



Original Research Communications

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Evidence for impaired lipolysis in abdominally obese men: postprandial study of apolipoprotein B-48- and B-100-containing lipoproteins¹⁻³

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ABSTRACT

Background: Abdominal obesity has been associated with postprandial hypertriglyceridemia. The contribution of intestinally and hepatically derived lipoproteins to this exaggerated postprandial lipemic response is not known.

Objective: We examined the associations between body fatness, fat distribution, and postprandial apolipoprotein (apo) B-48 and apo B-100 concentrations measured in triacylglycerol-rich lipoproteins (TRLs).

Design: Dietary fat tolerance was investigated in 50 men aged 28–67 y. The subjects were given a test meal containing 60 g fat/m² body surface area and providing 64% of energy from fat, 18% from carbohydrates, and 18% from protein. The meal provided 7524–9196 kJ, depending on body surface area. Blood samples were collected every 2 h over an 8-h period.

Results: The increase in plasma triacylglycerol after the meal resulted from increases in both apo B-48- and apo B-100-containing lipoproteins. The apo B-100 concentration was the strongest contributor ($R^2 = 69.6\%$, $P = 0.0001$) to postprandial triacylglycerol in total TRLs; the postprandial increase in triacylglycerol was best predicted by the apo B-48 concentration ($R^2 = 32.7\%$, $P = 0.0001$). Visceral abdominal fat was significantly associated with high postprandial TRL apo B-48 and apo B-100 concentrations ($r = 0.30-0.44$, $P < 0.05$). After the meal, the apo B-100 concentration in small TRLs decreased in 12 subjects. These men showed features of the insulin resistance-dyslipidemic syndrome, including more visceral fat ($P = 0.07$) and an altered fasting metabolic profile.

Conclusion: A lower lipolytic capacity may contribute to the exaggerated and prolonged postprandial lipemia among abdominally obese men. *Am J Clin Nutr* 2002;76:311–8.

KEY WORDS Abdominal obesity, visceral adipose tissue, postprandial lipemia, apolipoprotein B-48, apolipoprotein B-100, men, hypertriglyceridemia, triacylglycerol-rich lipoproteins

INTRODUCTION

Abdominal obesity, especially when accompanied by an excess of visceral adipose tissue (AT), has been associated with numerous metabolic disturbances that increase the risk of cardiovascular disease (1–3). For instance, visceraally obese subjects frequently have high fasting triacylglycerol concentrations, low HDL-cholesterol concentrations, elevated apolipoprotein (apo) B and

insulin concentrations, and an increased proportion of small, dense LDL particles (3–5). In addition to these disturbances in the fasting metabolic profile, abdominal obesity and excessive visceral adipose tissue accumulation have also been associated with postprandial hyperlipidemia (6–10). We previously reported that this relation is independent of obesity per se (6), and it is generally believed that the association between visceral AT and postprandial hyperlipidemia is the result of the concomitant fasting hypertriacylglycerolemia state (7, 11, 12) found in visceraally obese patients, which could delay the clearance of newly synthesized triacylglycerol-rich lipoproteins (TRLs).

Yet, although fasting hypertriacylglycerolemia may indeed be an important contributor to the increased postprandial lipemia observed in visceraally obese patients, very little is known about the actual contribution of liver-derived compared with that of intestinally derived TRLs to the postprandial response. Because chylomicrons and VLDL show considerable variation in size and density, they cannot be adequately separated by ultracentrifugation. However, the measurement of apo B-48 and apo B-100, the structural proteins of chylomicrons and VLDL, respectively (13), allows the distinction of intestinally and hepatically derived lipoproteins. Furthermore, because each TRL particle contains only one apo B molecule, its plasma concentration has been used as a marker of lipoprotein particle number (13). Although both plasma apo B-48 and apo B-100 concentrations have been shown

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to increase after consumption of a high-fat meal (14–19), little is known about the relations between abdominal fat accumulation and postprandial changes in TRL particle number. Therefore, the present study was undertaken to investigate the potential associations between body fatness and AT distribution indexes and postprandial apo B-48 and apo B-100 concentrations in men.

SUBJECTS AND METHODS

Subjects

Fifty men (mean age \pm SD: 46 ± 9 y) were recruited through the media and selected to cover a wide range of body fatness values. The subjects gave their written consent to participate in the study, which was approved by the Medical Ethics Committee of Laval University. The subjects were all nonsmokers, and persons with diabetes or cardiovascular disease were excluded from the study. None of the subjects were on medication known to affect insulin action or plasma lipoprotein concentrations. With the exception of being restrained from alcohol consumption for 48 h and from physical activity for 24 h before the test meal, no dietary recommendations were made to the subjects before the study.

Anthropometry, body composition, and body fat distribution

Body weight, height, and waist and hip circumferences were measured by following standardized procedures (20). Body density was measured by the hydrostatic weighing technique (21). The mean of 6 measurements was used in the calculation of percentage body fat from body density with the use of the equation of Siri (22). Fat mass was obtained by multiplying body weight by percentage body fat. Abdominal visceral and subcutaneous AT accumulations were assessed by computed tomography, which was performed on a Siemens Somatom DRH scanner (Erlangen, Germany) with the use of previously described procedures (23, 24).

