Very Low-Carbohydrate and Low-Fat Diets Affect Fasting Lipids and Postprandial Lipemia Differently in Overweight Men[1]

Matthew J. Sharman,[2] Ana L. Gómez, William J. Kraemer, and Jeff S. Volek

Human Performance Laboratory, Department of Kinesiology, University of Connecticut, Storrs, CT 06269-1110

ABSTRACT Hypoenergetic very low-carbohydrate and low-fat diets are both commonly used for short-term weight loss; however, few studies have directly compared their effect on blood lipids, with no studies to our knowledge comparing postprandial lipemia, an important independently identified cardiovascular risk factor. The primary purpose of this study was to compare the effects of a very low-carbohydrate and a low-fat diet on fasting blood lipids and postprandial lipemia in overweight men. In a balanced, randomized, crossover design, overweight men ($n = 15$; body fat >25%; BMI, 34 kg/m^2) consumed 2 experimental diets for 2 consecutive 6-wk periods. One was a very low-carbohydrate (<10% energy as carbohydrate) diet and the other a low-fat (<30% energy as fat) diet. Blood was drawn from fasting subjects on separate days and an oral fat tolerance test was performed at baseline, after the very low-carbohydrate diet period, and after the low-fat diet period. Both diets had the same effect on serum total cholesterol, serum insulin, and homeostasis model analysis-insulin resistance (HOMA-IR). Neither diet affected serum HDL cholesterol (HDL-C) or oxidized LDL (oxLDL) concentrations. Serum LDL cholesterol (LDL-C) was reduced ($P < 0.05$) only by the low-fat diet (−18%). Fasting serum triacylglycerol (TAG), the TAG/HDL-C ratio, and glucose were significantly reduced only by the very low-carbohydrate diet (−44, −42, and −6%, respectively). Postprandial lipemia was significantly reduced when the men consumed both diets compared with baseline, but the reduction was significantly greater after intake of the very low-carbohydrate diet. Mean and peak LDL particle size increased only after the very low-carbohydrate diet. The short-term hypoenergetic low-fat diet was more effective at lowering serum LDL-C, but the very low-carbohydrate diet was more effective at improving characteristics of the metabolic syndrome as shown by a decrease in fasting serum TAG, the TAG/HDL-C ratio, postprandial lipemia, serum glucose, an increase in LDL particle size, and also greater weight loss ($P < 0.05$). J. Nutr. 134: 880–885, 2004.

KEY WORDS: • *weight loss* • *postprandial lipemia* • *lipoprotein subclasses* • *triglycerides* • *metabolic syndrome*

The popularity of diets that restrict carbohydrates has increased dramatically in recent years despite review articles cautioning against their use (1–3). Because these diets are often high in saturated fat and cholesterol, there is an understandable concern regarding potential risk for cardiovascular disease (CVD),[3] and this line of research has been a focus in our laboratory (4). To shed light on how excessive carbohydrate restriction affects CVD risk independently of weight loss, we initially studied isoenergetic very low-carbohydrate diets in normal-weight men and women (5–8). In our first study, we demonstrated that a very low-carbohydrate diet rich in monounsaturated fat and supplemented with (n-3) fatty acids significantly reduced fasting triacylglycerols (TAG), postprandial lipemia, and fasting insulin in men (5). In a follow-up study in a similar population, we reported similar improvements in fasting lipids, postprandial lipemia, and insulin after consumption of a very low-carbohydrate diet that was unrestricted in the type of fat and not supplemented with (n-3) fatty acids (6,7). Additionally, there was an increase in peak LDL particle size in subjects who started with a predominance of small LDL particles (6). Most recently, we also showed that a very low-carbohydrate diet significantly increases HDL cholesterol (HDL-C) and significantly decreases TAG and postprandial lipemia in normal-weight women (8).

Our earlier work with very low-carbohydrate diets was in normal-weight men and women. Because the majority of individuals who consume a very low-carbohydrate diet do so with the intention of losing weight, the primary purpose of this study was to examine the effect of a hypoenergetic very low-carbohydrate diet on CVD risk in overweight men. We compared responses to a low-fat diet in the same subjects (i.e., within-subjects design) because of the large variability in lipid responses to diet interventions and the difficulty in adequately matching subjects for confounding factors such as genetics, which can affect lipid responses to diet interventions (9).

