A Randomized Trial Comparing Low-Fat and Low-Carbohydrate Diets Matched for Energy and Protein

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Abstract

SEGAL-ISAACSON, CJ, SHANNAH JOHNSON, VLAD TOMUTA, BRANDY COWELL, AND DANIEL T. STEIN. A randomized trial comparing low-fat and low-carbohydrate diets matched for energy and protein. *Obes Res.* 2004;12:130S–140S.

Several recent studies have found greater weight loss at 6 months among participants on a very-low-carbohydrate (VLC) weight-loss diet compared with a low-fat (LF) weight-loss diet. Because most of these studies were not matched for calories, it is not clear whether these results are caused by decreased energy intake or increased energy expenditure. It is hypothesized that several energy-consuming metabolic pathways are up-regulated during a VLC diet, leading to increased energy expenditure. The focus of this study was to investigate whether, when protein and energy are held constant, there is a significant difference in fat and weight loss when fat and carbohydrate are dramatically varied in the diet. The preliminary results presented in this paper are for the first four of six postmenopausal overweight or obese participants who followed, in random order, both a VLC and an LF diet for 6 weeks. Other outcome measures were serum lipids, glucose, and insulin, as well as dietary compliance and side effects. Our results showed no significant weight loss, lipid, serum insulin, or glucose differences between the two diets. Lipids were dramatically reduced on both diets, with a trend for greater triglyceride reduction on the VLC diet. Glucose levels were also reduced on both diets, with a trend for insulin reduction on the VLC diet. Compliance was excellent with both diets, and side effects were mild, although participants reported more food cravings and bad breath on the VLC diet and more burping and flatulence on the LF diet.

Key words: low carbohydrate diet, carbohydrate metabolism, weight loss, protein, ketogenic diet

Introduction

The main objective of this pilot study was to investigate, under controlled dietary conditions, whether more energy is expended during a very-low-carbohydrate (VLC)[1] diet (≤5% to 10% of energy as carbohydrate) compared with a low-fat (LF) diet when the energy and protein content of the diets are the same.

The results presented in this paper and in a companion paper are based on very preliminary results from the first four of six participants being studied. This paper focuses on the dietary methodology of the study and our preliminary weight, lipid, and quality-of-life results.

Clinical Trials Comparing VLC Diets to LF Diets

Recent clinical trials comparing LF diets to VLC higher protein diets (VLC diets) have tended to show that study participants on VLC diets lose more weight through the first 6 months of the diet (1,2). Most of these studies have chosen a design where calories are not matched between groups but imitate "natural conditions," in which participants follow a diet book or a self-help manual with only a modest amount of dietary counseling (1,3,4).

In studies where calories have been matched, there have been conflicting results. No weight-loss differences have been observed between VLC and LF diets in studies with very low energy levels of 800 to 1000 kcal, as exemplified by the study conducted by Yang and Van Itallie (5). It is

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[1] Nonstandard abbreviations: VLC, very-low-carbohydrate; LF, low-fat; REE, resting energy expenditure; DASH, Dietary Approaches to Stop Hypertension; LDL, low-density lipoprotein; HDL, high-density lipoprotein; MET, metabolic equivalent; SCL-90, Symptom Checklist-90.

possible, however, that the extreme energy reduction of these diets may eliminate weight-loss differences, making it difficult to extrapolate to diets with more moderate energy reductions.

Similarly, a recent study by Stadler et al. (6) has found no significant weight-loss differences when 25 participants were either randomized to a VLC diet or to the LF Dietary Approaches to Stop Hypertension (DASH) diet (7). Participants on the VLC diet were started before those on the DASH diet and were given meals totaling 125% of their predicted energy requirements. They were told to eat as much as they needed not to be hungry. The VLC group spontaneously consumed only 67% of their predicted energy requirements. The energy level of the DASH diet group was matched to this reduced VLC diet group by kilocalorie average. Although not significant, there was a trend toward greater weight loss in the VLC diet group.

Greene et al. (8) also has found a trend toward greater weight loss in a small VLC to LF isoenergetic randomized controlled feeding trial of 21 participants for 12 weeks, where men were provided 1800 kcal/d and women were provided 1500 kcal/d. The weight loss for the VLC group was 23 $\pm$ 4.6 lb compared with 17 $\pm$ 2.3 lb.

At present, it is not clear whether, on energy-matched diets, VLC diets cause greater resting energy expenditure (REE).

Potential Metabolic Energy Inefficiencies on VLC Diets

Hypothetically, VLC diets might increase REE through up-regulating one or more metabolic pathways that are less energy efficient than glycolytic pathways. These pathways might include increased gluconeogenesis from protein catabolism to meet obligate glucose needs, direct use of amino acid 2- and 3-carbon fragments for energy, increased triglyceride cycling, and increased glyceroneogenesis.

Because the focus of this pilot study was to investigate metabolic energy inefficiencies related to fat metabolism, only the latter two phenomena—triglyceride cycling and glyceroneogenesis—will be reviewed here. In the companion paper, a third possible mechanism—an up-regulation of mitochondrial uncoupling proteins with a resultant wasting of ATP as heat—will be reviewed.

