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Dietary glycemic load assessed by food-frequency questionnaire in relation to plasma high-density-lipoprotein cholesterol and fasting plasma triacylglycerols in postmenopausal women[1–3]

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ABSTRACT

Background: In metabolic studies, both greater carbohydrate intakes and higher glycemic indexes (GIs) raise fasting triacylglycerol concentrations. In epidemiologic studies, dietary glycemic load (GL) is positively associated with risk of coronary artery disease and type 2 diabetes.

Objective: We examined both the physiologic relevance of GI and GL and the ability of dietary questionnaires to measure these variables.

Design: In the Nurses' Health Study, we measured plasma triacylglycerol concentrations in fasting blood samples from 185 healthy postmenopausal women and HDL-cholesterol concentrations in an additional 95 nonfasting samples. Dietary carbohydrate, GI, and GL were assessed by use of semiquantitative food-frequency questionnaires. The cross-sectional associations between these 3 variables and plasma triacylglycerol and HDL were assessed, with adjustment for potential confounding factors.

Results: For the lowest and highest quintiles of GL, the multivariate-adjusted geometric mean triacylglycerol concentrations were 0.98 and 1.75 mmol/L (87 and 155 mg/dL; P for trend <0.001). Both overall GI (P for trend = 0.03) and carbohydrate (P for trend <0.01) contributed independently to the strong positive association between GL and fasting triacylglycerol concentrations. GL was also inversely associated with HDL-cholesterol concentrations. For the lowest and highest quintiles of GL, the mean HDL-cholesterol concentrations were 1.50 and 1.34 μmol/L (58 and 52 mg/dL; P for trend = 0.03). The relation between GL and fasting triacylglycerol concentrations differed significantly by body mass index (BMI; in kg/m^2) categories ($P < 0.001$ for interaction). For the lowest to the highest quintiles of GL, the mean triacylglycerol concentrations were 0.92 and 2.24 mmol/L (81 and 198 mg/dL) in women with BMIs >25 (P for trend <0.001) and 1.02 and 1.42 mmol/L (90 and 126 mg/dL) in women with BMIs ≤ 25 (P for trend <0.001).

Conclusion: These data support the physiologic relevance of the GL as a potential risk factor for coronary artery disease in free-living women, particularly those prone to insulin resistance. These findings also document the ability of a semiquantitative food-frequency questionnaire to assess dietary GIs and GLs. *Am J Clin Nutr* 2001;73:560–6.

KEY WORDS Triacylglycerol, high-density lipoprotein, carbohydrate, glycemic index, glycemic load, women, dietary questionnaire, dietary assessment, coronary artery disease

INTRODUCTION

Early research on the classic diet-heart hypothesis focused almost exclusively on dietary fats (1–3). The results of animal experiments (4), cross-cultural studies (5), and metabolic studies (6, 7) relating dietary fats to serum lipids suggest that diets high in saturated fat and cholesterol increase the risk of coronary artery disease (CAD). These observations led to recommendations in the United States and elsewhere to replace total dietary fat with carbohydrate (8). However, increased intake of carbohydrates can raise fasting plasma triacylglycerol concentrations (3, 9–12) and reduce HDL-cholesterol concentrations (3, 10, 13), creating a lipid profile that would be predicted to increase the risk of CAD (14–17). Carbohydrates differ in their ability to increase blood glucose. The glycemic index value of each carbohydrate-containing food is a measure of how much that food raises blood glucose in comparison with a standard food of either glucose or white bread per unit of carbohydrate. The glycemic index is thus an indicator of carbohydrate quality. Previous studies showed that even when the amount of carbohydrate is held constant, foods with a higher glycemic index increase fasting triacylglycerol concentrations (18, 19).

