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Effects of low- and high-glycemic index/glycemic load diets on coronary heart disease risk factors in overweight/obese men

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Abstract

Chronic insulin resistance contributes to subclinical inflammation, thrombosis/impaired fibrinolysis, and dyslipidemia. The effect of dietary carbohydrate, specifically of glycemic index (GI) and glycemic load (GL), on established and emerging coronary heart disease risk factors has not been elucidated fully. We conducted a randomized crossover feeding study of matched diets differing only in GI and GL in 24 overweight or obese but otherwise healthy men to investigate the effects on insulin sensitivity, inflammation, thrombosis/fibrinolysis, lipoproteins/lipids, and body composition. All meals for the high- and low-GI/GL diets were prepared in a metabolic kitchen. Each participant consumed both diets in random order for 4 weeks each, with a 4-week washout period in between. Each participant underwent a frequently sampled intravenous glucose tolerance test for assessment of insulin sensitivity; blood sampling for the measurement of inflammatory markers, coagulation factors, and lipoproteins/lipids; and dual-energy x-ray absorptiometry for assessment of body composition at the beginning and end of each dietary period. There were no statistically significant differences in glucose metabolism factors, inflammatory markers, or coagulation factors after 4 weeks on the high- and low-GI/GL diets. The high-GI/GL diet resulted in a slightly greater reduction in fat mass and a slightly greater increase in lean mass compared with the low-GI/GL diet. The high-GI/GL diet resulted in significant, but unexpected, reductions in total and low-density lipoprotein cholesterol, whereas high-density lipoprotein cholesterol concentration was significantly reduced on the high-GI/GL diet compared with the low-GI/GL diet. Overall, high- and low-GI/GL diets of 4 weeks' duration had no consistent effects on coronary heart disease risk factors in this group of overweight/obese men.

1. Introduction

Coronary heart disease (CHD) results in significant morbidity and mortality in the United States [1]. Chronic insulin resistance likely plays an important role in the etiology of this disease by promoting subclinical inflammation and thrombosis/impaired fibrinolysis, in addition to its more established association with dyslipidemia [2-4]. Plasma mediators of chronic inflammation, such as C-reactive protein (CRP), tumor necrosis factor–α (TNF-α), and interleukin-6 (IL-6), and other acute phase reactants, such as fibrinogen and plasminogen activator inhibitor–1 (PAI-1), are some of the emerging risk factors and biomarkers being evaluated as early manifestations of insulin resistance [5].

Early intervention aimed at decreasing insulin resistance, including dietary intervention, may play a role in CHD risk reduction. Continuous excessive intake of carbohydrates may lead to chronic hyperinsulinemia, insulin resistance, and eventually CHD [4]. However, carbohydrates elicit a wide spectrum of blood glucose and insulin responses, influenced by both the quality and quantity of the carbohydrate. Glycemic index (GI) is a ranking of foods based on their postprandial blood glucose responses and is a measure of carbohydrate quality [6]. Glycemic load (GL) is a measure that incorporates both the quantity and quality of dietary carbohydrates [7].

Although observational studies have shown associations of GI and/or GL and markers of inflammation and thrombosis/impaired fibrinolysis [8-10], there is a paucity

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of randomized controlled trials (RCTs) evaluating the effects of dietary interventions differing in GI and GL on comprehensive measures of insulin resistance, inflammation, and thrombosis/fibrinolysis. In addition, several RCTs that have been reported were conducted in participants with diabetes [11-13]. Relatively few studies have evaluated healthy participants, although existing data have confirmed the applicability of the concept of GI in healthy states for disease risk reduction [14]. Furthermore, previous studies may have been confounded by failure to match total energy intake and macronutrient content (most notably dietary fiber) between the low- and high-GI diets [13,15,16].

To address this, we conducted a randomized, crossover, controlled feeding study of matched diets differing only in GI and GL in overweight or obese, but otherwise healthy, African American and white men to investigate the effects of the diets on insulin sensitivity, inflammation, thrombosis/fibrinolysis, lipoproteins/lipids, and body composition.

