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Effect of short-term low- and high-fat diets on low-density lipoprotein particle size in normolipidemic subjects

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ABSTRACT

High-fat, low-carbohydrate diets have been shown to raise plasma cholesterol levels, an effect associated with the formation of large low-density lipoprotein (LDL) particles. However, the impact of dietary intervention on time-course changes in LDL particle size has not been investigated. To test whether a short-term dietary intervention affects LDL particle size, we conducted a randomized, double-blind, crossover study using an intensive dietary modification in 12 nonobese healthy men with normal plasma lipid profile. Participants were subjected to 2 isocaloric 3-day diets: high-fat diet (37% energy from fat and 50% from carbohydrates) and low-fat diet (25% energy from fat and 62% from carbohydrates). Plasma lipid levels and LDL particle size were assessed on fasting blood samples after 3 days of feeding on each diet. The LDL particles were characterized by polyacrylamide gradient gel electrophoresis. Compared with the low-fat diet, plasma cholesterol, LDL cholesterol, and high-density lipoprotein cholesterol were significantly increased (4.45 vs 4.78 mmol/L, P = .04; 2.48 vs 2.90 mmol/L, P = .005; and 1.29 vs 1.41 mmol/L, P = .005, respectively) following the 3-day high-fat diet. Plasma triglycerides and fasting apolipoprotein B-48 levels were significantly decreased after the high-fat diet compared with the low-fat diet (1.48 vs 1.01 mmol/L, P = .0003 and 9.6 vs 5.5 mg/L, P = .008, respectively). The high-fat diet was also associated with a significant increase in LDL particle size (255.0 vs 255.9 Å; P = .01) and a significant decrease in the proportion of small LDL particle (<255.0 Å) (50.7% vs 44.6%, P = .01). As compared with a low-fat diet, the cholesterol-raising effect of a high-fat diet is associated with the formation of large LDL particles after only 3 days of feeding.

1. Introduction

Low density lipoprotein (LDL) particles are heterogeneous in terms of density, size, lipid composition, electrical charge, and pathogenic properties [1]; and it is now recognized that small dense LDL particles are associated with an increased risk of coronary heart disease (CHD) [2] even in the presence of relatively normal plasma LDL cholesterol (LDL-C) concentrations [3]. Intrinsic properties of small dense LDL particles have been suggested to be biologically responsible for increasing the risk of developing CHD; and in fact, several characteristics link small LDL subfractions to atherogenesis, including

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enhanced susceptibility to oxidation [4] and long residence time in plasma as well as enhanced capacity to bind to intimal proteoglycans associated with increased permeability through the endothelial barrier [5]. Furthermore, subtle variations in LDL particle composition and diameter have been shown to induce important conformational changes of apolipoprotein (apo) B-100, which may alter epitope exposure, and cause changes in LDL receptor binding affinity [6,7]. Together, these findings support the hypothesis that small dense LDL particles contribute to an increased risk of future CHD and that the distribution and concentration of these atherogenic lipoproteins may be used to evaluate response to lipid therapy [8].

Several lines of evidence suggest that heterogeneity in LDL particle size is most likely attributable to a complex network of genetic, metabolic, and environmental factors including dietary composition [9-12]. In general terms, most studies that have compared low-fat and high-fat diets consumed under isocaloric conditions have shown an association between increases in dietary carbohydrates and reductions in LDL size [12]. Indeed, the metabolic effects of low-fat, high-carbohydrate diets are complex and include not only a reduction in LDL particle size but also increased plasma levels of triglyceride-rich lipoproteins, reduced high-density lipoprotein cholesterol (HDL-C) concentrations, and increased insulin levels [13], a constellation of factors associated with increased cardiovascular risk [14]. So far, the reduction in LDL size associated with low-fat, high-carbohydrate diets has been reported in the context of long-term dietary intervention. By contrast, little is known about early changes of LDL particle size that could occur in response to short-term dietary intervention. These potential changes deserve to be characterized, especially when considering the significance of small dense LDLs as a cardiovascular risk factor. For this study, which intended to analyze whether such early changes in LDL particle size occurred, we conducted a randomized, double-blind, crossover intervention using a short-term, intensive dietary modification in 12 healthy men with normal plasma lipid profile.