Oral lipid tolerance test

After the subjects fasted for 12 h overnight, blood was drawn by an intravenous catheter inserted into their forearm veins for sampling. Each participant was given a test meal containing 60 g fat/m² body surface area as previously described (6). The meal (total energy: 7524–9196 kJ, depending on body surface area) provided 64% of energy from fat, 18% from carbohydrates, and 18% from protein and was well tolerated by all subjects. Participants were forbidden to eat for 8 h after consumption of the meal but were given free access to water. Blood samples were drawn before the meal and every 2 h after the meal over the 8-h period.

Plasma lipoprotein concentrations

Plasma was separated immediately after blood collection by centrifugation at $2500 \times g$ for 10 min at 4 °C. Triacylglycerol and cholesterol concentrations in total plasma were determined enzymatically (Randox Co, Crumlin, United Kingdom) on an RA-500 analyzer (Bayer Corporation Inc, Tarrytown, NY), as previously described (25). Each plasma sample (4 mL) was then subjected to a 12-h ultracentrifugation ($180\,000 \times g$) in a Beckman 50.3 Ti rotor (Beckman Coulter, Fullerton, CA) at 4 °C in 6 mL Beckman Quickseal tubes, which yielded 2 fractions: total TRLs [density (d) < 1006 g/L] and triacylglycerol-poor lipoproteins (d > 1006 g/L). The distilled water layering technique and the modified method of Ruotolo et al (26) were

used to further separate the total TRL fraction into 3 subclasses of TRLs: large, medium, and small, as previously described (6). Large TRLs consist of lipoproteins with a Svedberg flotation (S_f) rate > 400, whereas the medium and small TRLs have an S_f of 20–400 (26). HDL particles were isolated from the d > 1006 g/L fraction after precipitation of apo B-containing lipoproteins with heparin and manganese chloride (27). The triacylglycerol and cholesterol contents of each fraction, ie, large, medium, and small TRLs as well as HDL, were quantified by enzymatic methods on the RA-500. All lipoprotein isolation procedures were completed within 2–3 d of the fat challenge. Fasting plasma apo B concentrations were measured in plasma by the rocket immunoelectrophoretic method (28). The lyophilized serum standard for apo B measurement in plasma was prepared in our laboratory and calibrated with reference standards obtained from the Centers for Disease Control and Prevention (Atlanta). Plasma nonesterified fatty acid concentrations were measured with a colorimetric method (29).

Postprandial apolipoprotein B-48 and B-100 measurements

Apo B-48 and apo B-100 concentrations were quantified in the different TRL fractions by densitometric scanning of apo bands separated by electrophoresis in 3–10% (by wt) sodium dodecyl sulfate polyacrylamide slab gels and stained with Coomassie blue, as previously described (30, 31). Briefly, delipidated TRL fractions were solubilized with 200–300 μ L sample buffer and 50- μ L portions were applied in duplicate to the gels. Gel electrophoresis was carried out in the Laemmli system at 50 V/gel for 30 min and then at 75 V/gel for 60–90 min in a Mini-Protean II vertical gel apparatus (Bio-Rad Laboratories, Hercules, CA) in which 2 minigels are run simultaneously. The gels were stained for 18–22 h in trays containing 100 mL 0.25% Coomassie Blue R-250 in methanol:water:acetic acid (5:5:1, by vol) at room temperature and under constant agitation on an orbital shaker. Finally, the gels were placed between 2 sheets of cellophane gel wrap (Biodesign Inc, New York) and allowed to dry completely in a fume hood at room temperature overnight before being analyzed (30, 31). Standards used for the calculation of apo B-48 and apo B-100 were proteins from a dialyzed, delipidated narrow-cut LDL fraction ($d = 1025$ – 1055 g/L), isolated by sequential ultracentrifugation as previously described (32). Briefly, plasma (4 mL) was overlaid with $d = 1025$ g/L solution and ultracentrifuged at $180\,000 \times g$ at 4 °C for 18 h with a Beckman 50.3 Ti rotor (Beckman Coulter, Fullerton, CA) in 6-mL Beckman Quickseal tubes. The resulting top fraction ($d < 1025$ g/L), consisting of VLDL and remnants, was discarded. The bottom fraction ($d > 1025$ g/L) was recovered and ultracentrifuged under the same conditions after addition of $d = 1.055$ g/L solution. The top fraction was recovered as LDL, and the bottom fraction was discarded. Proteins in this narrow-cut fraction consist almost exclusively of apo B-100 with little or no contamination by apoE (30). Because human apo B-48 and apo B-100 have the same chromogenicities (31, 33), a unique apo B-100 standard curve can be used to determine their respective concentrations in the different TRL samples.

