective cohort study of ≈59,000 black women aged 21–69 y at baseline (1995). The participants were enrolled through self-administered questionnaires mailed to subscribers of *Essence* magazine, members of several black professional organizations, and friends and relatives of early respondents. The baseline questionnaire collected information on demographics, medical and reproductive history, and lifestyle factors, including diet. Follow-up questionnaires are mailed every 2 y to update exposures and identify new illnesses; >80% of the cohort has been retained through 2007. BWHS respondents reside in various regions throughout the United States—most in California, New York, Illinois, Michigan, Georgia, and New Jersey. The Institutional Review Board of Boston University Medical Center approved the study protocol.

Assessment of exposure and covariates

Diet was assessed in 1995 and 2001 with a version of the National Cancer Institute (NCI)–Block short-form food-frequency questionnaire (FFQ) (43) that had been modified to include several food items specific to a black female population, based on write-in items from our pilot study. For each food, the participant was asked to fill in how often, on average, she had consumed the food during the previous year, and her usual portion size. There were 9 options for frequency. These options ranged from "never or <1 per month" to a maximum of either "≥2 per day" for food items or "≥6 per day" for beverage items." The serving sizes used on the 1995 FFQ were small, medium, and large; on the 2001 FFQ, we added a fourth category: super-size. "Small" was equal to half the medium serving size, "large" was 1.5 times the medium size, and "super-size" was twice as large as the medium size.

The FFQ was validated by using a 3-d food diary and up to three 24-h dietary recalls among a sample of 408 BWHS participants (44). Comparisons of FFQ data with data from recalls and diaries indicated acceptable validity for deriving intakes of carbohydrate, fat, protein, dietary fiber, calcium, iron, vitamin C, folate, and β-carotene, with deattenuated and energy-adjusted correlation coefficients ranging from 0.5 to 0.8.

Nutrient estimates from the FFQ were calculated by using version 1.4.1 of the National Cancer Institute (Rockville, MD) DietCalc software. The National Cancer Institute Diet History Questionnaire Database provided serving size- and sex-specific GL and carbohydrate values (34). We calculated overall dietary GL and carbohydrates by multiplying each serving-size specific value by the mean number of servings per day and then summing the resulting value over all foods (45). When computing GL per serving, the Diet History Questionnaire Database uses the GI value relative to an equivalent quantity of glucose and multiplies it by the digestible carbohydrates in a serving of food: the USDA-based value for grams of total carbohydrate minus the USDA-based value for grams of dietary fiber. Subtracting dietary fiber from total carbohydrate results in a GL value that is an indicator of the blood glucose response to the digestible carbohydrates in a serving of food, and failure to subtract dietary fiber might result in an overestimate of this effect (34). Each participant's average dietary GI was calculated by dividing her dietary GL by her daily intake of digestible carbohydrates. We adjusted dietary GI and GL by using the nutrient residual method to measure the variation in nutrient intake attributable to the nutrient composition of the diet, independent of total energy intake (46).

The baseline and follow-up questionnaires collected information on several potential risk factors for UL, including age at menarche, parity, age at each birth, body mass index (BMI; in kg/m^2), cigarette smoking, alcohol intake, education, marital status, occupation, and diabetes. The 2007 questionnaire assessed recency of pelvic exam screening: <5 y ago, 5–9 y ago, ≥10 y ago, and never. Hours of vigorous physical activity were reported on all questionnaires through 2001. Education and occupation were reported on the baseline questionnaire, household income was reported on the 2003 questionnaire, and marital status was updated for each questionnaire cycle, with the exception of 2001.

Assessment of outcome

On the 1999, 2001, and 2003 follow-up questionnaires, women were asked whether they received a diagnosis of "uterine fibroids" in the previous 2-y interval, the calendar year in which they were first diagnosed and whether their diagnosis was confirmed by pelvic exam and/or by ultrasound/hysterectomy." In 2003 and subsequent questionnaires, the question about diagnostic method asked whether the diagnosis was confirmed by "ultrasound" and/or by "surgery (eg, hysterectomy)" to identify women who may have had other surgical procedures. Respondents were classified as cases if in 1999 or 2001 they reported a diagnosis of uterine fibroids confirmed by "ultrasound/hysterectomy" or in 2003, 2005, or 2007 they reported a diagnosis confirmed by "ultrasound" or "surgery," with a valid year of diagnosis (≥1997). The index date for each case was defined as the midpoint of the reported calendar year in which the diagnosis was made.

Our outcome definition included cases diagnosed by ultrasound as well as by surgery because the latter represent only 10–30% of cases for whom ultrasound evidence is available and because an analysis restricted to such cases may spuriously identify risk factors associated with disease severity or treatment preference. Ultrasound, the standard used to confirm diagnoses in clinical practice (47), has high sensitivity (99%) and specificity (91%) relative to histologic evidence (48, 49). To maximize the specificity of outcome classification (50), we treated diagnoses made by pelvic exam only (n = 548) as "noncases" in the analysis because they could represent other gynecologic pathologies (51).

The accuracy of self-reported UL was assessed in a random sample of 248 cases reporting a diagnosis by ultrasound or surgery. Cases were mailed supplemental surveys regarding their initial date of diagnosis, method of confirmation, symptoms, and treatment, and they were asked for permission to review their medical records. We obtained medical records from 127 of the 128 women who gave us permission and confirmed the self-report by medical record in 122 (96%). There were no material differences between cases who did and did not release their medical records with respect to established risk factors for UL, which suggests that those who released their medical records represented the larger case group (52).