Because both the amount and the quality of carbohydrates in a food are important determinants of fasting plasma triacylglycerol concentrations and the postprandial plasma glucose response, we proposed the glycemic load as a measure that incorporates both the quantity and the quality of the dietary carbohydrates

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consumed. The glycemic load of a specific food—calculated as the product of that food's carbohydrate content and its glycemic index value—has direct physiologic meaning in that each unit can be interpreted as the equivalent of 1 g carbohydrate from white bread (or glucose depending on the reference used in determining the glycemic index). The concept of glycemic load addresses the concern about rating foods as good or bad solely on the basis of their glycemic index (20). For example, although the glycemic index for carrots is reported to be as high as 131 (21), the glycemic load for one serving of carrots is small because the amount of carbohydrate in one serving of carrots is minimal (≈7 g carbohydrate). Indeed, ≈700 g carrots (which provides 50 g carbohydrate) must be consumed to produce an incremental glucose response 1.31 times that of 100 g white bread containing 50 g carbohydrate.

We reported recently that a high dietary glycemic load is associated directly with increased risk of CAD (22) and type 2 diabetes (23, 24). Nevertheless, the physiologic relevance of the glycemic index for mixed meals and the ability of a food-frequency questionnaire to measure dietary glycemic load remain contentious (25–27). In this study we evaluated the relations of dietary glycemic load assessed by a food-frequency questionnaire to plasma concentrations of HDL and triacylglycerol in 280 apparently healthy postmenopausal women. Documentation of direct associations between dietary glycemic load and plasma lipid concentrations would support the physiologic relevance of dietary glycemic load and glycemic index for predicting risk of CAD and would also provide evidence of the validity of assessing dietary glycemic load.

SUBJECTS AND METHODS

Nurses' Health Study subjects and blood sample collection

The Nurses' Health Study (NHS) cohort was established in 1976 when 121 700 female registered nurses between the ages of 30 and 55 y answered a mailed questionnaire about their medical history and lifestyle. The cohort has since been followed up every 2 y to assess risk factors and incident diseases. In 1989–1990 we collected blood samples from 32 826 NHS participants who were 43–69 y of age at the time. As described previously in detail (28, 29), we sent each woman a kit containing all the supplies needed for blood collection plus a supplemental questionnaire about menopausal status, recent postmenopausal hormone use, time since last meal, and time of day of blood sampling. Participants arranged to have their blood drawn and then mailed the whole-blood sample cooled with an enclosed ice pack via overnight mail. We previously documented the stability of these blood samples during the period of transport (28, 29). After they were received in our laboratory, the samples were centrifuged (20 min, 1320.6375 × *g*, 4 °C), divided, and frozen in the vapor phase of liquid nitrogen freezers (−130 °C or colder). A total of 280 women were included in this analysis, all of whom were control subjects from 2 nested case-control studies of breast cancer and myocardial infarction. All 280 women were postmenopausal (ie, no menses for ≥12 mo before blood sampling) and had not used postmenopausal hormones for ≥3 mo before the blood collection. They also did not have previously diagnosed cancer (except nonmelanoma skin cancer), cardiovascular disease, or diabetes and were not taking any cholesterol-lowering drugs. Triacylglycerol concentrations were measured only in the overnight fasting plasma samples provided by 185 women. This study was approved by the Institutional Review Board of Brigham and Women's Hospital, Boston.

Assays for HDL and triacylglycerol

Plasma HDL cholesterol and fasting plasma triacylglycerols were measured enzymatically with a Hitachi 704 Analyzer (Boehringer Mannheim Diagnostics, Indianapolis) after precipitation of other lipoproteins with a manganese chloride–heparin solution (30). These assays were analyzed in the lipid research laboratory of Brigham and Women's Hospital. This laboratory participates in the Lipid Standardization Program of the Centers for Disease Control and Prevention–National Heart, Lung, and Blood Institute (31). The CVs for these assays were 2.7% for HDL and 1.8% for triacylglycerol.

Assessment of diet by a semiquantitative food-frequency questionnaire

Dietary intake was measured in 1986 and 1990 with a semiquantitative food-frequency questionnaire (SFFQ). For each food, a commonly used unit or portion size (eg, one slice of bread) was specified and each participant was asked how often on average during the previous year she had consumed that amount. Nine responses were possible, ranging from "never" to "six or more times per day." Nutrient scores were computed by multiplying the frequency of consumption of each unit of food from the SFFQ by the nutrient content of the specified portion size according to the food-composition tables of the US Department of Agriculture (32) and other sources. A full description of the SFFQ and of the procedures for calculating nutrient intake, as well as data on reproducibility and validity in this cohort, were reported previously (33, 34). The correlation coefficient for energy-adjusted carbohydrate intake between the SFFQ and a 7-d diet record was 0.73 (34). The performance of the SFFQ for assessing individual foods high in carbohydrate was also documented previously (35, 36). For example, correlation coefficients were 0.71 for white bread, 0.77 for dark bread, 0.66 for potatoes, and 0.94 for yogurt (35).

