Effects of Dietary Fat Restriction on Particle Size of Plasma Lipoproteins in Postmenopausal Women

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Hypertriglyceridemia is an independent risk factor for coronary artery disease (CAD) and is also commonly associated with other coronary risk factors, ie, small, dense low-density lipoprotein (LDL) particles and low plasma levels of high-density lipoprotein cholesterol (HDL-C). Dietary fat restriction is recommended for the prevention of nutrition-related cancers. Low-fat, high-carbohydrate intake can increase plasma triglyceride (TG) and decrease HDL-C. In general, plasma TG levels are inversely related to the particle size of LDL. We investigated the effects of dietary fat restriction on the concentration and particle size of plasma lipoproteins in 14 healthy postmenopausal women (aged 61 ± 11 years). During a 4-month period of eucaloric controlled feeding, dietary fat was reduced stepwise from a habitual intake of 33% ± 8% to 23% and then to 14% of daily energy. Changes in the plasma lipid level and particle size of very-low-density lipoprotein (VLDL), LDL, and HDL were determined at the end of each dietary phase. Increasing carbohydrate intake without weight loss was associated with an increase in plasma TG (1.86 ± 0.30 *v* 2.47 ± 0.37 mmol/L) and decreases in total cholesterol (5.82 ± 0.25 *v* 5.40 ± 0.21 mmol/L), LDL-C (3.07 ± 0.18 *v* 2.61 ± 0.21 mmol/L), HDL-C (1.42 ± 0.1 *v* 1.24 ± 0.1 mmol/L), and apolipoprotein (apo) A1 (5.14 ± 0.25 *v* 4.61 ± 0.36 mmol/L), whereas plasma apo B did not change. The particle size of VLDL increased (42.7 ± 1.4 *v* 47.0 ± 0.9 nm). However, there was no change in either LDL (25.1 ± 0.2 *v* 25.3 ± 0.2 nm) or HDL particle size. Although at each level of dietary fat intake LDL particle size correlated inversely with plasma TG and apo B, there was no relationship between the increase in plasma TG and LDL particle size. These results show that hypertriglyceridemia caused by a eucaloric high-carbohydrate intake is not associated with a decrease in LDL particle size. Therefore, carbohydrate-induced hypertriglyceridemia may not have the same atherogenic potential as genetic hypertriglyceridemias.

DIETARY FAT RESTRICTION has been widely recommended for the prevention of coronary artery disease (CAD) and nutrition-related cancers.[1,2] Low-fat, and consequently high-carbohydrate, diets reduce low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C), but may increase plasma triglyceride (TG).[3-5] Hypertriglyceridemia is now considered an independent risk factor for CAD.[6,7] In addition, hypertriglyceridemia is associated with other CAD risk factors such as small, dense LDL particles and low plasma levels of HDL-C.[8,9]

The major carriers of plasma TGs during fasting are very-low-density lipoproteins (VLDLs).[4] A portion of these lipoproteins become cholesterol-rich LDLs during a lipolytic process initiated by lipoprotein lipase (LpL).[10-12] A second lipolytic enzyme, hepatic TG lipase, plays a role in the latter phases of VLDL to LDL conversion.[13] Particle size and TG content of VLDLs affect their metabolic fate. Larger, TG-rich VLDLs are taken up by the liver, whereas smaller, TG-poor VLDLs are directed to the LDL production pathway.[14-17] In hypertriglyceridemic states, a relatively TG-rich LDL particle may initially be produced. These particles may then be rapidly hydrolyzed into smaller, denser LDLs by hepatic TG lipase.[18] Individuals with smaller and denser LDL particles, pattern B, have a threefold increase in CAD risk compared with pattern A subjects with larger LDLs.[19-23] The particle size and subclass distribution of LDLs are determined by both genetic and environmental factors.[24-26]

We speculated that if carbohydrate-induced hypertriglyceridemia increases the size and TG content of VLDL particles, these may be removed directly by the liver without entering the LDL production cascade. Therefore, the particle size of LDLs may not be significantly altered. In contrast, if there is an increase in the number of smaller VLDLs, these may convert easily to LDLs, producing smaller and denser particles. The effects of dietary fat restriction on LDL particle size have been investigated previously, but these dietary interventions were performed mostly in men, in combination with hypocaloric diets and exercise to achieve weight loss.[27-29] In some of these studies, a high-carbohydrate intake was associated with a decrease in plasma TG, due to the decrease in energy intake and the increase in exercise.[29] None of these investigations determined the changes in VLDL particle size.