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[2] To whom correspondence should be addressed.
E-mail: matthew.sharman@uconn.edu.
[3] Abbreviations used: AUC, area under the curve; CVD, cardiovascular disease; HDL-C, HDL cholesterol; HOMA-IR, homeostasis model analysis-insulin resistance; IDL, intermediate density lipoprotein; LDL-C, LDL cholesterol; oxLDL, oxidized LDL; TAG, triacylglycerol; TC, total cholesterol.

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Further, no published very low-carbohydrate diet studies have assessed postprandial lipemia and none have taken more than 1 blood sample at each time point, a practice highly recommended to account for day-to-day variability in blood lipids (10). Based on our earlier work in normal-weight men, we hypothesized that a hypoenergetic very low-carbohydrate diet in overweight men would have a more favorable effect on characteristics of the metabolic syndrome (i.e., fasting TAG, postprandial lipemia, HDL-C, LDL particle size, and insulin resistance) because men with increased body fat tend to exhibit enhanced postprandial lipemia and other characteristics of the metabolic syndrome (11,12).

SUBJECTS AND METHODS

Subjects. Overweight (percentage body fat > 25%) but otherwise healthy men ($n = 15$) volunteered to participate in this investigation. Their physical characteristics were (mean ± SD); age, 33.2 ± 11.3 y; body mass, 109.1 ± 17.8 kg; body fat, 34.9 ± 5.2%; and BMI, 34.3 ± 5.6 kg/m^2. The subjects had been weight stable for the past month (± 2 kg), were not adhering to special diets, were not regular consumers of nutritional supplements (except a daily multivitamin/mineral). They habitually consumed between 29 and 42% of energy as fat (assessed via a 7-d food diary at baseline). All subjects were nonsmokers and not prescribed any medication known to affect serum lipoproteins. Subjects were either sedentary or moderately active and maintained the same level of physical activity throughout the study. Physical activity was recorded on log sheets, which were part of the packets the subjects received to complete food records and ketone monitoring, and also included diet prescriptions. The study was conducted in accordance with the guidelines of the Institutional Review Board at the University of Connecticut.

Experimental design. In a balanced, randomized, cross-over design, subjects consumed 2 experimental diets for 6-wk periods, a low-fat and a very low-carbohydrate diet. There was no washout period between the experimental diet periods. Two blood draws from fasting subjects were performed at the same time of day on separate days to account for diurnal and day-to-day variation in lipids, and an oral fat tolerance test was performed at baseline after the very low-carbohydrate diet period and after the low-fat diet period. On the basis of earlier work, we determined that the length of the diet periods was sufficient to achieve stabilization of blood lipids (5,6).

Diet interventions. Both experimental diets were designed to be hypoenergetic (−2.1 MJ/d). Energy levels were assigned to the nearest 837-kJ increment based on resting energy expenditure obtained using indirect calorimetry at the start of the study and appropriate activity factors. Resting energy expenditure measurements were made by indirect calorimetry (MedGraphics CPX/D, Medical Graphics) after an overnight fast (>12 h) with subjects resting supine in comfortable thermoneutral conditions (13). Standard diabetic exchange lists were used to ensure a constant energy and macronutrient balance of protein (~20% energy), fat (~25% energy), and carbohydrate (~55% of energy) during the low-fat diet period. The low-fat diet was also designed to contain <10% of total energy as saturated fat and <300 mg cholesterol (i.e., a Step-I diet). We developed customized diabetic exchange lists for the very low-carbohydrate diet period to ensure a stable energy intake of protein (~30% energy), fat (~60% energy), and carbohydrate (~10% of energy) throughout the study. There were no restrictions on the type of fat from saturated and unsaturated sources or cholesterol levels. Foods commonly consumed during the very low-carbohydrate diet period included beef (e.g., hamburger, steak), poultry (e.g., chicken, turkey), fish, oils, various nuts/seeds and peanut butter, moderate amounts of vegetables, salads with low-carbohydrate dressing, moderate amounts of cheese, eggs, protein powder, and water or low-carbohydrate diet drinks. Low-carbohydrate bars and shakes (Atkins Nutritionals) were provided to subjects during the very low-carbohydrate diet period. A daily multivitamin/mineral complex that provided micronutrients at levels ≤ 100% of the RDA was given to subjects during both experimental diet periods.

