Original Research

Comparison of a Very Low-Carbohydrate and Low-Fat Diet on Fasting Lipids, LDL Subclasses, Insulin Resistance, and Postprandial Lipemic Responses in Overweight Women

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Objective: Very low-carbohydrate diets are widely used for weight loss yet few controlled studies have determined how these diets impact cardiovascular risk factors compared to more traditional low-fat weight loss diets. The primary purpose of this study was to compare a very low-carbohydrate and a low-fat diet on fasting blood lipids, LDL subclasses, postprandial lipemia, and insulin resistance in overweight and obese women.

Methods: Thirteen normolipidemic, moderately overweight (body fat >30%) women were prescribed two hypocaloric (−500 kcal/day) diets for 4 week periods, a very low-carbohydrate (<10% carbohydrate) and a low-fat (<30% fat) diet. The diets were consumed in a balanced and randomized fashion. Two fasting blood draws were performed on separate days and an oral fat tolerance test was performed at baseline, after the very low-carbohydrate diet, and after the low-fat diet.

Results: Compared to corresponding values after the very low-carbohydrate diet, fasting total cholesterol, LDL-C, and HDL-C were significantly ($p \leq 0.05$) lower, whereas fasting glucose, insulin, and insulin resistance (calculated using the homeostatic model assessment) were significantly higher after the low-fat diet. Both diets significantly decreased postprandial lipemia and resulted in similar nonsignificant changes in the total cholesterol/HDL-C ratio, fasting triacylglycerols, oxidized LDL, and LDL subclass distribution.

Conclusions: Compared to a low-fat weight loss diet, a short-term very low-carbohydrate diet did not lower LDL-C but did prevent the decline in HDL-C and resulted in improved insulin sensitivity in overweight and obese, but otherwise healthy women. Small decreases in body mass improved postprandial lipemia, and therefore cardiovascular risk, independent of diet composition.

INTRODUCTION

Very low-carbohydrate diets have been promoted for several decades as a superior alternative weight loss approach, best exemplified by the best-selling Atkins diet having sold several million copies [1]. Very low-carbohydrate diets have recently been examined in several clinical trials that primarily focused on weight loss. Results generally indicate that very low-carbohydrate diets result in greater weight loss compared to traditional low-fat diets [2–5]. However, few studies have rigorously examined the effects of very low-carbohydrate diets on risk factors for cardiovascular disease including postprandial lipemia, a significant and independent risk factor for coronary artery disease [6,7]. Although carbohydrate restriction could favorably impact certain aspects of lipid metabolism compared to low-fat diets, such as decreasing hepatic production of triacylglycerols [8], they are inherently high in saturated fat and cholesterol, and therefore could be potentially atherogenic.

In addition to studies aimed at determining the effects of carbohydrate restriction on weight loss and body composition, an understanding of the effects on accepted risk factors for

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cardiovascular disease should be known in different populations before this diet is widely recommended. To address this concern, our laboratory has assessed the effects of very low-carbohydrate diets in normal-weight men and women under conditions of weight maintenance to isolate the effects of the diet independent of weight loss. Collectively these studies have shown that short-term carbohydrate restriction (<10% of total energy) for 4 to 8 weeks reduces fasting triacylglycerols, postprandial lipemic responses to a fat-rich meal, and insulin levels, and increases HDL-C, LDL-C, and LDL particle size [9–12]. Whether similar responses occur in overweight women consuming a hypocaloric very low-carbohydrate weight loss diet is unknown.

Thus, the primary purpose of this study was to shed light on the short-term cardiovascular risk responses to consumption of a hypocaloric very low-carbohydrate diet in overweight women. Since weight loss alone tends to improve risk status, the responses were compared to those achieved after consumption of a traditional low-fat diet. We tested the hypothesis that a very low-carbohydrate diet would not have a detrimental effect on cardiovascular risk status compared to a low-fat diet. Because blood lipid responses to diet are quite variable, we utilized a within subjects design in order enhance statistical power and the chances of detecting significant differences between diets.