2. Materials and methods

2.1. Participants

Potential participants were recruited through flyers posted around the University of Alabama at Birmingham (UAB) campus, advertisements in the campus employee and student newspapers, and word of mouth. Inclusion criteria included men aged 20 to 50 years, body mass index (BMI) from 25 to 33 kg/m^2, and ability to read and write English. Exclusion criteria included current chronic disease (CHD, diabetes, hypertension, kidney or liver disease, or uncontrolled thyroid disease); use of medications known to influence body composition or blood glucose, insulin, or lipid concentrations; use of anti-inflammatory medications; current smoking; greater than 2 hours of vigorous exercise per week; alcohol consumption greater than 2 drinks per day; illicit use of drugs; currently on a special diet; significant mental illness; or inability or unwillingness to submit to informed consent. Interested persons were screened for initial eligibility by telephone. Eligible persons attended a screening visit at the UAB General Clinical Research Center (GCRC) outpatient clinic after an overnight fast. At this visit, blood was drawn for screening laboratory tests (creatinine, albumin, total bilirubin, direct bilirubin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, thyroid-stimulating hormone, and glucose); height and weight were measured, and BMI was calculated; and questionnaires were completed (sociodemographic, medical history, medication use, and physical activity). Participants completed a 4-day food record during screening to determine general eating habits and assess compatibility with the study diets. Participants who were eligible after calculation of BMI, review of laboratory tests, and review of questionnaire responses were entered into the study. A total of 30 participants were enrolled in 5 separate waves. A total of 24 participants completed both dietary periods and all 4 overnight GCRC visits. The study was approved by the Institutional Review Board for Human Use at UAB, and all participants provided written informed consent.

2.2. Study design

In a crossover design, participants consumed for 4 weeks each 2 study diets: a high-GI/GL diet and a low-GI/GL diet. The order of the diets was randomly determined. Participants were admitted to the GCRC for an overnight stay at the beginning and end of each dietary intervention period, for a total of 4 such visits. At each visit, participants were admitted during the evening; and height (first visit only), weight, and blood pressure were measured. Participants then were provided with dinner, followed by an overnight (12-hour) fast. At approximately 8:00 AM the following day, participants underwent a frequently sampled intravenous glucose tolerance test (FSIGT). Additional blood was drawn for the measurement of inflammatory markers, coagulation factors, and lipoproteins/lipids. Participants underwent dual-energy x-ray absorptiometry after the FSIGT. Participants began their prescribed diet the same day and continued until the second overnight admission 4 weeks later, during which the same protocol was followed. There was a 4-week washout period between the 2 dietary intervention periods, during which participants were free to consume foods of their own choosing, without monitoring by study personnel. After this period, participants had their third overnight admission and began the second 4-week dietary intervention period, culminating in the fourth overnight admission. During the second and fourth overnight admissions (the visits at the end of the 4-week dietary intervention periods), participants received the dinner that corresponded to the diet to which they had been assigned during the preceding 4 weeks.

2.3. Study diets

High- and low-GI/GL diets were designed to be isoenergetic within individual participants, with approximately equal macronutrient composition and dietary fiber content. Energy content of the diets was individualized to participants to ensure weight maintenance throughout the dietary intervention periods and was calculated using the Harris Benedict equation × 1.35 [17]. The high-GI/GL diet was modeled after the Therapeutic Lifestyle Changes diet developed by the National Cholesterol Education Program [18]. The low-GI/GL diet was a modification of this diet, with the underlying principle being the replacement of high-GI carbohydrates with low-GI carbohydrate alternatives. The GI and GL values were obtained from a published list of such values [19]. All dietary analyses, including determination of overall dietary GI and GL values, were conducted with Nutrition Data System for Research software [20].

All meals for the high- and low-GI/GL diets were prepared, stored, and dispensed in the Bionutrition Department of the GCRC. Meals for each diet were designed by

GCRC research dietitians in collaboration with the principal investigator. Meals were prepared by research cooks in the GCRC metabolic kitchen under the direction of the Bionutrition Research Manager, a registered dietitian. Meals were prepared on a 4-day menu cycle with 12 meals. Four unique daily menus were designed for both the high- and low-GI/GL diets. The 4-day rotation ensured that participants did not consume the same dinner each Sunday, for example, which has promoted dietary adherence in other feeding studies conducted in the GCRC. Participants reported to the Bionutrition Department early in the morning 3 times a week to pick up meals. On Mondays, participants picked up meals for Monday and Tuesday; on Wednesdays, participants picked up meals for Wednesday and Thursday; and on Fridays, participants picked up meals for Friday, Saturday, and Sunday. Meals were packaged in 2 separate insulated containers. One container contained foods that were to remain frozen until use. The second container contained foods that were to be refrigerated until use, along with foods not requiring refrigeration.

