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Fasting and Postprandial Remnant-Like Particle Cholesterol Concentrations in Obese Participants Are Associated with Plasma Triglycerides, Insulin Resistance, and Body Fat Distribution[1,2]

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Abstract

Elevated plasma concentrations of remnant-like particle cholesterol (RLP-C) are atherogenic. However, factors that determine RLP-C are not fully understood. This study evaluates which factors affect RLP-C in the fasting and postprandial state, using multiple regression analyses in a large cohort of lean and obese participants. All participants ($n = 740$) underwent a test meal challenge containing 95 energy % (en%) fat (energy content 50% of predicted daily resting metabolic rate). Fasting and postprandial concentrations of circulating metabolites were measured over a 3-h period. Obese participants ($n = 613$) also participated in a 10-wk weight loss program (−2510 kJ/d), being randomized to either a low-fat or a high-fat diet (20–25 vs. 40–45en% fat). Postprandial RLP-C was associated with fasting RLP-C, waist:hip ratio (WHR), $HOMA_{IR}$ (homeostasis model assessment index for insulin resistance) ($P < 0.001$), and age, independently of BMI and gender [adjusted R^2 (adj. R^2) = 0.70). These factors were also related to fasting RLP-C ($P < 0.010$), along with gender and physical activity (adj. $R^2 = 0.23$). The dietary intervention resulted in significantly lower fasting RLP-C concentrations, independently mediated by weight loss, improvements in $HOMA_{IR}$, and the fat content of the prescribed diet. However, after inclusion of plasma triglyceride (TG), HDL-cholesterol, and FFA concentrations in the models, $HOMA_{IR}$ and WHR no longer significantly predicted fasting RLP-C, although WHR remained a predictor of postprandial RLP-C ($P = 0.002$). Plasma TG was strongly associated with both fasting and postprandial RLP-C ($P < 0.001$). In conclusion, plasma RLP-C concentrations are mainly associated with plasma TG concentrations. Interestingly, the high-fat diet was more effective at decreasing fasting RLP-C concentrations in obese participants than the low-fat diet. J. Nutr. 138: 2399–2405, 2008.

Introduction

Insulin-resistant conditions like obesity and type 2 diabetes mellitus are strongly associated with hyperlipidemia and an increased risk for atherosclerosis and cardiovascular disease (1). An atherogenic lipoprotein profile is characterized by high plasma concentrations of triglyceride (TG)[11]-rich lipoproteins (TRL), small, dense LDL, and low plasma concentrations of HDL-cholesterol (HDL-C) (2). Moreover, high plasma concentrations of remnant-like particles

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[11] Abbreviations used: adj. R^2, adjusted R^2; en%, energy %; HDL-C, HDL-cholesterol; $HOMA_{IR}$, homeostasis model assessment index for insulin resistance; iAUC, incremental area under the curve; LDL-C, LDL cholesterol; NUGENOB, Nutrient-Gene Interactions in Human Obesity–Implications for Dietary Guidelines; RLP, remnant-like lipoprotein particle; RLP-C, remnant-like particle cholesterol; TG, triglyceride; TRL, triglyceride-rich lipoprotein; WHR, waist:hip ratio.

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(RLP), which are formed when TRL are partly depleted of TG by lipoprotein lipase, are considered to be highly atherogenic (2,3). In this context, it has been suggested that plasma RLP-cholesterol (RLP-C), and not plasma TG, is an independent risk factor for the development of cardiovascular disease (4–6).

Several studies have been performed to determine which factors may play a role in RLP metabolism and show associations with insulin resistance, BMI, upper body obesity, other blood lipids, gender, and age (7–15). However, most of these studies were performed in a relatively small number of participants so that multiple factors could not be taken into account. Moreover, data on the influence of lifestyle factors such as diet and physical activity are limited.

Results of a study investigating the effect of dietary composition on plasma RLP-C suggest that a 2-wk high-carbohydrate diet [60 energy % (en%) carbohydrate] increased plasma TG and decreased plasma HDL-C concentrations but also led to increased fasting and postprandial RLP-C concentrations compared with a 2-wk low-carbohydrate diet (40en% carbohydrate) (16). On the other hand, it has been shown that reducing the total fat content of the diet causes weight loss and better weight maintenance, which can also have a favorable effect on the blood lipid profile (17). Nevertheless, little information is available on the relative effects of weight loss and dietary fat modification on plasma RLP-C concentrations.