2. Subjects and methods

2.1. Subjects

Twelve healthy men were recruited in the Québec city metropolitan area to participate in the study. The participants were aged between 18 and 50 years; were nonsmokers; had a body mass index between 20.0 and 30.0 kg/m^2; and had normal plasma LDL-C, HDL-C, and triglyceride levels. None of the subjects was vegetarian or had some extreme dietary practices. Subjects were excluded if they had monogenic hyperlipidemia, such as familial hypercholesterolemia; had a history of cardiovascular events or taking medications known to affect lipoprotein metabolism; had diabetes mellitus; had history of cancer; had hematologic, digestive, or central nervous system disorders; had impairment of renal function, dysproteinemia, nephritic syndrome, or other renal disease; had coagulopathy; had human immunodeficiency virus; or had history of mental instability and of drug and alcohol abuse. The participants were maintaining their current physical activities throughout the study. The characteristics of the subjects at the time of screening are shown in Table 1. The research protocol was approved by the Laval University Medical Center ethical review committee, and written informed consent was obtained from each subject.

2.2. Experimental design

The study was performed as a double-blind, randomized, crossover intervention with 2 experimental phases where the participants received a high-fat diet and low-fat diet in random order. Each experimental phase consisted of 3 feeding day periods, each separated by a 2-week washout period where participants returned to their habitual ad libitum diets. Meals were prepared at the Institute of Nutraceuticals and Functional Foods Research Unit of Laval University for consumption on site of at least 2 of the 3 meals including breakfast. The other meal was available for takeout. The subjects were instructed to consume their entire meal provided to them and not to supplement their diet with any other food or drink except water and a maximum of 2 cups of coffee per day. Subjects were weight stable for at least 3 months before the start of the study and were required to not consume any drugs throughout the study. A validated food frequency questionnaire was administered to the participants by a registered dietitian at the beginning of the study to estimate the energy intake of the participants [15]. Each participant was then assigned to a level of energy intake for each diet. Fasting blood samples were obtained after each dietary phase.

2.3. Experimental diets

During each experimental phase, subjects consumed a solid food diet typical of those consumed in North America. The

Table 1 – Baseline characteristics of the subjects (N = 12)

Variables	
Age (y)	27.1 ± 3.9
Weight (kg)	81.0 ± 11.5
Body mass index (kg/m^2)	25.2 ± 3.0
Waist circumference (cm)	86.2 ± 9.1
Total cholesterol (mmol/L)	4.70 ± 0.59
LDL-C (mmol/L)	2.72 ± 0.64
HDL-C (mmol/L)	1.43 ± 0.34
Plasma triglycerides (mmol/L)	1.20 ± 0.58
Fasting glucose (mmol/L)	4.96 ± 0.41
Mean of daily calories intake (kcal)	3229 ± 1040
Proteins (% kcal)	16.0 ± 3.0
Carbohydrates (% kcal)	49.0 ± 7.5
Total fibers (g)	31.3 ± 8.8
Fat (% kcal)	33.8 ± 5.0
Saturated (%kcal)	11.6 ± 2.7
Monounsaturated (% kcal)	13.8 ± 2.5
Polyunsaturated (% kcal)	5.8 ± 1.7
Trans (g)	5.9 ± 3.2
Alcohol (% kcal)	3.3 ± 3.3
Cholesterol (mg)	444 ± 252

Values are presented as means ± SD.

high-fat diet reflected as closely as possible current North American men averages [16,17]. The low-fat diet represented the recommendations of the National Cholesterol Education Program Adult Treatment Panel III [18]. Both diets were identical in terms of menu, calories, proteins, fibers, and monounsaturated and polyunsaturated fatty acids (Table 2). The quantities of vegetable and animal protein and of soluble and nonsoluble fibers were also identical between the 2 diets. Experimental diets were formulated by using Nutrition Data System software (version 4.03_31; Nutrition Coordinating Center, Minneapolis, MN).

