ABSTRACT

Background: There remains no consensus about the optimal dietary composition for sustained weight loss.

Objective: The objective was to examine the effects of 2 dietary macronutrient patterns with different glycemic loads on adherence to a prescribed regimen of calorie restriction (CR), weight and fat loss, and related variables.

Design: A randomized controlled trial (RCT) of diets with a high glycemic load (HG) or a low glycemic load (LG) at 30% CR was conducted in 34 healthy overweight adults with a mean (±SD) age of 35 ± 6 y and body mass index (kg/m²) of 27.6 ± 1.4. All food was provided for 6 mo in diets controlled for confounding variables, and subjects self-administered the plans for an additional 6 mo. Primary and secondary outcomes included energy intake measured by doubly labeled water, body weight and fatness, hunger, satiety, and resting metabolic rate.

Results: All groups consumed significantly less energy during CR than at baseline (P < 0.01), but changes in energy intake, body weight, body fat, and resting metabolic rate did not differ significantly between groups. Both groups ate more energy than provided (eg, 21% and 28% CR at 3 mo and 16% and 17% CR at 6 mo with HG and LG, respectively). Percentage weight change at 12 mo was −8.04 ± 4.1% in the HG group and −7.81 ± 5.0% in the LG group. There was no effect of dietary composition on changes in hunger, satiety, or satisfaction with the amount and type of provided food during CR.

Conclusions: These findings provide more detailed evidence to suggest that diets differing substantially in glycemic load induce comparable long-term weight loss.

KEY WORDS Glycemic load, caloric restriction, body weight, metabolism

INTRODUCTION

The prevalence of obesity and overweight continues to increase nationally and worldwide (1–3). Calorie restriction (CR) remains the cornerstone of most weight-management strategies, but there remains no consensus over the role of dietary macronutrient composition in optimizing long-term weight loss.

In part, the lack of consensus probably reflects the fact that most studies in this area have provided dietary advice, rather than food, with resulting uncertainty in the true extent of dietary change. For example, recent studies have examined whether low-carbohydrate or low-glycemic-load (GL) diets facilitate greater long-term weight loss than do conventional recommendations based on national dietary guidelines (4, 5); most (6–10), but not all (11), of the studies reported transiently greater weight loss at 6 mo in individuals consuming low-carbohydrate or low-GL diets that was attenuated in studies continuing to 12 mo (8, 10). However, unbiased assessments of adherence to the tested regimens were not performed, and there may have been differences between tested diets that influenced the results. It is recognized that dietary change in the absence of provided food is difficult because of formidable barriers, such as the need to alter central lifestyle factors such as established shopping and cooking habits and food preferences (12–16). For this reason, perhaps, subjects tend to inflate self-reports of the magnitude of dietary change (17). Moreover, in most of the reports of high-compared with low-carbohydrate regimens and weight loss, differential behavioral support was given to each treatment group because they were testing popular diet prescriptions rather than specifically different dietary compositions, which confounded the results (8, 11, 18). Thus, additional studies that use more detailed and consistent methods are needed to resolve the effects of different dietary patterns on long-term weight loss.

We describe here a detailed 1-y randomized controlled trial (RCT) designed to examine the effects of dietary patterns differing...
in glycemic load and fed at 30% CR on adherence to the regimens, weight and body fat losses, and underlying explanations for differential responses to the diets.