All subjects received extensive initial instruction and follow-up by registered dietitians on how to translate foods/meals into diabetic exchanges. Subjects were also provided with a packet outlining specific lists of appropriate foods, recipes, and sample meal plans that were compatible with their individual preferences for both experimental diets. Subjects received follow-up counseling on a weekly basis during which time body mass was measured, compliance was assessed, and further dietetic education provided if necessary.

Subjects received thorough instructions for completing detailed weighed food records during wk 1, 3, and 5 of each experimental diet period (21 d total). Food measuring utensils and scales were provided to subjects to ensure accurate reporting of food/beverage amounts consumed. Food diaries were analyzed for energy and macro/micronutrient content (NUTRITIONIST PRO, Version 1.3, First Databank, The Hearst Corporation). To ensure that carbohydrates were restricted throughout the very low-carbohydrate diet period, subjects tested their urine daily using reagent strips (Bayer). The test is specific for acetoacetic acid, which produces a relative color change when it reacts with nitroprusside. We found this to be a very sensitive indicator of carbohydrate restriction and compliance with a very low-carbohydrate diet in our earlier studies (5–7). Compliance during the low-fat diet period was assessed through analysis of food records and measurement of respiratory exchange ratio obtained after the diet.

Blood collection. Blood samples were obtained on 2 separate days before and after each 6-wk experimental diet period. Samples were obtained after an overnight fast and abstinence from alcohol and strenuous exercise for 24 h. Subjects reported to the laboratory between 0700 and 0900 h, rested quietly for 10 min in the supine position, and a blood sample was obtained from an antecubital vein and collected into a tube coated with a silicone-gel. Blood was separated by centrifugation at 1500 × *g* for 15 min at 4°C and serum stored at −80°C for subsequent analysis.

Oral fat tolerance test. An oral fat tolerance test was performed at baseline and after each experimental diet period using standard procedures in our laboratory (5,6). Subjects arrived at the laboratory after a 12-h overnight fast and abstinence from alcohol and strenuous exercise for 24 h. A flexible catheter was inserted into a forearm vein and blood samples were obtained from a 3-way stopcock connected to the end of the catheter. Blood was collected with a syringe and transferred to a silicone gel–coated tube for processing as above for determination of TAG. The catheter was kept patent with a constant saline drip. Subjects rested in a seated position for 10 min and 2 baseline blood samples separated by 10 min were obtained. The test meal (240 mL heavy whipping cream, sugar-free pudding, 30 mL canola oil, 36.1 g macadamia nuts) was then consumed. This meal provided 5.44 MJ, 11% energy as carbohydrate, 3% energy as protein, 86% energy as fat. Postprandial blood samples were obtained in a seated position immediately after the meal and hourly for a total of 8 h. Subjects rested quietly and consumed exactly 1 L of water only during the 8 h postprandial period.

Determination of serum lipids, oxidized LDL, glucose, and insulin. Serum collected for the determination of insulin, LDL particle size, and oxidized LDL (oxLDL) concentrations was immediately stored at −80°C. The remaining serum (~3 mL) was sent to a certified medical laboratory (Quest Diagnostics) for determination of glucose, total cholesterol (TC), HDL-C, and TAG concentrations using automated enzymatic procedures (Olympus America) with calculated precision values < 3%. The Friedewald formula (14) was used to calculate LDL cholesterol (LDL-C): [LDL-C = TC – (HDL-C + TAG/5)], which was then converted to mmol/L by dividing by 38.7. An ELISA with a sensitivity of <1 mU/L (#008–10-1143–01, American Laboratory Products) was used to determine oxLDL in duplicate from fasting subjects; the ELISA is based on the direct sandwich technique in which two monoclonal antibodies are directed against separate antigenic determinants on the oxidized apolipoprotein B molecule (15). The intra-assay CV was 7.9%. Serum insulin concentrations of fasting subjects were determined in duplicate using an ELISA kit with a sensitivity of 1.81 pmol/L (#10–1600, Diagnostic Systems Laboratory). The intra-assay CV was 5.5%. Absorbances were read on a multilabel counter (VersaMax, Molecular Devices). An estimation of insulin resistance was calculated using the homeostasis model analysis (HOMA-IR) using the formula: glucose (mU/L) · [insulin (pmol/L)/22.5] (16). Normal-weight, normal sub-

jects aged <35 y usually have a HOMA-IR value of 1; a value > 3.8 would represent insulin resistance (17).