Triglyceride Cycling

Triglyceride turnover (lipolysis and resynthesis of triglyceride) increases substantially during fasting conditions and is an energy-consuming process. As much as 60% of triglycerides during fasting are hydrolyzed and resynthesized. A large portion of this triglyceride turnover occurs in white adipose tissue. Triglyceride turnover is up-regulated by epinephrine and glucagon during fasting and down-regulated in the fed state by higher insulin levels (9). Hanson and Reshef (9) have pointed out that it is not yet known whether this futile cycling confers any survival advantage to mammals, because it would seem more logical to conserve rather than expend additional calories during the fasting state. They have suggested that the advantage of ready fuel for "emergencies" in the form of free fatty acids may outweigh the cost of calories spent resynthesizing triglyceride.

Because VLC diets are associated with lower ambient insulin and glucose levels (10,11) and higher free fatty acid levels (11) and because triglyceride cycling is also driven by the available concentration of free fatty acids (12), the higher free fatty acid levels of VLC diets could hypothetically lead to increased triglyceride turnover with its concomitant energy dissipation.

Glyceroneogenesis

Glyceroneogenesis, the second futile cycle mentioned above, occurs under both fasting conditions and when carbohydrate is absent or nearly absent in the diet. Glyceroneogenesis refers to the synthesis of glycerol from lactate, pyruvate, or alanine rather than glucose, the precursor for glycerol under fed conditions when carbohydrate is present in the diet (9,13).

Glycerol can also be converted to glucose through the process of gluconeogenesis. In fact, fasting has been shown to dramatically increase the amount of glycerol converted to glucose. The amount of glycerol that is converted to glucose increases from 5% in the fed state on a carbohydrate-containing diet to 20% after a 3- to 4-day fast (14). Thus, it is possible that, even without considering energy inefficiencies related to protein metabolism, there may be modest but persistent increases in energy expenditure related to fat metabolism on a VLC diet.

As stated earlier, one of the primary purposes of this study was to determine whether a VLC diet independent of its protein content might perceptibly enhance weight loss compared with an LF diet with the same protein content. This paper presents the extremely preliminary findings on weight loss from the first four participants in a pilot crossover controlled feeding trial of six participants. It will also present data on compliance, frequency of side effects of both diets, physical activity patterns, and psychological well-being on both diets.

Although beyond the scope of this paper, additional objectives of the study were to 1) compare the 24-hour REE of both diets to baseline measures through indirect calorimetry using a bubble canopy (Delatrac II Metabolic Monitor; Datex USA, Tewksbury, MA) by measuring participants for 20 minutes every hour for 15 hours, followed by a final measurement at hour 24; 2) measure total fat oxidation rates using a dietary bolus of ^{13}C-triolein tracer and then measure its appearance in breath samples; 3) measure free fatty acid and triglyceride turnover rates by 2,2-H-palmitate and d5-

Table 1. Diet composition

	VLC diet	High-protein LF diet
Energy*	REE − 200 kcal	REE − 200 kcal
Protein	30%	30%
Carbohydrate	5%	50% (as starches and fruit)
Fat	65%	20%
Monounsaturate	22%	8%
Polyunsaturate	21%	6%
Saturate	22%	6%

*Kilocalories are individualized for participants and set at their REE − 200 kcal as measured by 20 minutes of indirect calorimetry under a bubble canopy calorimeter (Delatrac II Metabolic Monitor).

glycerol tracers; 4) measure the effects of the two diets on total body fat by the total body water body dilution technique, using the appearance of deuterated water (^2H_2O) in the saliva; 5) evaluate the effects of the two diets on visceral fat by magnetic resonance imaging, using ^{1}H-spectroscopy (Philips NT 1.5 T Clinical MR System, Philips Medical Systems, Andover, MA); 6) determine through hyperinsulinemic euglycemic clamp studies whether the percentages of fat and carbohydrate intake in a weight-loss diet affects insulin sensitivity; 7) measure the effects of both diets on levels of intramyocellular lipids; and 8) follow participants who have completed the 12-week trial to the 1-year time-point to assess further weight loss, weight loss maintenance, dietary compliance, satisfaction and quality of life—participants will select the trial diet with which they were most comfortable and transition to preparing their own food.

Research Methods and Procedures

Study Design

This study was a 12-week cross-over controlled feeding study in which participants consume both an LF and VLC diet for 6 weeks each. The study used a random order cross-over design to control for diet order effects. Of the four participants' results reported in this paper, two started with the VLC diet and two started with the LF diet. The diets were isocaloric and isonitrogenous. Measurements were collected at baseline, 6 weeks, and 12 weeks. Table 1 shows the dietary composition of each diet. The study was approved by the Committee on Clinical Investigations of the Albert Einstein College of Medicine.

After the end of the 12-week diet trial, participants were given the opportunity to continue for an additional 9 months (to the 1-year time-point) with whichever of the two diets they preferred. During this period, participants transitioned to preparing their own food but received monthly dietary counseling. Lipids, REE, and body composition were measured at the 6- and 12-month time-points.