Postheparin plasma lipoprotein lipase activity

Plasma lipoprotein lipase (LPL; EC 3.1.1.34) and hepatic lipase (EC 3.1.1.3) activities were also measured on one occasion in fasted subjects, 10 min after an intravenous injection of heparin (60 IU/kg body wt). The activity was measured by using

TABLE 1
Physical characteristics and fasting metabolic profile of the subjects¹

Variable	Value
Age (y)	46 ± 9 (28–67)
Body weight (kg)	88.1 ± 12.5 (64–118)
BMI (kg/m ²)	29.1 ± 4.3 (20–41)
Fat mass (kg)	25.3 ± 8.5 (8–46)
Waist circumference (cm)	98.5 ± 10.0 (80–123)
Abdominal adipose tissue (cm ²)	
Visceral	150 ± 64 (38–357)
Subcutaneous	283 ± 110 (35–525)
Cholesterol	5.03 ± 0.76 (3.55–6.81)
LDL (mmol/L)	3.27 ± 0.69 (2.09–5.02)
HDL (mmol/L)	0.90 ± 0.20 (0.55–1.62)
Total:HDL	5.48 ± 1.29 (3.22–8.04)
Triacylglycerol (mmol/L)	1.78 ± 0.92 (0.49–4.37)
Apolipoprotein B (g/L)	1.07 ± 0.20 (0.66–1.46)
Glucose (mmol/L)	5.07 ± 0.63 (3.57–6.99)
Insulin (pmol/L)	90.9 ± 48.5 (28–280)

¹ $\bar{x} \pm SD$; range in parentheses. $n = 50$.

a modification of the method of Nilsson-Ehle and Ekman (34), as previously described (35) and expressed as nmol oleic acid released · mL plasma⁻¹ · min⁻¹.

Glucose and insulin concentrations

Fasting and postprandial plasma glucose concentrations were determined with the glucose oxidase assay (Sigma, St Louis; 36). Plasma insulin concentrations were measured by a commercial double-antibody radioimmunoassay (Linco Research, St Louis) that shows little cross-reactivity (<0.02%) with proinsulin (37).

Statistical analyses

Spearman correlation coefficients were used to quantify associations between variables (nonparametric variables). Differences between negative and positive small TRL apo B-100 responders were tested by analysis of variance followed by Tukey's studentized range test. Analysis of variance for repeated measures was also performed to test the effects of response group, time, and the response group × time interaction term on the postprandial changes in TRL composition parameters. The independent contributions of the response of postprandial total TRL apo B-48 and apo B-100 to the variance of the postprandial plasma triacylglycerol response were quantified by multiple regression analyses. Total TRL data were calculated by summing individual values of the large, medium, and small TRL fractions and the different areas under the total (AUC) and incremental curves of TRL. Triacylglycerol, apo B-48, and apo B-100 concentrations were determined by the trapezoid method. All analyses were conducted with the SAS statistical package (version 8.0; SAS Institute, Cary, NC).

RESULTS

The physical and metabolic characteristics of the men recruited for the study are shown in **Table 1**. By design, the group had a wide range of body fatness and fat distribution values. As a group, the subjects were abdominally obese, as shown by high mean values for waist circumference (≈100 cm), and had visceral AT accumulation higher than the 130-cm² proposed cutpoint value associated with a higher risk of metabolic disturbances (3). The fasting metabolic profile was also concordant with that generally

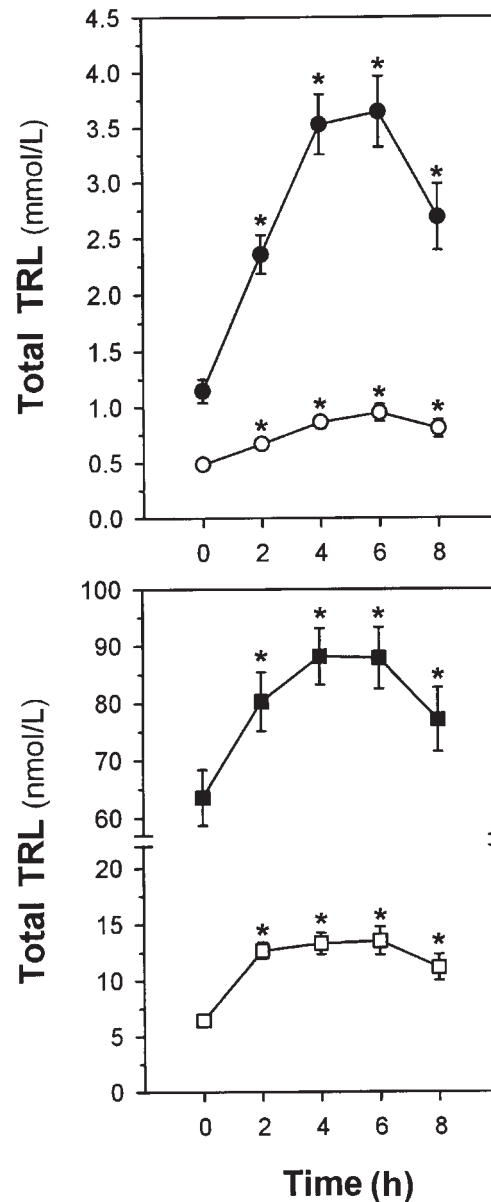


FIGURE 1. Postprandial triacylglycerol (●), cholesterol (○), apolipoprotein (apo) B-48 (□), and apo B-100 (■) concentrations in total triacylglycerol-rich lipoproteins (TRLs) in the group of 50 men. Values are presented as means ± SEM. *Significantly different from baseline, $P < 0.0001$.

found among men with abdominal obesity. Indeed, the subjects had moderately elevated fasting plasma triacylglycerol (≈2.0 mmol/L), low HDL-cholesterol (≈0.9 mmol/L), and high apo B (≈1.0 g/L) and insulin (≈100 pmol/L) concentrations.