Participants were provided with detailed instructions on the proper storage, selection (ie, menus), and preparation of foods. Foods supplied required as little preparation before consumption as possible. In most cases, preparation entailed heating in a microwave oven. Participants were instructed to consume no foods or beverages outside of those provided by the study, with the exception of water, which was not limited on either diet. They also were instructed to consume all of the foods and beverages provided. In the event of a missing food item, the participant was instructed to substitute a food item from another day; and the missing item was replaced as quickly as possible. During each meal pickup, participants were questioned about adherence to the study diets.

2.4. Anthropometry and body composition

Body height was measured, without footwear, to the nearest 0.1 cm with a calibrated, wall-mounted digital stadiometer (Heightronic model 235; Measurement Concepts, North Bend, WA). Body weight was measured, with participants wearing light clothing and no footwear, to the nearest 0.1 kg with a calibrated digital scale (model 6002; Scale-Tronix, Carol Stream, IL). Besides being measured at the beginning and end of each dietary period, weight also was measured during participants' thrice-weekly visits to the GCRC to pick up study meals. Any fluctuation of body weight of more than 2 kg from the previous weight was reported to study dietitians, who adjusted energy content of the participant's diet accordingly. Body composition was assessed at the beginning and end of each dietary period by dual-energy x-ray absorptiometry with a GE Lunar Prodigy bone densitometer (GE Healthcare, Waukesha, WI).

2.5. Frequently sampled intravenous glucose tolerance test

Whole-body insulin sensitivity was assessed on an inpatient basis in the GCRC after an overnight fast with an insulin-modified FSIGT. Before testing, flexible intravenous catheters were placed in the antecubital spaces of both arms. Three 2.0-mL blood samples were taken over a 20-minute period for determination of basal glucose and insulin concentrations (the average of the values was used for basal "fasting" concentrations). At time 0, glucose (50% dextrose, 11.4 g/m^2) was administered intravenously. Insulin (0.02 U/kg, Humulin; Eli Lilly, Indianapolis, IN) was injected at 20 minutes post–glucose injection. Blood samples (2.0 mL) were collected at the following times relative to glucose administration: 2, 3, 4, 5, 6, 8, 10, 12, 15, 19, 20, 21, 22, 24, 26, 28, 30, 35, 40, 45, 50, 55, 60, 70, 80, 100, 120, 140, and 180 minutes. Sera were stored at −85°C until analyzed.

2.6. Laboratory analyses

Glucose and insulin analyses were performed in the Core Laboratory of the GCRC and the Clinical Nutrition Research Center (CNRC) at UAB. Serum glucose was measured with the glucose oxidase method using a SIRRUS analyzer (Stanbio Laboratory, Boerne, TX), with an interassay coefficient of variation (CV) of 3%. Insulin was assayed with Linco Research (St Charles, MO) reagents, with an intraassay CV of 4% and an interassay CV of 6%. Glucose and insulin values were entered into the minimal model of glucose dynamics (MINMOD computer program, Millennium version; 2001, Richard N Bergman, Los Angeles, CA) for determination of the insulin sensitivity index (S_i), glucose effectiveness (S_g), and the acute insulin response to glucose (AIR_g) [21-23]. The AIR_g was calculated as the incremental area under the curve for the first 10 minutes after glucose administration, as determined by the trapezoidal method. Intravenous glucose tolerance (K_g) was calculated as the inverse slope of time vs the natural log of glucose concentration during minutes 8 to 19 after glucose administration. It was expressed in percentage per minute (disappearance of glucose).

Inflammatory marker and coagulation factor assays were conducted at the Laboratory for Clinical Biochemistry Research within the College of Medicine at the University of Vermont. C-reactive protein was measured by a BNII nephelometer (Dade Behring, Deerfield, IL) using a particle-enhanced immunonephelometric assay. Interleukin-6 was measured by ultrasensitive enzyme-linked immunosorbent assay (ELISA) (R&D Systems, Minneapolis, MN). Tumor necrosis factor–α was measured by Luminex technology multiplex ELISA using the Human Serum Adipokine Panel B LINCOplex Kit (Linco Research). Tumor necrosis factor–α receptor II (TNF-RII) was measured using an ultrasensitive ELISA assay (R&D Systems). Fibrinogen concentrations were quantified by the STAR automated coagulation analyzer (Diagnostica Stago, Parsippany, NJ) and the clotting method of Clauss [24]. Plasminogen activator inhibitor–1 assay was performed as a 2-site ELISA. Interassay CVs for these assays ranged from 2% (CRP) to 15% (IL-6).

