Postprandial Triglyceride Response in Visceral Obesity in Men

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Although metabolic disturbances are often observed in obese patients, increased accumulation of visceral adipose tissue (AT) has been shown to be more closely associated with high fasting triglyceride (TG) and insulin levels as well as with low HDL cholesterol concentrations than with excess body fatness per se. Interestingly, the fasting concentration of plasma TGs has been shown to be an important determinant of the magnitude and duration of the postprandial TG response. Yet little is known about the respective contributions of obesity versus excess visceral AT to the variation in postprandial TG clearance. In the present study, we examined potential differences in postprandial triglyceride-rich lipoprotein (TRL) responses in subjects characterized by high versus low levels of visceral AT. In a sample of 43 men (mean age: 41.3 ± 9.6 years), we found that both excess body fat and visceral obesity were associated with increased postprandial TG responses in total TRL (r = 0.33–0.45). We also found a strong relationship between fasting plasma TG levels and postprandial total TRL–TG concentrations (r = 0.79, P < 0.0001). When matched for total body fat mass, individuals with high levels of visceral AT (≥130 cm^2; n = 10) as assessed by computed tomography were characterized by increased medium- and small-TRL–TG responses (P < 0.05) compared with subjects with low visceral AT accumulation (<130 cm^2; n = 10). Moreover, this elevated response of small-TRL triglycerides noted in men with high levels of visceral AT was not accompanied by a concomitant increased retinyl palmitate response in this TRL fraction, suggesting that visceral obesity in men is accompanied by higher postprandial VLDL production than is found in obese men with lower levels of visceral AT. Increased postprandial insulin and free fatty acid (FFA) responses were also noted in men with high levels of visceral AT. Finally, postheparin plasma lipoprotein lipase activity was negatively correlated with the total-TRL–TG response in a subsample of 32 individuals (r = –0.37, P < 0.05). The results of the present study suggest that visceral obesity is associated with an impaired postprandial TG clearance. Furthermore, the exaggerated postprandial FFA response observed in subjects with high visceral AT suggests that visceral obesity may contribute to fasting and postprandial hypertriglyceridemia by altering FFA metabolism in the postprandial state. *Diabetes* 47:953–960, 1998

Numerous alterations in plasma lipid and lipoprotein concentrations are found in obese patients (1,2). Indeed, obese individuals, especially those with an increased accumulation of abdominal adipose tissue (AT), are characterized by higher fasting plasma triglyceride (TG) (3–6) and lower HDL cholesterol (7–10) concentrations compared with lean individuals. These alterations are known to increase the risk of coronary heart disease. Increased visceral AT accumulation—which promotes increased VLDL and apolipoprotein B secretion as well as reduced lipoprotein lipase (LPL) activity—measured in the plasma of obese subjects is believed to play a significant role among factors involved for the dyslipidemic state of abdominal obesity (11).

Most studies on the characterization of plasma lipoprotein levels in obesity have been done in the fasting state, with postprandial lipoproteins generally being neglected. The interest in postprandial studies grew when Zilversmit (12) hypothesized that the development of atherosclerosis could be a postprandial phenomenon. Since then, postprandial lipoproteins have received more attention. It has been reported that dietary fat tolerance is affected by numerous factors, such as age (13,14), sex (13,15), diet (16), physical activity (17), and NIDDM (18,19). Disturbances in dietary fat tolerance have also been related to anthropometric indexes of body composition. Indeed, Lewis et al. (20) reported a greater 24-h postprandial response (area under the incremental curve) for plasma TG in obese subjects (BMI ~44 kg/m^2). However, because obesity was defined only on the basis of BMI, the relationship between visceral AT accumulation and postprandial lipemia was not investigated. Visceral obesity has been related to alterations in the fasting lipoprotein profile (11,21), but little is known about the potential relationship of visceral AT accumulation to postprandial TG response. Whether the hypertriglyceridemic state that characterizes visceral obesity is an important determinant of the magnitude and duration of the postprandial TG response is also unknown.

Therefore, the aim of the present study was to examine the postprandial responses of various triglyceride-rich lipoproteins (TRLs) and their potential relationship with excess fat-

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AT, adipose tissue; AUC, area under the curve; AUIC, area under the incremental 0- to 8-h triglyceride curve; FFA, free fatty acid; HPLC, high-performance liquid chromatography; LPL, lipoprotein lipase; PH, postheparin; RA, retinyl acetate; RP, retinyl palmitate; TG, triglyceride; TRL, triglyceride-rich lipoprotein; WHR, waist-to-hip ratio.

ness in comparison with high levels of visceral AT. For this purpose, 43 adult men were investigated and their plasma TRL responses measured over an 8-h period after a meal with a high fat content. Results from the present study suggest that visceral AT accumulation is associated with an impaired postprandial clearance of plasma TRLs. Furthermore, alterations in postprandial free fatty acid (FFA) metabolism could contribute to the disturbances in postprandial TRL clearance in visceral obesity.