Determination of lipoprotein particle size. Lipoprotein particle size was determined using nongradient polyacrylamide gel electrophoresis (Lipoprint LDL System, Quantimetrix). The method was described in detail in a recent publication by our laboratory (6) and others (18) and verified by nondenaturing gradient gel electrophoresis and NMR spectroscopy (19). Seven bands of LDL, 3 bands of intermediate density lipoprotein (IDL), and VLDL were quantitatively evaluated using computer software (NIH imaging software, utilizing the Lipoprint LDL macro). The scanned gel image is divided at designated R_f values identified by their relative mobility, which is based on particle size (smaller particles migrate further). The area under the curve (AUC) was calculated for each fraction. The percentage of LDL, IDL, and VLDL in each band and mean and peak LDL particle diameter are reported.

Statistical analysis. All statistical analyses were done with Statistica software, version 5.5 (StatSoft). Means for fasting serum TC, HDL-C, LDL-C, and TAG were calculated from the 2 fasting samples obtained at each time point and used for statistical analysis. A 1-way repeated-measures ANOVA was used to evaluate changes over time (baseline, post-very low-carbohydrate diet, and post-low-fat diet) for all variables. The TAG total AUC was calculated from individual values obtained during the oral fat tolerance test using the trapezoidal method. Significant main effects were further analyzed using Tukey's post-hoc test. Differences were considered significant at $P < 0.05$.

RESULTS

All dietary macronutrients were significantly different when the men consumed the very low-carbohydrate diet compared with the low-fat diet with the exception of alcohol (**Table 1**). We achieved our goals for each diet with 23% of total energy coming from fat for the low-fat diet and 8% of total energy coming from carbohydrate for the very low-carbohydrate diet. All subjects were in ketosis throughout the very low-carbohydrate diet period as indicated by color changes on the urinary reagent strips (data not shown), indicating compliance in terms of carbohydrate restriction. Subjects lost significantly more weight during the very low-carbohydrate diet period (−6.1 ± 2.9 kg) compared with the low-fat diet period (−3.9 ± 3.4 kg).

Serum TC was significantly reduced by both the very low-carbohydrate (−11%) and low-fat (−15%) diets, with no difference in the extent of the decrease (**Table 2**). Serum LDL-C was significantly reduced only by the low-fat diet (−18%). Serum HDL-C was not affected by either diet but there was a trend for the TC/HDL-C ratio to decrease after consumption of both diets ($P = 0.10$). Serum TAG and the TAG/HDL-C ratio were significantly reduced only by the very low-carbohydrate diet (−44 and −42%, respectively). Serum oxLDL was not affected by either diet. Serum glucose was significantly reduced only after consumption of the very low-carbohydrate diet (−6%). Serum insulin and insulin resistance were significantly reduced to the same extent by both the very low-carbohydrate (−42 and −43%, respectively) and low-fat (−28 and −30%, respectively) diets.

There were no changes in the relative percentage of lipoprotein fractions after men consumed the low-fat diet (**Table 3**). There were significant increases in the relative percentage and concentration of the larger LDL-1 fraction and significant decreases in the smaller LDL-3 and LDL-4 particles after the very low-carbohydrate diet period. There were also significant decreases in the relative percent and concentration of VLDL after consumption of the very low-carbohydrate diet. This shift to larger particles was reflected by significant increases in the mean and peak LDL particle diameters. Twelve subjects were classified as "*pattern B*" at baseline and 75% had switched to "*pattern A*" after the very low-carbohydrate diet period whereas only 42% had switched after the low-fat diet period (**Table 4**). Of the three "*pattern A*" subjects at baseline, two remained "*pattern A*" after consuming the very low-carbohydrate diet, whereas only one remained "*pattern A*" after consuming the low-fat diet.

Postprandial TAG values generally peaked ~4 h after the meal and gradually returned to baseline after 7–8 h (**Fig. 1**). Postprandial lipemia (total AUC) was significantly reduced by both diets compared with baseline (22.1 ± 5.4 mmol/L × 8 h), but the reduction was significantly greater after the very low-carbohydrate diet period (13.8 ± 3.6 mmol/L × 8 h) compared with the low-fat diet period (17.8 ± 6.0 mmol/L × 8 h). Compared with baseline, peak TAG responses were also significantly reduced after the very low-carbohydrate (−34%) and low-fat (−23%) diet periods.