3. Anthropometric measurements and blood pressure

Body weight and waist circumference were measured according to standardized procedure [19] at the beginning of the intervention. At the same time, systolic and diastolic blood pressures were taken after a 10-minute rest in the sitting position. They were measured on the right arm using an automated blood pressure monitor (BPM 300-BpTRU Vital Signs Monitor, VSM MedTech Ltd., Coquitlam, BC, Canada).

3.1. *Plasma lipids, lipoproteins, and apolipoproteins*

Venous blood samples were collected from an antecubital vein into Vacutainer tubes containing K_3EDTA (1 mg/mL, final concentration) after a 12-hour fasting period. Samples were then immediately centrifuged at 4°C for 10 minutes at 3000 rpm to obtain plasma and were stored at 4°C until processed. Cholesterol and triglycerides levels were determined in plasma; and lipoprotein fractions were quantified by enzymatic methods (Randox, Crumlin, UK) using a RA-500 analyzer (Bayer, Tarrytown, NY, USA), as previously described [20]. Heparin and manganese chloride [21] were added to precipitate apoB-containing LDL, leaving the HDL in solution. The LDL-C was calculated according to the equation described by Friedewald et al [22] (LDL-C = total cholesterol – HDL-C – plasma triglyceride/2.2). Plasma apoA-I and apoB levels were measured using a Behring Nephelometer BN-100 (Behring Diagnostic, Westwood, MA, USA) with reagents and calibrators (Dade Behring, Mississauga, Ontario) provided by the manufacturer. Plasma apoB-48 was assessed by a sandwich enzyme-linked immunosorbent assay method using monoclonal antibody (Shibayagi, Gumma, Japan) [23].

Table 2 – Composition of the 2 experimental diets

Nutrients	Low fat	High fat
Proteins (% kcal)	15.0	15.0
Carbohydrates (% kcal)	61.8	49.8
Total fibers[a] (g)	20.4	20.3
Fats (% kcal)	25.0	37.0
Saturated (% kcal)	6.0	15.0
Monounsaturated (% kcal)	12.0	12.7
Polyunsaturated (% kcal)	4.9	4.3
Trans (% kcal)	Trace	3.5
Cholesterol[a] (mg)	189	383
Phytosterol[a] (mg)	180	120
P/S ratio	0.81	0.28

P/S indicates polyunsaturated to saturated fat ratio.
[a] For 2500 kcal/d.

3.2. *Measurement of glucose, insulin, and free fatty acids*

Plasma glucose was measured enzymatically, whereas plasma insulin was measured by radioimmunoassay with polyethylene glycol separation [24]. Free fatty acid levels were measured with an enzymatic detection kit (ZenBio, Research Triangle Park, NC, USA).

3.3. *Cholesterol ester transfer protein measurements*

Plasma cholesterol ester transfer protein (CETP) mass concentration was determined by a commercial sandwich enzyme-linked immunosorbent assay kit (Wako Chemicals, Richmond, VA, USA) as previously described [11]. Plasma CETP mass concentration and plasma CETP activity are strongly correlated [25].