Postprandial triacylglycerol and cholesterol concentrations in total TRLs ($d < 1006$ g/L) are presented in **Figure 1**. We noted significant increases in plasma concentrations of these variables after meal consumption. However, the rise in total TRL triacylglycerol was greater (2.4-fold increase from fasting to the 6-h peak concentration, $P < 0.0001$) than the change in total TRL cholesterol (1.1-fold increase at 6 h, $P < 0.0001$). In addition, this



TABLE 2

Total area under the curve and total area under the incremental curve of postprandial triacylglycerol, apolipoprotein (apo) B-48, and apo B-100 concentrations in total triacylglycerol-rich lipoproteins (TRLs)¹

Variable	Value
Total area under the curve	
Triacylglycerol (mmol · 8 h/L)	1373 ± 788 (259–3516)
Apo B-48 (μmol · 8 h/L)	5.8 ± 3.0 (1.4–13.1)
Apo B-100 (μmol · 8 h/L)	39.2 ± 16.8 (11.1–80.5)
Total area under the incremental curve	
Triacylglycerol (mmol · 8 h/L)	823 ± 490 (162–2195)
Apo B-48 (μmol · 8 h/L)	2.7 ± 1.8 (1.6–8.6)
Apo B-100 (μmol · 8 h/L)	8.8 ± 5.1 (–2.2–20.1)

¹ $\bar{x} \pm SD$; range in parentheses. $n = 50$.

increase in the triacylglycerol content of total TRLs resulted from increases in both intestinal and hepatic TRL particles, as indicated by the concomitant elevation of apo B-48 (1.4-fold increase, $P < 0.0001$) and apo B-100 (0.5-fold increase, $P < 0.0001$) concentrations. Although both apo B-48 and apo B-100 concentrations increased during the postprandial period, ≈85% of the postprandial increase in particle number was accounted for by apo B-100-containing TRLs, and apo B-48-containing TRLs accounted for only ≈15% of this increase. Postprandial total and incremental responses of triacylglycerol, apo B-48, and apo B-100 in total TRLs are shown in **Table 2**.

The results of the multiple regression analyses conducted to quantify the independent contributions of postprandial total TRL apo B-48 and apo B-100 concentrations to the variance in postprandial total TRL triacylglycerol concentrations are shown in **Table 3**. Postprandial total TRL apo B-100 AUC was by far the best predictor of postprandial total TRL triacylglycerol concentrations, accounting for ≈70% of the variance. In contrast, the area under the incremental curve of total TRL apo B-48 concentrations showed the greatest contribution to the response of total TRL triacylglycerol.

Associations between body composition, fat distribution indexes, and postprandial apo B-48 and apo B-100 AUC in total TRLs as well as in the large, medium, and small TRL fractions are presented in **Table 4**. Total body fat mass, expressed in kilograms, showed no association with postprandial apo B-48 AUC but was significantly associated with a greater apo B-100 AUC in all TRL fractions, although this relation was not statistically significant in the small TRL fraction. In contrast, preferential accumulation of fat in the abdominal region, expressed as a high waist circumference, was positively correlated with both apo B-48 and apo B-100 concentrations during the postprandial period with the

TABLE 3

Multivariate regression analyses showing the independent contributions of postprandial apolipoprotein (apo) B-48 and apo B-100 concentrations to the postprandial triacylglycerol concentrations in total triacylglycerol-rich lipoproteins (TRLs)

Dependent variable	Independent variables	Partial (R^2)	P	Total (R^2)
		%		%
Area under the curve				
Total TRL triacylglycerol	Apo B-100	69.6	0.0001	73.6
	Apo B-48	4.0	0.0105	
Area under the incremental curve				
Total TRL triacylglycerol	Apo B-48	32.7	0.0001	32.7

TABLE 4

Spearman correlation coefficients between body composition, adipose tissue distribution, and postprandial area under the curve (AUC) of apolipoprotein (apo) B-48 and apo B-100 concentrations in triacylglycerol-rich lipoproteins (TRLs)

	Postprandial TRL apo B AUC			
	Total	Large	Medium	Small
Apo B-48				
Fat mass	0.19	0.25	0.25	0.12
Waist circumference	0.31 ¹	0.32 ¹	0.36 ¹	0.25
Abdominal adipose tissue areas				
Visceral	0.37 ²	0.36 ²	0.37 ²	0.33 ¹
Subcutaneous	0.13	0.11	0.20	0.08
Apo B-100				
Fat mass	0.32 ¹	0.32 ¹	0.32 ¹	0.26
Waist circumference	0.32 ¹	0.40 ³	0.36 ¹	0.23
Abdominal adipose tissue areas				
Visceral	0.35 ¹	0.44 ³	0.33 ¹	0.30 ¹
Subcutaneous	0.23	0.21	0.24	0.20

¹ $P < 0.05$.