Sample Size

Preliminary data with adolescents from Sondike et al. (4) have shown a 12-week weight loss of 8.5 ± 8.3 lb for the LF group and 19.0 ± 12.4 lb for the VLC group. The mean difference in total weight loss for the two groups was 10.5 lb. Based on this, a sample size of six participants in each dietary group would provide 88% power to detect a 4 ± 2-lb fat loss and 64% power to detect a 3 ± 2-lb fat loss between the two diets at 6 weeks ($\alpha = 0.05$).

Participants

Participants were limited to a relatively homogenous sample of overweight or obese postmenopausal women who had a waist-to-hip ratio of at least 0.8 and a BMI of at least 28 kg/m^2 and <40 kg/m^2 to maximize potential effects and minimize hormonal variability. The maximum weight was limited to ≤250 lb, because this was the limit of the Philips NT 1.5 T Clinical Magnetic Resonance system. Exclusion criteria also included a history of cardiovascular disease or diabetes, the current use of any medications known to affect weight or insulin sensitivity, a history of eating disorders, triglycerides >400 mg/dL, a weight change >5 lb in the past 3 months, use of a low-carbohydrate weight loss diet within the past 6 months, claustrophobia, ferromagnetic foreign bodies, or veins difficult to access for venipuncture.

Preliminary characteristics of the participants are listed in Table 2. Baseline dietary data were collected through self-report using the Dietary History Questionnaire food frequency questionnaire (15). It is likely that participants underreported their average calorie intake, possibly because of lack of familiarity with the instrument.

Overall, the REE at baseline was between 1300 and 1400 kcal/d. The mean weight was 82.2 ± 10.3 kg, and BMI was 33.3 ± 3.2 kg/m^2. Serum glucose was high normal. Cholesterol and low-density lipoprotein (LDL) were also high normal, and high-density lipoprotein (HDL) was within the normal range.

Dietary Intervention

A modular dietary pattern was developed for both diets so that calorie levels could be easily individualized to achieve an REE − 200 kcal energy deficit for each participant. Each diet consisted of interchangeable breakfasts, lunches, dinners, snacks, and 100-kcal adjustment foods. There were approximately five choices for breakfasts and snacks and seven choices for lunches/dinners. The 100-kcal adjustment foods allowed for finer calorie gradations and consisted

Table 2. Preliminary characteristics of participants ($n = 4$)

	Mean	SD	Percentage of kilocalories
Age	52.3	3.8	
Race: 2 White, 2 Latina			
Kilocalories	1252	523	
Protein (g)	56	27	18%
Total fat (g)	52	21	37%
Saturated fat (g)	18	6	13%
Monounsaturated fat (g)	18	7	13%
Polyunsaturated fat (g)	13	6	9%
Carbohydrate (g)	143	61	46%
Dietary cholesterol (mg)	152	58	
Fiber (g)	12	8	
REE (kcal/d)	1375	126	
Weight (kg)	82.2	10.3	
BMI (kg/m^2)	33.3	3.2	
Waist-to-hip ratio	0.88	0.09	

of either an ounce of specific cheeses for the VLC diet or 1 cup of 1% low-fat milk, soymilk, or low-fat plain yogurt for the LF diet. The basic 1400-kcal diet consisted of a 300-kcal breakfast, a 450-kcal lunch and dinner, and a 200-kcal snack with each meal, following the macronutrient distribution of the overall diet described in Table 1. Participants were also allowed noncaloric herbs, spices, and limited amounts of lemon juice, diet soda, and diet gelatin. Neither diet contained any added sugar. Carbohydrates were provided in the LF diet as low glycemic starches or as small portions of fruits. The meal choices and recipes were developed by the study nutrition staff using the FoodWorks dietary analysis computer program (FoodWorks Version 3.01; The Nutrition Co., Long Valley, NJ).

An electronic digital scale (model 3001; Salter Housewares Ltd, Tonbridge, England), a set of calibrated measuring spoons, and a calibrated measuring cup were provided to each participant so that participants could measure and prepare their own breakfasts, snacks, and calorie adjustment foods according to specific study recipes. Participants were tested on their ability to accurately measure and portion foods three times during the study. Lunches and dinners were prepared by a licensed caterer who was supervised by study nutrition staff. The meals were frozen and distributed to participants in vacuum-sealed reheatable plastic bags in insulated carrying bags with ice once each week after their nutrition counseling session. Table 3 shows the entrées developed for each diet. One entrée in each condition was designed to contain significant amounts of ω3-fatty acids. Participants could eliminate one or more entrée if they disliked it but were provided the same weekly pattern of entrées over the 6-week diet. No participant rejected more

Table 3. Dinner and lunch entrée choices

VLC entrées	LF entrées
Roast chicken with green salad	Chicken breast oreganato, linguine, and spinach
Salmon teriyaki with spinach	Halibut teriyaki, brown rice with sesame seeds, and broccoli
Lamb chop with string beans and toasted sunflower seeds	Roast leg of lamb, broccoli, and sweet potatoes
Chinese beef and broccoli	Bean and ground turkey enchiladas, green salad
Roast beef and green salad	Burgundy beef stew
Coconut chicken curry and asparagus	Braised honeyed boneless chicken, couscous, and green beans
Veal scallopine with smokey chard	Spinach-tofu lasagne

than one entrée. Participants were also provided a therapeutic vitamin-mineral supplement (Basic 1; Atkins Nutritionals, Ronkonkoma, NY)

The lunches and dinners were prepared in two batches by the caterer. For each batch, a sample of each entrée was sent to Covance Laboratories (Madison, WI) for analysis of protein, fat, water, and by deduction, carbohydrate content.