Calculation of dietary glycemic load

We calculated each food's glycemic load by multiplying the carbohydrate content of one serving by the food's glycemic index value (20, 22, 37). For example, the glycemic load per serving of cooked potatoes was 38, which was the product of the glycemic index (102%) and the number of grams of carbohydrate per serving of potatoes (37 g). We then multiplied this glycemic load value by the frequency of consumption (1 time/d = 1, 2–3 times/d = 2.5, etc) and summed these products over all food items to produce the dietary glycemic load. Dietary glycemic load thus represents the quality and quantity of carbohydrates and their interaction. (The multiplication means that a higher glycemic index will have a greater effect at higher carbohydrate intakes.) Each unit of dietary glycemic load represents the equivalent of 1 g carbohydrate from white bread. Additionally, the overall dietary glycemic index, a variable representing the overall quality of carbohydrate intake for each participant, was created by dividing the dietary glycemic load by the total amount of carbohydrate consumed. By representing the dietary glycemic load per unit of carbohydrate, this measure essentially matches carbohydrate contents gram by gram and thus reflects the overall quality of carbohydrate intake in a whole diet. The formula for the calculation of overall dietary glycemic index is the following:

Overall dietary glycemic index =

$$\sum_{i=1}^{n} \mathrm{GI}_i \times \mathrm{CHO}_i \times \mathrm{FPD}_i / \sum_{i=1}^{n} \mathrm{CHO}_i \times \mathrm{FPD}_i \qquad (1)$$

where GI_i is the glycemic index for food i, CHO_i is the carbohydrate content in food i (grams per serving), and FPD_i is the frequency of servings of food i per day during the past year. The numerator is dietary glycemic load and the denominator is total carbohydrate intake. Thus, overall dietary glycemic index can be considered as the weighted average of the glycemic index values of all carbohydrate-containing foods, with the weight being the amount of carbohydrate consumed. In the current analysis, dietary variables from the 1986 and the 1990 SFFQs were averaged for each woman to reduce within-person variation.

Statistical analysis

We first calculated the means (±SDs) and proportions of covariates for this sample of women. We determined whether the plasma concentrations of HDL and fasting triacylglycerol were distributed normally. We treated each major dietary variable (ie, dietary glycemic load, overall dietary glycemic index, and carbohydrate intake) as either continuous or categorical (by quintiles) variables. Using multiple linear regression to adjust for potential confounding factors including age, parental family history of myocardial infarction before the age of 60 y, family history of diabetes, body mass index (BMI; in kg/m^2) at the age of 18 y, weight change since the age of 18 y, smoking status, alcohol intake, level of physical activity, and intakes of dietary fiber, protein, and total energy, we calculated the changes in plasma HDL and fasting triacylglycerol concentrations associated with 25-unit changes in glycemic load, which correspond to ≈2 slices white bread. In addition, we calculated the mean plasma HDL and fasting triacylglycerol concentrations according to quintiles of dietary glycemic load, overall dietary glycemic index, or total carbohydrate intake by using multiple linear regression. We also calculated the adjusted geometric means by first regressing the natural logarithm of HDL or triacylglycerol concentrations on dietary variables and then exponentiating the resulting mean logarithmic HDL or triacylglycerol concentrations. The robust variance was used to ensure valid inference even if the regression residuals were not normally distributed (38). Statistical analyses were conducted with SAS software (version 6; SAS Institute Inc, Cary, NC). The effect of a high–glycemic load diet is most pronounced in the setting of increased insulin resistance, particularly with increased BMI (11, 22, 39). We therefore repeated several of the analyses with the subjects stratified by BMI (> or <25).