3.4. *LDL particle size characterization*

Nondenaturing 2% to 16% polyacrylamide gel electrophoresis was performed as described previously [3]. Low-density lipoprotein particle size was determined on 8 × 8-cm polyacrylamide gradient gels prepared in batches in our laboratory. Aliquots of 3.5 μL of whole plasma samples were mixed in a 1:1 volume ratio with a sample buffer containing 20% sucrose and 0.25% bromophenol blue and loaded onto the gels. A 15-minute prerun at 75 V preceded electrophoresis of the plasma samples at 150 V for 3 hours. Gels were stained for 1 hour with Sudan black (0.07%) and stored in a 0.81% acetic acid/4% methanol solution until analysis by the Imagemaster 1-D Prime computer software (Amersham Pharmacia Biotech, Piscataway, NJ, USA). Low-density lipoprotein size was extrapolated from the relative migration of 4 plasma standards of known diameter. The estimated diameter for the major peak in each scan was identified as the LDL–peak particle diameter (PPD). An integrated (or mean) LDL diameter was also computed by using a modification of the approach described previously [3]. This integrated LDL particle size corresponds to the weighted mean size of all LDL subclasses in each individual. It was calculated as a continuous variable and was computed as the sum of the diameter of each LDL subclass multiplied by its relative area. Analysis of pooled plasma standards revealed that measurement of LDL-PPD was highly reproducible, with an interassay coefficient of variation of less than 2%. The relative proportion of LDL having a diameter less than 255 Å (LDL% <255 Å) was ascertained by computing the relative area of the densitometric scan less than 255 Å [26]. The absolute concentration of cholesterol among particles less than 255 Å (LDL-$C_{<255\ Å}$) was calculated by multiplying the plasma LDL-C levels by the relative proportion of LDL with a diameter less than 255 Å [26]. A similar approach was used to assess the relative and absolute concentrations of cholesterol in particles with a diameter between 255 and 260 Å or greater than 260 Å.

Table 3 – Plasma lipid/lipoprotein profile and LDL particle characteristics after 3 days of low-and high-fat diets in 12 healthy men

Lipids	Low-fat diet	High-fat diet	Changes (%) [a]	P
Lipid/lipoprotein profile				
Plasma-C (mmol/L)	4.45 ± 0.73	4.78 ± 0.52	6.4 (-0.5, 20.1)	.04
LDL-C (mmol/L)	2.48 ± 0.64	2.90 ± 0.59	19.7 (2.4, 34.4)	.005
HDL-C (mmol/L)	1.29 ± 0.25	1.41 ± 0.30	7.0 (2.8, 18.3)	.005
Triglycerides (mmol/L)	1.48 ± 0.77	1.01 ± 0.39	-36.0 (-41.7, -17.3)	.0003
Plasma-C/HDL-C	3.63 ± 1.17	3.55 ± 0.97	-1.7 (-8.7, 3.4)	.5
Plasma apoB (g/L)	0.83 ± 0.22	0.88 ± 0.20	4.8 (-1.8, 17.9)	.2
Plasma apoB-48 (mg/L)	9.6 ± 5.2	5.8 ± 2.4	-42.7 (-54.5, -1.8)	.008
Plasma apoA-I (g/L)	1.42 ± 0.12	1.50 ± 0.17	2.4 (-1.7, 7.8)	.1
Glucose (mmol/L)	5.65 ± 0.48	5.88 ± 0.57	4.6 (-0.7, 9.7)	.1
Insulin (pmol/L)	80.8 ± 58.3	65.9 ± 46.0	-15.7 (-39.3, 15.4)	.2
Free fatty acids (mmol/L)	393.1 ± 191.5	364.4 ± 131.2	-2.5 (-21.8, 29.7)	.4
CETP (μg/mL)	1.20 ± 0.29	1.34 ± 0.30	14.0 (3.8, 26.8)	.01
LDL particle size				
LDL-size (Å)	255.0 ± 1.5	255.9 ± 1.1	0.5 (-0.1, 0.6)	.01
LDL-PPD (Å)	255.1 ± 1.5	255.5 ± 1.1	0.2 (-0.1, 0.8)	.4
Relative distribution among LDL subclass (%)				
Large LDL	10.6 ± 5.1	11.8 ± 5.4	20.9 (0.1, 35.1)	.2
Medium LDL	38.7 ± 11.4	43.6 ± 9.2	17.8 (-4.4, 29.9)	.03
Small LDL	50.7 ± 13.3	44.6 ± 11.6	-11.9 (-25.8, 3.2)	.04
Cholesterol levels among LDL subclass (mmol/L)				
Large LDL-C >260 Å	0.28 ± 0.21	0.35 ± 0.19	41.7 (11.4, 70.1)	.03
Medium LDL-C 255-260 Å	0.93 ± 0.27	1.25 ± 0.35	25.5 (16.7, 52.5)	.0003
Small LDL-C <255 Å	1.28 ± 0.49	1.30 ± 0.46	3.6 (-13.6, 27.2)	.8

C indicates cholesterol.
[a] Changes (%) are represented by medians of the individual percentage changes with quartiles.