Measures

Participant were weighed to the nearest 0.25 kg on the same calibrated balance scale at each measurement point wearing a paper hospital gown and underwear but no shoes. Weights were collected after fasting and voiding. Body composition was determined by the total body water method, as described by Wolfe, using deuterated water as the stable isotope (16). An analysis of the body composition measures is pending.

Participants completed three types of daily monitoring forms to assess dietary compliance, quality of life, side effects, and physical activity levels. All checklists, forms, and returned food packaging were reviewed on a weekly basis with the study nutritionist. Dietary compliance was assessed with daily checklists. Participants were responsible for checking off their food choices and amounts eaten as well as adding any additional foods they might have consumed. Participants were also asked to bring in the packaging from all food provided for a further compliance check. Symptom checklists were used to assess quality-of-life parameters, such as well-being, energy, and mood, as well as the presence of physical symptoms, such as bad breath, nausea, headaches, and gastrointestinal disturbances. Participants were asked to remain relatively sedentary and not change their level of physical activity during the trial. Participants completed the Seven-Day Activity Recall on a daily basis to assess physical activity levels (17). The Seven-Day Activity Recall has been shown to have good validity compared with doubly labeled water measurements (18).

Results

Compliance

Dietary compliance with both diets was excellent. All participants completed their daily dietary checklists for the entire 12 weeks. The checklists documented that participants were consuming the food and not consuming nonintervention foods. Participants were satisfied with the taste and convenience of the frozen meals provided for them. Physical activity logs and symptom checklists were also appropriately completed for all participants.

Compliance was also excellent with the request to maintain the same level of physical activity over the 12-week trial. As estimated from the Seven-Day Activity Recall, physical activity did not vary significantly between the diets. The metabolic equivalents (METS) were 32.90 ± 2.51 for the LF diet group and 35.18 ± 2.95 for the VLC diet group ($p = 0.58$). METS are the ratio of activity-related energy expenditure to REE, where 1 MET is defined as 1 kcal/kg per hour and is approximately the energy cost of sitting quietly (19).

Table 4. Diet-related symptoms ($n = 4$)

Symptom	Number of days participants reported symptom: VLC diet	LF diet	Pearson χ^2	p
Constipation	22	12	3.450	.063
Food cavings	17	4	8.814	0.003
Flatulence	6	34	22.092	<0.001
Burping	5	21	10.524	0.001
Fruity or foul breath	67	26	26.663	<0.001
Hunger	12	12	0.001	0.974

Symptoms

Participants reported more burping and flatulence on the LF diet and more bad breath and food cravings on the VLC diet. There was no significant differences between the two diets for constipation or hunger (Table 4).

The Symptom Checklist-90 (SCL-90) was used to evaluate negative feelings at baseline and at the end of each diet period. SCL-90 answers range from "not at all" to "extremely" on a five-point scale. Total scores range from 0 to 360. The mean baseline SCL-90 score ($n = 4$) was 36.25 ± 30.60. Scores did not differ significantly between the VLC group (29.35 ± 25.03) and the LF group (36.50 ± 30.92). The low scores suggest that participants had a generally positive mood both before and during both interventions.

Weight Loss

There was no significant difference in weight loss ($p = 0.509$) between the LF and VLC diets. The average weight loss for the VLC diet was 5.88 ± 1.20 kg and for the LF diet was 4.35 ± 1.32 kg (Figure 1).

There was also no significant diet order weight-loss effect; three of four participants lost as well with the second diet as with the first diet, although the fourth participant lost more weight on the VLC diet (Figure 2).

Extension Diet

All four participants decided to participate in the 9-month extension study. Three of the participants chose to continue

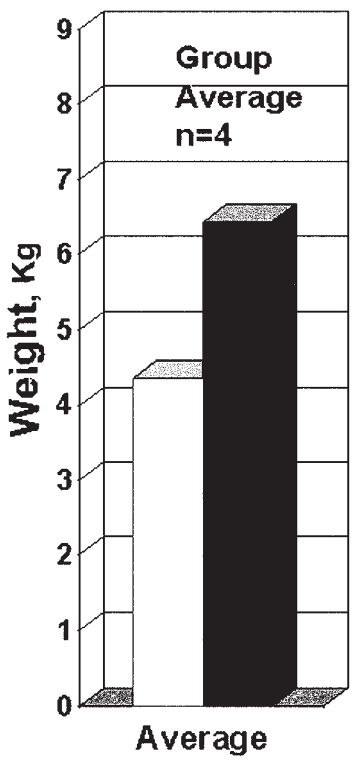

Figure 1: Comparison of weight loss between diets. Student's *t* test for average weight loss, $p = 0.359$. VLC diet: 6.45 ± 2.15 kg; LF diet: 4.35 ± 1.32 kg. Black, VLC diet; white, LF diet.