The objective of this part of the European multicenter trial Nutrient-Gene Interactions in Human Obesity–Implications for Dietary Guidelines (NUGENOB) was to take the drawbacks of earlier studies into account and investigate the factors that affect plasma RLP-C concentrations in a large cohort of lean and obese participants with a detailed phenotype, both in the fasting state and postprandially after the consumption of a high-fat meal. Second, we investigated determinants of change in fasting RLP-C concentration after a 10-wk hypo-energetic diet with either a high- or low-fat content in the obese participants who participated in the NUGENOB trial.

Materials and Methods

The study was a randomized, parallel, 2-arm, open-label, 10-wk dietary intervention of 2 hypo-energetic diets performed in 8 different centers across 7 European countries: United Kingdom, The Netherlands, France (2 centers), Spain, Czech Republic, Sweden, and Denmark. The trial was part of the multicenter EU FP5 project NUGENOB.

Participants. In total, 740 Caucasian participants (552 women) were included in the NUGENOB study. Inclusion criteria were age 20–50 y, BMI between 18.5 and 25 kg/m^2 for lean participants and BMI $\geq$30.0 kg/m^2 for obese participants. After baseline measurements, only the obese participants were allowed to enter the weight loss program. Details on participant recruitment and exclusion criteria are described elsewhere (18).

All participants were informed about the nature of the study and gave written informed consent prior to study participation. The study protocol was approved by the ethical committee at each of the participating centers.

Experimental design. All participants underwent a 1-d clinical investigation protocol. Participants arrived at the research center after a 12-h overnight fast and a preceding 3-d dietary run-in period, during which they were to keep their habitual diet and avoid excessive physical activity and alcohol consumption. After the participants voided their bladders, they underwent anthropometric and body composition assessments [as described in Petersen et al. (18)]. Thereafter, participants stayed on a bed for 3.5 h, during which circulating hormones and metabolites were determined before and after a high-fat test meal. At least 30 min before the start of the resting measurement, a catheter was inserted in an antecubital forearm vein for blood sampling. Blood was drawn in the fasting state and every 60 min following the test meal for the next 3 h. Plasma concentrations of glucose, insulin, FFA, TG, total cholesterol, HDL-C, and RLP-C were determined pre- and postprandially. Furthermore, postprandial RLP-C was also measured 6 h postprandially in a subgroup of 113 participants to compare 3-h and 6-h RLP-C concentrations. During the whole experiment, the room was kept thermoneutral at 25°C.

The obese participants who participated in the weight loss program also underwent a second clinical investigation; at the end of the 10-wk dietary intervention, anthropometric measurements and body composition assessments were repeated and a venous blood sample was obtained after an overnight fast.

Test meal. The fluid test meal (double cream with 40% fat/100 g adjusted with butter in 2 centers) consisted of 95 en% (percent of total energy content fat load) fat, 60% of which was saturated fat, 3 en% carbohydrate, and 2 en% protein. Based on the predicted metabolic rate, the energy content was fixed at 50% of the predicted basal metabolic rate (19) and ranged from 1697 to 6590 kJ. Participants were asked to drink the test meal within 10 min.

Dietary intervention. Stratified block randomization was used with center, gender, and 3 age groups (20–29, 30–39, and 40–50 y) as strata and a block size of 12 to assign obese participants to either a low-fat diet or a high-fat diet. The target macronutrient composition of the low-fat diet was 20–25% of total energy from fat, 15% from protein, and 60–65% from carbohydrate. The target macronutrient composition of the high-fat diet was 40–45% of total energy from fat, 15% from protein, and 40–45% from carbohydrate. Both diets were designed to provide 2510 kJ/d less than the individually estimated energy requirement based on an initial resting metabolic rate multiplied by 1.3. Information about how the diet was controlled is given in detail elsewhere (18).