SUBJECTS AND METHODS

Study population

The subjects were 34 overweight [body mass index (in kg/m²): 25–30] but otherwise healthy men and women aged 24–42 y who were recruited through a variety of local advertisements. Twelve additional subjects were recruited and randomly assigned to 2 different control groups for the purpose of gaining experience in retaining a control group but are not described here because the groups are very small (n = 5 in the HG group and n = 4 in the LG group at 12 mo). This study constitutes the first phase of the CALERIE (Comprehensive Assessment of the Long-term Effects of Restricting Intake of Energy) trial at Tufts University. CALERIE is a coordinated multicenter study of CR in human health and aging. During this first phase, independent studies were conducted at the different sites. Eligibility for the Tufts study was determined on the basis of a normal health-history questionnaire and a screening examination that included blood and urine tests, physical and psychological examinations, and assessment of anticipated lifestyle changes, such as pregnancy or moving out of the area. Additional exclusion criteria included high physical activity levels (ie, participation in sports or training for >12 h/wk), weight fluctuations (>6.8 kg in the past year), inability to complete an accurate 7-d dietary record (accuracy defined as 70–130% of estimated energy requirements), and any disease or medications that might influence the results obtained (including diabetes, cancer, coronary heart disease, endocrine disorders, psychiatric diagnosis, or eating disorder). The study was conducted at the Metabolic Research Unit of the Jean Mayer US Department of Agriculture Human Nutrition Research Center on Aging at Tufts University with approval by the Institutional Review Board of Tufts–New England Medical Center Hospital. All subjects gave written informed consent before participating and were provided with a stipend. The study was independently monitored annually for overall compliance and data accuracy by an external clinical trial monitor from the Duke Clinical Research Institute, Durham, NC, and the safety and efficacy of the clinical trial were monitored by a Data Safety Monitoring Board.

Study protocol

As shown in Figure 1, this yearlong intervention study included a 7-wk baseline period (phase 1), during which time the subjects were requested to maintain a stable weight and continue eating their usual diet. Baseline weight-maintenance energy requirements [assumed to be equal to total energy expenditure (TEE), as measured by doubly labeled water (19)] and key outcome variables were assessed. Following phase 1, there was a 24-wk CR phase (phase 2: ≈6 mo) during which the subjects were randomly assigned to a diet with a low glycemic load (LG) or a high glycemic load (HG), and all food was provided at 70% of individual baseline weight-maintenance energy requirements. The last phase of the study consisted of a 24-wk CR phase (phase 3: ≈6 mo) during which the subjects were instructed to take overall responsibility for food preparation and to continue their phase 2 regimen. The subjects were expected to visit the research

FIGURE 1. Flow of study participants from screening through study completion. The numbers shown in the figure are specific to the group that was prescribed a regimen of 30% calorie restriction (CR). Twelve subjects were randomly assigned to a 10% CR control group (data not shown). HG, high glycemic load; LG, low glycemic load.
TABLE 1
Composition of the 2 diets

<table>
<thead>
<tr>
<th></th>
<th>HG diet</th>
<th>LG diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrate (% of energy)</td>
<td>60</td>
<td>40 (^2)</td>
</tr>
<tr>
<td>Fat (% of energy)</td>
<td>20</td>
<td>30 (^2)</td>
</tr>
<tr>
<td>Protein (% of energy)</td>
<td>20</td>
<td>30 (^2)</td>
</tr>
<tr>
<td>Fiber (g/1000 kcal)</td>
<td>15.1 ± 0.8 (^3)</td>
<td>15.3 ± 0.6</td>
</tr>
<tr>
<td>Energy density (kcal/g)</td>
<td>1.0 ± 0.0</td>
<td>1.0 ± 0.0</td>
</tr>
<tr>
<td>Glycemic index</td>
<td>85.6 ± 2.8</td>
<td>52.4 ± 4.4 (^4)</td>
</tr>
<tr>
<td>Glycemic load (g/1000 kcal)</td>
<td>118.3 ± 4.1</td>
<td>45.4 ± 4.6 (^4)</td>
</tr>
<tr>
<td>Variety (food items/3/d)</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Appearance (100-mm VAS)</td>
<td>55.0 ± 12.3</td>
<td>56.6 ± 12.1</td>
</tr>
<tr>
<td>Taste (100-mm VAS)</td>
<td>64.5 ± 13.7</td>
<td>62.8 ± 11.8</td>
</tr>
<tr>
<td>Smell (100-mm VAS)</td>
<td>61.5 ± 12.6</td>
<td>61.6 ± 9.3</td>
</tr>
</tbody>
</table>

\(^1\) VAS, visual analogue scale (5-point anchors ranging from “not at all” to “extremely” at opposite ends).
\(^2\) Significantly different from the HG diet, \(P < 0.001\) (independent-sample \(t\) test).
\(^3\) ± SD (all such values).
\(^4\) Mixed dishes were considered as one food item.
\(^5\) Paired-sample \(t\) tests were used for comparisons between groups because an independent group tested both diets before the study began; no significant differences were observed.

center weekly throughout the study for a variety of activities, including weekly behavioral support groups, individual meetings with the study dietitian, safety monitoring, and outcome testing.