TABLE 1
Baseline characteristics of 21,861 women according to dietary glycemic load and glycemic index: the Black Women's Health Study, United States, 1997[1]

	Quintile of dietary glycemic load (range)				Quintile of dietary glycemic index (range)			
	1 (26–83)	3 (93–101)	5 (112–198)	*P* for trend[2]	1 (37–52)	3 (55–56)	5 (58–68)	*P* for trend[2]
No. of women	4007	4112	5272	—	4380	4097	4883	—
Age (y)	35.5 ± 7.3	34.5 ± 7.2	34.2 ± 7.2	<0.001	35.7 ± 7.4	34.5 ± 7.1	34.2 ± 7.2	<0.001
BMI (kg/m^2)	28.6 ± 7.4	27.5 ± 6.8	27.8 ± 6.9	<0.001	27.5 ± 6.5	27.8 ± 6.8	28.4 ± 7.5	<0.001
Age at menarche (y)	12.4 ± 1.6	12.3 ± 1.6	12.4 ± 1.6	0.02	12.3 ± 1.6	12.3 ± 1.5	12.4 ± 1.6	0.05
Parity (births)	1.1 ± 1.3	1.1 ± 1.2	1.1 ± 1.21	0.51	1.0 ± 1.2	1.1 ± 1.2	1.2 ± 1.2	<0.001
Age at first birth (y)[3]	23.0 ± 5.4	23.5 ± 5.2	22.8 ± 5.0	0.04	23.5 ± 5.4	23.4 ± 5.2	22.6 ± 5.0	<0.001
Time since last birth (y)[3]	10.1 ± 7.5	9.8 ± 7.6	10.4 ± 7.6	0.01	9.9 ± 8.1	9.8 ± 7.3	10.3 ± 7.5	0.003
Vigorous exercise (h/wk)	1.5 ± 2.4	1.7 ± 2.5	1.7 ± 2.6	0.005	2.3 ± 2.9	1.6 ± 2.4	1.2 ± 2.1	<0.001
Education (y)	14.8 ± 1.8	15.0 ± 1.7	14.8 ± 1.7	0.06	15.1 ± 1.7	14.9 ± 1.7	14.7 ± 1.8	<0.001
Oral contraceptive use (y)	4.6 ± 4.7	4.7 ± 4.6	4.5 ± 4.5	0.06	4.4 ± 4.7	4.7 ± 4.7	4.7 ± 4.6	0.004
Current use of progestin-only injectables or implants (%)	3.5	2.8	2.8	0.65	2.4	2.9	3.0	0.15
Alcohol intake (drinks/wk)	1.8 ± 3.8	1.3 ± 2.6	1.1 ± 2.6	<0.001	1.3 ± 2.8	1.2 ± 2.6	1.4 ± 3.0	0.11
Dairy intake (servings/wk)	9.7 ± 11.3	7.9 ± 7.7	5.0 ± 5.6	<0.001	13.0 ± 13.2	6.7 ± 5.8	4.2 ± 4.1	<0.001
Glycemic load	74.0 ± 8.3	96.8 ± 2.4	125.1 ± 12.4	—	90.9 ± 16.2	99.7 16.7	108.3 ± 22.0	<0.001
Glycemic index	54.0 ± 4.0	55.3 ± 3.1	57.0 ± 2.8	<0.001	50.5 ± 2.1	55.6 ± 0.44	59.6 ± 1.35	—
Diabetes (%)	4.9	2.7	2.5	<0.001	3.2	3.0	3.0	0.53
Current smoker (%)	17.0	13.4	14.2	0.003	11.2	12.8	18.4	<0.001
Married (%)	38.3	41.4	39.1	0.59	40.0	40.3	38.2	0.14
Household income <$25,000 in 2003 (%)	13.1	9.2	11.5	0.02	9.0	10.3	13.0	<0.001
White collar occupation (%)	56.7	60.9	58.7	0.08	63.1	59.6	54.7	<0.001
Region of residence in USA (%)								
West	21.6	17.8	15.4	<0.001	21.0	19.0	14.6	<0.001
Midwest	24.7	23.3	19.8	<0.001	21.2	21.7	23.4	0.005
Northeast	22.2	26.8	31.7	<0.001	29.0	28.5	25.4	<0.001
South	31.5	32.2	33.2	0.25	28.7	30.8	36.6	<0.001

[1] With the exception of age, means and percentages were standardized to the age distribution of the cohort in 1997.
[2] *P* values from the age-adjusted test for linear trend across all quintiles.
[3] Restricted to 12,452 participants who were parous at the start of follow-up.

Restriction criteria

Follow-up for UL incidence began in March 1997, the start of the second questionnaire cycle, because the self-reported method of diagnosis was first elicited on the 1999 questionnaire. We restricted the sample to premenopausal women with intact uteri because UL is rare after menopause. Of the 53,153 women who completed the 1997 questionnaire, we excluded women who were postmenopausal (n = 16,594). Women who reported a UL diagnosis before 1997 (n = 10,626), who reported UL without information on year of diagnosis (n = 125) or method of diagnosis (n = 120), who did not complete a follow-up questionnaire (n = 980), or who had missing data on key covariates (n = 582) were excluded. Women who did not complete the 1995 FFQ, who left >10 FFQ items blank (n = 418), or who had implausible total energy intake values on the 1995 FFQ (<500 or ≥3800 kcal/d, n = 1,847) were also excluded, which left a final sample of 21,861 premenopausal women at risk of UL in 1997. Those excluded had lower educational attainment than did respondents, but were similar with respect to age, parity, age at menarche, and other determinants of UL risk.

Data analysis

Each participant contributed person-time from 1 March 1997 until the diagnosis of UL, menopause, death, loss to follow-up, or end of follow-up (1 March 2007), whichever came first. We used Cox regression models, stratified by age and time period, to estimate incidence rate ratios (IRRs) and 95% CIs for the associations of interest (53). Covariates that changed over time (eg, BMI and parity) were treated as time-dependent variables in the analysis.