RESEARCH DESIGN AND METHODS

Subjects. We recruited 43 men, ages 22–56 years (mean age: 41.3 ± 9.6 years), through the media and selected them to cover a wide range of body fatness values. Subjects gave their written consent to participate in the study, which was approved by the Medical Ethics Committee of Laval University. Men with diabetes or coronary heart disease were excluded from the study. None of the subjects was on medication known to affect insulin action or plasma lipoprotein levels.

Anthropometric and body composition measurements. Body weight, height, and waist and hip circumferences were measured following standardized procedures (22), and the waist-to-hip ratio (WHR) was calculated. Body density was measured by the hydrostatic weighing technique (23). The mean of six measurements was used in calculating the percent of body fat from body density using the equation of Siri (24). Fat mass was obtained by multiplying body weight by percent body fat.

Computed tomography. Visceral AT accumulation was assessed by computed tomography, which was performed on a Somatom DRH scanner (Siemens, Erlagen, Germany) using previously described procedures (25,26). Briefly, the subjects were examined in the supine position with both arms stretched above the head. The scan was performed at the abdominal level (between L4 and L5 vertebrae) using an abdominal scout radiograph to standardize the position of the scan to the nearest millimeter. Total AT area was calculated by delineating the abdominal scan with a graph pen and then computing the AT surface with attenuation range of –190 to –30 Hounsfield units (25–27). The abdominal visceral AT area was measured by drawing a line within the muscle wall surrounding the abdominal cavity. The abdominal subcutaneous AT area was calculated by subtracting the visceral AT area from the total abdominal AT area.

Oral lipid tolerance test. After a 12-h overnight fast, an intravenous catheter was inserted into a forearm vein for blood sampling. Each participant was given a test meal containing 60 g fat/m^2 body surface area and 60,000 IU of vitamin A (Aquasol A; Astra, Westborough, MA) (28). The meal consisted of eggs, cheese, toast, peanut butter, peaches, whipped cream, and milk. Composition of the meal was 64% fat, 18% carbohydrate, and 18% protein. The test meal was well tolerated by all subjects. After the meal, subjects were not allowed to eat for the next 8 h but were given free access to water. Blood samples were drawn before the meal and every 2 h after the meal over an 8-h period; samples were handled in a dimmed light to avoid deterioration of vitamin A.

Fasting and postprandial plasma lipoprotein concentrations. Plasma was separated immediately after blood collection by centrifugation at 3,000 rpm for 10 min at 4°C and placed in aluminum foil–wrapped tubes. Triglyceride and cholesterol concentrations in total plasma were determined enzymatically on an RA-1000 Auto-Analyzer (Technicon, Tarrytown, NY), as previously described (29). Each plasma sample (4 ml) was then subjected to a 12-h ultracentrifugation (50,000 rpm) in a Beckman 50.3Ti rotor (Beckman, Palo Alto, CA) at 4°C, in 6-ml Beckman Quickseal tubes, which yielded two fractions—the top fraction containing TRL (total TRL; density (d) < 1.006 g/ml) and the bottom fraction (d > 1.006 g/ml) containing TG-poor lipoproteins. Using the distilled water–layering technique and modified method of Ruotolo et al. (30), the total TRL fraction was further separated through a 5-min spin (40,000 rpm) at 4°C using the same tubes and rotor into three subclasses of TRLs: large, medium, and small. A small volume (100 µl) of d = 1.019 g/ml saline solution was added to the total TRL fraction to facilitate water layering. The large TRL fraction was collected by tube slicing, and was then made up to a final volume of 1 ml with 0.15 mol/l NaCl. The next 3 ml of the middle layer were collected by aspiration as medium TRL, and the final 2 ml were considered as the small TRL fraction. HDL particles were isolated from the bottom fraction (d > 1.006 g/ml) after precipitation of apolipoprotein B–containing lipoproteins with heparin and $MnCl_2$ (31). The triglyceride and cholesterol contents of the large, medium, and small fractions as well as of the HDL particles were quantified on the Auto-Analyzer. All lipoprotein isolation procedures were completed within 2–3 days of the fat load, and samples were protected from light at all times for later assays. Plasma FFA levels were measured at 0, 2, 4, 6, and 8 h using a colorimetric method (32).

Postheparin plasma LPL activity. Plasma LPL activity was measured on one occasion in subjects after a 12-h overnight fast, 10 min after an intravenous injection of heparin (60 IU/kg body wt). The activity was measured using a modification of the method of Nilsson-Ehle and Ekman (33), as previously described (34), and expressed as nanomoles of oleic acid released per milliliter of plasma per minute.