Biochemical analyses. All blood analyses were performed in the laboratory of one of the centers. Plasma glucose concentrations (ABX diagnostics), TG (Sigma; ABX diagnostics), and total cholesterol (cholesterol 100; ABX diagnostics) were measured on a COBAS MIRA automated spectrophotometric analyzer (Roche Diagnostica). Plasma FFA (NEFA C kit; Wako Chemicals) and HDL-C (HDL-C Roche) were measured on a COBAS FARAH centrifugal spectrophotometer (Roche Diagnostica). Standard samples with known concentrations were included in each analysis for quality control. Plasma insulin concentrations were measured with a double antibody RIA (Insulin RIA 100; Kabi-Pharmacia). RLP-C concentrations were measured in plasma using an immunoseparation technique developed by Nakajima et al. (20). The RLP fraction was prepared by mixing 5 μL of plasma with 300 μL immunoseparation gel suspension, containing a mixture of 2 monoclonal antibodies, i.e. anti-human apolipoprotein A-I (H-12) and anti-human apolipoprotein-B-100 (JI-H). The reaction mixture was gently shaken for 2 h at room temperature on a special mixer (RLP-mixer J100-A, Photal, Otsuka Electronics). After incubation, 200 μL of supernatant was used for the measurements of cholesterol (RLP-C) on a COBAS MIRA S auto-analyzer (ABX diagnostics).

Calculations. The homeostasis model assessment for insulin resistance ($HOMA_{IR}$) was calculated from fasting glucose and fasting insulin according to the equation of Matthews et al. (21). An estimate of total habitual physical activity was obtained by means of the Baecke questionnaire using the sum of work, sport, and leisure scores of the questionnaire (22,23). For comparing postprandial responses, we calculated the incremental area under the curve (iAUC) according to the trapezium rule. Postprandial RLP-C is expressed as the plasma concentration of RLP-C at $t = 180$ min, because only baseline and 3-h values of RLP-C were available.

Statistical methods. Statistical analyses were performed using SPSS 14.0 for Windows (SPSS Inc.). All variables were checked for normal distribution and non-normally distributed data were ln-transformed to

satisfy conditions of normality. Student's t test for unpaired samples was used to compare participant characteristics at baseline (lean vs. obese, low- vs. high-fat diet group) and repeated-measures ANOVA was used to test for differences in time between groups.

Multiple regression analysis was performed to evaluate which factors were associated with plasma RLP-C concentrations, both in the fasting state and postprandially after a high-fat meal. The dependent variable in each multiple regression model was ln-transformed to satisfy conditions of normality. Independent variables were included in the analyses in 2 steps; gender, BMI, age, $HOMA_{IR}$, waist:hip ratio (WHR), baseline dietary fat intake, total physical activity, and/or fasting plasma RLP-C were included in model 1 and plasma concentrations of TG, FFA, and HDL-C (fasting or as iAUC in the postprandial model) were included in model 2.

Determinants of change (Δ) in fasting RLP-C were also evaluated in 2 models, with the independent variables gender, diet, age, Δ weight, Δ $HOMA_{IR}$, and Δ WHR in model 1 and change in fasting plasma TG, FFA, and HDL-C in model 2. The Δ was calculated as (10 wk − 0 wk) and the models were corrected for the mean values of each Δ variable (10 wk + 0 wk/2). Furthermore, all models as described above were corrected for center (dummy variables) and, in the postprandial model, for the energy content of the high-fat test meal. To avoid multicollinearity, predictors with a correlation > 0.80 were not included in the model simultaneously. The relative impact of the predictors is demonstrated as the standardized β-coefficient and its significance value. The adjusted R^2 (adj. R^2) of each model is indicated in the tables. Significance was set at $P < 0.05$.

Results

At baseline, obese participants had higher plasma concentrations of RLP-C, TG, FFA, and total cholesterol and a higher $HOMA_{IR}$ than lean participants ($P < 0.001$) (**Table 1**). Furthermore, the obese participants in the low- and high-fat groups at baseline did not differ. Fasting plasma RLP-C concentrations decreased in both groups due to the hypocaloric diet, with a greater reduction in the high-fat group (−0.07 ± 0.01 mmol/L) than in the low-fat group (−0.03 ± 0.01 mmol/L; $P = 0.019$). Also, the decrease in fasting TG was greater in the high-fat group (−0.17 ± 0.03 mmol/L) than in the low-fat group (−0.03 ± 0.02 mmol/L; $P = 0.007$), whereas participants that consumed the low-fat diet had a greater reduction in plasma total cholesterol and HDL-C concentrations (Table 1). Dietary goals were achieved in this study (**Table 2**) and are, along with the flow of participants in the NUGENOB study, described in detail elsewhere (18).