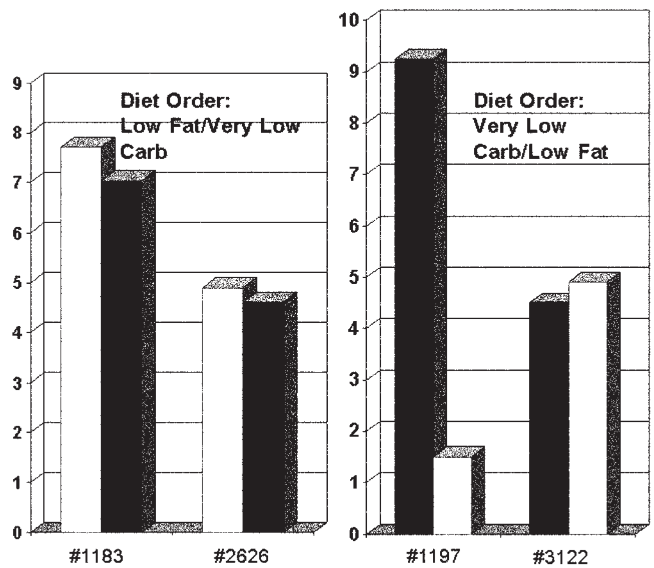

Figure 2: Comparison between LF and VLC diets. For averages, see Figure 1. Black, VLC diet; white, LF diet.

with the VLC diet, and one decided to continue with the LF diet. All did very well with either losing additional weight or sustaining the majority of their weight loss during the extension study. The patterns of weight loss during the 12-week controlled feeding study and the 9-month extension study are shown in Figure 3. For the three participants who chose the VLC extension diet, carbohydrate intake rose to 23% and fat intake decreased to 52% of kilocalories by 6 months. By 12 months, carbohydrate intake increased to 30% of kilocalories and fat intake remained constant at 52% of kilocalories, as participants' diets reverted toward their baseline macronutrient composition. For the participant who chose the LF extension diet, her 6-month carbohydrate

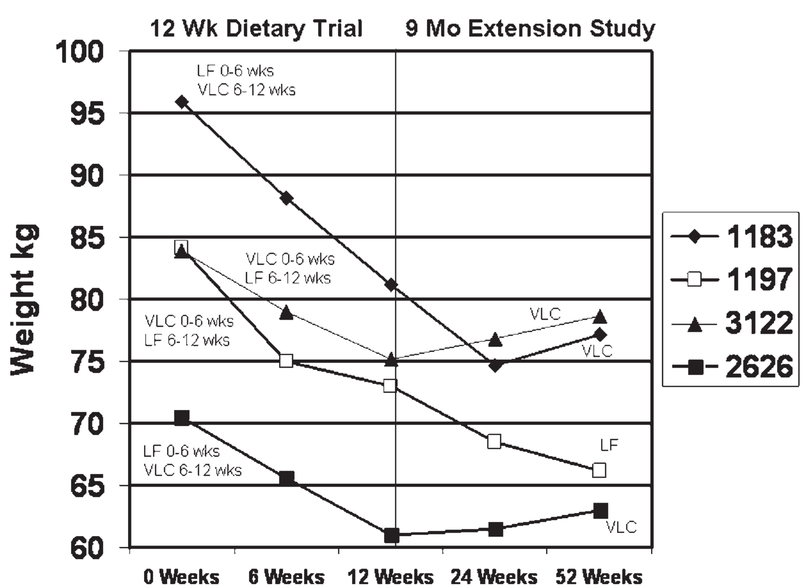

Figure 3: Weight patterns in first four participants. ♦, participant 1183; □, participant 1197; ▲, participant 3122; ■, participant 2626.

Table 5. Comparison of fasting lipids and selected hormones during the 12-week dietary trial ($n = 4$)

	Baseline [mean (SD)]	VLC diet [mean (SD)]	LF diet [mean (SD)]	*t* (VLC to LF)	*p* (VLC to LF)
Cholesterol (mg/dL)	212 (17)	143 (30)*	130 (7)*	1.03	0.378
Triglyceride (mg/dL)	97 (20)	53 (11)*	75 (20)	−2.86	0.065
LDL (mg/dL)	138 (19)	92 (23)*	82 (7)*	1.15	0.333
HDL (mg/dL)	55 (6)	41 (12)*	34 (6)*	2.13	0.123
Serum glucose (g/dL)	95.4 (10.2)	78.6 (11.6)*	84.0 (9.1)*	−1.60	0.206
Serum insulin (μg/dL)	4.8 (2.4)	1.8 (1.29)	4.0 (1.5)	−1.99	0.141

*Significantly different from baseline ($p \leq 0.05$).

intake was 53% of kilocalories and her fat intake was 26% of kilocalories. By 12 months her carbohydrate intake decreased to 47% of kilocalories and her fat intake increased to 32% of kilocalories, as her dietary pattern also reverted toward her baseline pattern.