Lipoprotein/lipid analyses were performed in the Core Laboratory of the GCRC and CNRC at UAB. Serum total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides were measured using a SIRRUS analyzer (Stanbio Laboratory). Low-density lipoprotein (LDL) cholesterol was calculated using the equation of Friedewald et al [25].

2.7. Statistical analyses

The primary purpose of the study was to assess the effect of high- and low-GI/GL diets on a variety of CHD risk factors, including measures of glucose metabolism, inflammatory markers, coagulation factors, lipids/lipoproteins, and body composition. This study was powered to detect a difference between the 2 diets with regard to change in serum glucose. Specifically, a 2-sided *t* test using 24 individuals in a crossover design would achieve 80% power to detect a difference in the mean change in serum glucose between diets of 5.1 mg/dL, assuming a within root mean square error of 6.0 mg/dL and an α of .05.

Given the crossover design of the study, analyses were conducted using the methods illustrated in Jones and Kenward [26]. Specifically, inferential tests were conducted for the effect of sequence (commonly referred to as *crossover effect*), effect of the diets, and effect of time periods. The analysis strategy first was to examine for sequence effects. If this test was nonsignificant ($P > .05$), the test of the effect of diets was examined using information from both time periods. However, when the test of sequence effect was statistically significant, this result was interpreted as indication of a carryover effect, whereby the effect of the first diet to which a participant was randomized had not completely "washed out" before commencing the second diet. When the test of sequence effect was statistically significant, the test of diet effect was conducted using only the data from the first time period. This was the case for HDL cholesterol because a statistical test indicated that, within the crossover design, a significant carryover effect may have occurred. Therefore, for this specific variable, comparison of the 2 diets is based only upon data obtained in the first phase. The distributional assumption of normality was examined using histograms and normal probability plots and tested using the Kolmogorov-Smirnov test. To examine the robustness of our finding to the distributional assumption of normality, all statistical tests were recast as 2-sample tests as illustrated by Hills and Armitage [27] and conducted using the nonparametric equivalent test (Wilcoxon rank sum) of the 2-sample *t* test. Because significance did not differ between the 2 approaches, only *P* values resulting from tests assuming normality are reported.

3. Results

3.1. Participants

The study enrollment scheme is presented in Fig. 1. A total of 172 men were screened by telephone for the study between September 2006 and April 2007. One hundred eight men immediately were excluded because they did not meet eligibility requirements. The remaining 64 men were scheduled for a screening visit at the GCRC, 42 of whom completed this visit. Based on screening testes, 30 of these men were eligible and were entered into the study. Six men dropped out of the study before completing all 4 GCRC visits because of the time commitment required. Twenty-four men completed both dietary intervention periods and all 4 overnight GCRC visits and were included in the data analysis. Participants included 14 white and 10 African American men (Table 1). The mean age of participants was 34.5 ± 8.1 years and mean BMI was 27.8 ± 3.5 kg/m^2, compared with a mean age of 25.0 ± 2.8 years ($P = .0019$ for difference) and mean BMI of 29.5 ± 4.3 kg/m^2 ($P = .2760$) in the men who dropped out.

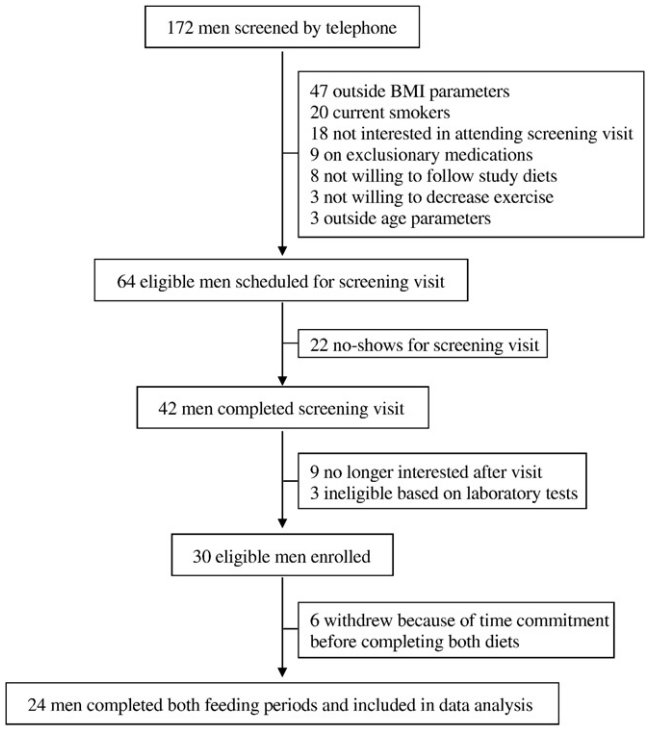

Fig. 1. Study enrollment scheme.