Hypertriglyceridemia can also affect the plasma level and particle size of HDL. Hypertriglyceridemic individuals usually have low plasma HDL-C.[8,9] The mechanism underlying this finding is that during LpL-mediated lipolysis of VLDL, excess surface lipids and apoproteins are transferred to HDL, contributing to HDL production.[10-12] Low-fat diets decrease the activity of LpL in muscle, and therefore impair HDL production.[30] In addition, the cholesterol core of HDL may be partially replaced by TG through the action of cholesterol ester transfer protein; further decreasing plasma HDL-C.[31] The effects of a low-fat intake on HDL particle size have also been studied primarily in men while simultaneously altering the energy intake and exercise.[27-29] The present study was designed to discriminate the effects of dietary fat and carbohydrate intake from the effects of changes in energy intake and weight. The investigation was performed in postmenopausal women because menopause is a CAD risk factor and low-fat diets are recommended more frequently for the prevention of breast cancer in this group.[32]

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SUBJECTS AND METHODS

Subjects and Study Design

Fourteen healthy postmenopausal women (aged 61 ± 11 years, mean ± SD) were included in the study after signing informed-consent forms approved by the Institutional Human Investigation Committee of the University of California at Davis. All participants were examined by the principal investigator, and chemistry-20 panels were obtained during fasting. Individuals with diabetes mellitus, liver or kidney disease, or plasma TG levels greater than 2.82 mmol/L or LDL-C levels greater than 4.26 mmol/L were excluded. Menopause was defined by at least a 9-month history of amenorrhea or surgical removal of both ovaries. Only women on continuous hormone replacement therapy were included; women on cyclical hormone replacement were excluded. Four women used hormone replacement: two estrogen only, and two a combination of estrogen and progesterone. Dosages of hormones and all other medications or supplements remained unchanged throughout the study. The exercise level was also kept constant and monitored by activity questionnaires.

Diet

Dietary intervention involved a 4-month period of eucaloric controlled feeding that provided all food intake. The study was designed to reduce fat intake stepwise to 15% of the daily energy intake. The participants' diet before the study was defined as "the habitual diet." After entering the study, participants consumed a 35% fat diet during the first 4 weeks. The goal was to have all the participants achieve the same fat intake level and to adjust the energy intake as a preparation for the low-fat diet phases. During this period, the initial energy intake was individualized based on each subject's energy expenditure (measured by indirect calorimetry) multiplied by a factor based on their physical activity level (estimated by physical activity questionnaire). Subjects were weighed five times each week, and the energy content of the diet was adjusted when the weight varied by more than 1 kg from the entry level, to maintain the body weight.

After stabilizing the weight and energy intake during the 35% fat period, participants were switched to a diet containing 25% fat for 6 weeks and 15% fat for another 6 weeks. Participants ate dinner 5 days per week at the study site, and received breakfast, lunch, snacks, and weekend meals in prepackaged form as take-outs. The food was served in 7-day menu cycles. They also kept daily records of additional dietary intake, and noncompliance was defined as a deviation of greater than 1% of calories from the experimental diet on more than one occasion per week. All subjects adhered to the diet satisfactorily. Alcohol was not included in the diet. One alcoholic drink per week was permitted as long as the intake was recorded in the food diary. The majority of women did not consume any alcohol. Food from an entire week during each diet period was homogenized and sent to the Hazelton Laboratory (Madison, WI) for analysis. Actual fat content of the diets was reported as 31%, 23%, and 14%, and carbohydrate content as 53%, 60%, and 67%, respectively.