² $P < 0.01$.

³ $P < 0.005$.

exception of the small TRL fraction. Furthermore, whereas no association was found between postprandial apo B-48 and apo B-100 AUC and the amount of abdominal subcutaneous AT, greater visceral AT accumulation was accompanied by a larger postprandial AUC of both apo B-48 and apo B-100 concentrations in all TRL fractions (Table 4).

Fasting plasma lipoprotein-lipid concentrations as well as insulin and glucose concentrations were also associated with postprandial apo B-48 and apo B-100 AUC (**Table 5**). Elevated fasting plasma apo B, glucose, and insulin concentrations were associated with exaggerated postprandial apo B-48 and apo B-100 AUC in all TRL fractions. Low fasting HDL cholesterol and an increased total-HDL cholesterol ratio were also associated with greater postprandial AUC for both apo B-48 and apo B-100. Nevertheless, fasting triacylglycerol was undoubtedly the best correlate of both postprandial apo B-48 and apo B-100 AUC, an observation that is reinforced by the fact that statistical adjustment for fasting triacylglycerol concentrations eliminated almost all associations between the metabolic variables measured and postprandial apo B-48 and apo B-100 AUC (data not shown).

The associations between the postprandial response or area under the incremental curve of triacylglycerol and apo B-100 in large, medium, and small TRLs are shown in **Figure 2**. We found positive and significant associations between both variables in the large and medium TRL fractions. Similar correlations were observed between the triacylglycerol and apo B-48 responses in



TABLE 5

Spearman correlation coefficients between fasting metabolic profile variables and the postprandial area under the curve (AUC) of apolipoprotein (apo) B-48 and apo B-100 concentrations in triacylglycerol-rich lipoproteins (TRLs)

Fasting value	Postprandial TRL apo B AUC			
	Total	Large	Medium	Small
Apo B-48				
Triacylglycerol	0.78 ¹	0.73 ¹	0.80 ¹	0.68 ¹
HDL cholesterol	-0.41 ¹	-0.54 ¹	-0.50 ¹	-0.30 ²
Apo B	0.49 ¹	0.53 ¹	0.55 ¹	0.40 ¹
Total:HDL cholesterol	0.55 ¹	0.69 ¹	0.65 ¹	0.41 ¹
Glucose	0.44 ¹	0.44 ¹	0.45 ¹	0.40 ¹
Insulin	0.47 ¹	0.47 ¹	0.50 ¹	0.38 ³
Apo B-100				
Triacylglycerol	0.84 ¹	0.78 ¹	0.74 ¹	0.79 ¹
HDL cholesterol	-0.54 ¹	-0.59 ¹	-0.51 ¹	-0.45 ¹
Apo B	0.59 ¹	0.55 ¹	0.58 ¹	0.50 ¹
Total:HDL cholesterol	0.68 ¹	0.69 ¹	0.66 ¹	0.57 ¹
Glucose	0.36 ²	0.47 ¹	0.36 ³	0.24
Insulin	0.40 ¹	0.48 ¹	0.41 ¹	0.31 ²

¹ $P < 0.005$.

² $P < 0.05$.

³ $P < 0.01$.

large, medium, and small TRLs (data not shown). However, postprandial triacylglycerol and apo B-100 responses were not associated in the small TRL fraction, suggesting that an increase in the number of apo B-100-containing particles was not a major contributing factor in the significant increase in triacylglycerol within that specific TRL fraction.

The results presented in Figure 2 also showed that some individuals were characterized by a negative response of small TRL apo B-100 concentrations, suggesting a reduction in the absolute number of small TRL particles in these subjects after the meal. This was noted despite the fact that these subjects also showed an increase in the triacylglycerol content of that same TRL fraction. To further investigate this observation, we matched subjects on the basis of their triacylglycerol response but separated them on the basis of their apo B-100 response in small TRLs (positive compared with negative response). Postprandial apo B-48 and apo B-100 concentrations in large, medium, and small TRLs and the triacylglycerol response for these respective TRL fractions in positive or negative small TRL apo B-100 responders are shown in Figure 3. We found that negative small TRL apo B-100 responders showed larger apo B-100, apo B-48, and triacylglycerol responses in large and medium TRLs compared with positive small TRL apo B-100 responders. Analysis of variance for repeated measures was performed to test the respective effects of response group (negative compared with positive responders) and time variables as well as of the time \times group interaction term on postprandial apo B-48 and B-100 concentrations within the different TRL fractions. Significant group effects were noted for all TRL apo B concentrations, with the exception of apo B-48 in small TRLs, indicating that concentrations of both apolipoproteins during the postprandial period were significantly different between negative and positive responders. Furthermore, significant time \times group interaction terms were found in large (apo B-48: $P = 0.0110$; apo B-100: $P = 0.0094$) and small TRL (apo B-48: $P = 0.0186$; apo B-100: $P = 0.0001$) fractions but not in medium TRLs. These results suggest that the accumulation of large TRL