We assessed the 1995 FFQ data in relation to incidence of UL occurring during 1997–2001 and the average of 1995 and 2001 in relation to UL incidence during 2001–2007, because the average is considered a better measure of long-term intake (54). For the 5437 participants who had missing or implausible data for the 2001 FFQ, we used 1995 FFQ data for the entire incident period. We divided women into groups based on quintiles of dietary exposure, and we conducted 2-sided tests for linear trend by modeling the median intake by quintile as a continuous variable. We also examined the possibility of a nonlinear relation of GI and GL with UL risk using restricted cubic splines (55). Tests for nonlinearity were computed by using the likelihood ratio test, comparing the model with the linear term to the model with the linear and spline terms (56).

We constructed 2 sets of multivariable models: model 1 controlled for age (1-y intervals), questionnaire cycle (1997–1999, 1999–2001, 2001–2003, 2003–2005, and 2005–2007), and total energy intake (quintiles)—strong potential confounders of the diet-UL associations. Model 2 additionally controlled for

TABLE 2
Risk of ultrasound- or hysterectomy-confirmed uterine leiomyomata in relation to dietary glycemic load and glycemic index: the Black Women's Health Study, United States, 1997–2007[1]

	Quintile of dietary intake					*P* for linear trend[2]
	1	2	3	4	5	
Glycemic load						
Cases	1092	1175	1202	1156	1175	
Person-years	32,573	32,503	32,470	32,539	32,519	
Model 1: IRR (95% CI)[3]	1.00[4]	1.09 (1.00, 1.18)	1.12 (1.03, 1.21)	1.07 (0.98, 1.16)	1.09 (1.00, 1.18)	0.11
Model 2: IRR (95% CI)[5]	1.00[4]	1.07 (0.98, 1.16)	1.08 (0.99, 1.17)	1.02 (0.94, 1.12)	1.03 (0.94, 1.12)	0.96
Glycemic index						
Cases	1088	1154	1147	1222	1189	
Person-years	32,589	32,534	32,519	32,455	32,507	
Model 1: IRR (95% CI)[3]	1.00[4]	1.07 (0.99, 1.16)	1.07 (0.99, 1.17)	1.15 (1.06, 1.24)	1.11 (1.02, 1.21)	0.003
Model 2: IRR (95% CI)[5]	1.00[4]	1.06 (0.98, 1.16)	1.05 (0.96, 1.15)	1.12 (1.02, 1.22)	1.09 (0.99, 1.19)	0.04

[1] IRR, incidence rate ratio.
[2] *P* values from the 2-sided test for linear trend, modeling the quintile median as a continuous variable.
[3] Adjusted for age, questionnaire cycle, and energy intake.
[4] Reference group.
[5] Adjusted for age, questionnaire cycle, total energy intake, servings of dairy foods, age at menarche, current use of hormonal contraception, BMI, diabetes, current alcohol consumption, cigarette smoking, vigorous physical activity, current US region of residence, marital status, household income, occupation, educational level, parity, age at first birth, and years since last birth.

dietary, reproductive, hormonal, and lifestyle factors shown to be associated with UL in our data set (57–60) or in other studies (8, 61) and socioeconomic factors that might influence both diet quality and detection of UL (62). These additional factors were as follows: age at menarche (11, 12–13, 14, and ≥15 y), parity (0, 1, 2, 3, and ≥4 births), age at first birth (<20, 20–24, 25–29, and ≥30 y), years since last birth (<5, 5–9, 10–14, 15–19, and ≥20), current use of hormonal contraception (combined oral contraceptives, progestin-only injectable or implant use, and none), BMI (<20, 20–24, 25–29, 30–34, and ≥35), physician-diagnosed diabetes (yes and no), current alcohol consumption (<1, 1–6, and ≥7 drinks/wk), cigarette smoking (current, former, and never smoker), vigorous physical activity (0, <1, 1, 2, 3–4, 5–6, and ≥7 h/wk), current region of residence (Northeast, South, Midwest, West, and outside US), educational attainment (≤12, 13–15, 16, and ≥17 y), marital status (single, married, and divorced/separated/widowed), household income (≤$25,000, $25,001–50,000, $50,001–100,000, and >$100,000), and occupation (white-collar, nonwhite collar, and not employed/other). Because dairy contributes to both GI and GL and is inversely associated with UL in our cohort (63), model 2 also controlled for servings of dairy foods (<1, 1–1.9, 2–3.9, and ≥4 servings/d). All analyses were carried out by using SAS statistical software (version 9.1) (64).

In subgroup analyses, we examined whether associations between GI and GL and UL risk were modified by selected participant characteristics (age, parity, education, vigorous physical activity, and BMI) or method of diagnosis (surgery or ultrasound). We conducted tests for statistical interaction using the likelihood ratio test, comparing model 2 with a model that included an interaction term between the potential effect modifier (categorical variable) and the quintile median (continuous variable). Because women younger than 35 y are less likely to be misclassified with respect to case status (5), we evaluated effect modification by age (<35 compared with ≥35 y). We also assessed differences in our associations by parity, because parity is an important protective factor for UL (8, 10, 13) and has been shown to modify the relation between diet and other reproductive outcomes, such as ovulatory infertility (65). We stratified on markers of insulin resistance, overweight (BMI: 25–29) or obesity (BMI ≥ 30), and vigorous physical activity, because several studies noted a stronger association of GL and endometrial cancer in obese women (37, 38) or in overweight women with low physical activity (66). Finally, we stratified by education because our FFQ validation study found moderately higher correlations between FFQ and 24-h recall in college-educated women for some nutrients, including calcium and β-carotene (44).