Study diets

Two diets approximating the range of current dietary recommendations for healthful macronutrient ranges and containing the Dietary Reference Intakes (DRIs) of micronutrients and essential fatty acids (4) were developed for use in this study at 30% CR relative to baseline energy requirements. Diet compositions are summarized in Table 1 for the HG and LG diets, and a list of actual foods that were provided for each type of diet is included in Appendix A. Both diets had consistent features designed to promote CR, including meeting DRIs for dietary fiber (4), limited inclusion of high-energy-density foods (20), limited liquid calories (21), and a relatively high variety of low-energy-density foods (eg, fruit and vegetables), and a relatively low variety of high-energy-dense foods (22). The diets differed in the ratio of macronutrients (HG: 60% carbohydrate, 20% fat, and 20% protein; LG: 40% carbohydrate, 30% fat, and 30% protein), and the carbohydrate sources in the LG diet had a lower glycemic index (GI) per published GIs of different carbohydrate sources (23). Because all 3 macronutrients varied between the diets, the study outcomes are most appropriately attributed to different dietary patterns. However, because the largest difference between the diets was in the GL, the diets are described as HG and LG diets. The daily glycemic load was calculated as [daily GI \(\times\) (total available carbohydrate (g/d)/1000 kcal)]. The amount of available carbohydrate for each food was calculated as total grams of carbohydrate – total dietary fiber. Please note that, although it was technically possible to change the GL of the diets by changing just the carbohydrate and fat contents (and leaving protein constant), it would have been hard to control other factors between the diets, including palatability and energy density. With the chosen approach, it was possible to match the diets for dietary variety and palatability [assessed by using a visual analogue scale (VAS) during a pilot test of the diets]. The subjects were also provided with a multivitamin supplement and 500 mg Ca/d to ensure that the DRIs of micronutrients were met.

All food was provided at the 30% reduced CR prescription to subjects during the first 6 mo of the CR intervention. The subjects were asked to consume only the provided food and were told that it was important to comply with the study but were also told that it was important to report both leftovers and any additional foods they consumed on data recording sheets that were provided for this purpose. After weeks 15–20 of the CR intervention, the subjects were allowed 1000 kcal/wk of discretionary foods not on the menu, and this amount was subtracted from the provided foods. The subjects were requested to bring back their leftover foods, which were weighed and the amounts recorded on the data recording sheets. The subjects were allowed to eat foods not included in the study diet on days such as Thanksgiving and Christmas (or other infrequent special occasions) and were given nonperishable foods and menu suggestions when traveling. Intakes were self-recorded during these times. The subjects or their designated representative came to the research center twice a week to pick up the meals.

During the second 6 mo of the study, the subjects were instructed to self-select and prepare their own food at home to maintain their randomization. To prepare for this phase, the subjects worked with the study dietitian to develop an individualized plan that included menus, recipes, portion sizes, and food lists that were consistent with their randomized diets, prescribed caloric levels, and food preferences. Food scales were provided to help with appropriate portioning, and the subjects participated in a preparatory grocery store tour and cooking class.

Recruitment and randomization

A total of 365 eligible subjects were screened for this study over a 1-y period from October 2002 to December 2003, and 34 subjects were enrolled to the 30% CR groups (Figure 1). A block randomization stratified on body mass index, sex, and diet group was used. All outcome-assessment staff were blinded to participant randomization, and the subjects were not informed of their randomization until month 3 of CR.