Lipids, Glucose, and Insulin Values

There were no significant differences in fasting lipids (cholesterol, triglycerides, LDL, and HDL) between the two diets, although there was a trend for lower triglyceride levels in the VLC diet group (VLC, 53 ± 11 mg/dL; LF, 75 ± 20 mg/dL; $p = 0.065$) as shown in Table 5. The lipid values for both diets were significantly lower than baseline values, except triglycerides for the LF diet, where there was a trend for a lower value ($p = 0.072$). Fasting serum glucose values were lower than baseline values for both diets, but serum insulin levels were not, although once again, there was a trend for lower values in the VLC group ($p = 0.061$).

The lipid patterns over the course of the 12-week controlled dietary trial and the 9-month extension study for the four participants are shown in Figures 4 to 8. Lipids rebounded to baseline levels after the dietary trial for all participants, regardless of weight-loss maintenance or the extension diet they selected by 12 months.

Discussion

The purpose of our study was to evaluate how weight loss and metabolism are affected by two diets when energy and protein are held constant, and dietary fat and carbohydrate are dramatically varied. It is possible that there is greater energy expenditure on a VLC diet, leading to increased weight loss from the increased turnover of triglycerides and synthesis of glycerol from noncarbohydrate substrates. This paper reports the preliminary findings for the first four participants. The planned final sample size for this pilot is six participants.

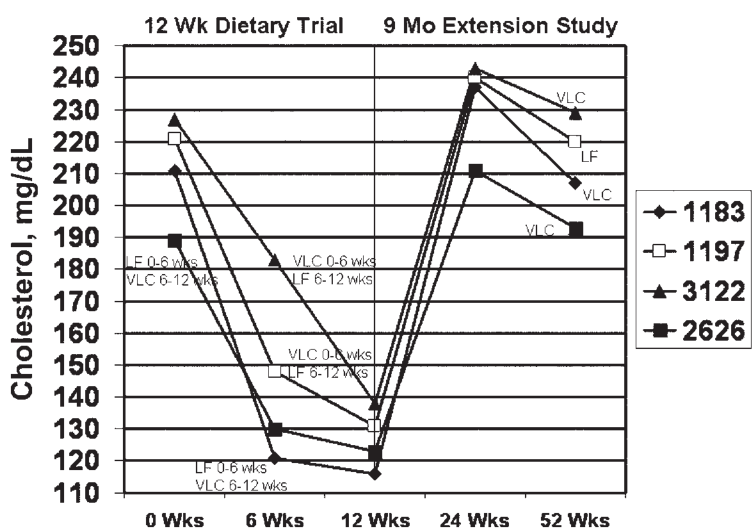

Figure 4: Cholesterol patterns in first four participants. ◆, participant 1183; □, participant 1197; ▲, participant 3122; ■, participant 2626.

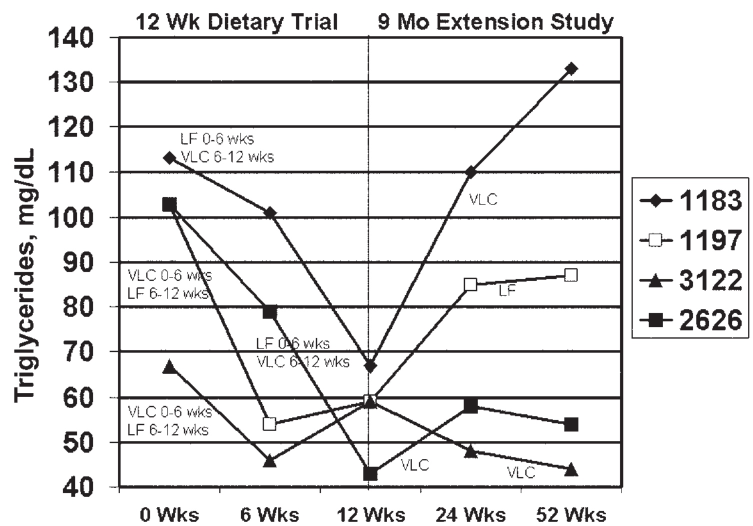

Figure 5: Triglyceride patterns in first four participants. ♦, participant 1183; □, participant 1197; ▲, participant 3122; ■, participant 2626.

Both diets were very well tolerated, although participants experienced some mild and transient side effects on both diets. Participants reported more food cravings and fruity or foul breath on the VLC diet but more flatulence and burping on the LF diet. There was a trend for more constipation on the VLC diet.

Participants consumed a LF and VLC diet for 6 weeks in random order, set at an individualized kilocalorie level of REE − 200 kcal/d. The LF diet had 10 times the carbohydrate of the VLC diet (50% of kilocalories compared with 5% of kilocalories), whereas the VLC diet had 3.25 times the amount of fat as the LF diet (65% of kilocalories compared with 20% of kilocalories).