After the high-fat meal, plasma RLP-C, TG, and insulin concentrations increased and there was a postprandial decrease in plasma FFA concentrations (**Fig. 1**).

Determinants of fasting RLP-C concentrations. In multiple regression, $HOMA_{IR}$, gender, age, WHR, and total physical activity were positively associated with fasting RLP-C (adj. $R^2 = 0.23$), with higher concentrations in men than in women (**Table 3**). In model 2, fasting TG was the strongest positive predictor ($P < 0.001$) for fasting RLP-C concentrations (adj. $R^2 = 0.60$), whereas the degree of insulin resistance and WHR were no longer significantly associated with fasting RLP-C.

Determinants of postprandial RLP-C after a high-fat load. Fasting RLP-C, $HOMA_{IR}$, WHR (all $P < 0.001$), and age ($P = 0.023$) were significantly associated with the plasma RLP-C response to the high-fat meal (adj. $R^2 = 0.70$) (**Table 4**). Means of postprandial RLP-C according to WHR and $HOMA_{IR}$ quartiles are illustrated in **Figure 2**. Furthermore, WHR was still associated with postprandial RLP-C after inclusion of TG, HDL-C, and FFA iAUC in model 2 ($P = 0.002$), whereas $HOMA_{IR}$ was not ($P = 0.274$). Plasma TG iAUC was strongly related to postprandial RLP-C ($\beta = 0.278$; $P < 0.001$) (adj. $R^2 = 0.76$), which was also confirmed in a correlation analysis (**Fig. 3**). Plasma concentrations of RLP-C at 3 and 6 h postprandially were strongly correlated ($r_s = 0.779$; $P < 0.001$) in a subgroup of 113 participants (data not shown).

Determinants of change in fasting RLP-C after dietary intervention. Both weight loss and improvement in insulin resistance were significantly related to a decrease in fasting RLP-C (adj. $R^2 = 0.29$) after dietary intervention (**Table 5**). Furthermore, model 1 confirmed the observation we described above, i.e. that the high-fat diet was more beneficial than the low-fat diet in improving RLP-C concentrations in obese participants ($\beta = -0.075$; $P = 0.030$) and this diet effect was independent

TABLE 1 Participant characteristics at baseline and after a 10-wk hypocaloric diet[1]

	Baseline		Δ after dietary intervention[2]	
	Lean	Obese	Low-fat diet	High-fat diet
n	127 (38 M)	613 (150 M)	317 (82 M)	296 (71 M)
Age, *y*	34 ± 1	37 ± 0[a]		
BMI, *kg/m²*	23.8 ± 0.3	36.0 ± 0.2[a]	−2.5 ± 0.1	−2.4 ± 0.1
WHR	0.81 ± 0.01	0.89 ± 0.00[a]	−0.02 ± 0.00	−0.02 ± 0.00
$HOMA_{IR}$	1.11 ± 0.06	2.61 ± 0.07[a]	−0.29 ± 0.09	−0.38 ± 0.10
Dietary fat intake, *% energy*	34.4 ± 0.6	36.4 ± 0.3[a]		
Total physical activity,[3] *AU*	8.22 ± 0.10	7.42 ± 0.05[a]		
Fasting metabolites				
Plasma RLP-C, *mmol/L*	0.25 ± 0.01	0.33 ± 0.01[a]	−0.03 ± 0.01	−0.07 ± 0.01[c]
Plasma TG, *mmol/L*	0.74 ± 0.03	1.10 ± 0.03[a]	−0.03 ± 0.02	−0.17 ± 0.03[b]
Plasma FFA, *μmol/L*	418 ± 12	520 ± 6[a]	−33 ± 10	−28 ± 11
Plasma HDL-C, *mmol/L*	1.34 ± 0.03	1.12 ± 0.01[a]	−0.09 ± 0.01	−0.04 ± 0.01[b]
Plasma total cholesterol, *mmol/L*	4.59 ± 0.08	4.92 ± 0.04[a]	−0.37 ± 0.04	−0.25 ± 0.03[b]

[1] Values are means ± SEM. [a] $P < 0.001$, lean vs. obese, Student's t test for unpaired samples; [b] $P < 0.01$; [c] $P < 0.05$, diet × time interaction, repeated-measures ANOVA.
[2] The change (Δ) of each value is calculated as (10 wk–baseline).
[3] AU, Arbitrary units.