MATERIALS AND METHODS

Subjects

Thirteen moderately overweight and obese (percentage body fat >30%) but otherwise healthy women volunteered to participate in this investigation. Their physical characteristics were (mean ± SD) age 34.0 ± 8.6 years, body mass 76.2 ± 12.9 kg, body fat 42.0 ± 5.1% (determined by dual-energy X-ray absorptiometry) and body mass index 29.6 ± 4.0 kg/m^2. The subjects had been weight stable for the past month (±2 kg), were not adhering to special diets or regular consumers of nutritional supplements (except a daily multi-vitamin/mineral) and habitually consumed between 27% and 41% of energy as fat (assessed via a seven-day food diary at baseline). All subjects were nonsmokers, not prescribed any medication known to affect serum lipoproteins, and premenopausal. All blood samples were obtained during days 2–4 of the follicular phase to control for possible effects of menstrual phase on lipoproteins, even though the variation is small [13]. Subjects were either sedentary or moderately active and maintained the same level of physical activity throughout the study documented by analysis of log sheets on which all exercise sessions were recorded. The study was conducted in accordance with the guidelines of the Institutional Review Board at the University of Connecticut.

Experimental Design

Subjects consumed two experimental weight loss diets for 4 week periods, a low-fat and a very low-carbohydrate diet. The diets were consumed in a balanced and randomized fashion. Two fasting blood draws 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 and after the low-fat diet.

Diet Interventions

Both experimental diets were designed to be hypoenergetic (−500 kcal/day). Energy levels were assigned to the nearest 200 kcal increment based on resting energy expenditure obtained using indirect calorimetry (MedGraphics CPX/D, Medical Graphics Corporation, St. Paul, MN) at the start of the study and appropriate activity factors. 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. The low-fat diet was also designed to contain <10% saturated fat and <300 mg cholesterol (i.e., a Step I diet). Foods encouraged during the low-fat diet included whole grains (breads, cereals and pastas), fruit/fruit juices, vegetables, vegetable oils, and low-fat dairy and meat products. We developed customized diabetic exchange lists for the very low-carbohydrate diet period in order to ensure a constant energy and balance of protein (~30% energy), fat (~60% energy) and carbohydrate (~10% of energy) throughout the day. There were no restrictions on the type of fat from saturated and unsaturated sources or cholesterol levels. Foods commonly consumed on the very low-carbohydrate diet were 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, Inc., Hauppauge, NY) were provided to subjects during the very low-carbohydrate diet. A daily multi-vitamin/mineral complex that provided micronutrients at levels ≤100% of the RDA was given to subjects during both experimental diets.

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.

Subjects received thorough instructions for completing detailed weighed food records during weeks 1, 3, and 4 of each experimental diet (21 days 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 Inc, The Hearst Corporation, San Bruno, CA). The program had no missing values for the nutrients reported. The database was extensively modified by our group to include new foods and recipes. To ensure that carbohydrates were restricted throughout the very low-carbohydrate diet, subjects tested their urine daily using reagent strips (Bayer Corporation, Elkhart, IN). The test is specific for acetoacetic acid, which produces a relative color change when it reacts with nitroprusside. We have found this to be a very sensitive indicator of carbohydrate restriction and compliance to a very low-carbohydrate diet in our prior studies [9–11].

Fasting Blood Collection

Blood samples were obtained on two separate days before and after each 4 week experimental diet. Samples were obtained following an overnight fast and abstinence from alcohol and strenuous exercise for 24 hours. Subjects reported to the laboratory between 0700 and 0900 hours, rested quietly for 10 minutes 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 minutes at 4°C.

Oral Fat Tolerance Test

An oral fat tolerance test was performed after each experimental diet using standard procedures in our laboratory [9–11]. Subjects arrived at the laboratory after a 12 hour overnight fast and abstinence from alcohol and strenuous exercise for 24 hours. 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 triacylglycerol. The catheter was kept patent with a constant saline drip. Subjects rested in a seated position for 10 minutes and two baseline blood samples were obtained separated by 10 minutes. The test meal (150 mL heavy whipping cream, sugar-free pudding, 5 mL canola oil, 28.5 g macadamia nuts) was then consumed. This meal provided 867 kcal, 13% carbohydrate, 3% protein, 84% fat, 38 g saturated fat, 33 g monounsaturated fat, 4 g polyunsaturated fat, and 207 mg cholesterol. Postprandial blood samples were obtained immediately after the meal and hourly for a total of eight hours. Subjects rested quietly in a seated position and consumed exactly one liter of water only during the 8 hour postprandial period.