Body weight, height, and composition

Height was measured at the research center, once at the beginning of the study, with a wall-mounted stadiometer to ±0.1 cm, and weight was measured at weekly intervals to ±50 g with a calibrated scale (model CN-20; DETECTO-Cardinal Scale Manufacturing Co, Webb City, MO). All subjects were provided with a home weight scale (model HS301 TANITA body weight scale; Tanita Corporation of America Inc, Arlington Heights, IL), and a daily home weight measure was obtained. Air-displacement plethysmography (BOD POD; Life Measurement Inc, Concord, CA) was used to measure body density in duplicate at baseline and at 3, 6, and 12 mo. The principles of this accurate density-based method and its validation and practical use are described elsewhere (24–26). The test-retest CV for percentage body fat measured by BOD POD in human adults is 1.7% ± 1.1% (24).

Resting metabolic rate

Resting metabolic rate (RMR) was measured on 2 mornings at baseline and at 6 mo and 12 mo of CR, after the subjects slept
weight loss of 7.4 kcal/g (36).

measurements (for a maximum of 28 days). The energy content of

is not in neutral energy balance), TEE data can be used to cal-

culate a value for energy intake unbiased by subject reporting, by

is described elsewhere (29, 30). Briefly, at the start of each

subject was discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

were discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

of the subjects was measured in duplicate over succes-
sive 14-d periods at baseline, and additional 14-d measure-
ments were made at 3, 6, and 12 mo of CR. This standard,
nonradioactive isotopic method has been extensively validated
and is described elsewhere (29, 30). Briefly, at the start of each

EEE measurement, the subjects fasted overnight and were given
an oral dose of doubly labeled water (2H218O) containing 0.22 g
H218O/kg estimated total body water and 0.115 g 2H2O/kg total
body water after collection of 2 independent baseline urine spec-
imens. The subjects were then required to remain fairly sedentary
and not to consume any food or water while urine samples were
collected from complete voids made at 3, 4.5, and 6 hours after
d ose administration. After completion of urine collections, the
subjects were discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

an oral dose of doubly labeled water (2H218O) containing 0.22 g
H218O/kg estimated total body water and 0.115 g 2H2O/kg total
body water after collection of 2 independent baseline urine spec-
imens. The subjects were then required to remain fairly sedentary
and not to consume any food or water while urine samples were
collected from complete voids made at 3, 4.5, and 6 hours after
dose administration. After completion of urine collections, the
subjects were discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

The TEE of the subjects was measured in duplicate over suc-
cessive 14-d periods at baseline, and additional 14-d measure-
ments were made at 3, 6, and 12 mo of CR. This standard,
nonradioactive isotopic method has been extensively validated
and is described elsewhere (29, 30). Briefly, at the start of each

of the subjects was measured in duplicate over success-
vie 14-d periods at baseline, and additional 14-d measure-
ments were made at 3, 6, and 12 mo of CR. This standard,
nonradioactive isotopic method has been extensively validated
and is described elsewhere (29, 30). Briefly, at the start of each

subject was discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

were discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

absorbed, but not to consume any food or water while urine samples were
collected from complete voids made at 3, 4.5, and 6 hours after
dose administration. After completion of urine collections, the
subjects were discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

absorbed, but not to consume any food or water while urine samples were
collected from complete voids made at 3, 4.5, and 6 hours after
dose administration. After completion of urine collections, the
subjects were discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

of the subjects was measured in duplicate over success-
vie 14-d periods at baseline, and additional 14-d measure-
ments were made at 3, 6, and 12 mo of CR. This standard,
nonradioactive isotopic method has been extensively validated
and is described elsewhere (29, 30). Briefly, at the start of each

subject was discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

of the subjects was measured in duplicate over success-
vie 14-d periods at baseline, and additional 14-d measure-
ments were made at 3, 6, and 12 mo of CR. This standard,
nonradioactive isotopic method has been extensively validated
and is described elsewhere (29, 30). Briefly, at the start of each

subject was discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

absorbed, but not to consume any food or water while urine samples were
collected from complete voids made at 3, 4.5, and 6 hours after
dose administration. After completion of urine collections, the
subjects were discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