TABLE 2 Composition of the habitual diet of lean and obese participants at baseline and the composition of the low- and high-fat hypocaloric intervention diets in obese participants[1,2]

	Habitual diet	Low-fat diet	High-fat diet
n	740	302[3]	285[3]
Energy intake, *kJ/d*	9118 ± 103	6518 ± 88	6846 ± 85[a]
Fat, *% energy*	36.1 ± 0.3	25.1 ± 0.3	41.3 ± 0.3[a]
Carbohydrate, *% energy*	45.8 ± 0.3	56.6 ± 0.3	41.5 ± 0.3[a]
Protein, *% energy*	16.3 ± 0.1	17.8 ± 0.2	17.0 ± 0.2[a]
Alcohol, *% energy*	1.8 ± 0.1	0.4 ± 0.1	0.2 ± 0.1[b]
Dietary fiber, *g/d*	18.5 ± 0.3	22.6 ± 0.4	19.1 ± 0.4[a]

[1] Values are means ± SEM. [a] $P < 0.01$; [b] $P < 0.05$, low-fat vs. high-fat diet, Student's *t* test for unpaired samples.
[2] The composition of the diets is based on a 3-d-weighed food record.
[3] A small number of participants did not complete a 3-d-weighed food record after the 10-wk dietary intervention period.

of the degree of weight loss and the change in insulin resistance. In model 2, however, these diet and $HOMA_{IR}$ effects disappeared and a decrease in fasting TG concentrations was the strongest predictor of a decrease in fasting RLP-C concentrations (adj. $R^2 = 0.51$).

Discussion

Elevated plasma concentrations of RLP-C are atherogenic and have been shown to be an independent risk factor for the development of cardiovascular disease (5). However, factors that are associated with plasma RLP-C concentrations are not fully understood. This study demonstrates that both fasting and postprandial plasma RLP-C are strongly related to $HOMA_{IR}$ and WHR, which is consistent with earlier indications from the literature (7–11,24,25). When adding plasma TG, FFA, and HDL-C to the models, however, plasma TG was the strongest predictor of both fasting and postprandial RLP-C, and in the fasting model, the associations with $HOMA_{IR}$ and WHR were no longer significant. It has been shown before in a study in obese children that fasting RLP-C was significantly associated with systolic blood pressure and $HOMA_{IR}$, whereas only TG was associated with RLP-C after inclusion of other lipids in the model (7). This may be due to the high correlation between plasma RLP-C and plasma TG, which is not surprising, because a large part of plasma TG is carried in TRL and RLP particles. It may well be that although RLP represent the more atherogenic fraction, measuring RLP-C is not necessary to assess this risk, because plasma TG mirrors plasma RLP-C.

Men had significantly higher fasting RLP-C concentrations than women and RLP-C concentrations increased with age, which is consistent with previous findings (14,26). In the postprandial response to the high-fat meal, however, the gender effects on plasma RLP-C were explained by the effect of body fat distribution; WHR was significantly associated with postprandial RLP-C, independent of gender, BMI, the degree of insulin resistance, and postprandial circulating TG concentrations, suggesting that body fat distribution is directly linked to RLP-C in the postprandial phase. Abdominal obesity plays an important role in postprandial TRL metabolism in both men and women (13,27). Based on our results, the association between WHR and postprandial RLP-C seems to be stronger than the association with gender.