3.2. Diets

Energy content of the low- and high-GI/GL diets was nearly identical and varied little over the 4-day menus for each diet (Table 2). Likewise, macronutrient composition of the diets was very similar. Whereas there were no clinically meaningful differences between the 2 diets in total monounsaturated fatty acids or total *trans*-fatty acids, total saturated fatty acids were slightly lower (by approximately 3 g/d) and total polyunsaturated fatty acids were slightly higher (by approximately 5 g/d) in the high-GI/GL diet, although these differences did not reach statistical significance (data not shown). Total dietary fiber content was

Table 1
Characteristics of study participants at baseline

Variable	All participants (N = 24)
Age (y)	34.5 ± 8.1
Race	
White	14 (58.3)
African American	10 (41.7)
Weight (kg)	90.5 ± 12.5
BMI (kg/m^2)	27.8 ± 3.5
Fat mass (%)	26.9 ± 6.1
Lean mass (%)	69.2 ± 5.8
Glucose (mg/dL)	101.9 ± 8.6
Insulin (mU/L)	7.1 ± 2.7
S_i ($\times 10^{-4} \times \text{min}^{-1}\ \text{mU}^{-1} \times \text{mL}^{-1}$)	4.0 ± 1.7
S_g ($\text{min}^{-1} \times 10^{-2}$)	1.8 ± 1.1
AIR_g (mU/L × min)	736 ± 580
K_g (%/min)	1.7 ± 1.1
CRP (mg/L)	1.4 ± 1.5
IL-6 (ng/L)	2.8 ± 2.2
TNF-α (ng/L)	2.6 ± 1.8
TNF-RII (mg/L)	1.93 ± 0.42
PAI-1 (μg/L)	37.9 ± 39.6
Fibrinogen (g/L)	2.75 ± 0.53
Total cholesterol (mg/dL)	182.0 ± 41.9
LDL cholesterol (mg/dL)	117.8 ± 38.5
HDL cholesterol (mg/dL)	40.8 ± 8.7
Triglycerides (mg/dL)	125.8 ± 114.2

Data are shown as mean ± SD except for race, which was expressed as number (percentage).

slightly higher (by approximately 2 g/d) in the low-GI/GL diet compared with the high-GI/GL diet, but this difference was not statistically significant. Mean GI in the low-GI/GL diet was 34.0% lower than that in the high-GI/GL diet (49.5 vs 75.0, respectively; $P = .0194$), whereas mean GL in the low-GI/GL diet was 35.5% lower than that in the high-GI/GL diet (158.3 vs 245.5, respectively; $P = .0209$). Participants were questioned by study dietitians about compliance with study diets during each visit to the GCRC to pick up their meals. Both diets were well tolerated by study participants. Although 2 participants reported that the amount of food was more than they were accustomed to and one said it was less than he was accustomed to, all participants reported upon questioning that they consumed all of their study foods; and none reported that they consumed foods or beverages outside of the study diets.

3.3. Anthropometry and body composition

As was the intent, body weight and BMI remained relatively stable on both diets over the dietary intervention periods, with no statistically significant differences in changes in weight or BMI between the groups (Table 3). Fat mass decreased slightly in both diet groups over the 4-week dietary periods. Although the percentage reduction was significantly greater in the high-GI/GL group, the absolute difference between the groups was small (−1.1% vs −0.5%, high-GI/GL and low-GI/GL diet, respectively).

3.4. Glucose metabolism factors

Glucose and insulin concentrations decreased slightly on both the high- and low-GI/GL diets (Table 4). Although the reductions were slightly larger in magnitude on the low-GI/GL diet, the differences were not statistically significant. There were no significant differences in changes in S_i, S_g, AIR_g, or K_g between the 2 diets.

3.5. Inflammatory markers and coagulation factors

There were no significant differences in changes observed in inflammatory markers (CRP, IL-6, TNF-α) or TNF-RII in response to the 2 dietary interventions (Table 5). Likewise, no significant differences in changes were noted between the diet groups for the coagulation factors (PAI-1, fibrinogen).