of the subjects was measured in duplicate over success-
vie 14-d periods at baseline, and additional 14-d measure-
ments were made at 3, 6, and 12 mo of CR. This standard,
nonradioactive isotopic method has been extensively validated
and is described elsewhere (29, 30). Briefly, at the start of each

subject was discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

of the subjects was measured in duplicate over success-
vie 14-d periods at baseline, and additional 14-d measure-
ments were made at 3, 6, and 12 mo of CR. This standard,
nonradioactive isotopic method has been extensively validated
and is described elsewhere (29, 30). Briefly, at the start of each

subject was discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

abdominal, but not to consume any food or water while urine samples were
collected from complete voids made at 3, 4.5, and 6 hours after
dose administration. After completion of urine collections, the
subjects were discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

abdominal, but not to consume any food or water while urine samples were
collected from complete voids made at 3, 4.5, and 6 hours after
dose administration. After completion of urine collections, the
subjects were discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

abdominal, but not to consume any food or water while urine samples were
collected from complete voids made at 3, 4.5, and 6 hours after
dose administration. After completion of urine collections, the
subjects were discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

subject was discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

subject was discharged from the unit and carried out their usual
daily activities for 14 days, with supervised urine specimen collec-
tion on days 7 and 14. All samples were portioned in duplicates
into airtight storage tubes (no. 62.547.004; Sarstedt, Inc, New-

}
TABLE 2
Characteristics of the subjects in the 2 diet groups at baseline

<table>
<thead>
<tr>
<th></th>
<th>HG diet (n = 4 M, 13 F)</th>
<th>LG diet (n = 4 M, 13 F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>34 ± 5</td>
<td>35 ± 6</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.5 ± 1.6</td>
<td>27.6 ± 1.2</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.1 ± 10.7</td>
<td>169.0 ± 10.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79.0 ± 12.1</td>
<td>79.1 ± 9.2</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>34.8 ± 7.1</td>
<td>34.9 ± 8.2</td>
</tr>
</tbody>
</table>

All values are x ± SD. HG, high glycemic load; LG, low glycemic load. There were no statistically significant differences between the diet groups (independent-sample t tests).

Baseline (P < 0.01). However, %CR was not statistically significantly different between the groups at 3, 6, or 12 mo of the intervention. On average, the subjects ate somewhat more food than prescribed at all time points. Consistent with the actual measured %CR values, percentage weight loss was significant over time in both groups (P < 0.0001) but was not significantly different between the groups (P = 0.59) (Figure 2). In other words, there was no difference in percentage weight loss between individuals randomly assigned to different diets, and mean values at 12 mo were not statistically significantly different (Table 4).

Baseline body weight, percentage body fat, and RMR, and percent change from baseline at 6 and 12 mo of CR, respectively, are also shown in Table 4. There was a statistically significant decrease in mean percentage fat over time (P < 0.0001) consistent with body weight change; however, the difference between diet groups was not statistically significant over time. RMR also decreased significantly from baseline to 6 and 12 mo (P < 0.01), but changes in RMR over time were not statistically significant between diet groups. There was no diet-by-time interaction for both the measured and percentage change data. It should be noted that there were also no group differences in changes in fat-free mass and fat mass with CR, and the change in RMR adjusted for the change in fat-free mass was also not significant (data not shown). Results for weight, fat loss, and change in RMR when all participants were included were not statistically different from the results obtained when noncompleters were.

Changes in self-reported hunger and satisfaction with the amount and type of provided food and the desire to eat nonstudy foods between baseline and 3 mo of CR were examined by using daily VAS. The first 3 mo of CR were chosen for this analysis because this is the period when adherence to the prescribed CR was at its highest; therefore, eating-behavior variables could be compared between groups to indicate true composition effects. The results from this analysis showed that there was a significant increase from baseline in the desire to eat nonstudy foods (P < 0.01) and a significant decrease in the satisfaction with the type of provided food (P < 0.05) within the HG group but not within the LG group. However, there was no statistically significant difference between the diet groups for change in these variables over time (data not shown).