RESULTS

The 280 postmenopausal women in the study ranged in age from 45 to 70 y; their mean age was 63 ± 5 y. Their reported mean carbohydrate intake was 198 ± 27 g/d. The average dietary glycemic load was 147 ± 23 and the average overall dietary glycemic index was 75 ± 4. The women's mean BMI was 26.3 ± 4.5, their mean plasma HDL concentration was 1.47 ± 0.43 mmol/L (56.9 ± 16.5 mg/dL), and their mean fasting triacylglycerol concentration was 1.41 ± 0.77 mmol/L (125 ± 68 mg/dL). About 20% of the participants were current smokers, 11% had a parental family history of myocardial infarction before the age of 60 y, and 19% had a family history of diabetes.

The unadjusted mean concentrations of plasma HDL decreased and those of fasting plasma triacylglycerol increased across quintiles of dietary glycemic load, overall dietary glycemic index, and total carbohydrate intake. For increasing quintiles of dietary glycemic load, the corresponding mean HDL-cholesterol concentrations were 1.55, 1.53, 1.50, 1.37, and 1.37 mmol/L (60, 59, 58, 53, and 53 mg/dL; P for trend = 0.02); mean triacylglycerol concentrations were 1.27, 1.33, 1.22, 1.41, and 1.74 mmol/L (112, 118, 108, 125, and 154 mg/dL; P for trend = 0.01). Similar relations were observed for overall dietary glycemic index or carbohydrate intake and triacylglycerol and HDL concentrations, albeit of lower magnitude.

Because the distributions of the plasma HDL and fasting plasma triacylglycerol concentrations were skewed to the right, we calculated their geometric mean concentrations by quintiles of dietary glycemic load, overall dietary glycemic index, and carbohydrate intake by using natural log transformations of plasma HDL and fasting plasma triacylglycerol concentrations. In multivariate analyses, dietary glycemic load, overall dietary glycemic index, and total carbohydrate intake were each inversely related to plasma HDL concentrations and positively related to fasting plasma triacylglycerol concentrations (**Table 1**). For the lowest and highest quintiles of dietary glycemic load, the multivariate-adjusted geometric mean HDL-cholesterol concentrations were 1.5 and 1.34 mmol/L (58 and 52 mg/dL), whereas the geometric mean triacylglycerol concentrations were 0.99 and 1.74 mmol/L (87 and 155 mg/dL). After further adjustment for carbohydrate intake, dietary glycemic load remained strongly positively associated with fasting triacylglycerol (P for trend = 0.03) and still tended to be inversely associated with the HDL-cholesterol concentration (P for trend = 0.06). In a multivariate model adjusting for the same covariates and treating dietary glycemic load as a continuous variable, a 25-unit increment in dietary glycemic load was associated with a 0.0303-mmol/L (1.17-mg/dL) reduction in HDL (P for trend = 0.02) and a 0.0284-mmol/L (2.51-mg/dL) increase in fasting triacylglycerol (P for trend < 0.001).

For the lowest and highest quintiles of overall dietary glycemic index, the multivariate-adjusted geometric mean HDL-cholesterol concentrations were 1.45 and 1.29 mmol/L (56 and 50 mg/dL) and the geometric mean triacylglycerol concentrations were 1.16 and 1.37 mmol/L (103 and 120 mg/dL). For lowest and highest quintiles of carbohydrate intake, the multivariate-adjusted geometric mean HDL-cholesterol concentrations were 1.42 and 1.37 mmol/L (55 and 53 mg/dL) and the geometric mean triacylglycerol concentrations were 1.10 and 1.59 mmol/L (97 and 141 mg/dL).

The relation between dietary glycemic load and fasting plasma triacylglycerol concentrations differed significantly by BMI categories (P < 0.001 for interaction), with different slopes for the regression lines for different BMI categories. There were 139 women (94 for whom fasting plasma samples were available) with BMIs >25. The dose-response gradient between dietary glycemic load and fasting triacylglycerol was stronger in women with BMIs >25 (**Figure 1**). For the lowest to the highest quintiles of dietary glycemic load, the multivariate-adjusted geometric mean triacylglycerol concentrations were 0.92 and 2.24 mmol/L (81 and 198 mg/dL) in women with BMIs >25 (P for trend < 0.001) and 1.02 and 1.42 mmol/L (90 and 126 mg/dL) in women with BMIs ≤25 (P for trend <0.001). The dose-response