3.5. *Statistical analysis*

The LDL-PPD and LDL integrated size were normally distributed. Spearman correlation coefficients were determined to assess the significance of associations. All analyzes were performed using JMP Statistical Software (version 8.0.1; SAS Institute, Cary, NC). Student paired *t* test for continuous measures was used to assess differences between the 2 dietary interventions.

4. Results

4.1. *Characteristics of the subjects*

Subject baseline characteristics at screening are presented in Table 1. The mean age and body mass index (±SD) of participants were 27.1 ± 3.9 years and 25.2 ± 3.0 kg/m^2, respectively. The mean plasma lipid levels were between the 40th and the 75th percentiles for men aged 25 to 34 years [27], with total cholesterol, LDL-C, HDL-C, and triglyceride concentrations at 4.70 ± 0.59, 2.72 ± 0.64, 1.43 ± 0.34, and 1.20 ± 0.58 mmol/L, respectively.

4.2. *Plasma lipid, lipoprotein, and apolipoprotein concentrations*

Table 3 shows the lipid/lipoprotein profile of subjects following each treatment phase with low-fat and high-fat diets. High-fat diet led to significant increases in the concentrations of plasma cholesterol (4.45 vs 4.78 mmol/L; $P = .04$), LDL-C (2.48 vs 2.90 mmol/L; $P = .005$), and HDL-C (1.29 vs 1.41 mmol/L; $P = .005$) and was associated with significant reductions in plasma triglyceride (1.48 vs 1.01 mmol/L; $P = .0003$) and fasting apoB-48 levels (9.6 vs 5.8 mg/L; $P = .008$). However, the high-fat diet had no significant impact on plasma apoB and apoA-I levels. High-fat diet decreased insulin and free fatty acid levels, but these reductions did not reach statistical significance. Finally, the high-fat diet led to a significant increase in CETP mass (1.20 vs 1.34 μg/mL; $P = .01$).

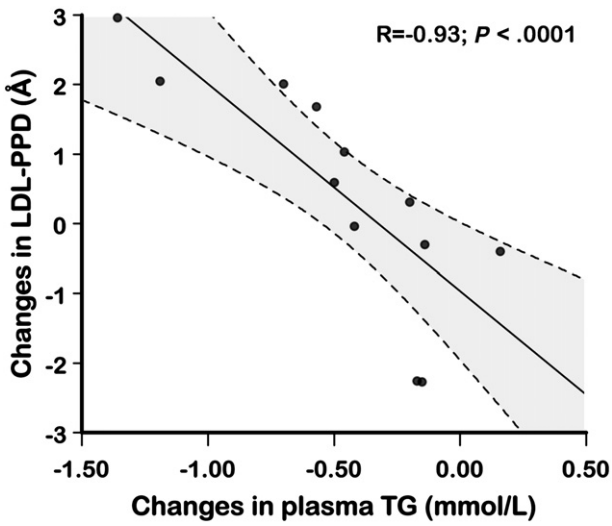

Fig. 1 – Correlation between changes in plasma triglyceride levels and changes in LDL-PPD between the 2 diets.

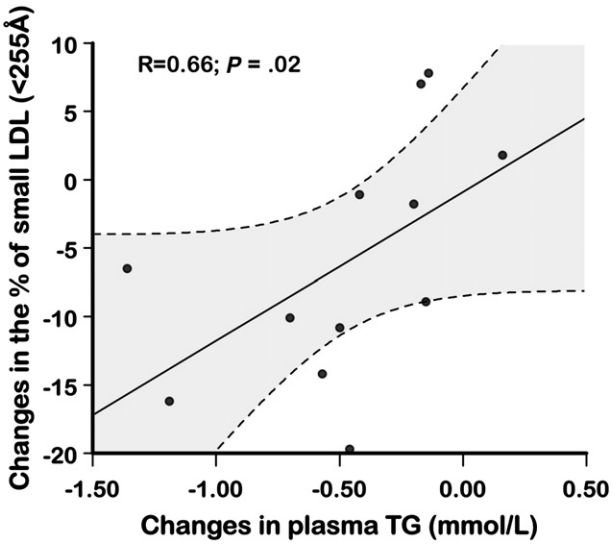

Fig. 2 – Correlation between changes in triglyceride levels and changes in the proportion of small LDL particles between the 2 diets.