Fasting values for triacylglycerols, insulin, glucose, and total, HDL, and LDL cholesterol at baseline and the percent change in these variables at 6 and 12 mo of CR are shown in Table 5. The decreases over time in percentage change from baseline were statistically significant for triacylglycerol (P < 0.001), insulin (P < 0.0001), and total (P < 0.001), and LDL (P < 0.05) cholesterol, but not for glucose. There were no statistically significant diet-by-group interactions over time for any of the variables. Insulin and glucose data for the 30% CR group with the 2 diets are reported in more detail elsewhere (39), but are summarized here for completeness.

DISCUSSION

This detailed RCT in healthy overweight women and men is the first to examine the effects of HG compared with LG diets on weight loss in a long-term protocol not confounded by group differences in other factors that strongly influence energy intake, including type of behavioral support, diet palatability, and dietary variety of the regimens. Under the conditions of this study, which tested diets that differed in all 3 macronutrients but mostly in the glycemic load (40% carbohydrate from low-GI sources compared with 60% of energy intake from high-GI sources), we found no significant difference between the groups in mean energy intake, weight loss, and body fat loss throughout the 12 mo study. These findings provide more rigorous support than available previously for the view that wide variability in the balance of different dietary macronutrients has little effect on mean long-term weight loss during CR (40).
TABLE 4
Resting metabolic rate (RMR) and body composition in the 2 diet groups

<table>
<thead>
<tr>
<th></th>
<th>Baseline $^2$</th>
<th>6 mo</th>
<th>12 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body weight (kg)$^5$</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HG diet ($n = 15$)</td>
<td>78.5 ± 12.3</td>
<td>−9.1 ± 4.2</td>
<td>−8.0 ± 4.1</td>
</tr>
<tr>
<td>LG diet ($n = 14$)</td>
<td>78.0 ± 9.3</td>
<td>−10.4 ± 4.1</td>
<td>−7.8 ± 5.0</td>
</tr>
<tr>
<td><strong>Body fat (%)$^5$</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HG diet</td>
<td>35.0 ± 7.1</td>
<td>−17.1 ± 11.6</td>
<td>−14.8 ± 8.8</td>
</tr>
<tr>
<td>LG diet</td>
<td>35.2 ± 8.7</td>
<td>−23.3 ± 16.6</td>
<td>−17.9 ± 12.5</td>
</tr>
<tr>
<td><strong>RMR (kcal/d)$^4$</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HG diet</td>
<td>1582 ± 255</td>
<td>−5.9 ± 5.7</td>
<td>−3.3 ± 7.1</td>
</tr>
<tr>
<td>LG diet</td>
<td>1605 ± 182</td>
<td>−6.6 ± 5.6</td>
<td>−2.2 ± 7.8</td>
</tr>
</tbody>
</table>

$^1$ All values are $\bar{x} \pm$ SD. HG, high glycemic load; LG, low glycemic load.
$^2$ There were no statistically significant differences at baseline between the groups (independent-sample $t$ tests).
$^3$ There was a statistically significant change over time (mixed-model analysis of repeated measures).

Several recent long-term studies have examined the effects of diet composition on weight loss and reported greater weight loss with LG diets than with HG diets at 6 mo, but no difference in mean weight loss at 12 mo (8, 10, 41). Perhaps the most important difference between those studies and the one described here is that those studies recommended dietary compositions to the subjects, whereas we provided subjects with a complete set of meals and snacks every day for 6 mo in menus controlled for other factors that have well-established influences on energy intake (42, 43). The compositions recommended in those studies were also more extreme (eg, less carbohydrate in the LG groups), but self-reported intakes indicated similar actual compositions to those used in this study. The greater initial weight loss seen in the LG groups in the previous studies may therefore have been due to inadvertent dietary changes that the subjects made to accommodate protocol requirements, for example, in dietary variety, palatability, and fiber (which are known to have independent effects on energy intake) rather than in macronutrients and glycemic load. By 12 mo, both the previous studies and our new investigation found no difference in weight loss between the HG and LG regimens and a tendency for weight and body fat regain in the LG groups. Taken together, these findings suggest that reduced energy intake may be somewhat harder to sustain with LG regimens in the long term. This could be true for a number of