TABLE 1
Geometric mean plasma concentrations of HDL and triacylglycerol according to energy-adjusted dietary glycemic load, glycemic index, and carbohydrate intake in apparently healthy postmenopausal women in the Nurses' Health Study[1]

Dietary variables	HDL	*P* for trend	Fasting triacylglycerol	*P* for trend
	μmol/L		*mmol/L*	
Quintile of glycemic load[2]				
Q1 [117]	1.50 (1.40, 1.60)		0.99 (0.84, 1.14)	
Q2 [134]	1.47 (1.37, 1.60)		1.06 (0.89, 1.28)	
Q3 [147]	1.42 (1.27, 1.55)	0.03	1.10 (0.92, 1.31)	<0.001
Q4 [159]	1.29 (1.19, 1.42)		1.36 (1.16, 1.59)	
Q5 [180]	1.34 (1.24, 1.45)		1.74 (1.46, 2.07)	
Quintile of glycemic index[2]				
Q1 [68]	1.45 (1.32, 1.53)		1.16 (0.99, 1.36)	
Q2 [73]	1.42 (1.32, 1.53)		1.20 (1.02, 1.41)	
Q3 [75]	1.42 (1.29, 1.58)	0.10	1.14 (0.96, 1.34)	0.03
Q4 [77]	1.40 (1.32, 1.53)		1.27 (1.08, 1.47)	
Q5 [81]	1.29 (1.19, 1.42)		1.37 (1.13, 1.64)	
Quintile of carbohydrate intake (g/d)[2]				
Q1 [162]	1.42 (1.32, 1.55)		1.10 (0.93, 1.38)	
Q2 [184]	1.40 (1.24, 1.58)		1.06 (0.89, 1.24)	
Q3 [198]	1.40 (1.29, 1.50)	0.76	1.16 (0.97, 1.38)	0.005
Q4 [212]	1.40 (1.32, 1.50)		1.25 (1.05, 1.50)	
Q5 [238]	1.37 (1.27, 1.47)		1.59 (1.34, 1.89)	

[1] 95% CI in parentheses. n = 56/quintile for HDL; n = 37/quintile for triacylglycerol. All models were adjusted simultaneously for age (5-y categories), laboratory batch (3 batches), time of day of blood draw (5 categories), parental family history of myocardial infarction before the age of 60 y (yes or no), family history of diabetes (yes or no), BMI at the age of 18 y (4 categories), weight change since the age of 18 y (7 categories), cigarette smoking (never, past, or current), alcohol intake (4 categories), physical activity (h/wk in 5 categories), protein intake (in quintiles), dietary fiber (in quintiles), and total energy intake (in quintiles). Glycemic load was defined as an indicator of blood glucose induced by an individual's total carbohydrate intake. Each unit of glycemic load represents the equivalent of 1 g carbohydrate from white bread. To convert HDL in mmol/L to mg/dL, divide by 0.02586. To convert triacylglycerol in mmol/L to mg/dL, divide by 0.0113.

[2] Mean value for each quintile in brackets.

gradients between dietary glycemic load and plasma HDL concentrations also differed somewhat by BMI categories, albeit with less magnitude and not significantly.

DISCUSSION

In this sample of 280 apparently healthy postmenopausal women, both the quantity and quality (as measured by overall dietary glycemic index) of carbohydrate intake were directly related to plasma HDL and fasting plasma triacylglycerol concentrations. Dietary glycemic load appeared to best capture the combined effects of the quantity and quality of the carbohydrate consumed. In a comparison of the 2 extreme quintiles of intake, the adjusted geometric mean plasma HDL concentration decreased 10% with increasing dietary glycemic load, 11% with increasing overall dietary glycemic index, and 4% with increasing carbohydrate intake; fasting triacylglycerol increased 76% with increasing dietary glycemic load, 17% with increasing overall dietary glycemic index, and 44% with increasing carbohydrate intake. When both dietary glycemic load and carbohydrate were considered simultaneously, glycemic load remained a significant predictor of fasting triacylglycerol concentrations, illustrating the value of carbohydrate quality in addition to quantity.