RESULTS

GI and GL were moderately positively correlated in our cohort (Spearman correlation coefficient = 0.32, $P < 0.0001$). Characteristics of the sample by quintile of GL and GI are shown in **Table 1**. Both GL and GI were inversely related to age, dairy intake, and residence in the West and Midwest US. GL was inversely associated with physician-diagnosed diabetes and smoking and positively associated with residence in the Northeast. GI was positively associated with BMI, smoking, and residence in the South and inversely associated with vigorous physical activity, education, white collar occupation, and household income.

There were 5800 incident cases of UL diagnosed by ultrasound or surgery during 162,604 person-years of follow-up from 1997 to 2007. Overall, there was no association of GL with UL risk (**Table 2**). GI was weakly associated with UL risk overall (P = 0.04; IRR for highest quintile relative to the lowest = 1.09; 95% CI: 0.99, 1.19). Visually, there was little evidence of a positive monotonic increase in UL risk with each successive quintile of GI, although the restricted cubic spline analyses did not show evidence of a nonlinear association (data not shown).

Results for the associations of GL and GI with UL risk stratified by age and education are shown in **Tables 3** and **4**.

TABLE 3
Risk of ultrasound- or hysterectomy-confirmed uterine leiomyomata in relation to dietary glycemic load, stratified by age and education: the Black Women's Health Study, 1997–2007[1]

	Quintile of glycemic load					*P* for linear trend[2]	*P* for statistical interaction[3]
	1	2	3	4	5		
Age <35 y							
Cases	287	370	395	403	470		
Person-years	10,721	11,489	12,581	13,120	14,105		
Model 1: IRR (95% CI)[4]	1.00[5]	1.20 (1.03, 1.40)	1.19 (1.02, 1.38)	1.16 (1.00, 1.35)	1.28 (1.11, 1.48)	0.005	
Model 2: IRR (95% CI)[6]	1.00[5]	1.19 (1.02, 1.39)	1.13 (0.97, 1.32)	1.09 (0.93, 1.26)	1.18 (1.02, 1.37)	0.15	0.04
Age ≥35 y							
Cases	805	805	807	753	705		
Person-years	21,852	21,014	19,889	19,419	18,414	0.95	
Model 1: IRR (95% CI)[4]	1.00[5]	1.05 (0.95, 1.16)	1.09 (0.99, 1.20)	1.03 (0.93, 1.14)	1.00 (0.91, 1.11)		
Model 2: IRR (95% CI)[6]	1.00[5]	1.03 (0.93, 1.14)	1.06 (0.96, 1.17)	0.99 (0.99, 1.10)	0.94 (0.85, 1.05)	0.19	
Education <16 y							
Cases	559	578	526	548	619		
Person-years	17,290	16,351	15,457	16,451	17,639		
Model 1: IRR (95% CI)[4]	1.00[5]	1.10 (0.98, 1.24)	1.07 (0.95, 1.20)	1.04 (0.93, 1.17)	1.10 (0.98, 1.24)	0.22	
Model 2: IRR (95% CI)[6]	1.00[5]	1.08 (0.96, 1.21)	1.02 (0.91, 1.16)	0.98 (0.87, 1.11)	1.03 (0.92, 1.16)	0.99	0.90
Education ≥16 y							
Cases	533	597	676	608	556		
Person-years	15,284	16,152	17,013	16,088	14,880		
Model 1: IRR (95% CI)[4]	1.00[5]	1.07 (0.96, 1.21)	1.15 (1.02, 1.29)	1.09 (0.97, 1.22)	1.07 (0.95, 1.21)	0.31	
Model 2: IRR (95% CI)[6]	1.00[5]	1.06 (0.94, 1.20)	1.12 (1.00, 1.26)	1.05 (0.94, 1.18)	1.02 (0.90, 1.15)	0.97	

[1] IRR, incidence rate ratio.
[2] *P* values for the 2-sided test for linear trend, modeling the quintile median as a continuous variable.
[3] *P* values for the likelihood ratio test, comparing model 2 with a model that was further adjusted for the interaction between the binary exposure used for stratification and the glycemic load quintile median.
[4] Adjusted for age, questionnaire cycle, and energy intake.
[5] Reference group.
[6] Adjusted for age, questionnaire cycle, total energy intake, servings of dairy foods, age at menarche, current use of hormonal contraception, BMI, diabetes, current alcohol consumption, cigarette smoking, vigorous physical activity, current US region of residence, marital status, household income, occupation, educational level, parity, age at first birth, and years since last birth.

There was a positive association between GL and UL risk in women younger than age 35 y (multivariable-adjusted IRR: 1.18; 95% CI: 1.02, 1.37) for the highest compared with the lowest quintile of GL (*P* for trend = 0.15) (Table 3). There was some evidence of effect modification by age on the association between GL and UL risk: *P* for interaction = 0.04. GI was positively associated with UL risk in college-educated women (Table 4). The multivariable-adjusted IRR was 1.18 (95% CI: 1.04, 1.34; *P* for trend = 0.004) in a comparison of the highest with the lowest quintile of GI in college-educated women, and the comparable IRR was 1.00 (95% CI: 0.88, 1.14) in noncollege-educated women (*P* for interaction = 0.06). Finer stratification of the college-educated group found similar GI-UL associations in women with and without postgraduate education (data not shown). There were no substantial differences in IRRs across categories of vigorous physical activity, BMI, and parity (data not shown).

The results did not differ appreciably when we examined the cases confirmed by surgery separately from those confirmed by ultrasound, when we included cases detected by pelvic exam in the case group or when we stratified the analysis by time period (1997–2001 compared with 2001–2007) (data not shown). Furthermore, the results were similar when we restricted the sample to 16,097 women who reported having received a pelvic exam within the past 5 y and when we excluded women with prevalent or incident diabetes (n = 1276).