Data Collection

At the end of each dietary period, blood samples were collected after a 12-hour overnight fast into tubes containing EDTA.

Nutrition data. Seven-day food records and food frequency questionnaires were obtained at entry to determine the habitual intake.[33] The 7-day food records were analyzed using an updated version of the Nutrition Data System (NDS 93; University of Minnesota, Minneapolis, MN). Food frequency questionnaires were analyzed by the Nutritionist 4 program (N-Squared Computing, Silverton, OR). Data obtained by these two independent methods were compared to determine the reliability. Data obtained by analysis of 7-day food records are reported. Since nutrient intake information was obtained using self-reported 7-day food records during the habitual diet and using chemical analysis of the food during the controlled feeding, these two sets of data could not be compared. Therefore, data obtained during the 31% fat intake and 14% fat intake periods of controlled feeding were used to determine the changes in plasma lipoproteins and lipoprotein particle size.

Lipid and Apolipoprotein Determinations

An aliquot of fresh plasma was subjected to ultracentrifugation for serial isolation of VLDL ($d < 1.019$), LDL ($1.019 < d < 1.063$), and HDL ($1.063 < d < 1.21$). Plasma and various lipoprotein fractions were used for determination of lipids, apolipoproteins, and particle size. TG and cholesterol levels were measured enzymatically using kits from Sigma (St Louis, MO). Each assay included appropriate standards and calibrators. The interassay coefficient of variation (CV) was 3.6% for TG and 1.9% for cholesterol. HDL and the HDL_3 subfraction were separated from the plasma by the serial precipitation method of Warnick et al[34] using dextran sulfate and magnesium chloride. The CV for HDL-C was 2% for the normal values and 5% for the extremes. Values for HDL_2 were calculated by subtracting the values for HDL_3 from HDL. Apolipoproteins (apos) B and A1 were determined by immunonephelometry (Beckman, Palo Alto, CA) with CVs of 3.6% and 3.3%, respectively.

Determination of Lipoprotein Particle Size

VLDL. Freshly isolated VLDL was used to determine particle size optically by dynamic light-scattering using a Microtrak Series 9200 Ultrafine particle analyzer (Leeds and Northrup, North Wales, PA).[35] Aliquots of VLDL were suspended as a 1:10 dilution in a NaCl solution ($d = 1.0063$ g/mL) and placed into the sample well. The system software and a 3-mW ($\lambda = 780$ nm) laser beam was activated. Light-scattering from the lipoprotein particles was recorded for 3 minutes, adapted to the audio range, and deconvoluted by system software. Using this method, light from the laser diode is scattered from each particle, and its frequency is subsequently Doppler-shifted by Brownian motion of the particle. The Doppler effect is proportional to the particle velocity. Velocity distribution is a known function of the particle size, fluid temperature, and fluid viscosity. Both temperature and viscosity of the suspending fluid are known, and thus with compensation the velocity distribution becomes a unique function of the particle size. Although considered a primary method, the validity of these measurements was regularly assessed using monosized latex beads (Bangs Laboratory, Carmel, IN).

LDL and HDL. Undialyzed aliquots of LDL and HDL were kept at −20°C. All samples from each feeding period for individual subjects were separated on the same gel. LDL and HDL fractions were subjected to nondenaturing gradient gel electrophoresis using gels with gradients of 2% to 16% and 4% to 30% polyacrylamide (Isolabs, Akron, OH), respectively, in a GE-2/4 LS vertical electrophoresis apparatus (Pharmacia, Uppsala, Sweden). Protein staining with Coomassie blue R-250 in methanol:acetic acid:water (45:10:45) for 24 hours was used to visualize lipoproteins Gels were destained in methanol:acetic acid: water (20:75:5) until backgrounds were clear. Migration of lipoproteins was measured and analyzed using a Shimatzu CS-9301 PC (Shimatzu Scientific, Columbia, MD) scanning densitometer. Particle sizes were calibrated in the digitized scans by comparison to migration distances of standard proteins of known hydrated diameters (Pharmacia, Piscataway, NJ) within each gel.[35,36]

Statistical Analysis

The results are presented as the mean ± SEM unless otherwise noted. Data were analyzed by ANOVA with repeated measures. Where necessary, log transformation of the data was made to conform to the assumptions of normality and homogeneity of variance. If a significant result was obtained ($P < .05$), Student's t test was performed to

evaluate differences between the various dietary intervention periods. Correlations among variables were calculated using Pearson's product-moment correlations. All analyses were performed using PC-SAS Release 6.04 (SAS Institute, Cary, NC).