TABLE 1

Daily intake of dietary energy and nutrients[1]

Nutrient	Baseline	Very low-carbohydrate	Low-fat
Energy, *MJ*	10.86 ± 2.47[a]	7.77 ± 1.81[b]	6.54 ± 1.19[c]
Protein, *g*	106 ± 24[b]	130 ± 30[a]	79 ± 18[c]
Protein, *% energy*	16 ± 2[c]	28 ± 5[a]	20 ± 4[b]
Protein, *g/kg body*	0.96 ± 0.19[b]	1.30 ± 0.33[a]	0.78 ± 0.19[c]
Carbohydrate, *g*	308 ± 77[a]	36 ± 18[c]	224 ± 56[b]
Carbohydrate, *% energy*	47 ± 5[b]	8 ± 3[c]	56 ± 7[a]
Total fat, *g*	104 ± 28[b]	130 ± 34[a]	39 ± 11[c]
Total fat, *% energy*	35 ± 4[b]	63 ± 4[a]	23 ± 7[c]
Saturated fat, *g*	35 ± 12[b]	46 ± 13[a]	13 ± 3[c]
Monounsaturated fat, *g*	29 ± 8[b]	48 ± 18[a]	10 ± 5[c]
Polyunsaturated fat, *g*	16 ± 4[b]	20 ± 6[a]	6 ± 3[c]
Alcohol, *% energy*	2 ± 3	1 ± 2	1 ± 1
Cholesterol, *mg*	303 ± 94[b]	731 ± 290[a]	170 ± 66[c]
Dietary fiber, *g*	16 ± 5[a]	8 ± 6[b]	17 ± 6[a]

[1] Values are means ± SD, $n = 15$. Means in a row with different superscripts differ, $P < 0.05$. Analysis was performed on 7 d of diet records during the baseline period and 21 d during the very low-carbohydrate and low-fat diet periods.

TABLE 2

Serum biochemistry of fasting overweight men after 6 wk of consuming hypoenergetic very low-carbohydrate and low-fat diets[1]

	Baseline	Very low-carbohydrate	Low-fat
TC, *mmol/L*	4.98 ± 0.83[a]	4.44 ± 0.95[b]	4.25 ± 0.75[b]
LDL-C, *mmol/L*	3.25 ± 0.73[a]	3.05 ± 0.80[a]	2.68 ± 0.67[b]
HDL-C, *mmol/L*	1.02 ± 0.16	0.99 ± 0.20	0.95 ± 0.16
TC/HDL-C	4.96 ± 1.03	4.53 ± 0.73	4.59 ± 1.17
TAG, *mmol/L*	1.55 ± 0.49[a]	0.87 ± 0.24[b]	1.32 ± 0.51[a]
TAG/HDL-C	1.56 ± 0.58[a]	0.90 ± 0.27[b]	1.43 ± 0.64[a]
Oxidized LDL, *mU/L*	4.72 ± 1.98	4.12 ± 1.14	4.32 ± 2.23
Glucose, *mmol/L*	5.23 ± 0.35[a]	4.93 ± 0.41[b]	5.03 ± 0.58[a]
Insulin, *pmol/L*	77.1 ± 32.7[a]	45.1 ± 27.5[b]	55.4 ± 26.8[b]
HOMA-IR[2]	2.49 ± 1.05[a]	1.41 ± 0.97[b]	1.74 ± 0.89[b]

[1] Values are means ± SD, $n = 15$. Means in a row with different superscripts differ, $P < 0.05$.

[2] HOMA-IR was calculated as glucose (mU/L) · [insulin (pmol/L)/22.5].