DISCUSSION

In this large prospective cohort study of US black women, dietary GI, but not GL, was associated with risk of UL overall. Whereas the linear trend for increasing quintile of GI was significant, the magnitude of the association was small. There was a positive association between GL and UL risk in young women aged <35 y and an association between GI and UL risk in college-educated women. Whether these differences in association were real or due to chance variation is unclear. UL is less likely to be misclassified in younger women (5), and women with more education may be better reporters of dietary intake (44, 67, 68). Thus, these 2 subgroups may include women among whom information bias is reduced. However, GI and GL did not show independent associations within the same subgroup analysis, and our assessment of 2 different exposure variables across multiple subgroups may have increased the potential for false-positive results. A recent cross-sectional study—in which all women were screened with ultrasound for the presence of UL—found no association between plasma concentrations of insulin and IGF-I and prevalence of UL in black women (31). Whereas a previous prospective study found evidence of an association between GL and endometrial cancer confined to women with low physical activity and high BMI (66), we found no evidence of effect modification by physical activity or BMI in stratified analyses.

TABLE 4
Risk of ultrasound- or hysterectomy-confirmed uterine leiomyomata in relation to dietary glycemic index, stratified by age and education: the Black Women's Health Study, 1997–2007[1]

	Quintile of glycemic index					*P* for linear trend[2]	*P* for statistical interaction[3]
	1	2	3	4	5		
Age <35 y							
Cases	327	356	390	422	430		
Person-years	10,931	1,1881	12,537	13,076	13,591		
Model 1: IRR (95% CI)[4]	1.00[5]	0.92 (0.79, 1.07)	1.01 (0.87, 1.17)	1.07 (0.92, 1.23)	1.07 (1.02, 1.23)	0.11	
Model 2: IRR (95% CI)[6]	1.00[5]	0.92 (0.79, 1.07)	0.99 (0.86, 1.16)	1.05 (0.90, 1.22)	1.04 (0.89, 1.21)	0.26	0.97
Age ≥35 y							
Cases	761	798	757	800	759		
Person-years	21,657	20,653	19,982	19,379	18,916		
Model 1: IRR (95% CI)[4]	1.00[5]	1.09 (0.99, 1.20)	1.07 (0.97, 1.19)	1.16 (1.05, 1.28)	1.11 (1.00, 1.22)	0.02	
Model 2: IRR (95% CI)[6]	1.00[5]	1.09 (0.98, 1.20)	1.06 (0.95, 1.17)	1.14 (1.02, 1.26)	1.09 (0.98, 1.22)	0.08	
Education <16 y							
Cases	471	544	550	645	620		
Person-years	14,539	15,417	16,900	17,681	18,651		
Model 1: IRR (95% CI)[4]	1.00[5]	1.10 (0.97, 1.24)	1.02 (0.90, 1.16)	1.15 (1.02, 1.29)	1.04 (0.92, 1.17)	0.36	
Model 2: IRR (95% CI)[6]	1.00[5]	1.08 (0.95, 1.22)	0.98 (0.86, 1.12)	1.10 (0.96, 1.25)	1.00 (0.88, 1.14)	0.98	0.06
Education ≥16 y							
Cases	617	610	597	577	569		
Person-years	18,050	17,117	15,619	14,774	13,856		
Model 1: IRR (95% CI)[4]	1.00[5]	1.04 (0.93, 1.17)	1.12 (1.00, 1.26)	1.15 (1.02, 1.29)	1.20 (1.07, 1.35)	0.0004	
Model 2: IRR (95% CI)[6]	1.00[5]	1.05 (0.93, 1.18)	1.12 (0.99, 1.25)	1.13 (1.00, 1.28)	1.18 (1.04, 1.34)	0.004	

[1] IRR, incidence rate ratio.
[2] *P* values for the 2-sided test for linear trend, modeling the quintile median as a continuous variable.
[3] *P* values for the likelihood ratio test, comparing model 2 with a model that was further adjusted for the interaction between the binary exposure used for stratification and the glycemic index quintile median.
[4] Adjusted for age, questionnaire cycle, and energy intake.
[5] Reference group.
[6] Adjusted for age, questionnaire cycle, total energy intake, servings of dairy foods, age at menarche, current use of hormonal contraception, BMI, diabetes, current alcohol consumption, cigarette smoking, vigorous physical activity, current US region of residence, marital status, household income, occupation, educational level, parity, age at first birth, and years since last birth.

Our study design had several strengths. We prospectively measured diet and known UL risk factors, thereby eliminating the potential for recall bias. We used a nutrient database that has rigorously evaluated its standard values of GI and GL (34, 69). A previous study using FFQ data from our cohort found a significant positive association of GI with risk of type 2 diabetes, suggesting low potential for exposure misclassification (45). The high rate of follow-up for each questionnaire period reduced the potential for bias from differential loss to follow-up. The large sample size and high number of incident cases provided excellent power to detect small effects and control for many putative risk factors for UL.

Our data analysis adjusted for many covariates because dietary factors correlate with other lifestyle factors, such as vigorous exercise and smoking, which may confound the association between diet and UL risk (61, 70). Dairy products were of particular interest because milk has been shown to be positively correlated with circulating IGF-I concentrations (71), and dairy products were inversely associated with UL in our cohort (63). However, associations of GI and GL with UL risk did not substantially change after adjustment for total dairy intake (data not shown), which suggests that dairy products are an unlikely confounder or mediator of our associations. GL was inversely associated with diabetes at baseline in our cohort (likely related to low-carbohydrate diets prescribed to diabetic persons), and diabetes was inversely associated with risk of UL in 3 of 4 studies that examined this relation (31, 60, 72, 73). The small number of UL cases who also had diabetes in our young cohort sample precluded a meaningful examination of whether diabetes modified the associations of UL with GI and GL.