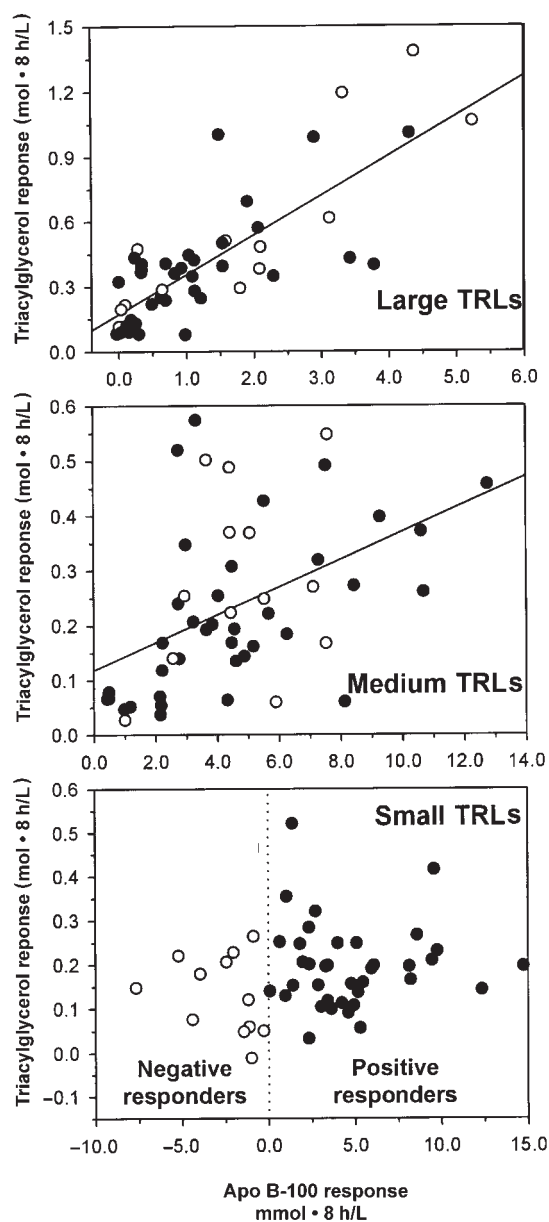


FIGURE 2. Associations between triacylglycerol and apolipoprotein (apo) B-100 responses (area under the incremental curve) in large ($r = 0.76$, $P < 0.0001$), medium ($r = 0.51$, $P < 0.0005$), and small ($r = 0.09$) triacylglycerol-rich lipoproteins (TRLs) in the group of 50 men. The subjects were separated on the area under the incremental curve of small TRL apo B into positive (●) and negative (○) responders.

particles was greater in negative than in positive small TRL apo B-100 responders.

As shown in Table 6, subjects with a postprandial decrease in small TRL apo B-100 concentrations tended to be characterized by higher visceral AT accumulation than were subjects with a positive response. High fasting triacylglycerol, insulin, total TRL apo B-48 and apo B-100 concentrations, lower HDL-cholesterol concentrations, and a higher total-HDL cholesterol ratio also characterized men with a postprandial decrease in the number of apo B-100-containing small TRL particles. The postprandial changes



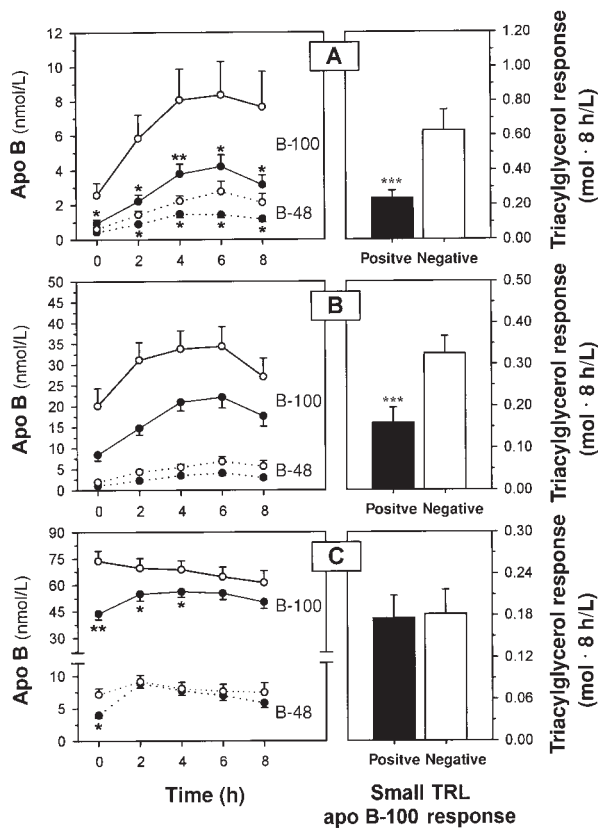


FIGURE 3. Postprandial apolipoprotein (apo) B-48 and apo B-100 concentrations and triacylglycerol responses (area under the incremental curve) in large (A), medium (B), and small (C) triacylglycerol-rich lipoproteins (TRLs) in men matched for small TRL triacylglycerol response but with either a positive (●, $n = 11$) or negative (○, $n = 11$) apo B-100 response in small TRLs after the meal. Values are presented as means \pm SEM. *, **, ***Significantly different from men with a negative small TRL apo B-100 response: * $P < 0.05$, ** $P < 0.005$, *** $P < 0.01$.