RESULTS

Changes in Nutrient Intake

During controlled feeding, the daily energy required to maintain weight was significantly higher than the self-reported values for the habitual diet. This is consistent with the underreporting observed by other researchers.[37] As fat intake decreased, cholesterol intake also decreased and fiber intake increased (Table 1).

Changes in Plasma Lipoproteins

Decreasing the amount of dietary fat intake was associated with increasing plasma TG levels (14% during the change from 31% fat to 23% fat intake, and 34% during the change from 23% fat to 14% fat intake). Plasma total cholesterol and LDL-C decreased only during the 14% fat intake (7% and 15%, respectively, $P < .05$). Apo B levels did not change. HDL-C decreased by 6% during the 23% fat diet and by 13% during the 14% fat diet. Apo A1 decreased only during the 14% fat diet, by 10% (Table 2).

Changes in Lipoprotein Particle Size

VLDL. When dietary fat was restricted to 14%, VLDL particle size increased (habitual diet, 42.5 ± 1.5 nm; 31% fat, 40.7 ± 0.8 nm; 23% fat, 41.2 ± 0.9 nm; and 15% fat, 47.1 ± 0.9 nm). Although the direction of the changes in VLDL particle size and plasma TG was similar, they did not correlate (Fig 1 and Table 3).

LDL. There was no change in LDL particle size.

HDL. Seven of 14 subjects had three HDL bands detected with nondenaturing gel electrophoresis. The remaining seven subjects did not have the largest HDL band (HDL_1). During fat restriction, despite the significant decrease in HDL-C levels, the size of the HDL bands did not change.

Relationships Between Weight and Plasma Lipoproteins and Lipoprotein Particle Size

When all time points were considered, weight correlated significantly with various components of HDL (HDL-C, $r = -.440$; HDL_2-C, $r = -.311$; HDL_3-C, $r = -.405$; plasma apo A1, $r = -.416$; and HDL-apo A1, $r = -.426$). Other plasma lipids or lipoproteins did not relate to weight. Weight correlated weakly with VLDL particle size during the habitual diet and 31% fat and 23% fat diets, but not during the 14% fat diet (Table 4). The particle size of LDL or HDL did not correlate with weight. However, the change in weight between the 31% fat and 14% fat diets correlated directly with the change in particle size of VLDL and inversely with the change in particle size of the largest HDL band (HDL_1) (Table 5).

Relationships Between Plasma Lipoproteins and Lipoprotein Particle Size

VLDL. During the habitual diet and 31% fat intake, VLDL particle size correlated inversely with HDL-C and HDL-TG and directly with HDL-apo A1. However, as dietary fat intake decreased, the relationships between VLDL particle size and HDL disappeared. During the habitual diet and 23% fat intake, VLDL particle size correlated inversely with LDL particle size ($r = -.298$, $P < .03$ and $r = -.667$, $P < .02$, respectively) (Table 4). The change in VLDL particle size correlated inversely with the change in plasma total cholesterol and directly with the change in apo A1 (Table 5).

LDL. Both during the habitual diet and at every level of eucaloric fat restriction, LDL particle size correlated inversely with plasma TG and apo B (Table 4). The change in LDL particle size also correlated inversely with the change in apo B, but not with the change in plasma TG (Table 5). Changes in LDL particle size correlated directly with changes in the particle size of smaller HDL bands (HDL_2 and HDL_3) but not the large HDL band (HDL_1) (Table 5).