A limitation of our study was that participants self-reported their UL diagnosis. However, our validation study confirmed 96% of UL diagnoses in the participants who released their medical records, and these cases were similar to cases who did not release their records with respect to reported symptoms, method of diagnosis, and predictors of UL (52). Because UL is often asymptomatic, true cases will have been missed. However, we expect any disease misclassification to be nondifferential because diet was assessed before the report of UL, and such misclassification usually results in bias toward the null (74). This could explain why we found a positive relation between GL and UL risk only among younger women, whose case status is less likely to be misclassified (5). Our case group likely represents women with symptomatic disease because most cases in the validation study (71%) reported symptoms before the initial diagnosis, a low percentage of cases (13%) were detected incidentally, and rates of UL diagnoses in our study are similar to rates for black women reported in other US studies (75).

Another limitation was error in measuring long-term nutrient intakes using FFQs, which would generally bias diet-disease associations toward the null. Given that our validation study

found greater accuracy in correlations between the FFQ and dietary recalls/records in more educated women, the positive GI-UL association in college-educated women may reflect reduced bias from nondifferential exposure misclassification (76). In addition, it may be more difficult to discern an association of dietary GL with UL in energy-adjusted analyses. Dietary GL is the product of dietary GI and carbohydrates, and isoenergetic comparisons of GL quintiles mix the effect of substituting a higher dietary GI with the effect of substituting the carbohydrate content for an isoenergetic quantity of fat and/or protein, which may produce different metabolic effects (77). However, protein and fat intakes were unrelated to UL risk in the BWHS, and adjustment for these factors did not change the results appreciably (data not shown).

In summary, we observed a small positive association of GI with UL risk overall and slightly stronger associations of GL with UL in younger women and GI with UL in college-educated women. Further studies of prospectively measured and validated dietary intake are needed to determine whether these findings reflect chance or real associations.