Determination of Serum Lipids, Oxidized LDL, Glucose, and Insulin

After processing, serum collected for the determination of insulin, LDL particle size and oxidized LDL (oxLDL) were immediately stored at −80°C. The remaining serum (~3 mL) was sent to a certified medical laboratory (Quest Diagnostics, Wallingford, CT) for determination of glucose, total cholesterol, HDL-C, and triacylglycerol concentrations using automated enzymatic procedures (Olympus America Inc., Melville, NY). The Friedewald formula [14] was used to calculate LDL-C: [LDL-C = total cholesterol − (HDL-C + triacylglycerols/5)]. Fasting oxidized LDL-C was determined in duplicate using an enzyme-linked immuno sorbent assay (American Laboratory Products Company, Windham, NH) that 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]. Intra-assay coefficient of variance was 7.9%. Fasting serum insulin concentrations were determined in duplicate using an ELISA kit with a sensitivity of 1.81 pmol/L (#10-1600, Diagnostic Systems Laboratory, Webster, TX). Intra-assay coefficient of variance was 5.5%. Absorbances were read on a multilabel counter (VersaMax, Molecular Devices, Sunnyvale, CA). The homeostasis model assessment (HOMA) was used to estimate insulin resistance using the formula: glucose (mmol/L) · [insulin (mU/L)/22.5] [16]. Normal-weight subjects aged <35 years have an insulin resistance of 1 [16].

Determination of Lipoprotein Particle Size

Lipoprotein particle size was determined using non-gradient polyacrylamide gel electrophoresis (Lipoprint LDL System, Quantimetrix Co., Redondo Beach, CA). The method has been described in detail in a recent publication by our laboratory [10] and others [17] and validated against non-denaturing gradient gel electrophoresis and nuclear magnetic resonance spectroscopy [18]. Seven bands of LDL, 3 bands of 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 Rf values identified by their relative mobility, which is based on particle size (smaller particles migrate further). The area under the curve is calculated for each fraction. The percentage of LDL, IDL, and VLDL in each band and mean and peak LDL particle diameter are reported. Based on the distribution of LDL subclasses, subjects were classified as either *Pattern A* (predominance of large LDL particles) or *Pattern B* (predominance of small LDL particles).

Statistical Analysis

All statistical analyses were done with Statistica software, Version 5.5 (StatSoft Inc, Tulsa, OK). Means for fasting serum total cholesterol, HDL-C, LDL-C, and triacylglycerols were calculated from both fasting samples obtained at each time point and used for statistical analysis. Paired comparison *t* tests (two-tailed) were used to evaluate values after each diet intervention. Triacylglycerol total area under curve (AUC) was calculated from individual values obtained during the oral fat

Table 1. Daily Intake of Dietary Energy and Nutrients[1]

Nutrient	Baseline	Very Low-Carbohydrate	Low-Fat
Energy (kcal)	1931 ± 306	1288 ± 281	1243 ± 291
Protein (g)	75.5 ± 16.0	87.6 ± 19.4	59.0 ± 13.6*
Protein (%)	15.4 ± 2.1	27.8 ± 2.4	18.9 ± 3.8*
Carbohydrate (g)	242.7 ± 34.6	28.7 ± 8.1	186.1 ± 44.1*
Carbohydrate (%)	50.3 ± 7.1	9.1 ± 2.0	58.9 ± 4.4*
Total Fat (g)	71.1 ± 18.8	88.4 ± 20.9	29.2 ± 8.1*
Total Fat (%)	32.4 ± 4.2	62.5 ± 2.5	20.6 ± 2.5*
Saturated Fat (g)	23.6 ± 5.0	33.7 ± 11.4	9.5 ± 3.0*
Monounsaturated Fat (g)	16.4 ± 6.0	28.7 ± 9.7	7.7 ± 2.5*
Polyunsaturated Fat (g)	10.3 ± 6.1	11.6 ± 2.9	4.5 ± 1.2*
Alcohol (%)	2.0 ± 3.1	0.5 ± 1.1	1.5 ± 2.9
Cholesterol (mg)	272 ± 111	470 ± 192	124 ± 42*
Dietary Fiber (g)	14.4 ± 4.1	7.6 ± 2.1	16.3 ± 4.3*

[1] Values are mean ± SD; n = 13.