TABLE 3

Lipoprotein fractions including LDL subclass percentages and mean and peak LDL particle diameters in response to hypoenergetic very low-carbohydrate and low-fat diets in overweight men[1]

Lipoprotein fraction[2]	Baseline	Very low-carbohydrate	Low-fat
		%	
VLDL	15.3 ± 4.7[a]	12.5 ± 2.6[b]	15.0 ± 4.7[a]
IDL-C	12.1 ± 1.0	12.2 ± 1.0	12.4 ± 2.6
IDL-B	8.1 ± 2.1	8.1 ± 2.2	7.8 ± 2.6
IDL-A	4.3 ± 0.8[b]	6.8 ± 2.6[a]	4.9 ± 1.5[b]
LDL-1 (27.7 nm)	12.7 ± 2.9[b]	18.1 ± 5.3[a]	13.7 ± 4.5[b]
LDL-2 (26.1 nm)	19.5 ± 3.5	17.3 ± 6.4	18.4 ± 4.7
LDL-3 (24.5 nm)	6.6 ± 3.0[a]	3.9 ± 3.0[b]	5.4 ± 3.6[a]
LDL-4 (23.0 nm)	1.0 ± 1.1[a]	0.5 ± 0.6[b]	0.8 ± 1.2[a]
LDL-5 (21.8 nm)	0.1 ± 0.3	0.0 ± 0.0	0.0 ± 0.0
LDL-6 (20.7 nm)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
LDL-7 (18.7 nm)	0.0 ± 0.0	0.0 ± 0.0	0.1 ± 0.3
		nm	
LDL particle size			
Mean diameter	26.4 ± 3.2[b]	26.7 ± 3.4[a]	26.4 ± 4.2[b]
Peak diameter	26.4 ± 3.7[b]	27.0 ± 6.5[a]	26.4 ± 5.3[b]

[1] Values are means ± SD, $n = 15$. Means in a row with different superscripts differ, $P < 0.05$.
[2] Values in parentheses indicate the mean particle size for that fraction.

DISCUSSION

The aim of this study was to compare directly the effects of very low-carbohydrate and low-fat weight loss diets on cardiovascular risk factors. Our previous research in normolipidemic individuals showed that very low-carbohydrate diets result in significant decreases in serum TAG, small increases in TC and LDL-C, increases in LDL particle size, and moderate increases in HDL-C that are independent of weight loss (5,6). Results of this study indicate that a hypoenergetic very low-carbohydrate diet that resulted in significant weight loss had a similar if not better effect on overall blood lipids than the low-fat diet.

Both the low-fat and very low-carbohydrate hypoenergetic diets resulted in significant and similar decreases in serum total cholesterol and no change in serum HDL-C or the TC/HDL-C ratio, indicating a similar effect on CVD risk. The greater weight loss during the very low-carbohydrate vs. the low-fat diet period would be expected to decrease serum LDL-C to a greater extent (20); however, in this study, only the low-fat diet significantly decreased serum LDL-C.

Similar to our earlier work, the very low-carbohydrate diet resulted in much greater reductions in fasting serum TAG, a response also consistently reported in other recent studies. Four studies published within the last 6 mo comparing low-fat and very low-carbohydrate weight loss diets (3–12 mo in duration) have reported larger reductions in fasting TAG levels with consumption of a very low-carbohydrate diet (21–24). Recent studies clearly indicate that increased TAG is an independent risk factor for CVD (25,26).

An increase in fasting TAG also tends to result in an exaggerated TAG response to a fat-rich meal (i.e., abnormal postprandial lipemia). Increased postprandial lipemia is associated with a constellation of potentially atherogenic changes that include production of chylomicron remnants, reduction in HDL, formation of small LDL particles that are more prone to oxidative modification, activation of blood coagulation, stimulation of inflammatory cytokines and leukocytes, and endothelial dysfunction (27–29), all of which contribute to the causal role for elevated postprandial lipemia in the pathogenesis and progression of CVD. We report for the first time that a very low-carbohydrate weight loss diet results in a significantly greater reduction in postprandial lipemia compared with a low-fat diet. The dyslipidemia associated with an enhanced lipemic response is central to the insulin resistance syndrome, which has most recently been labeled the metabolic

TABLE 4

Individual changes in overweight men in LDL subclass pattern after 6 wk intake of hypoenergetic very low-carbohydrate and low-fat diets[1,2]

Subject	Baseline	Very low-carbohydrate	Low-Fat
		Pattern	
1	B	B	B
2	B	A	B
3	B	B	A
4	B	A	A
5	B	A	B
6	B	A	A
7	B	A	A
8	A	B	A
9	B	A	B
10	B	A	B
11	A	A	B
12	A	A	B
13	B	A	B
14	B	A	A
15	B	B	B

[1] Individual changes of subjects ($n = 15$) classified as "pattern A" or "pattern B" at baseline and their responses to the experimental diets.
[2] Individuals with "pattern A" have a predominance of large LDL particles and those with "pattern B" have a predominance of smaller atherogenic LDL particles.