4.3. *Electrophoretic characteristics of LDL particles*

As shown in Table 3, high-fat diet significantly increased LDL particle size by 0.9 Å (P = .008) as compared with the low-fat diet, whereas no change was observed in LDL-PPD. The high-fat diet also increased the percentage of large$_{>260\ Å}$ and medium$_{255Å\text{-}260\ Å}$ LDL particles and decreased the percentage of small$_{<255\ Å}$ LDL particles. The concentration of cholesterol in the large$_{>260\ Å}$ and the medium$_{255Å\text{-}260\ Å}$ LDL particles was increased by the high-fat diet as compared with the low-fat diet, without any change in the concentration of cholesterol in the small$_{<255\ Å}$ LDL particles. Fig. 1 shows a negative correlation between changes in plasma triglyceride levels and changes in LDL-PPD (r = –0.93, P = <.0001). Furthermore, a positive association was observed between changes in percentage of small$_{<255\ Å}$ LDL particles and concurrent changes in plasma triglyceride levels (r = 0.66, P = .02) (Fig. 2).

5. Discussion

The present study was designed to investigate the impact of a short-term high-fat diet on the fasting lipid profile and LDL subclasses compared with a low-fat diet in healthy subjects. The results indicate that 3 days of a high-fat diet significantly increased plasma cholesterol, LDL-C, and HDL-C concentrations compared with a low-fat diet. Plasma triglycerides and fasting apoB-48 levels were significantly reduced following a high-fat diet compared with a low-fat diet. The high-fat diet was also associated with a significant increase in LDL particle size and a reduction of the proportion of small LDL particles. Finally, the reduction in plasma triglyceride concentration following the high-fat diet was directly associated with the corresponding increase in LDL particle size and decrease in the proportion of small LDL particles. These findings suggest that the cholesterol-raising effect of a high-fat diet is associated with the formation of large LDL particles after only 3 days of feeding as compared with a low-fat diet. However, because the present study was only conducted in men, the results cannot be generalized to the whole population.

Cross-sectional and metabolic studies provide evidence that dietary nutrients influence plasma lipids and lipoproteins. Dietary fat was associated with a reduction in plasma triglyceride levels, relative to dietary carbohydrate [28]. A postprandial study of postmenopausal women making graded changes to reduce dietary fat intake and increase carbohydrate intake showed sequential elevations in fasting triglyceride concentration as dietary carbohydrate increased from 50% to 67% of energy [29]. Fasting triglyceride levels were higher with the 67% carbohydrate diet, and higher absolute concentrations of circulating triglyceride from very low-density lipoprotein (VLDL) and chylomicrons in the postprandial period were observed. In fact, several lines of evidence suggest that elevation of plasma triglycerides during high-carbohydrate feeding can be observed even after a single meal. Harbis et al [30] fed 4 test meals varying in glycemic index to healthy men and reported that apoB-48-containing lipoprotein concentrations were significantly higher after meals with high glycemic index compared with those with low glycemic index, a finding supporting the concept that high postprandial glucose and insulin concentrations stimulate de novo lipogenesis and secretion of intestinal and hepatic triglyceride-rich lipoproteins. In an animal model of insulin resistance [31], chronic fructose feeding was associated with overproduction of intestinal apoB-48 and enhanced intestinal lipid synthesis in the form of free cholesterol, cholesterol ester, and triglyceride, as well as increases in both mass and activity of microsomal triglyceride transfer protein. A study by Hudgins et al [32] extended these observations to humans by showing that healthy subjects fed high-carbohydrate diets exhibited elevated hepatic de novo lipogenesis. In contrast, however, a study with hypertriglyceridemic subjects switching from a high-fat to a high-carbohydrate diet showed a significant increase in triglyceride-rich lipoprotein apoB-48 levels and VLDL apoB-100 associated with a reduction in VLDL-triglyceride catabolism and no impact on VLDL secretion and de novo lipogenesis [33]. Therefore, these studies suggest 2 potential mechanisms responsible for the elevation of plasma triglyceride and apoB-48 levels after a low-fat diet: (1) a stimulation of de novo lipogenesis leading to enhanced lipoprotein production and, alternatively, (2) a reduction in VLDL clearance most likely due to concomitant elevation in triglyceride-rich lipoproteins of intestinal origin. The present study demonstrated that this phenomenon was rapid because a significant reduction in plasma triglyceride and apoB-48 levels was found after only 3 days of high-fat feeding.