TABLE 5
Clinical indicators in the 2 diet groups

<table>
<thead>
<tr>
<th></th>
<th>Baseline $^2$</th>
<th>6 mo</th>
<th>12 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Triacylglycerol (mg/dL)$^4$</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HG diet ($n = 15$)</td>
<td>90.6 ± 47.2</td>
<td>−14.3 ± 21.9</td>
<td>−16.5 ± 29.9</td>
</tr>
<tr>
<td>LG diet ($n = 14$)</td>
<td>98.6 ± 33.1</td>
<td>−24.7 ± 27.7</td>
<td>−15.2 ± 24.8</td>
</tr>
<tr>
<td><strong>Total cholesterol (mg/dL)$^4$</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HG diet</td>
<td>168.4 ± 25.3</td>
<td>−11.1 ± 8.3</td>
<td>−4.2 ± 9.3</td>
</tr>
<tr>
<td>LG diet</td>
<td>176.7 ± 26.7</td>
<td>−13.4 ± 12.1</td>
<td>−5.3 ± 10.5</td>
</tr>
<tr>
<td><strong>HDL cholesterol (mg/dL)$^3$</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HG diet</td>
<td>55.4 ± 8.5</td>
<td>−2.8 ± 10.6</td>
<td>13.3 ± 16.2</td>
</tr>
<tr>
<td>LG diet</td>
<td>51.0 ± 11.5</td>
<td>−3.1 ± 19.1</td>
<td>11.9 ± 10.2</td>
</tr>
<tr>
<td><strong>LDL cholesterol (mg/dL)$^3$</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HG diet</td>
<td>96.9 ± 21.5</td>
<td>−13.2 ± 11.0</td>
<td>−7.1 ± 11.3</td>
</tr>
<tr>
<td>LG diet</td>
<td>107.6 ± 24.2</td>
<td>−13.4 ± 18.2</td>
<td>−7.0 ± 17.5</td>
</tr>
<tr>
<td><strong>Glucose (mg/dL)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HG diet</td>
<td>83.5 ± 6.1</td>
<td>−2.5 ± 6.1</td>
<td>−2.3 ± 6.2</td>
</tr>
<tr>
<td>LG diet</td>
<td>84.4 ± 5.8</td>
<td>−1.8 ± 7.8</td>
<td>5.0 ± 9.9</td>
</tr>
<tr>
<td><strong>Insulin (µIU/mL)$^4$</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HG diet</td>
<td>10.5 ± 3.6</td>
<td>−14.9 ± 20.0</td>
<td>−18.0 ± 15.0</td>
</tr>
<tr>
<td>LG diet</td>
<td>12.1 ± 4.3</td>
<td>−25.4 ± 24.2</td>
<td>−21.2 ± 16.7</td>
</tr>
</tbody>
</table>

$^1$ All values are $\bar{x} \pm$ SD. HG, high glycemic load; LG, low glycemic load. There were no statistically significant differences between diet groups over time.
$^2$ There were no statistically significant differences at baseline between the groups (independent-sample $t$ tests).
$^3$ There was a statistically significant change over time (mixed-model analysis of repeated measures).
$^4$ There was a statistically significant change over time at the 12-mo time point only, $P < 0.001$, $P < 0.0001$, $P < 0.05$. 
$^5$ There was a statistically significant change over time at the 12-mo time point only, $P < 0.0001$ (mixed-model analysis of repeated measures).
reasons, including the difficulty in sustaining a self-selected LG diet because of the challenges in maintaining acceptable variety and palatability or, perhaps, to the difficulties associated with the significant lifestyle changes required to shop and cook for an unfamiliar LG regimen.