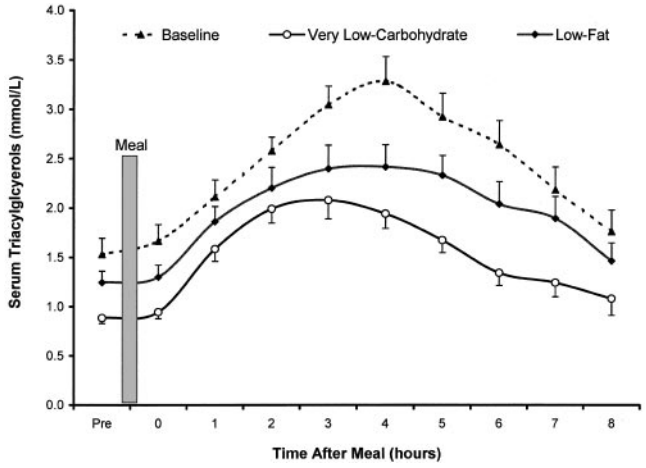

FIGURE 1 Serum TAG responses of overweight men after ingestion of a high-fat meal at baseline and after 6 wk of consuming hypoenergetic very low-carbohydrate and low-fat diets. Values are means ± SEM, $n = 15$. TAG total AUC was calculated from individual values obtained during the oral fat tolerance test using the trapezoidal method. The total TAG AUC differed: Baseline > Low-Fat > Very Low-Carbohydrate, $P < 0.05$.

syndrome (30) and afflicts an estimated 42% of adults in the United States (31). In addition to improving the lipid disorders of the metabolic syndrome, the very low-carbohydrate diet favorably affected HOMA-IR and the TAG/HDL-C ratio, a surrogate marker of insulin resistance (32).

Fasting TAG levels and enhanced postprandial lipemia are inversely related to peak LDL size (33); thus we expected that the very low-carbohydrate diet would increase the distribution of larger LDL particles, previously shown to occur in normal-weight men consuming a very low-carbohydrate diet (6). Individuals with a predominance of small, dense LDL particles have been classified as *"pattern B,"* whereas those with larger LDL particles are *"pattern A."* Individuals exhibiting higher levels of small dense LDL have a greater than threefold increased risk of CVD (34,35). The majority of men were *"pattern B"* at the start of the study, which was expected because obesity is associated with the metabolic syndrome (10,11). Weight loss was shown to increase LDL particle size in men with *"pattern B"* (36); however, in our study, more men with *"pattern B"* had switched to *"pattern A"* after 6 wk of intake of a very low-carbohydrate diet (75%) compared with a low-fat diet (42%). This dietary-induced change in particle size is consistent with other work that has manipulated dietary fat and carbohydrate content (37–39) and suggests that a relation may exist between the ratio of carbohydrate to fat in the diet and LDL particle size.

There are several limitations in this study. The duration was short (6 wk), and it is not known whether these changes in lipids would persist over longer periods of time. The study was also conducted on a small sample ($n = 15$) of overweight but otherwise young, healthy men. We used a crossover design to eliminate interindividual differences in the response of blood lipids to the diet interventions. However, because this was a weight loss study, we chose not to employ a washout period between the 2 diet periods because we wanted subjects to continue to lose weight at a constant rate throughout the experiment. Our present study focused on measuring risk factors for CVD, yet we did not measure all CVD biomarkers such as those related to inflammation, endothelial function, and thrombosis, nor did we assess other important clinical end points such as renal function or bone health. Nevertheless, this study demonstrates that a short-term hypoenergetic low-fat diet was more effective at lowering serum LDL-C in overweight men, but a very low-carbohydrate diet was more effective at improving characteristics of the metabolic syndrome as determined by decreased fasting serum TAG, the TAG/HDL-C ratio, postprandial lipemia, and improved LDL subclass distribution. Thus, in principle, a very low-carbohydrate diet appears safe and may be more beneficial for individuals with metabolic syndrome; however, future research is warranted to completely understand the overall health implications.

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