3.6. Lipoproteins/lipids

Concentrations of total, LDL, and HDL cholesterol decreased after 4 weeks on the high-GI/GL diet (Table 6). Total and LDL cholesterol concentrations increased on the low-GI/GL diet, whereas HDL cholesterol was virtually unchanged. Overall, the changes in total, LDL, and HDL cholesterol were significantly different comparing the 2 diets, with the high-GI/GL diet resulting in improvements in total and LDL cholesterol, but worsening HDL cholesterol.

Table 2
Composition of the study diets

Day	Energy (kcal)	Fat (% of energy)	Protein (% of energy)	Carbohydrate (% of energy)	Dietary fiber (g)	GI	GL
Low-GI/GL load diet							
1, 5	2483	29.6	18.2	54.8	19.2	50	161
2, 6	2496	29.2	16.5	55.6	24.6	53	172
3, 7	2480	28.6	18.4	54.7	27.6	45	141
4, 8	2473	28.3	17.2	55.2	21.4	50	159
Mean (SD)	2483 ± 9.6	28.9 ± 0.6	17.6 ± 0.9	55.1 ± 0.4	23.2 ± 3.7	49.5 ± 3.3	158.3 ± 12.8
High-GI/GL diet							
1, 5	2529	30.1	16.5	54.8	16.1	76	250
2, 6	2478	30.4	16.3	55.1	23.2	76	240
3, 7	2482	27.0	16.5	58.4	26.2	69	233
4, 8	2519	30.9	16.1	54.9	18.3	79	259
Mean (SD)	2502 ± 25.8	29.6 ± 1.8	16.4 ± 0.2	55.8 ± 1.7	21.0 ± 4.6	75.0 ± 4.2	245.5 ± 11.4

Table 3
Effects of the high- and low-GI/GL diets on body composition

Variable	High-GI/GL diet			Low-GI/GL diet			P^a
	Baseline	Follow-up	Change	Baseline	Follow-up	Change	
Weight (kg)	88.3 ± 10.5	87.6 ± 10.9	−0.7 ± 1.9	88.1 ± 11.1	87.1 ± 10.2	−1.0 ± 1.6	.7530
BMI (kg/m^2)	27.5 ± 3.4	27.1 ± 3.5	−0.3 ± 0.6	27.4 ± 3.7	27.0 ± 3.3	−0.4 ± 0.7	.4777
Fat mass (%)	26.4 ± 6.3	25.3 ± 6.7	−1.1 ± 1.3	26.0 ± 6.5	25.5 ± 6.6	−0.5 ± 1.3	.0244
Lean mass (%)	69.7 ± 6.1	70.8 ± 6.4	1.1 ± 1.3	70.1 ± 6.3	70.6 ± 6.4	0.5 ± 1.3	.0175

Data are shown as mean ± SD.
[a] P value for difference in change between high- and low-GI/GL diets.

There was no difference in the change in triglycerides between the 2 diets.

4. Discussion

In this randomized clinical trial, we observed no statistically significant differences in glucose metabolism factors, inflammatory markers, or coagulation factors after 4 weeks on high- or low-GI/GL diets. The high-GI/GL diet resulted in a slightly greater reduction in fat mass and a slightly greater increase in lean mass compared with the low-GI/GL diet. The high-GI/GL diet resulted in significant, but unexpected, reductions in total and LDL cholesterol, whereas HDL cholesterol concentration was significantly reduced on the high-GI/GL diet compared with the low-GI/GL diet. Overall, there were no consistent effects of high- and low-GI/GL diets on CHD risk factors in this group of overweight and obese men.

We observed no differences in glucose metabolism parameters between the high- and low-GI/GL diets. These results were in agreement with those from an RCT investigating the effects of 6-month high- and low-GL diets on glucose tolerance and inflammation in healthy but overweight participants conducted by Pittas and colleagues [28]. However, the diets employed by Pittas and colleagues were energy restricted, unlike the diets we employed. Several other RCTs also have shown no differences in changes in glucose, insulin, or homeostasis model assessment of insulin resistance comparing high- and low-GI and/or GL diets [16,29-31].

Our CRP results were in general agreement with those from previous studies, including an RCT reported by McMillan-Price and colleagues [30], in which there were no differences in changes in CRP levels in overweight or obese participants assigned to 1 of 4 diets varying in GL for 12 weeks. Likewise, there was no significant difference in change in CRP comparing low- and high-GI diets in the Canadian Trial of Carbohydrates in Diabetes [13].