* $p \leq 0.05$ *vs.* Low-Fat value.

Analysis performed on 7 days of diet records during baseline and 21 days during the very low-carbohydrate and low-fat diets.

tolerance test using the trapezoidal method. The alpha level for significance was set at 0.05.

RESULTS

Dietary Intakes

All dietary macronutrients were significantly different when women were on the very low-carbohydrate diet compared to the low-fat diet with the exception of total dietary energy and alcohol (Table 1). We achieved our goals for each diet with 21% of total energy coming from fat on the low-fat diet and 9% of total energy coming from carbohydrate on the very low-carbohydrate diet. All subjects were in ketosis throughout the very low-carbohydrate diet 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 on the very low-carbohydrate diet (−2.96 ± 1.45 kg) compared with the low-fat diet (−1.06 ± 2.07 kg).

Fasting Lipids, Glucose, and Insulin

Fasting total cholesterol, LDL-C, and HDL-C were significantly lower after the low-fat diet but there was no significant difference between diets for the total cholesterol/HDL-C ratio. Fasting triacylglycerol responses were not different between diets but the triacylglycerol/HDL-C ratio was significantly lower after the very low-carbohydrate diet. Fasting oxidized LDL was unchanged by either diet. Fasting glucose, insulin, and insulin resistance HOMA were significantly lower after the very low-carbohydrate diet (Table 2).

Lipoprotein Particle Size

All but one subject was classified as *Pattern A* at the start of the study, which is reflected by the low percentage of smaller LDL-3 particles (<1%). There were no differences in the relative percent of lipoprotein fractions or LDL size responses between diets with the exception of VLDL, which was significantly lower after the very low-carbohydrate diet. There was a

Table 2. Fasting Blood Lipid and Metabolic Responses to a Hypoenergetic Very Low-Carbohydrate and Low-Fat Diet in Overweight Women[1]

	Baseline	Very Low-Carbohydrate	Low-Fat
TC (mg/dL)	183 ± 34	185 ± 26	170 ± 30*
LDL-C (mg/dL)	113 ± 30	119 ± 29	107 ± 27*
HDL-C (mg/dL)	52 ± 14	53 ± 12	48 ± 10*
TC/HDL-C	3.66 ± 0.83	3.66 ± 0.92	3.68 ± 0.85
TAG (mg/dL)	89 ± 34	69 ± 31	79 ± 36
TAG/HDL-C	1.91 ± 1.03	1.37 ± 0.75	1.83 ± 1.20*
Oxidized LDL (mU/L)	6.9 ± 1.8	6.8 ± 1.2	6.9 ± 2.2
Glucose (mg/dL)	86 ± 4	83 ± 8	88 ± 6*
Insulin (pmol/L)	41.0 ± 21.6	37.4 ± 16.1	50.5 ± 33.9*
Insulin Resistance$_{HOMA}$	1.28 ± 0.68	1.10 ± 0.46	1.63 ± 1.06*

[1] Values are mean ± SD, n = 13.

TC = total cholesterol, TAG = triacylglycerol, HOMA = homeostasis model assessment calculated as glucose (mU/L) · [insulin (pmol/L)/22.5].

* $p \leq 0.05$ *vs.* Very Low-Carbohydrate value.

Table 3. Lipoprotein Fractions Including VLDL, Intermediate Density Lipoproteins (IDL), and LDL Subclass Percentages and Mean and Peak LDL Particle Diameters in Response to a Hypoenergetic Very Low-Carbohydrate and Low-Fat Diet in Overweight Women[1]