Retinyl palmitate measurements. The retinyl palmitate (RP) content of total- as well as large-, medium-, and small-TRL fractions was analyzed using high-performance liquid chromatography (HPLC) as previously described (30). Briefly, aliquots of 100 µl of total and large TRLs and 500 ml of medium and small TRLs were used for the analysis. The volume of total- and large-TRL fractions was adjusted to 500 µl with 0.15 mol/l NaCl. A volume of 200 µl of retinyl acetate (RA; 200 ng/ml; Sigma, St. Louis, MO) was added to each sample as an internal standard. The extraction of RP from the samples was obtained by adding 500 µl of methanol followed by 500 µl of mobile phase buffer prepared from 90 ml hexane, 15 ml n-butyl chloride, 5 ml acetonitrile, and 0.01 ml acetic acid (82:13:5 by volume with 0.01 ml of acetic acid). Tubes were mixed thoroughly after each addition. All solvents used were HPLC graded (Caledon Laboratories, Georgetown, Ontario). Samples were then centrifuged for 15 min at 1,500 rpm (room temperature). This procedure yielded two distinct phases. The upper phase, containing the RP and RA, was carefully removed and placed in separate autosampler vials. The vials were then placed in an autosampler (Shimadzu, Kyoto, Japan) and samples were analyzed with an HPLC system (Waters, Milford, MA). The RP and RA peaks were detected at 325 nm. The RP concentration (in RA equivalent) of every fraction was calculated according to the equation of Ruotolo et al. (30): RP (ng RA/ml) = (RP peak area/RA peak area) × (1/vol of sample used) × 40 ng RA.

Glucose and insulin concentrations. Fasting and postprandial plasma glucose concentrations were determined using the glucose oxidase assay (35) (Sigma). Plasma insulin levels were measured by a commercial double-antibody radioimmunoassay (Linco, St. Louis, MO) that shows little cross-reactivity (< 0.02%) with proinsulin (36).

Statistical analyses. All analyses were conducted using the SAS statistical package (SAS Institute, Cary, NC). Pearson product-moment correlation coefficients were used to quantify associations between variables. Subjects matched for body fat mass were also subclassified on the basis of visceral AT accumulation in accordance with previously proposed cutoff points (37): low visceral AT (<130 cm^2; n = 10) and high visceral AT (≥130 cm^2; n = 10). Differences between these two subgroups were tested for significance using Student's t test. Analysis of variance for repeated measures was performed within each subgroup of visceral AT accumulation to test overall differences in total-, large-, medium-, and small-TRL TG levels over time. The same procedure was performed with plasma insulin, glucose, and FFA concentrations. The different areas under the curve (AUCs) of TG, FFA, insulin, glucose, and RP concentrations were determined by the trapezoid method. Statistical adjustment of data was performed with the general linear model procedure, with adjustments for age and/or fasting plasma TG concentrations. Data are given as means ± SD unless otherwise noted.

RESULTS

Physical and metabolic variables were characterized by substantial variation among individuals (Table 1), as would be expected from the selection of subjects. Associations between body fatness and AT distribution variables with fasting and postprandial TG concentrations in total TRL are shown in Table 2. All adiposity indexes showed positive correlations with TRL TG levels assessed in the fasting or postprandial states. All adiposity variables were also significantly correlated with the postprandial TG response in total TRL (defined as the incremental area below the 0- to 8-h TG curve; AUIC). Furthermore, although all adiposity indexes showed comparable correlation coefficients, visceral AT cross-sectional area (in centimeters squared) and total body fat mass (in kilograms) were the best correlates of postprandial TRL concentrations.

Table 3 shows the relationship of fasting plasma and lipoprotein-lipid concentrations to fasting as well as postprandial TRL TG levels. A strong correlation was found between fasting plasma TG levels and both the AUC and AUIC for total-TRL TGs. We also found significant correlations between fasting insulin levels and total-TRL TG concentrations measured during both the fasting and postprandial periods. On the other hand, fasting HDL cholesterol concentra-

TABLE 1
Physical characteristics and fasting metabolic profile of the sample of 43 men

Age (years)	41 ± 10	(22–56)
BMI (kg/m^2)	29.3 ± 4.6	(20–41)
Body fat (%)	26.2 ± 7.1	(11–41)
Fat mass (kg)	24.3 ± 9.3	(8–46)
Waist girth (cm)	101.7 ± 12.2	(76–129)
WHR	0.97 ± 0.07	(0.76–1.15)
Abdominal adipose tissue areas (cm^2)		
Subcutaneous	282 ± 117	(35–525)
Visceral	154 ± 73	(38–357)
Plasma cholesterol (mmol/l)	5.15 ± 0.84	(3.55–6.81)
Plasma triglycerides (mmol/l)	2.09 ± 0.98	(0.68–4.37)
HDL cholesterol (mmol/l)	0.90 ± 0.22	(0.55–1.63)
FFAs (mmol/l)	0.65 ± 0.25	(0.14–1.43)
Insulin (pmol/l)	101 ± 51	(35–250)
Glucose (mmol/l)	5.2 ± 0.6	(3.6–6.9)

Data are means ± SD (range).

tions were negatively correlated with fasting and postprandial total-TRL TG levels.