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REFERENCES

1. Wilcox LS, Koonin LM, Pokras R, Strauss LT, Xia Z, Peterson HB. Hysterectomy in the United States, 1988-1990. Obstet Gynecol 1994;83:549–55.
2. Farquhar CM, Steiner CA. Hysterectomy rates in the United States 1990-1997. Obstet Gynecol 2002;99:229–34.
3. Marshall LM, Spiegelman D, Barbieri RL, et al. Variation in the incidence of uterine leiomyoma among premenopausal women by age and race. Obstet Gynecol 1997;90:967–73.
4. Brett KM, Marsh JV, Madans JH. Epidemiology of hysterectomy in the United States: demographic and reproductive factors in a nationally representative sample. J Womens Health 1997;6:309–16.
5. Day Baird D, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol 2003;188:100–7.
6. Buttram VC, Reiter RC. Uterine leiomyomata: etiology, symptomatology, and management. Fertil Steril 1981;36:433–45.
7. Rein MS. Advances in uterine leiomyoma research: the progesterone hypothesis. Environ Health Perspect 2000;108:791–3.
8. Ross RK, Pike MC, Vessey MP, Bull D, Yeates D, Casagrande JT. Risk factors for uterine fibroids: reduced risk associated with oral contraceptives. Br Med J (Clin Res Ed) 1986;293:359–62.
9. Parazzini F, La Vecchia C, Negri E, Cecchetti G, Fedele L. Epidemiologic characteristics of women with uterine fibroids: a case-control study. Obstet Gynecol 1988;72:853–7.
10. Parazzini F, Negri E, La Vecchia C, Chatenoud L, Ricci E, Guarnerio P. Reproductive factors and risk of uterine fibroids. Epidemiology 1996;7:440–2.
11. Romieu I, Walker AM, Jick S. Determinants of uterine fibroids. Post Marketing Surveillance 1991;5:119–33.
12. Samadi AR, Lee NC, Flanders WD, Boring JR, Parris EB. Risk factors for self-reported uterine fibroids: a case-control study. Am J Public Health 1996;86:858–62.
13. Marshall LM, Spiegelman D, Goldman MB, et al. A prospective study of reproductive factors and oral contraceptive use in relation to the risk of uterine leiomyomata. Fertil Steril 1998;70:432–9.
14. Faerstein E, Szklo M, Rosenshein N. Risk factors for uterine leiomyoma: a practice-based case-control study. I. African-American heritage, reproductive history, body size, and smoking. Am J Epidemiol 2001;153:1–10.
15. Renehan AG, Zwahlen M, Minder C, O'Dwyer ST, Shalet SM, Egger M. Insulin-like growth factor (IGF)-I, IGF binding protein-3, and cancer risk: systematic review and meta-regression analysis. Lancet 2004;363:1346–53.
16. Peiris AN, Sothmann MS, Aiman EJ, Kissebah AH. The relationship of insulin to sex hormone-binding globulin: role of adiposity. Fertil Steril 1989;52:69–72.
17. Jones JI, Clemmons DR. Insulin-like growth-factors and their binding-proteins—biological actions. Endocr Rev 1995;16:3–34.
18. Baserga R, Sell C, Porcu P, Rubini M. The role of the IGF-I receptor in the growth and transformation of mammalian cells. Cell Prolif 1994;27:63–71.
19. Dunn SE, Kari FW, French J, et al. Dietary restriction reduces insulin-like growth factor I levels, which modulates apoptosis, cell proliferation, and tumor progression in p53-deficient mice. Cancer Res 1997;57:4667–72.
20. Resnicoff M, Abraham D, Yutanawiboonchai W, et al. The insulin-like growth factor I receptor protects tumor cells from apoptosis in vivo. Cancer Res 1995;55:2463–9.
21. van der Ven LT, Van Buul-Offers SC, Gloudemans T, et al. Modulation of insulin-like growth factor (IGF) action by IGF-binding proteins in normal, benign, and malignant smooth muscle tissues. J Clin Endocrinol Metab 1996;81:3629–35.
22. Strawn EY, Novy MJ, Burry KA, Bethea CL. Insulin-like growth factor I promotes leiomyoma cell growth in vitro. Am J Obstet Gynecol 1995;172:1837–44.
23. Boehm KD, Daimon M, Gorodeski IG, Sheean LA, Utian WH, Ilan J. Expression of the insulin-like and platelet-derived growth factor genes in human uterine tissues. Mol Reprod Dev 1990;27:93–101.
24. Giudice LC, Irwin JC, Dsupin BA, et al. Physiology: insulin-like growth factor (IGF), IGF binding protein (IGFBP), and IGF receptor gene expression and IGFBP synthesis in human uterine leiomyomata. Hum Reprod 1993;8:1796–806.
25. Englund K, Lindblom B, Carlstrom K, Gustavsson I, Sjoblom P, Blanck A. Gene expression and tissue concentrations of IGF-I in human myometrium and fibroids under different hormonal conditions. Mol Hum Reprod 2000;6:915–20.
26. Wei J, Chiriboga L, Mizuguchi M, Yee H, Mittal K. Expression profile of tuberin and some potential tumorigenic factors in 60 patients with uterine leiomyomata. Mod Pathol 2005;18:179–88.
27. Wolanska M, Bankowski E. An accumulation of insulin-like growth factor I (IGF-I) in human myometrium and uterine leiomyomas in various stages of tumour growth. Eur Cytokine Netw 2004;15:359–63.
28. Dixon D, He H, Haseman JK. Immunohistochemical localization of growth factors and their receptors in uterine leiomyomas and matched myometrium. Environ Health Perspect 2000;108:795–802.
29. Swartz CD, Afshari CA, Yu L, Hall KE, Dixon D. Estrogen-induced changes in IGF-I, Myb family and MAP kinase pathway genes in human uterine leiomyoma and normal uterine smooth muscle cell lines. Mol Hum Reprod 2005;11:441–50.
30. Zhao Y, Zhang W, Wang S. The expression of estrogen receptor isoforms alpha, beta and insulin-like growth factor-I in uterine leiomyoma. Gynecol Endocrinol 2008;24:549–54.
31. Baird DD, Travlos GS, Wilson R. Uterine leiomyomata in relation to insulin-like growth factor-I, insulin, and diabetes. Epidemiology 2009;20:604–10.
32. Jenkins DJ, Wolever TM, Taylor RH. Glycemic index of foods: a physiological basis for carbohydrate exchange. Am J Clin Nutr 1981;34:362–6.
33. Wolever TM, Nuttall FQ, Lee R. Prediction of the relative blood glucose response of mixed meals using the white bread glycemic index. Diabetes Care 1985;8:418–28.
34. Flood A, Subar AF, Hull SG, Zimmerman TP, Jenkins DJA, Schatzkin A. Methodology for adding glycemic load values to the National Cancer Institute Diet History Questionnaire database. J Am Diet Assoc 2006;106:393–402.
35. Brand-Miller JC, Thomas M, Swan V, Ahmad ZI, Petocz P, Colagiuri S. Physiological validation of the concept of glycemic load in lean young adults. J Nutr 2003;133:2728–32.
36. Folsom AR, Demissie Z, Harnack L. Glycemic index, glycemic load, and incidence of endometrial cancer: The Iowa Women's Health Study. Nutr Cancer 2003;46:119–24.