Low-density lipoprotein particle size is influenced by genetic determinants [34], age, sex [35,36], and metabolic factors affecting plasma triglyceride levels [36], including abdominal adiposity [37] and insulin resistance [38]. Furthermore, it is well recognized that diets high in saturated fat and cholesterol cause progressive elevations in LDL particle size because of an increase in cholesterol ester content [39-41]. Dreon et al [39] investigated whether LDL subclasses are associated with response of plasma

lipoprotein levels to changes in dietary fat and carbohydrate content in healthy nonobese normolipidemic men who consumed high- (46% of energy) and low-fat (24% of energy) diets for 6 weeks each in a randomized, crossover design. The results showed that the reduction in LDL-C seen during consumption of a low-fat high-carbohydrate diet was associated with a shift from larger, more cholesterol-enriched LDL to smaller, cholesterol-depleted LDL. Our study is consistent with these findings and extend these observations to short-term dietary interventions, having shown a significant increase in LDL particle size and a shift from smaller LDL to more buoyant LDL particle size after only 3 days of high-fat diet. Interestingly, previous studies [42-44] indicated that a single meal does not significantly modulate LDL particle size, suggesting that the effects on LDL size observed in the present study are not the result of the last meal, but rather are cumulative effects of the short-term dietary intervention.

Cholesteryl ester transfer protein (CETP) plays a major role in the remodeling of lipoprotein particles by mediating the transfer of cholesteryl ester from HDL to apoB-containing lipoproteins in exchange for triglycerides. Several lines of evidence support the notion that CETP is linked to LDL particle size heterogeneity [11,45]. Previous human studies showed that a high-fat diet [46-49] was associated with an increase in plasma CETP concentrations, and it has been suggested that the elevation of plasma CETP concentrations could in turn cause an elevation in plasma LDL-C concentrations [50,51]. Our study is consistent with these previous observations, having shown a significant elevation of CETP mass following a high-fat diet. However, the causal relationship between changes in CETP and plasma lipid concentrations induced by the diet has not been clearly established. Because several conditions associated with hypercholesterolemia also elevate plasma CETP concentrations, it is possible that the activity of this protein may be regulated by plasma cholesterol levels per se. In vitro, the elevation of the intracellular content of cholesterol in human adipose tissue raises CETP messenger RNA concentrations and causes the secretion of CETP [52]. It has been suggested that the combination of dietary saturated fatty acids and cholesterol may alter the intracellular cholesterol-regulating pool in hepatocytes and that the lower levels of these nutrients found in the low-fat diet decreases CETP secretion in parallel with the fall in plasma LDL-C levels induced by this diet [53]. Further studies are needed to clarify the mechanisms underlying the elevation of CETP mass and activity associated with high-fat diets.

In conclusion, as compared with a low-fat diet, the cholesterol-raising effect of a high-fat diet is associated with the formation of large LDL particles after only 3 days of feeding. These results indicate that dietary fat content is an important determinant responsible for acute regulation of LDL particle size. However, it should be acknowledged that the short-term effects of these diets on lipoprotein profile may not necessarily reflect chronic effects. Therefore, the impact of these short-term changes in lipoprotein levels and composition on cardiovascular risk should be interpreted with caution.

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Conflict of Interest

None of the authors had a conflict of interest.

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