These findings are consistent with data from metabolic studies showing that high-carbohydrate, low-fat diets reduce HDL and increase triacylglycerol concentrations (11, 40, 41) and that fasting triacylglycerol is more sensitive than is HDL to dietary intake. These effects are observed in both diabetic and nondiabetic subjects and are graded among individuals prone to insulin resistance (11, 42). In an intervention study of 444 hypercholesterolemic men, Knopp et al (41) used diet records to measure reported fat intake in 4 intervention groups with different low-fat, high-carbohydrate diets (mean percentages of energy from fat of 27%, 26%, 25%, and 22%). After 1 y of intervention, weight loss was virtually identical in the different intervention groups. However, serum triacylglycerol concentrations increased by 10%, 3%, 22%, and 39% in the groups consuming 27%, 26%, 25%, and 22% of energy from fat ($P < 0.05$). HDL cholesterol also decreased by 3% in subjects consuming diets containing <25% of energy from fat ($P < 0.05$). In a randomized crossover trial of 10 healthy postmenopausal women (11), fasting plasma glucose, insulin, and triacylglycerol concentrations were higher in women consuming a diet containing 60% of energy from carbohydrate than in women consuming a diet containing 40% of energy from carbohydrate. Also, baseline insulin resistance was significantly correlated with postprandial plasma insulin concentrations ($r = 0.82$, $P < 0.02$), total triacylglycerols ($r = 0.77$, $P < 0.05$), and a triacylglycerol sedimentation fraction >400 ($r = 0.77$, $P < 0.05$), indicating that the adverse metabolic effects of a low-fat, high-carbohydrate diet increase with the underlying degree of insulin resistance (11). At present, the biological mechanisms related to carbohydrate-induced dyslipidemia remain to be elucidated (12).

Our findings that dietary glycemic load and overall dietary glycemic index assessed by a food-frequency questionnaire predict plasma HDL-cholesterol and fasting plasma triacylglycerol concentrations have several implications. First, they provide evidence that the total carbohydrate intake, the overall dietary

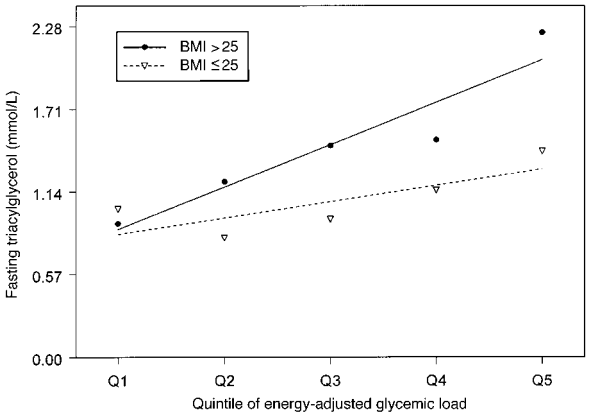

FIGURE 1. Adjusted geometric mean plasma concentrations of fasting triacylglycerol according to quintiles (Q) of energy-adjusted dietary glycemic load in postmenopausal women in 2 BMI categories: BMI > 25 (n = 94) and BMI ≤ 25 (n = 91). Adjusted for all the covariates mentioned in Table 1. P for trend < 0.001 for BMI > 25, P for trend = 0.03 for BMI ≤ 25, and P < 0.001 for the interaction between BMI and dietary glycemic load. To convert mmol/L to mg/dL, divide by 0.0113.