HDL. At each time point, the particle size of all three HDL bands correlated strongly with each other, but not with VLDL or LDL particle size.

Table 1. Daily Nutrient Intake During the Habitual Diet and Eucaloric Diets

Nutrient Intake	Habitual Diet	Eucaloric Diet		
	33% Fat	31% Fat	24% Fat	14% Fat
Energy (kcal)	1,695 ± 366	2,246 ± 525	2,257 ± 518	2,279 ± 554
Fat, g (%)				
Total	63 ± 22 (33 ± 8)	75 (31)	57 (23)	36 (14)
Saturated	20 ± 9 (10 ± 3)	22 (10)	15 (6)	9 (3)
MUFA	24 ± 9 (13 ± 3)	31 (12)	22 (10)	16 (7)
PUFA	14 ± 4 (8 ± 2)	21 (9)	17 (7)	11 (4)
Cholesterol	259 ± 159	237	201	167
CHO, g (%)	216 ± 64 (51 ± 7)	296 (53)	337 (60)	381 (67)
Fiber (g)	17 ± 3	21	25	25
Protein, g (%)	71 ± 16	98 (17)	99 (18)	108 (19)

NOTE. Data for the habitual diet were obtained by analysis of 7-day food records using the NDS-93 computer program (mean ± SD). Data for the eucaloric diets were obtained by direct chemical analysis of the food, and therefore, there is no SD associated with these values.

Abbreviations: MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; CHO, carbohydrate.

Table 2. Changes in Weight (kg) and Plasma Lipids, Lipoproteins, and Apolipoproteins (mmol/L) at Baseline and During Eucaloric Dietary Fat Restriction (N = 14, mean ± SEM)

	Habitual Diet	Eucaloric Diet		
Variable	33% Fat	31% Fat	24% Fat	14% Fat
Weight	82.7 ± 6.8[a]	82.7 ± 6.8[a]	82.7 ± 6.8[a]	82.3 ± 6.8[a]
TG	1.86 ± 0.30[a]	1.85 ± 0.28[a]	2.10 ± 0.26[b]	2.47 ± 0.37[c]
TC	5.82 ± 0.25[a]	5.64 ± 0.21[a]	5.72 ± 0.21[a]	5.40 ± 0.21[b]
Apo B	1.92 ± 0.17	1.94 ± 0.11	2.11 ± 0.15	2.0 ± 0.15
Apo A1	5.14 ± 0.25[a]	4.93 ± 0.36[a]	4.93 ± 0.29[a]	4.61 ± 0.36[b]
LDL-C	3.07 ± 0.18[a]	2.89 ± 0.18[a]	2.93 ± 0.21[a]	2.61 ± 0.21[b]
HDL-C	1.42 ± 0.1[a]	1.34 ± 0.1[b]	1.32 ± 0.1[b]	1.24 ± 0.1[c]
HDL_2-C	0.26 ± 0.05[a]	0.13 ± 0.05[b]	0.13 ± 0.05[b]	0.18 ± 0.05[a]
HDL_3-C	1.16 ± 0.08[a]	1.21 ± 0.1[a]	1.19 ± 0.08[a]	1.06 ± 0.1[b]

NOTE. Values with different superscripts are significantly different from each other ($P < .05$).

Abbreviation: TC, total cholesterol.

Changes in Nutrient Intake, Plasma Lipoproteins, and Lipoprotein Particle Size

The increase in VLDL particle size did not correlate with changes in intake of any of the nutrients. Changes in LDL particle size correlated directly with both the changes in energy and in protein intakes. Changes in HDL_1 particle size also correlated directly with the changes in energy, protein, and carbohydrate intake. Among all the lipoprotein fractions, the changes in HDL_1 particle size were most strongly related to the changes in nutrient intake (Table 5).