The postprandial response after the high-fat meal was measured over a 3-h period, which is a relatively short time for studying postprandial lipid profiles. Therefore, we analyzed RLP-C concentrations 6 h postprandially in a subgroup of the

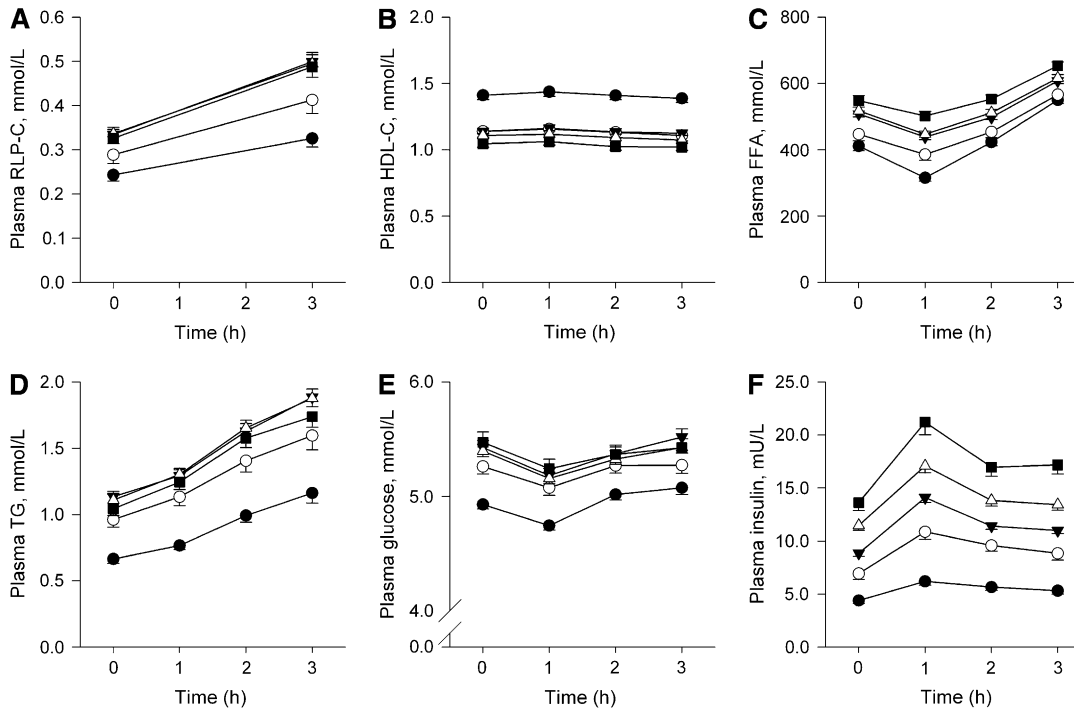

FIGURE 1 Plasma concentrations of RLP-C (*A*), HDL-C (*B*), FFA (*C*), TG (*D*), glucose (*E*), and insulin (*F*) during fasting ($t = 0$) and after consumption of a high-fat meal according to BMI categories: BMI <25 kg/m^2 (●) ($n = 92$), BMI 25–30 kg/m^2 (○) ($n = 35$), BMI 30–35 kg/m^2 (▲) ($n = 294$), BMI 35–40 kg/m^2 (△) ($n = 185$), and BMI >40 kg/m^2 (■) ($n = 106$). Values are means ± SEM.

TABLE 3 Determinants of fasting plasma RLP-C in multiple regression analyses[1]

	Model 1[2]		Model 2[2]	
$n = 740$	β	*P*-value	β	*P*-value
(Constant)		<0.001		<0.001
Gender, *male vs. female*	0.156	<0.001	0.109	0.001
BMI, *kg/m²*	0.041	0.315	0.082	0.008
Age, *y*	0.096	0.007	0.042	0.102
$HOMA_{IR}$	0.235	<0.001	−0.029	0.326
WHR	0.157	0.004	0.011	0.781
Dietary fat intake, *% energy*	0.027	0.463	0.030	0.266
Total physical activity, *AU*	0.085	0.012	0.074	0.003
Plasma TG (fasting), *mmol/L*	—	—	0.712	<0.001
Plasma FFA (fasting), *μmol/L*	—	—	−0.020	0.474
Plasma HDL-C (fasting), *mmol/L*	—	—	−0.001	0.985

[1] The dependent is fasting plasma RLP-C in mmol/L. For statistical analyses, the dependent variable was ln-transformed. —, variable not included in model 1.
[2] Both models include the indicated variables in addition to center. Model 1 adj. $R^2 = 0.23$, model 2 adj. $R^2 = 0.60$.

total cohort and showed that RLP-C concentrations at 3 h were highly correlated with 6-h values. Although this indicates that our postprandial model reflects conditions after a 6-h postprandial period, it remains a limitation of this study that we could not measure RLP-C accumulation over the total postprandial period.