	Baseline	Very Low-Carbohydrate	Low-Fat
Lipoprotein Fraction (%)			
VLDL	17.2 ± 7.0	13.9 ± 4.2	16.6 ± 4.6*
IDL-C	10.7 ± 3.8	10.2 ± 3.0	9.2 ± 2.7
IDL-B	6.6 ± 1.9	6.4 ± 1.9	6.1 ± 1.7
IDL-A	9.0 ± 4.2	8.0 ± 2.4	7.4 ± 3.5
LDL-1 (27.7 nm)[2]	20.0 ± 3.2	21.1 ± 4.1	21.6 ± 5.5
LDL-2 (26.1 nm)	7.7 ± 5.6	8.6 ± 4.8	10.4 ± 5.5
LDL-3 (24.5 nm)	0.6 ± 0.8	0.9 ± 1.2	1.2 ± 1.3
LDL-4 (23.0 nm)	0.0 ± 0.2	0.1 ± 0.3	0.2 ± 0.6
LDL-5 (21.8 nm)	0.0 ± 0.0	0.0 ± 0.0	0.1 ± 0.2
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	0.0 ± 0.0
LDL Particle Size (nm)			
Mean Diameter	27.2 ± 0.3	27.2 ± 0.3	27.1 ± 0.3
Peak Diameter	27.8 ± 0.5	27.7 ± 0.5	27.6 ± 0.5

[1] Values are mean ± SD; n = 13.

[2] Values in parentheses indicate the average particle size for that fraction.

* $p \leq 0.05$ *vs.* Very Low-Carbohydrate value.

significant relation between peak LDL size at the start of the study and the change in LDL peak size after the very low-carbohydrate (r = 0.59) but not the low-fat (r = 0.49) diet (Table 3), (Fig. 1).

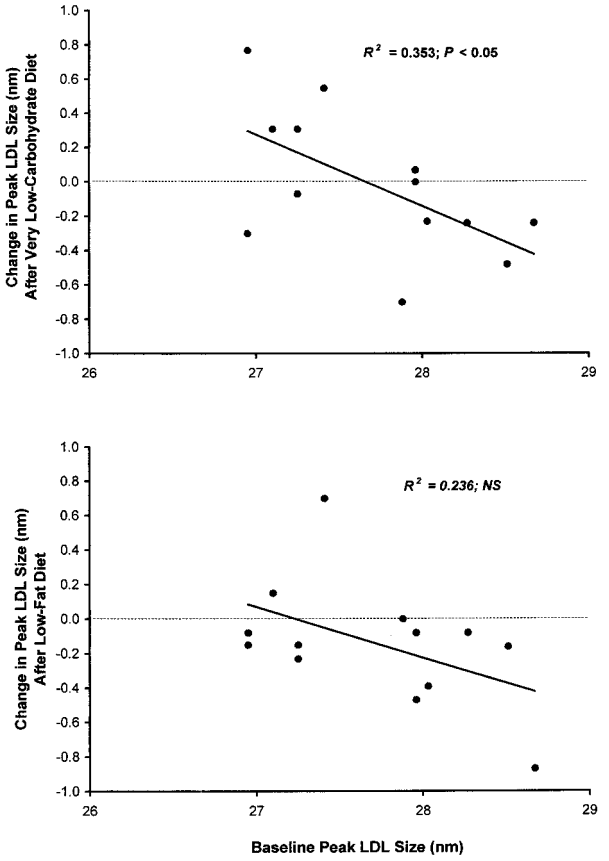

Fig. 1. Relationship between baseline peak LDL size and the change in peak LDL after a 4 week very low-carbohydrate and low-fat diet in overweight women (n = 13). NS = nonsignificant.

Oral Fat Tolerance Test

Postprandial triacylglycerol values generally peaked about 3 hours after the meal and gradually returned to baseline after 7 to 8 hours (Fig. 2). Compared to the baseline triacylglycerol AUC (1304 ± 555 mg/dL × 8 hours), postprandial lipemic responses were reduced to a similar extent after the very low-carbohydrate (927 ± 452 mg/dL × 8 hours) compared to the low-fat (984 ± 444 mg/dL × 8 hours) diet.

DISCUSSION

Interest in very low-carbohydrate diets for the purpose of weight loss has increased in recent years. These diets have been criticized because they differ from traditional recommendations for healthy weight loss [19–21]. We studied overweight, but otherwise healthy women with normal lipid profiles. In this population, the results of this study demonstrate both a short-term hypocaloric very low-carbohydrate and low-fat diet had a similar effect on cardiovascular risk as shown by similar changes in the total cholesterol/HDL-C ratio and fasting and postprandial triacylglycerols. However, a very low-carbohydrate diet was more effective than a low-fat diet at improving insulin sensitivity as measured by the homeostatic model assessment using fasting glucose and insulin, but the significance of this small decrease is probably not physiological relevant in terms of glucose clearance or insulin effectiveness.