in the ratio of triacylglycerol to apo B (B-48 + B-100) in total TRLs in negative and positive small TRL apo B-100 responders are shown in **Figure 4**. We observed that from the 4-h time point, negative small TRL apo B-100 responders were characterized by higher total TRL triacylglycerol–apo B ratios than were positive responders. These results were concordant with the lower ($P < 0.05$) postheparin LPL activity found in negative than in positive small TRL apo B-100 responders (**Figure 4**).

DISCUSSION

The results of the present study show that the postprandial increase in total TRL triacylglycerol concentrations results from increases of both intestinally and hepatically derived TRL particles. The contribution of TRLs produced by the liver to postprandial triacylglycerol was previously reported (15, 19, 38). In our study, liver-derived TRLs (containing apo B-100) accounted for most of the increase in particle number postprandially. However, in stepwise multiple regression analysis, the increase in postprandial total TRL triacylglycerol was best predicted by the apo B-48 response to the fat load rather than by the rise in apo B-100 con-

TABLE 6

Features of the insulin resistance–dyslipidemic syndrome in men matched on the basis of their postprandial apolipoprotein (apo) B response area under the incremental curve in small triacylglycerol-rich lipoproteins (TRLs)¹

Variable	Postprandial small TRL apo B response		<i>P</i>
	Positive ($n = 11$)	Negative ($n = 11$)	
Waist circumference (cm)	94.6 \pm 8.3	100.8 \pm 11.8	0.2022
Abdominal adipose tissue (cm ²)			
Visceral	133 \pm 32	188 \pm 86	0.0702
Subcutaneous	244 \pm 86	321 \pm 122	0.1049
Triacylglycerol (mmol/L)			
Plasma	1.42 \pm 0.68	2.63 \pm 1.00	0.0034
Total TRLs	0.81 \pm 0.48	1.83 \pm 0.86	0.0027
Large TRLs	0.07 \pm 0.12	0.18 \pm 0.14	0.0660
Medium TRLs	0.17 \pm 0.14	0.56 \pm 0.36	0.0059
Small TRLs	0.56 \pm 0.28	1.09 \pm 0.46	0.0040
HDL cholesterol (mmol/L)	0.94 \pm 0.16	0.79 \pm 0.12	0.0228
Total:HDL cholesterol	5.1 \pm 1.3	6.6 \pm 1.19	0.0086
Total TRL apo B-48 (nmol/L)	5.4 \pm 2.9	9.8 \pm 4.2	0.0090
Total TRL apo B-100 (nmol/L)	44.6 \pm 16.7	97.9 \pm 34.9	0.0004
Insulin (pmol/L)	77 \pm 41	133 \pm 71	0.0355

¹ $\bar{x} \pm$ SD.

centrations in total TRLs. In accordance with our results, it had been suggested that apo B-100 TRLs are responsible for transporting a significant proportion of triacylglycerol during the postprandial period but that the increase in plasma TRL triacylglycerol concentrations in the fed state is predominantly the result of an increase in apo B-48–containing TRLs (19, 38). This hypothesis was later confirmed in a study that used immunoaffinity chromatography to separate apo B-48– from apo B-100–containing TRLs; the investigators reported that although both apo B-48– and apo B-100–containing TRLs contribute to postprandial lipemia,

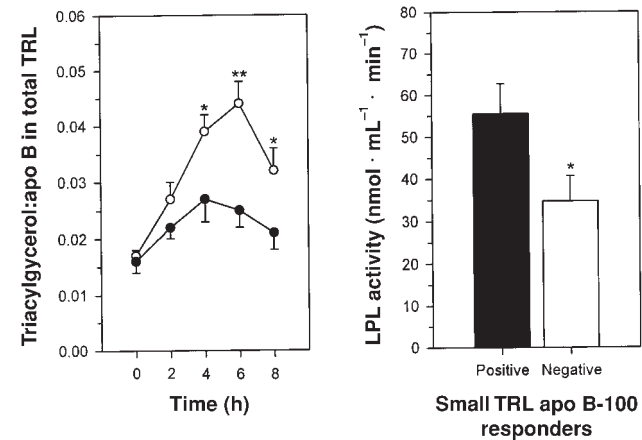


FIGURE 4. Postprandial changes in the ratio of triacylglycerol to apolipoprotein (apo) B (B-48 + B-100) in all triacylglycerol-rich lipoproteins (TRLs; left) and postheparin plasma lipoprotein lipase (LPL; right) in men matched for small TRL triacylglycerol response but with either a positive (●, $n = 11$) or negative (○, $n = 11$) apo B-100 response in small TRLs after the meal. Values are presented as means \pm SEM. *, **Significantly different from men with a positive small TRL apo B-100 response: * $P < 0.05$, ** $P < 0.005$.

particles containing apo B-48 account for most of the increase in triacylglycerol postprandially (39). Our results on the contribution of apo B-48 and apo B-100 concentrations to postprandial triacylglycerolemia are concordant with these previous observations.