To detect disturbances in lipid metabolism, a pure high-fat load was administered as a metabolic stressor. We acknowledge that the very slight insulin response after this high-fat load may have induced slightly different postprandial lipid responses in this study compared with, e.g., a high-fat mixed meal. Despite this, we observed similar associations between plasma RLP-C and $HOMA_{IR}$, WHR, and plasma TG concentrations to those shown previously (10,11).

TABLE 4 Determinants of postprandial plasma RLP-C after a high-fat meal containing 95en% fat[1]

	Model 1[2]		Model 2[2]	
$n = 712$	β	*P*-value	β	*P*-value
(Constant)		<0.001		<0.001
Gender, *male vs. female*	0.041	0.156	0.029	0.269
BMI, *kg/m²*	0.028	0.288	0.032	0.185
Age, *y*	0.052	0.023	0.036	0.079
$HOMA_{IR}$	0.104	<0.001	0.026	0.274
WHR	0.142	<0.001	0.100	0.002
Dietary fat intake, *% energy*	0.025	0.307	0.009	0.685
Total physical activity, *AU*	0.040	0.067	0.018	0.358
Plasma RLP-C (fasting), *mmol/L*	0.669	<0.001	0.599	<0.001
Plasma TG iAUC, *mmol/L·180 min*	—	—	0.278	<0.001
Plasma FFA iAUC *μmol/L·180 min*	—	—	0.045	0.022
Plasma HDL-C iAUC, *mmol/L·180 min*	—	—	−0.031	0.109

[1] The dependent is 3-h plasma RLP-C in mmol/L. For statistical analyses, the dependent variable was ln-transformed. —, variable not included in model 1.
[2] Both models include the indicated variables in addition to center and the energy% fat meal of measured basal metabolic rate. Model 1 adj. $R^2 = 0.70$, model 2 adj. $R^2 = 0.76$.

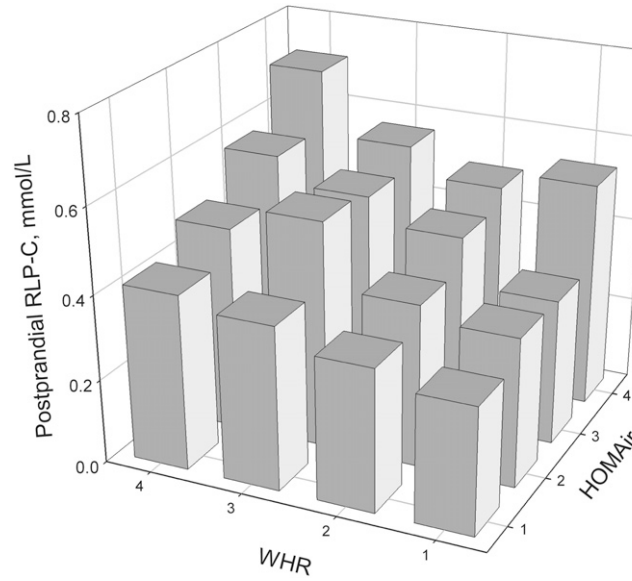

FIGURE 2 Postprandial plasma RLP-C concentrations (3 h) according to WHR and $HOMA_{IR}$ quartiles. Quartile 1 corresponds to the lowest WHR and $HOMA_{IR}$ values and quartile 4 to the highest values. Values are means.

We observed a small positive association between habitual physical activity and fasting RLP-C, which is not consistent with earlier findings about the relationship between total physical activity and plasma lipoprotein concentrations (12,28,29). The underlying mechanisms for this association remain to be elucidated.