Few previous intervention studies included IL-6 and TNF-α or its receptors. A clinical study showed that adipocyte TNF-α production was not influenced by dietary GI in an RCT of premenopausal women [32]. Similarly, in a short-term metabolic study in premenopausal, overweight women, the effects of high- and low-GL single meals on plasma levels of TNF-α and IL-6 did not differ [33]. In an observational study using the Nurses' Health Study cohort, dietary GI, but not GL, was positively associated with TNF-RII levels [9]. We showed no significant difference in changes in PAI-1, a CHD risk factor [34], on the low- and high-GI/GL diets. This was in contrast to 2 previous RCTs that demonstrated beneficial effects of low-GI/GL diets on PAI-1 levels [35,36].

The cholesterol findings in this study were somewhat at odds with the results of previous low-GI/GL interventions, although previous results are somewhat mixed. There were no significant differences in changes in total, LDL, or HDL cholesterol after low-GI and/or GL diets in several RCTs conducted in obese or overweight men and women [15,16,36-38]. Although there were no significant differences in the changes in total or HDL cholesterol in 2 RCTs of low- and high-GI diets in healthy overweight women, LDL cholesterol was significantly reduced in the low-GI compared with the high-GI diet [29,35]. There was a larger mean increase in HDL cholesterol in a reduced-GL diet relative to

Table 4
Effects of the high- and low-GI/GL diets on measures of glucose metabolism

Variable	High-GI/GL diet			Low-GI/GL diet			P^a
	Baseline	Follow-up	Change	Baseline	Follow-up	Change	
Glucose (mg/dL)	101.9 ± 7.8	99.6 ± 6.3	−2.2 ± 7.4	103.5 ± 8.0	98.4 ± 6.8	−5.1 ± 6.96	.1378
Insulin (mU/L)	7.2 ± 3.0	5.8 ± 2.9	−1.4 ± 2.7	7.6 ± 4.8	5.7 ± 3.3	−1.9 ± 4.5	.4344
S_i (x 10^{-4} × min^{-1} mU^{-1} × mL^{-1})	4.0 ± 1.7	3.7 ± 2.6	−0.3 ± 2.1	5.0 ± 3.9	4.4 ± 2.4	−0.6 ± 3.0	.5548
S_g (min^{-1} × 10^{-2})	1.8 ± 0.9	1.6 ± 0.6	−0.1 ± 0.9	1.9 ± 1.3	1.6 ± 1.0	−0.3 ± 1.0	.3640
AIR_g (mU/L × min)	726 ± 475	737 ± 537	11 ± 450	742 ± 588	658 ± 570	−85 ± 468	.1881
K_g (%/min)	1.9 ± 1.0	1.6 ± 0.1	−0.3 ± 1.1	2.0 ± 1.3	2.0 ± 1.3	0.0 ± 1.5	.9876

Data are shown as mean ± SD.
[a] P value for difference in change between high- and low-GI/GL diets.

Table 5
Effects of the high- and low-GI/GL diets on inflammatory markers and coagulation factors

Variable	High-GI/GL diet			Low-GI/GL diet			P^a
	Baseline	Follow-up	Change	Baseline	Follow-up	Change	
CRP (mg/L)	2.1 ± 1.8[1]	1.7 ± 1.9	−0.4 ± 2.0	1.3 ± 1.2	1.3 ± 1.2	0.0 ± 0.7	.7259
IL-6 (ng/L)	3.2 ± 2.8	3.1 ± 3.4	−0.1 ± 3.5	2.5 ± 1.9	2.3 ± 1.7	−0.2 ± 1.8	.5762
TNF-α (ng/L)	2.7 ± 1.6	2.8 ± 1.7	0.1 ± 0.5	2.7 ± 1.7	2.6 ± 1.5	−0.1 ± 0.7	.5370
TNF-RII (mg/L)	1.89 ± 0.38	1.85 ± 0.38	−0.04 ± 0.30	1.87 ± 0.41	1.80 ± 0.36	−0.07 ± 0.21	.7202
PAI-1 (μg/L)	28.0 ± 22.7	32.2 ± 29.2	4.2 ± 30.8	38.4 ± 38.7	38.8 ± 39.2	0.4 ± 52.8	.9335
Fibrinogen (g/L)	2.88 ± 0.82	2.76 ± 0.83	−0.12 ± 0.73	2.68 ± 0.56	2.64 ± 0.60	−0.04 ± 0.49	.9260

Data are shown as mean ± SD.
[a] *P* value for difference in change between high- and low-GI/GL diets.

the control diet in overweight and obese adults [31]. It should be noted that it is possible that the slightly higher polyunsaturated fatty acid and slightly lower saturated fatty acid content of the high-GI/GL diet in the present study may have contributed to the improvements in total and LDL cholesterol on this diet.