DISCUSSION

The present investigation addressed the effects of carbohydrate-induced hypertriglyceridemia on the particle size of VLDL, LDL, and HDL. Dietary fat restriction to 14% with increased carbohydrate intake to 67% was associated with increased VLDL particle size. VLDL size was correlated directly with body weight during every dietary period. In addition, changes in weight correlated directly with the change in VLDL particle size. Adipose tissue is the main source of fatty acids for hepatic TG synthesis, which is then incorporated into VLDL.[38] Interestingly, plasma TG levels correlated with VLDL particle size only during the 23% fat intake, and the increase in plasma TG did not correlate with the increase in VLDL particle size. Furthermore, neither the increased carbohydrate intake nor the decreased fat intake correlated with the changes in VLDL size. There was an inverse correlation between VLDL particle size and plasma HDL-C during the habitual diet and 31% fat and 23% fat diets. This finding could be due to the role of LpL in both the catabolism of VLDL and the production of HDL.[10-12,30] It is possible that one of the reasons for increased VLDL particle size and decreased HDL-C during a low-fat intake is the decrease in LpL activity, as previously reported by our group and others.[3,30] Taken together, it appears that VLDL particle size is not a direct function of plasma TG. Factors that regulate both the production and catabolism of VLDL may affect its particle size.

An important and novel finding of this study is that carbohydrate-induced hypertriglyceridemia did not cause a decrease in LDL particle size. It has been well documented that plasma TG level is an important determinant of LDL particle size.[23,26,36,39]

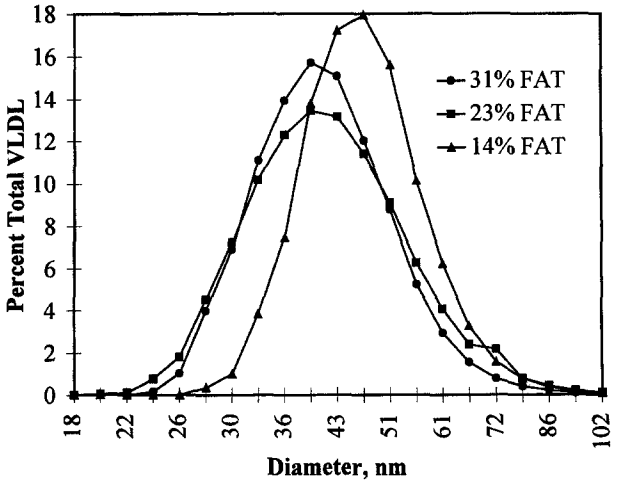

Fig 1. Effects of dietary fat restriction on VLDL particle size volume distribution as measured by dynamic light-scattering in 14 healthy postmenopausal women. During controlled feeding, the mean particle diameter of VLDL was 40.7 ± 0.6 nm on 31% fat, 41.6 ± 0.8 nm on 23% fat, and 47.0 ± 0.9 nm on 14% fat intake (N = 14, mean ± SEM).

Table 3. Particle Size (nm) of VLDL, LDL, and HDL at Baseline and During Eucaloric Dietary Fat Restriction (N = 14, mean ± SEM)

	Habitual Diet	Eucaloric Diet		
Particle	33% Fat	31% Fat	24% Fat	14% Fat
VLDL	42.7 ± 1.4[a]	40.7 ± 0.6[a]	41.6 ± 0.8[a]	47.0 ± 0.9[b]
LDL	25.3 ± 0.2[a]	25.3 ± 0.2[a]	25.2 ± 0.1[a]	25.1 ± 0.2[a]
HDL_1	11.9 ± 0.3[a]	11.9 ± 0.3[a]	11.9 ± 0.4[a]	12.1 ± 0.5[a]
HDL_2	11.1 ± 0.4[a]	11.0 ± 0.4[a]	11.0 ± 0.4[a]	11.1 ± 0.4[a]
HDL_3	9.9 ± 0.4[a]	9.9 ± 0.4[a]	9.9 ± 0.4[a]	10.0 ± 0.3[a]

NOTE. Values with different superscripts are significantly different from each other ($P < .05$).