37. Silvera SA, Rohan TE, Jain M, Terry PD, Howe GR, Miller AB. Glycaemic index, glycaemic load and risk of endometrial cancer: a prospective cohort study. Public Health Nutr 2005;8:912–9.
38. Mulholland HG, Murray LJ, Cardwell CR, Cantwell MM. Dietary glycaemic index, glycaemic load and endometrial and ovarian cancer risk: a systematic review and meta-analysis. Br J Cancer 2008;99: 434–41.
39. Augustin LS, Polesel J, Bosetti C, et al. Dietary glycemic index, glycemic load and ovarian cancer risk: a case-control study in Italy. Ann Oncol 2003;14:78–84.
40. Silvera SA, Jain M, Howe GR, Miller AB, Rohan TE. Glycaemic index, glycaemic load and ovarian cancer risk: a prospective cohort study. Public Health Nutr 2007;10:1076–81.
41. Cust AE, Slimani N, Kaaks R, et al. Dietary carbohydrates, glycemic index, glycemic load, and endometrial cancer risk within the European Prospective Investigation into Cancer and Nutrition cohort. Am J Epidemiol 2007;166:912–23.
42. George SM, Mayne ST, Leitzmann MF, et al. Dietary glycemic index, glycemic load, and risk of cancer: a prospective cohort study. Am J Epidemiol 2009;169:462–72.
43. Block G, Hartman A, Naughton D. A reduced dietary questionnaire: development and validation. Epidemiology 1990;1:58–64.
44. Kumanyika Sk, Mauger D, Mitchell D, Phillips D, Wright H, Palmer J. Relative validity of food frequency questionnaire nutrient estimation in the Black Women's Health Study. Ann Epidemiol 2003;13:111–8.
45. Krishnan S, Rosenberg L, Singer M, et al. Glycemic index, glycemic load, and cereal fiber intake and risk of type 2 diabetes in US black women. Arch Intern Med 2007;167:2304–9.
46. Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. Am J Epidemiol 1986;124:17–27.
47. Stewart EA. Uterine fibroids. Lancet 2001;357:293–8.
48. Loutradis D, Antsaklis A, Creatsas G, et al. The validity of gynecological ultrasonography. Gynecol Obstet Invest 1990;29:47–50.
49. Dueholm M, Lundorf E, Hansen ES, Ledertoug S, Olesen F. Accuracy of magnetic resonance imaging and transvaginal ultrasonography in the diagnosis, mapping, and measurement of uterine myomas. Am J Obstet Gynecol 2002;186:409–15.
50. Rothman KJ, Greenland S, Lash TL. Modern epidemiology. New York, NY: Lippincott Williams & Wilkins, 2008.
51. Myers ER, Bastian LA, Havrilesky LJ, et al. Management of adnexal mass. Evid Rep Technol Assess (Full Rep) 2006;Feb:1–145.
52. Wise LA, Palmer JR, Harlow BL, et al. Reproductive factors, hormonal contraception and risk of uterine leiomyomata in African-American women: a prospective study. Am J Epidemiol 2004;159:113–23.
53. Cox DR, Oakes D. Analysis of survival data. London, United Kingdom: Chapman Hall, 1984.
54. Hu FB, Stampfer MJ, Rimm E, et al. Dietary fat and coronary heart disease: a comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. Am J Epidemiol 1999; 149:531–40.
55. Durrleman S, Simon R. Flexible regression models with cubic splines. Stat Med 1989;8:551–61.
56. Li R, Hertzmark E, Louie M, Chen L, Spiegelman D. The SAS LGTPHCURV8 Macro. Boston, MA: The Channing Laboratory, 2004.
57. Wise LA, Palmer JR, Harlow BL, et al. Risk of uterine leiomyomata in relation to tobacco, alcohol and caffeine consumption in the Black Women's Health Study. Hum Reprod 2004;19:1746–54.
58. Wise LA, Palmer JR, Rosenberg L, Adams-Campbell LL. Risk of uterine leiomyomata according to birthplace and geographic region in the Black Women's Health Study. Ann Epidemiol 2004;14:622 (abstr).
59. Wise LA, Palmer JR, Spiegelman D, et al. Influence of body size and body fat distribution on risk of uterine leiomyomata in U.S. black women. Epidemiology 2005;16:346–54.
60. Wise LA, Palmer JR, Stewart EA, Rosenberg L. Polycystic ovary syndrome and risk of uterine leiomyomata. Fertil Steril 2007;87:1108–15.
61. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. Association of physical activity with development of uterine leiomyoma. Am J Epidemiol 2007;165:157–63.
62. Darmon N, Drewnowski A. Does social class predict diet quality? Am J Clin Nutr 2008;87:1107–17.
63. Wise LA, Radin RG, Kumanyika S, Palmer JR, Rosenberg L. A prospective study of dairy intake and risk of uterine leiomyomata. Am J Epidemiol 2009;171:221–32.
64. SAS Institute Inc. SAS/STAT user's guide. Version 9.1. Cary, NC: SAS Institute, 2004.
65. Chavarro JE, Rich-Edwards JW, Rosner BA, Willett WC. A prospective study of dietary carbohydrate quantity and quality in relation to risk of ovulatory infertility. Eur J Clin Nutr 2009;63:78–86.
66. Larsson SC, Friberg E, Wolk A. Carbohydrate intake, glycemic index and glycemic load in relation to risk of endometrial cancer: a prospective study of Swedish women. Int J Cancer 2007;120:1103–7.
67. Krebs-Smith SM, Graubard BI, Kahle LL, Subar AF, Cleveland LE, Ballard-Barbash R. Low energy reporters vs others: a comparison of reported food intakes. Eur J Clin Nutr 2000;54:281–7.
68. Klesges RC, Eck LH, Ray JW. Who underreports dietary intake in a dietary recall? Evidence from the Second National Health and Nutrition Examination Survey. J Consult Clin Psychol 1995;63:438.
69. Subar AF, Midthune D, Kulldorff M, et al. Evaluation of alternative approaches to assign nutrient values to food groups in food frequency questionnaires. New York, NY: Oxford University Press, 2000:279–86.
70. Schwartz SM. Epidemiology of uterine leiomyomata. Clin Obstet Gynecol 2001;44:316–26.
71. Holmes MD, Pollak MN, Willett WC, Hankinson SE. Dietary correlates of plasma insulin-like growth factor I and insulin-like growth factor binding protein 3 concentrations. Cancer Epidemiol Biomarkers Prev 2002;11:852–61.
72. Faerstein E, Szklo M, Rosenshein NB. Risk factors for uterine leiomyoma: a practice-based case-control study. II. Atherogenic risk factors and potential sources of uterine irritation. Am J Epidemiol 2001;153:11–9.
73. Templeman C, Marshall SF, Clarke CA, et al. Risk factors for surgically removed fibroids in a large cohort of teachers. Fertil Steril 2009;92: 1436–46.
74. Greenland S. Analysis of polytomous exposures and outcomes. In: Rothman KJ, Greenland S, Lash TL, eds. Modern epidemiology. Philadelphia, PA: Lippincott Williams & Wilkins, 2008:303–27.
75. Wise LA, Palmer JR, Stewart EA, Rosenberg L. Age-specific incidence rates for self-reported uterine leiomyomata in the Black Women's Health Study. Obstet Gynecol 2005;105:563–8.
76. Willett WC. Nature of variarion in diet. In: Willett WC, ed. Nutritional epidemiology. 2nd ed. New York, NY: Oxford University Press, 1998: 33–49.
77. Barclay AW, Brand-Miller JC, Wolever T. Glycemic index, glycemic load, and glycemic response are not the same. Diabetes Care 2005;28: 1839–40.