Some short-term studies have also examined the effects of HG compared with LG diets on weight and body composition (44–46). However, those studies did not control the diets for other factors, such as dietary variety (42), palatability (42), and fiber (43), which are known to have substantial independent effects on energy intake, and typically had other differences between diet groups, such as different methods for self-reporting relevant variables, such as energy intake. In the present study, energy intake was measured by using the objective doubly labeled water method by calculating energy intake from TEE (19) and the change in energy balance during the measurement period based on body weight change as outlined previously (35). This was an important element of the protocol because underreporting of dietary intake by the subjects in self-reports is essentially a universal phenomenon, with the extent of underreporting varying between 5% and 50%, depending on the population (35, 47–49). Using the doubly labeled water method, we found that, although both groups of 30% CR subjects consumed some nonstudy food, there was no significant difference in the degree of nonadherence between the dietary groups.

It should also be noted that there were no differences in self-assessments of changes in hunger over time by subjects in the HG and LG groups during the first 12 wk of the protocol, when adherence was generally highest. This finding of no difference in hunger between the HG and LG diet groups might have been due to a lack of power in this relatively small study, especially because the desire to eat nonstudy foods increased in the HG group but not in the LG group. It is also possible, however, that the suggested greater satiation from high-protein meals and low-GI meals than from low-protein and high-GI meals in previous studies (50, 51) was not seen here because of the common features anticipated to minimize hunger in both the diets, including very high amounts dietary fiber (43), low energy density (20), and low amounts of liquid energy sources (21). We speculate that these common satiety-inducing features may have overridden any possible additional satiety effects of the higher-protein content and lower GI of the LG diet.

This long-term and detailed RCT, which provided diets extensively matched for confounding variables, found no evidence of any differential effect of dietary GL on group mean values for energy intake, hunger, satiety, metabolic rate, and weight and body fat loss up to 12 mo. Although the results obtained cannot be attributed to any one macronutrient, because we aimed to create different macronutrient patterns that mimicked common patterns of consumption, the present results suggest that a broad range of healthy diets can successfully promote weight loss.

We thank the subjects for their committed participation in this study and the staff of the Metabolic Research Unit and the Nutrition Evaluation Laboratory for their expert assistance throughout the study.

The authors’ responsibilities were as follows—SKD: study design, clinical trial coordination and outcome assessment, intervention management, data management and analysis, and manuscript preparation; CHG: clinical trial intervention implementation, data management, and manuscript review; JKG, AGP, and PJF: clinical trial outcome assessment and manuscript review; RAC: clinical trial intervention implementation and manuscript review; ST: clinical trial outcome assessment; MT: clinical trial outcome assessment and data management; MAM and AHL: clinical trial outcome assessment and manuscript review; GED: statistical expertise and manuscript review; CD: study design and manuscript review; MVB: data analysis and manuscript review; JPD: doubly labeled water assessment, data analysis, and manuscript review; ES: assessment of adverse events, medical monitoring, and manuscript review; SBR (principal investigator): study design, clinical trial intervention implementation management, and manuscript preparation. None of the authors had a conflict of interest.

REFERENCES


APPENDIX A
Sample of foods provided in the diets with a high glycemic load (HG) or low glycemic load (LG)

HG diet
Candied sweet potatoes
Carrots
Chicken and pea casserole
Chef salad
Chicken and rice
Coconut
English muffins and bagels
Jelly
Jasmine rice
Lactose-free skim milk
Oatmeal
Pizza
Sugar cookies and graham crackers
Shepherd’s pie with mashed potatoes
Sweet and sour chicken
Turkey with cranberry sauce
Tuna sandwich
Waffles
Yogurt with added fruit—canned pears, peaches, figs, pineapple, oranges, and bananas

LG diet
Baked chicken
Bean and barley stew
Bulgur and beans
Broccoli and beans
Cottage cheese, low-fat
Curried lentils
Fish
Fruit: oranges, grapefruit, plums, pears, apples, and berries
Flaxseed cookies
Green salad
Kashi and Muesli cereal
Lentils with tomato sauce
Nuts
Pumpernickel bread
Salisbury steak
Skim milk
Tomato cucumber bean salad
Wheat berry salad
Yogurt

1 Lactaid; McNeil Nutritional, LLC, Fort Washington, PA.
2 Kashi, La Jolla, CA.
3 Kellogg’s Co, Battle Creek, MI.