Weight loss improved fasting RLP-C concentrations, even after correction for age, gender, and changes in $HOMA_{IR}$ and WHR, showing that weight loss per se can be an appropriate tool to improve fasting and postprandial RLP concentrations (30). Furthermore, weight loss was comparable after both diets, indicating that it was not the macronutrient composition of the diet that influenced a reduction in body weight but the total energy intake, because both diets were designed to provide 2510 kJ/d less than the individually estimated daily energy requirement (18). Therefore, it is interesting that despite a similar weight loss, a high-fat diet leads to a better improvement in both

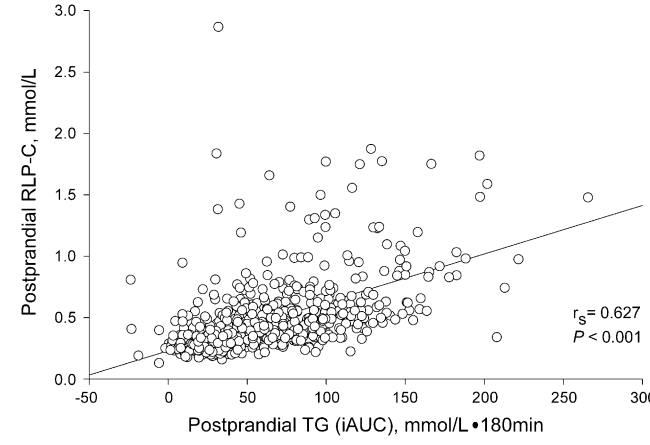

FIGURE 3 Strong relationship between the postprandial response of plasma TG (iAUC) and plasma RLP-C (3 h) after a high-fat meal. r_s and *P* are shown in the figure.

TABLE 5 Determinants of changes in fasting plasma RLP-C after a 10-wk hypo-energetic diet containing either 20–25 or 40–45en% fat[1]

	Model 1[2]		Model 2[2]	
$n = 613$	β	*P*-value	β	*P*-value
(Constant)		0.615		0.520
Gender, *male vs. female*	−0.042	0.384	0.046	0.273
Diet, *high vs. low fat*	−0.075	0.030	−0.006	0.841
Age, *y*	−0.053	0.157	−0.004	0.905
Δ Weight,[3] *kg*	0.240	<0.001	0.149	<0.001
Δ $HOMA_{IR}$	0.121	0.001	0.051	0.104
Δ WHR	−0.007	0.847	−0.012	0.683
Δ Plasma TG (fasting), *mmol/L*	—	—	0.534	<0.001
Δ Plasma FFA (fasting), *μmol/L*	—	—	0.054	0.078
Δ Plasma HDL-C (fasting), *mmol/L*	—	—	−0.018	0.598

[1] The dependent is the change in fasting plasma RLP-C in mmol/L. For statistical analyses, the dependent variable was ln-transformed. —, variable not included in model 1.

[2] Both models include the indicated variables in addition to center and the mean values (10 wk + 0 wk) / 2) of each change variable. Model 1 adj. $R^2 = 0.29$, model 2 adj. $R^2 = 0.51$.

[3] The change (Δ) of each variable was calculated as (10 wk – 0 wk).

fasting RLP-C concentrations and fasting TG concentrations than a low-fat diet in obese participants. This observation extends the results of Abbasi et al. (16), showing that in healthy participants, both fasting and postprandial RLP-C concentrations are significantly lower after a high-fat diet than after a low-fat diet and may be explained by the higher carbohydrate content of the low-fat diet compared with the high-fat diet. It has been described previously for the total NUGENOB cohort that the beneficial effects of the dietary intervention on plasma TG, LDL-C, and total cholesterol were mainly the result of weight loss per se, with additional effects of diet composition (18).

Furthermore, improvements in insulin resistance were also significantly related to a decrease in fasting RLP-C, independent of weight loss. Again, after inclusion of fasting TG in the model, these effects disappeared and only weight loss and a decrease in fasting TG were associated with decreased plasma RLP-C, emphasizing the outcomes of the baseline fasting and postprandial models.

In summary, this multicenter study demonstrates that plasma RLP-C concentrations are related to body fat distribution (WHR) and the degree of insulin resistance ($HOMA_{IR}$), both fasting and 3 h postprandial after a high-fat load. However, taking other plasma lipid concentrations into account, plasma TG appeared to be a strong determinant of plasma RLP-C.

The present mode of dietary intervention shows that, independent of weight loss, a high-fat diet is more effective in lowering fasting plasma RLP-C concentrations in obesity than a low-fat diet.

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