glycemic index, and the dietary glycemic load have important metabolic implications in free-living postmenopausal women. Both total carbohydrate intake and overall dietary glycemic index contribute to lipid perturbations and the dietary glycemic load best summarizes their combined effects. Previous observational studies suggest that for each 0.02586-mmol/L (1-mg/dL) decrease in HDL cholesterol, CAD risk increases by 3.2% in women (43). Thus, the 0.181-mmol/L (7-mg/dL, or 11%) decrease in HDL cholesterol we observed when comparing the lowest and highest quintiles of dietary glycemic load would theoretically translate into a 21% increase in CAD risk (43). A recent meta-analysis of 17 prospective studies suggested that an ≈0.99-mmol/L (≈88-mg/dL) difference in fasting triacylglycerol predicts a 76% increase in risk of CAD risk (17). In our data, even with relatively high mean HDL concentrations in these postmenopausal women, the difference in fasting triacylglycerol concentrations between the 2 extreme quintiles of dietary glycemic load was 0.76 (67 mg/dL), which would translate into a 58% difference in CAD risk. In the current study, the dose-response relations of dietary glycemic load with plasma concentrations of HDL and fasting triacylglycerol were even stronger in women with BMIs >25 (Figure 1). Thus, a greater risk of CAD would be predicted by the same difference in dietary glycemic load in these women who were more insulin resistant. The combined risk associated with the decrease in HDL and the increase in triacylglycerol concentrations approximates that seen for the entire NHS cohort, especially for women with higher BMIs. Comparing the highest and the lowest quintiles of dietary glycemic load, the relative risk of CAD was 1.85 (95% CI: 1.34, 2.54) in 10 y of follow-up (22). However, the relation between fasting triacylglycerol concentrations and CAD risk appears to be complex. The relation may not be independent of the relation between HDL and CAD risk but instead may be associated with the formation of more atherogenic forms of LDL as well as interactions between triacylglycerol and the fibrinolytic-coagulation system (44).

Our findings also provide strong evidence of the validity of our food-frequency questionnaires as measures of total carbohydrate intake, overall dietary glycemic index, and dietary glycemic load in this group of free-living women. Although plasma HDL and fasting plasma triacylglycerol concentrations respond to other dietary factors beside carbohydrate quantity and quality, these indexes can serve as an "alloyed gold standard" (45) because they provide an objective and independent measure of physiologic response. In multivariate analyses in which other known determinants of blood lipids were taken into account, clear associations between dietary variables and blood lipids remained. These results apply directly to the postmenopausal women in the NHS and should be examined in other populations. The apparently different dose-response gradients between dietary glycemic load and fasting triacylglycerol for the 2 different BMI groups observed in our data (the slopes of the 2 regression lines in Figure 1) are consistent with findings by Jeppesen et al (11). The women in our study appear similar to those studied by Jeppesen et al and it is likely that associations with blood lipids may be less strong in groups who are younger, leaner, and more active because these individuals would have a lower degree of insulin resistance.

Our data on overall dietary glycemic index and fasting plasma triacylglycerol concentrations are also consistent with results from most metabolic studies that examined glycemic index in mixed meals. Some researchers have questioned the clinical usefulness of the glycemic index for mixed meals, suggesting that no significant differences in glucose responses are apparent when different foods with different glycemic indexes are consumed in mixed meals (25, 26, 46, 47). However, most studies showed that the glycemic index of a mixed meal can be predicted consistently as the weighted mean of the glycemic index values of each of the component foods (weighted by their proportion of carbohydrate contents) (20, 48, 49) and that these glycemic index values can be used across different individuals (49). In particular, studies showed that although fat and protein affect the absolute glycemic response, they do not affect the relative differences between foods (20, 50, 51). Studies using standardized methods indicated that the correlation between the glycemic index of mixed meals and the average glycemic index values of individual component foods ranges from 0.84 to 0.99 (20, 48, 52). In addition, the glycemic index concept has been shown to be useful in the dietary management of diabetes, hyperglycemia, and hyperlipidemia (18, 20, 48, 49, 53–56). Furthermore, 10 of 11 long-term studies lasting from 1 wk to 3 mo showed that a reduction in overall dietary glycemic index of >12 units reduces triacylglycerol concentrations by an average of 9% (19). Two independent national surveys conducted in Britain and the United States in 1999 reported inverse relations between dietary glycemic index and plasma HDL concentrations in free-living adults (57, 58).

In conclusion, in this sample of 280 apparently healthy postmenopausal women, dietary glycemic load and overall dietary glycemic index were inversely related to plasma HDL concentrations and positively related to fasting plasma triacylglycerol concentrations, independent of BMI, weight change, total energy intake, and other known CAD risk factors. These data support the physiologic relevance in free-living women of dietary glycemic load as a potential risk factor for CAD. These findings also document the ability of a semiquantitative food-frequency questionnaire to assess dietary glycemic load and overall dietary glycemic index.

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