In this study, participants rated both diets similarly with respect to hunger and satiety levels. It is possible that this occurred because the diets were matched for protein at 30% of kilocalories. In a recent review, Anderson and Moore have summarized several lines of evidence, suggesting that protein contributes more to satiety than either fat or carbohydrate (20). Data from the Controlled Carbohydrate Assessment Registry Bank Study, a 3-year prospective Internet-based study with a cohort of 2509 people, has found that 94.9% of participants reported they liked low-carbohydrate diets because they are less hungry on them. The average protein intake of Controlled Carbohydrate Assessment Registry Bank Study participants is 23.5% (Segal-Isaacson, unpublished data) compared with the average intake of 15% reported for men and women surveyed for the National Health and Nutrition Examination Studies 1988 to 1994 (21).

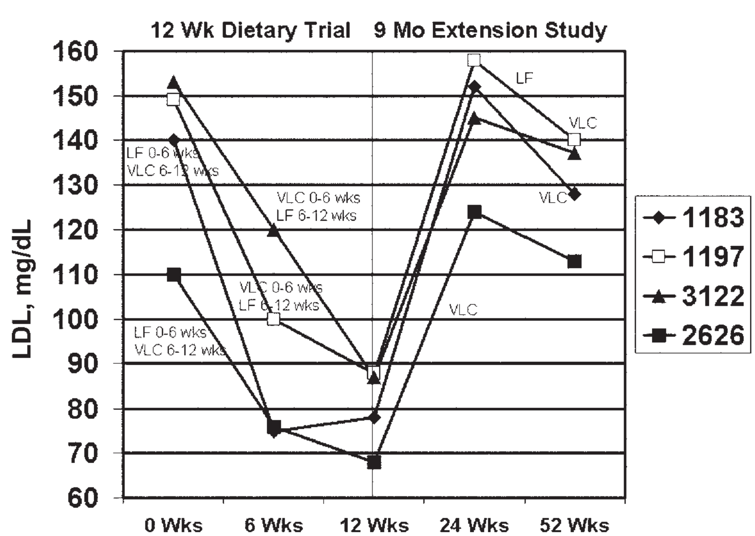

Figure 6: LDL patterns in first four participants. ♦, participant 1183; □, participant 1197; ▲, participant 3122; ■, participant 2626.

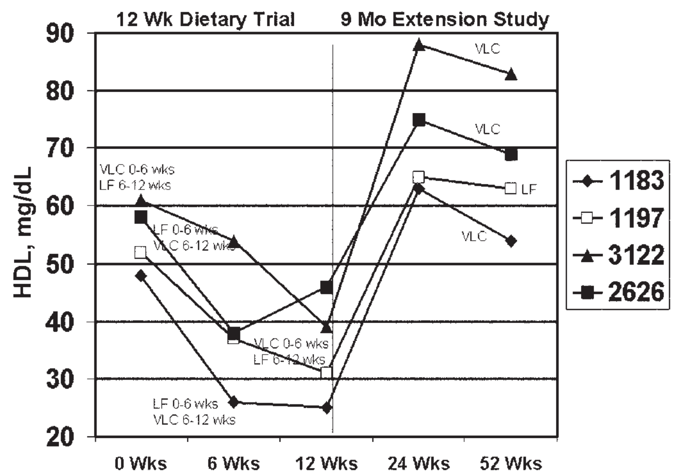

Figure 7: HDL levels in first four participants. ♦, participant 1183; □, participant 1197; ▲, participant 3122; ■, participant 2626.

The weight-loss data for the first four participants showed no significant weight-loss differences between diets at the same protein level, although there was a modest trend for greater weight loss during the low-carbohydrate phase of the intervention. This suggests that weight-loss differences found between VLC and LF diets are unlikely to be predominantly from increased cycling of triglyceride synthesis and neoglycerogenesis because of the replacement of fat for carbohydrate. However, the small trend for increased weight loss in the preliminary VLC diet group suggests that a modest increase in REE cannot yet be ruled out. Our preliminary results for 24-hour REE measurements under both diet conditions will be explored in the companion paper.

With respect to other randomized trials comparing VLC to LF diets, both Foster et al. (1) and Brehm et al. (2) have found a greater weight loss in the low-carbohydrate diet group at 3 and 6 months. In both studies, kilocalories and protein intake had not been matched between groups. Brehm et al. have reported no significant caloric differences between groups, although protein intake was significantly higher and carbohydrate intake significantly lower in the VLC group at both 3 and 6 months. Stadler et al. (6) did match calories and have found no significant weight-loss difference between the participants on a VLC compared with an LF diet but did find a small trend in favor of the VLC diet. Protein intake was higher on VLC diet.