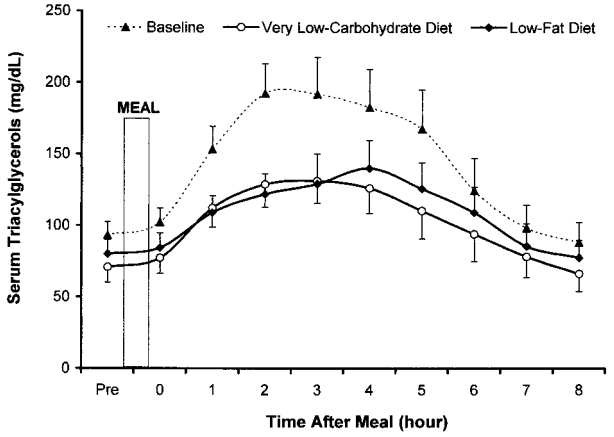

Fig. 2. Values are means ± SEM, n = 13. Serum triacylglycerol responses after ingestion of a high-fat meal at baseline and after a 4 week very low-carbohydrate diet and a 4 week low-fat diet in overweight women.

Our prior work in men indicated that a very low-carbohydrate diet improved the lipid abnormalities characteristic of the metabolic syndrome (i.e., the diet decreased fasting and postprandial triacylglycerols, increased HDL-C, and increased LDL size distribution) [9,10]. The magnitude of these improvements was related to the severity of the dyslipidemia. That is men who started with higher triacylglycerols, lower HDL-C, and/or smaller LDL particles, demonstrated the greatest improvements in response to the very low-carbohydrate diet. In the present study, there were no significant differences between the very low-carbohydrate and low-fat diets on fasting and postprandial triacylglycerols and LDL particle distribution. Different from the men in our prior studies, the overweight women in this study showed little evidence of any dyslipidemia. In fact only one woman was characterized as *Pattern B* at baseline. This is consistent with other research showing that women have larger less atherogenic LDL particles than men [22–25]. Similar to our prior work [9–11], we did observe an inverse correlation between baseline peak LDL size and the change in LDL size to the very low-carbohydrate indicating that women who have smaller more atherogenic LDL particles do increase LDL size in response to a very low-carbohydrate diet.

As expected the low-fat diet decreased both LDL-C and HDL-C resulting in no change in the total cholesterol/HDL-C ratio. The very low-carbohydrate diet did not lower LDL-C, but it prevented the decline in HDL-C also resulting in no change in the total cholesterol/HDL-C ratio. The lack of a decrease in LDL-C on a very low-carbohydrate diet could be of concern because several clinical trials clearly show that LDL-lowering therapy reduces risk of coronary heart disease and is therefore a primary target of therapy [26]. The goal of this study was not to isolate a particular nutrient but rather to examine how a diet pattern characterized by a very low-carbohydrate intake affects cardiovascular risk factors. However, the lower fiber intake on the very low-carbohydrate diet could be an important factor that contributed to the lack of a decrease in LDL-C because fiber alters metabolic pathways of hepatic cholesterol and lipoprotein metabolism, resulting in lowering of plasma LDL-C [27].

Caution should be taken when interpreting these short-term changes in lipids, because whether subjects are weight stabilized or actively losing weight will affect the magnitude of the LDL-C and the direction of the HDL-C responses [28,29]. Regardless of whether weight is stabilized or at a plateau, HDL-C responses are better maintained or increased and LDL-C does not decrease as much on a very low-carbohydrate diet compared to a low-fat diet [9–11] and a recent study showed that this pattern of LDL-C and HDL-C response is sustained for one year [2].