Table 4. Significant Correlates of VLDL, LDL, and HDL Particle Size During the Habitual Diet and Eucaloric Fat Restriction

	Habitual Diet	Eucaloric Diet		
Variable	33% Fat	31% Fat	24% Fat	14% Fat
VLDL particle size				
Weight	.411†	.480*	.568*	.385†
TG			.631	
HDL-C	−.503*	−.563	−.506*	
HDL-TG	−.607			
Apo B				
Apo A1		−.654		
HDL-apo A1	.474	−.670		
LDL particle size	−.298		−.667	
LDL particle size				
TG	−.849	−.788	−.740	−.749
Apo B	−.806	−.657	−.503	−.589
HDL_1 particle size				
HDL_2 particle size	.925	.682	.982	.984
HDL_3 particle size	.913	.551	.920	.985

NOTE. Values without superscripts are all $P < .05$.

*$.1 < P > .05$.

†$.2 < P > .1$.

Table 5. Significant Correlations for the Changes in VLDL, LDL, and HDL Particle Size and Weight, Nutrient Intake, and Plasma Lipids, Lipoproteins, and Apolipoproteins Between the 31% Fat and 14% Fat Diets (N = 14, mean ± SEM)

	Particle Size		
Variable	VLDL	LDL	HDL_1
Weight	.536*		−.933
Diet			
Energy		.508*	.873
Carbohydrate			.952
Protein		.456†	.920
Plasma level			
TG			
TC	−.386†		
LDL-C			
HDL-C			
Apo B		−.496	
Apo A1	.416*		
Particle size			
HDL_2		.573	
HDL_3		.483*	

NOTE. Values without superscripts are all $P < .05$.
*$.1 < P > .05$.
†$.2 < P > .1$.

Therefore, it might be expected that increased plasma TG should result in decreased LDL size. Although we found an inverse relationship between plasma TG and LDL particle size at every dietary phase, there was no correlation between the change in plasma TG and LDL size. This was unexpected, because previous studies have shown that a decrease in plasma TG by diet or exercise increases LDL particle size.[27-29] Unfortunately, these studies did not measure VLDL size.

It is possible that as plasma TG decreases, VLDLs become smaller and TG-poor. These particles may become a better precursor for the VLDL to LDL cascade,[14] affecting LDL production and LDL particle size. However, the opposite may not necessarily be true. When increased plasma TG is associated with increased VLDL size, these larger particles may be directly removed by hepatic uptake.[17] Therefore, there may not be a change in either the production or particle size of LDL.

There was also an inverse correlation with the LDL particle size and plasma apo B level, as previously reported.[36] Furthermore, the change in LDL particle size inversely correlated with the change in apo B. This is not surprising, because each LDL particle carries a single apo B molecule, and therefore, for the same level of LDL-C, subjects with larger LDLs have fewer particles.[40]

This study also demonstrated that although a low-fat intake decreases both HDL-C and apo A1 levels, it does not alter the overall particle size of HDL bands. It appeared that among the three HDL bands, only the largest (HDL_1) was affected by changes in weight and nutrient intake. Increased energy, carbohydrate, and protein intakes correlated directly with the size of this band, but changes in weight correlated inversely. The various HDL subfractions have been shown to respond to diet and exercise differently.[28]

The age and menopausal status of our subjects may have influenced the findings of the study. Although, in general, women have larger LDL particles and pattern A, postmenopausal women have a significant decrease in LDL size and frequently pattern B distribution of LDL.[41,42] Four of 14 participants in our study were on continuous hormone replacement. Estrogen replacement reduces LDL size both in healthy[43] and in dyslipidemic[44] postmenopausal women. Since hormone treatment was continuous and the dose remained stable, we expect that our findings were not significantly affected by hormone replacement. It is known that men with LDL subclass pattern B respond differently to low-fat diets compared with men with pattern A.[27] Thus, it is also possible that carbohydrate-induced hypertriglyceridemia may affect LDL particle size differently in premenopausal women or in men. The findings of this study show that in postmenopausal women, carbohydrate-induced hypertriglyceridemia does not reduce LDL particle size and therefore may not have the same atherogenic implications as the genetic disorders such as combined hyperlipidemia or hypertriglyceridemia.

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