Visceral fat has been associated with postprandial hypertriglycerolemia (6, 7, 9). The results of the present study show that an excessive accumulation of fat in the abdominal region is also associated with an increase in the number of apo B-48- and apo B-100-containing TRL particles after a meal. Furthermore, visceral obesity could be an important factor contributing to such a relation. Indeed, visceral but not subcutaneous abdominal AT accumulation was significantly associated with high apo B-48 and apo B-100 concentrations during the postprandial phase. To the best of our knowledge, this association, derived with the use of apoprotein markers of TRLs of intestinal compared with hepatic origin, was not reported before.

The well-documented importance of fasting triacylglycerol concentrations in postprandial hyperlipidemia (6, 11, 12) is also underlined in the present study, because this was the variable that best predicted postprandial apo B-48 and apo B-100 responses. Because fasting hypertriglycerolemia is a common feature of visceral obesity (1, 2), these high fasting triacylglycerol concentrations could explain, at least in part, the associations between abdominal obesity, visceral AT accumulation, and postprandial TRL particle number. A plausible physiologic mechanism has been proposed to explain these associations. Visceral adipocytes are characterized by a lively lipolytic activity that is poorly inhibited by insulin, resulting in an increase of nonesterified fatty acids in the portal circulation and in the plasma (40). Furthermore, Basu et al (41) recently reported that abdominal subcutaneous AT supplies an important quantity of nonesterified fatty acids to the systemic circulation. The increased flux of nonesterified fatty acids to the liver would elevate triacylglycerol concentrations through increased esterification of nonesterified fatty acids, reduced hepatic degradation of apo B, and ultimately overproduction of VLDL particles by the liver. This hypothesis is further supported by previously published reports of an impaired postprandial plasma nonesterified fatty acid metabolism in upper-body obesity (6, 42). On their entry into the circulation, both newly synthesized and endogenous TRLs have been shown to compete for LPL to be hydrolyzed (43); thus, the increased number of TRL particles in the fasting state could contribute to delaying the clearance of both apo B-48 and apo B-100 TRLs during the postprandial period, as previously proposed (44).

In the present study, ≈ 1 of 4 subjects was characterized by a negative response of small TRLs (mainly due to a decrease in apo B-100-containing particles) and a positive triacylglycerol response in small TRLs. In other words, the significant increase in the triacylglycerol content of small TRLs after the meal was not associated with an increase in the absolute number of small TRL particles. This postprandial lowering of small TRL apo B-100 supports previous observations by Björkegren et al (45) in nonobese hypertriglyceridemic subjects. When compared with subjects matched for their postprandial triacylglycerol response in small TRLs but with a concomitant increase in small TRL apo B-100 (positive responders), individuals with a negative small TRL apo B-100 response (negative responders) were characterized by features of the insulin resistance–dyslipidemic syndrome such as higher visceral fat deposition, although the difference was not statistically significant ($P = 0.07$), higher

fasting triacylglycerol and insulin concentrations, and a higher total-HDL cholesterol ratio. They also had more intestinally and hepatically derived TRL particles in the fasting state, as revealed by their higher total TRL apo B-48 and apo B-100 concentrations, respectively.

On the other hand, LPL, an enzyme closely related to the hydrolysis of triacylglycerol from chylomicrons and VLDL, was also shown to promote the hepatic clearance of TRL particles (46). Lower LPL activity of small TRL apo B-100 in negative than in positive responders could prevent the formation of smaller TRL particles through reduction of the hydrolysis of larger particles and thus explain the fall in small TRL apo B-100 concentrations. This concept was previously proposed for nonobese individuals (44, 45), and our observations tend to support such a hypothesis because larger TRL particles accumulated after the meal in the negative responders.

In summary, the present study confirms previous observations that increases in both apo B-48- and apo B-100-containing TRLs contribute to postprandial lipemia. Furthermore, our results also indicate that abdominal fat accumulation, particularly in the presence of an excess of visceral AT, is associated with a higher number of postprandial apo B-48 (intestinal) and apo B-100 (hepatic) TRL particles. Results in the literature suggest that the insulin-resistant state associated with visceral obesity could promote the production of VLDL particles by the liver, possibly causing saturation of the lipolytic pathway. Reduced LPL activity per se may also lead to the accumulation of larger TRL particles during the postprandial period in abdominally obese subjects. Consequently, postprandial alterations in the catabolism of apo B-48 and apo B-100 particles in abdominally obese men are likely to induce triacylglycerol enrichment of LDL and HDL cholesterol and subsequently produce smaller, denser LDL and HDL particles, which have the potential to increase the risk of cardiovascular disease. 

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