Elevated postprandial lipemia is a significant and independent risk factor for cardiovascular disease [6,7]. Fasting and postprandial triacylglycerols are higher in obesity, especially abdominal obesity [30]; however, few studies have examined the effect of moderate weight loss on postprandial lipemia. Women in this study demonstrated a "normal" postprandial lipemic response to the fat-rich meal, consistent with their relatively low fasting triacylglycerols. However, the small weight loss resulted in rather dramatic improvements in the total area under the triacylglycerol curve. We hypothesized the magnitude of the reduction would be greater after the very low-carbohydrate diet based on our prior work in normal-weight men [9,10], normal-weight women [11], and overweight men [31]. However, the decrease on the very low-carbohydrate diet (−29%) was similar to the low-fat diet (−25%). The reason for this difference is unclear. Women have been shown to have lower postprandial lipemic responses compared to men [32], an anti-atherogenic trait shown to be due to a greater contribution of skeletal muscle to lipid clearance [33]. One important feature of the design used in this study was that the fat tolerance test was similar in composition to the very low-carbohydrate diet and therefore may have gave an advantage to this diet because individuals tend to metabolize a meal that reflects the composition of their background diet more effectively [34]. From this perspective, a hypocaloric low-fat diet could be viewed as having an advantage because it resulted in a similar reduction in postprandial lipemia despite being quite different in composition to the test meal.

Women lost more weight on the very low-carbohydrate diet (−2.96 kg) than the low-fat diet (−1.06 kg). Based on the expected changes in lipids with weight loss [35], the change in body weight alone should have decreased TC, LDL-C, HDL-C, and triacylglycerols by 5.7, 2.3, 0.8, and 3.9 mg/dL, respectively, on the very low-carbohydrate diet and by 2.1, 0.8, 0.3, and 1.4 mg/dL, respectively, on the low-fat diet. This is much different than the actual changes observed (Table 2), suggesting that the composition of the diet, not weight loss *per se*, is the major stimulus for changes in lipids.

There is concern that very low carbohydrate diets, especially diets high in saturated fat, might lead to insulin resistance; however we observed a significant reduction in insulin resistance after the very low-carbohydrate diet as measured by the homeostatic model assessment technique [16], which uses fasting levels of glucose and insulin. Adaptation to a three-week very low carbohydrate diet (8% carbohydrate, 75% fat) in healthy subjects resulted in no change in resting or insulin-stimulated total glucose disposal [36]. There was however a significant decrease in insulin-stimulated glucose oxidation and a proportional increase in nonoxidative glucose metabolism, presumably glycogen formation [36]. This study also showed that insulin-stimulated suppression of lipid oxidation was nearly prevented (i.e., insulin was ineffective at inhibiting oxidation of fat) after a low carbohydrate diet compared to an 80% reduction after a standard diet [36]. Similar results were obtained in healthy men who consumed 3 isoenergetic liquid diets equal in protein (15% of energy) but different in carbohydrate (2%, 44% and 85% of energy) [37]. Glucose disposal was similar between all three diets but the low carbohydrate

diet resulted in lower rates of insulin-stimulated glucose oxidation and increased nonoxidative glucose disposal. The low carbohydrate diet also prevented insulin-stimulated inhibition of lipid oxidation. Collectively, these findings do not support the notion that very low carbohydrate diets exacerbate risk of type II diabetes mellitus and insulin resistance.

The results of this study indicate that, although short-term hypocaloric low-fat and very low-carbohydrate diets have different effects on HDL-C and LDL-C metabolism, they have a similar effect on the total cholesterol/HDL-C ratio. This study shows that even small reductions in body mass resulting from either type of diet can result in significant improvements in the postprandial lipemic response to a fat-rich meal. The overall clinical significance of these changes in lipids and insulin sensitivity are unknown, and it remains to be determined if these short-term responses can be sustained or are reflective of long term benefits that are associated with reduced morbidity and mortality. Limitations of this study include a short duration, small sample size, and the fact that we did not measure all cardiovascular biomarkers such as those related to inflammation, endothelial function and thrombosis, nor did we assess other important clinical endpoints such as renal function or bone health. These data should be viewed as pilot data that warrant further in-depth studies to determine the robustness and ability to generalize these data. The findings do support the concept that overweight individuals have some flexibility and can choose different dietary strategies depending on a number of factors such as food preference, baseline lipid profile, degree of obesity and the like.

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