Most previous studies have shown minimal effects of low-GI/GL interventions on measures of body composition [37,38]. Conversely, 12 weeks on a low-GL diet compared with a control diet led to a greater reduction in fat mass (although the difference was small and not likely to be clinically meaningful); and there was a slightly greater reduction in fat-free mass in participants on the reduced-GL diet [31]. There was a significantly greater (albeit small) decrease in fat mass in a low-GI diet relative to a high-GI diet in overweight nondiabetic men [15]. Reduction in fat mass was significantly greater in the low-GI relative to the high-GL diet in a 10-week study of low- and high-GI diets in healthy overweight women [29].

This study had several strengths. To eliminate the effects of differences in other dietary components, the study diets were designed to be nearly equal in macronutrient content, especially in regard to dietary fiber. Many low-GI foods are high in soluble fiber (eg, fruits and legumes), and soluble fiber potentially can affect many of the outcomes analyzed in this study (eg, PAI-1 and blood lipids). Therefore, fiber potentially can confound any association between GI/GL and these outcomes, which statistical control may not eliminate [39]. Many previous studies either did not report fiber content of their study diets or made no attempt to equalize fiber intakes. Another strength of this study was that the low- and high-GI/GL diets were well characterized, with mean GI and GL reported for each day of each diet. In addition, study diets were provided to participants, offering some measure of control of dietary intake. Finally, body weight of participants was assessed during each visit to the GCRC to pick up meals. This allowed for any fluctuations in weight to be detected early and energy content of the diets to be adjusted to maintain body weight, preventing changes in body weight from potentially confounding results.

Limitations of the study include the relatively short dietary intervention period; the self-reporting of dietary compliance; and the small, all-male sample from which there was some attrition. It is possible that longer intervention periods may have allowed differences in the effects of the 2 diets on the various measures to become evident. Although strict compliance with the diets was universally reported by study participants, it is possible that some participants did not consume all of the study-provided foods and/or consumed non–study-provided foods but were hesitant to report this. This dietary noncompliance, especially if differential, could have biased the results. Finally, when considering the requirements of the study—the frequent visits to pick up study meals and the 4 required overnight GCRC visits—the attrition rate of 20% seems reasonable.

In summary, 4-week high- and low-GI/GL diets had little effect on glucose metabolism factors, inflammatory markers, or coagulation factors; and their effects on other risk factors

Table 6
Effects of the high- and low-GI/GL diets on lipoproteins/lipids

Variable	High-GI/GL diet			Low-GI/GL diet			P^a
	Baseline	Follow-up	Change	Baseline	Follow-up	Change	
Total cholesterol (mg/dL)	185.4 ± 39.9	171.4 ± 38.5	−14.0 ± 25.1	170.3 ± 38.4	178.4 ± 30.8	8.1 ± 26.1	.0013
LDL cholesterol (mg/dL)	120.8 ± 39.5	108.0 ± 34.9	−12.8 ± 20.4	107.4 ± 34.4	113.4 ± 29.6	6.0 ± 21.4	.0019
HDL cholesterol (mg/dL)	44.6 ± 7.5	40.2 ± 9.9	−4.3 ± 4.6	38.5 ± 8.8	38.3 ± 11.1	−0.1 ± 4.6	.0447
Triglycerides (mg/dL)	111.5 ± 66.5	115.5 ± 79.2	4.0 ± 45.1	119.5 ± 112.9	134.4 ± 111.5	14.9 ± 52.3	.3291

Data are shown as mean ± SD. A statistical test indicated that, within the crossover design, a significant carryover effect may have occurred for HDL cholesterol. This carryover effect implies that the outcomes observed in the second phase of the design could be dependent upon the first-phase results. Therefore, for this specific variable, comparison of the 2 diets is based upon only data obtained in the first phase.
[a] *P* value for difference in change between high- and low-GI/GL diets.

were not consistent. However, future larger, longer-term studies of low-GI/GL diets in more diverse populations may be informative.

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