Foster et al. (1) have found that, compared with the LF group, the VLC group had generally higher lipid values (total cholesterol, HDL, LDL, and triglycerides), although not at all measurement time periods. The most sustained differences were higher HDL and lower triglyceride levels

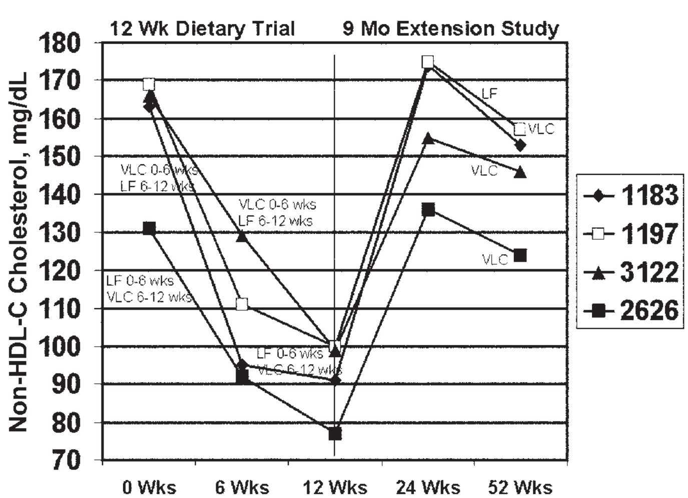

Figure 8: Non-HDL-C cholesterol patterns in first four participants. ♦, participant 1183; □, participant 1197; ▲, participant 3122; ■, participant 2626.

in the low-carbohydrate group. In this study, we found a trend for lower triglyceride levels in the VLC group, but no other substantial lipid differences between the two diets. This may be because of a much smaller number of participants, the shorter acute intervention time (6 weeks vs. 6 months), and that participants were on isocaloric diets, and therefore, losing weight steadily on both diets. It is also possible that the lipid results were also similar than in other studies because the dietary fat for both intervention diets was evenly distributed between saturated, monounsaturated, and polyunsaturated fats, albeit at different percentages of energy.

Perhaps one of the most surprising findings was that all measured lipids profoundly increased during the 9 months of the extension diet for all four participants, despite the fact that none of them regained weight during this period but either maintained their weight loss or continued to lose weight, albeit more slowly. This suggests that the lipid-lowering effect of either diet may have more to do with the rapidity of weight loss than its macronutrient profile. Rapid weight loss has been associated with a dramatic improvement in lipids (22).

Finally, and in a more anecdotal vein, there has been a resurgence of interest in the last few years in the efficacy of using meal replacements as part of a weight-loss strategy. Typically such meals consist of either a liquid protein shake or a high-protein bar. A number of studies have found that meal replacement foods can help individuals effectively lose weight (23,24). This effect has been attributed to the portion control and the convenience that meal replacement foods provide.

In this controlled feeding study, participants were supplied prepared portioned lunches, dinners, and some snacks that they found convenient and palatable. Although not a planned study objective, one of the remarkable findings was the extent to which this extremely structured approach seemed to help participants with compliance. All of the participants in this trial had tried to lose weight on their own in the recent past and had failed repeatedly. The big attraction to them of being in this dietary trial was that it provided them both the meals and the nutrition monitoring they believed they needed to stay on track. All four participants remarked at how much easier they found dietary compliance with the prepared meals. Their success with compliance leading to steady weight loss contributed to participants' growing sense of self-efficacy and confidence about both losing weight and sustaining their weight loss. This "can-do" confidence also carried participants through the transition to home food preparation during the extension study. Each one of the participants remarked that she had gained an appreciation of appropriate portion sizes from the prepared meals and a sense of trust that the portion sizes were sufficient to sustain her without hunger until the next meal.

Portion-controlled meals may be an easily translatable model for clinical use. A variety of modalities currently exist: frozen portion-controlled meals are available in most supermarkets, and home-delivered dieters' meal services have become available in many cities.

Although portion-control meals may work for some and not for others, the relevant construct is less about the specific approach than the crucial need to help individuals succeed at weight loss from the start and help them develop their own road map of how to keep that success moving forward.

In conclusion, additional controlled feeding studies are needed to determine whether protein and gluconeogenesis contribute toward greater weight loss on VLC diets. Such studies may want to compare VLC diets against both isonitrogenous and lower-protein LF diets to determine whether, if there is greater energy expenditure, it is protein per se or protein in the context of carbohydrate restriction that is the operative mechanism.

Additional studies are also needed to determine whether the consistent pattern of greater short-term weight loss with VLC diets under "natural conditions" (where calories are not strictly controlled) is caused by increased energy expenditure, restriction of food choices, greater satiety, or some combination of all three.

Acknowledgments

We gratefully acknowledge the generous support of our funders: The Robert C. Atkins Foundation, National Institute of Diabetes, Diet and Kidney Diseases Grant R01DK61644, and the General Clinical Research Center of the Albert Einstein College of Medicine. We also acknowledge Atkins Nutritionals for providing protein powder and vitamin supplements used in this study. We also thank the following people for their unstinting time and encouragement: Dr. Judith Wylie-Rosett for excellent comments on this manuscript and Dr. Abby Bloch for making both this supplement and the original conference possible.

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