To better isolate the contribution of visceral AT accumulation to the altered postprandial TRL responses in obesity, we matched subjects on the basis of total body fat mass and compared two groups with high versus low levels of visceral AT (Fig. 1,Table 4). Individuals with high levels of visceral AT were older than those with low visceral AT (mean age: 48.0 ± 6.3 vs. 36.0 ± 10.3 years; $P < 0.01$).

Figure 2 illustrates TG concentrations in total- as well as in large-, medium-, and small-TRL fractions before and after meal ingestion among subjects matched for fat mass but with different levels of visceral AT. No differences were found in fasting TG concentrations contained in total and in large, medium, and small TRL levels. However, subjects characterized by a high visceral AT accumulation showed higher concentrations of total-TRL TGs at the 8-h time point compared with subjects with low levels of visceral AT ($P < 0.05$). Furthermore, individuals with high visceral AT accumulation tended to be characterized by an increased total-TRL TG AUIC compared with those with low visceral AT deposition ($P = 0.06$). Although no difference in postprandial large-TRL TG AUICs was found between the two subgroups, increased medium- and small-TRL TG AUICs were noted in men with high levels of visceral AT (Fig. 2). We also noted that TG concentrations of total as well as large, medium, and small TRLs at 8 h were back to fasting values among men with low levels of visceral AT. However, among subjects with excess visceral AT accumulation, medium- and small-TRL TGs measured at the 8-h time point remained significantly higher than fasting levels ($P < 0.01$).

Postprandial changes in RP in total- as well as in large-, medium-, and small-TRL subfractions are illustrated in Fig. 3. We found that subjects with elevated visceral AT were characterized by significantly increased RP AUICs for total, large, and medium TRLs. Except at the 6-h time point, no difference in RP contained in small TRLs was observed between men with low versus high levels of visceral AT.

We noted an increased postprandial insulin AUIC among men with high levels of visceral AT, whereas no difference was observed in postprandial glucose concentrations between the two subgroups (Fig. 4). Although no difference was noted in postprandial FFA levels before 8 h, we found an increased FFA AUIC in individuals characterized by a high visceral AT accumulation. Furthermore, differences in the postprandial FFA profiles of the two subgroups were noted. We observed rather stable postprandial FFA concentrations in the low visceral AT subgroup, whereas FFA levels progressively increased after the meal among men characterized by a high visceral AT accumulation. An analysis of variance on repeated measures revealed no time-related difference in FFA concentrations among subjects with low levels of visceral AT, whereas subjects with a high visceral AT accumulation had FFA concentrations at 8 h that were significantly higher than fasting levels. In addition, postprandial plasma FFA responses were associated positively with total-TRL TG responses (Fig. 5).

Finally, Fig. 6 illustrates the relationship of total-TRL TG response to postheparin (PH)-LPL activity. We found that PH-LPL activity was negatively associated with the total-TRL TG response. Although visceral AT accumulation was not corre-

TABLE 2
Correlations between body fatness and adipose tissue distribution variables versus fasting and postprandial plasma triglyceride concentrations in total TRL in the sample of 43 men

	Total TRL triglycerides		
	Fasting (mmol/l)	AUC (mmol · l^{-1} · [8 h]$^{-1}$)	AUIC (mmol · l^{-1} · [8 h]$^{-1}$)
Age	0.21	0.27	0.28
BMI	0.40†	0.41†	0.37*
Body fat %	0.43‡	0.40†	0.33*
Fat mass	0.46‡	0.46‡	0.41*
Waist girth	0.38*	0.42‡	0.40*
WHR	0.31*	0.34*	0.33*
Abdominal adipose tissue areas			
Visceral	0.39*	0.45‡	0.45‡
Subcutaneous	0.38*	0.34*	0.28

*$P < 0.05$; †$P < 0.01$; ‡$P < 0.005$.

TABLE 3
Correlations between fasting lipid profile versus fasting and postprandial triglyceride concentrations in total TRL in the sample of 43 men

	Total TRL triglycerides		
Fasting variables	Fasting (mmol/l)	AUC (mmol · l^{-1} · [8 h]$^{-1}$)	AUIC (mmol · l^{-1} · [8 h]$^{-1}$)
Plasma cholesterol	0.37*	0.39†	0.36*
Plasma triglycerides	0.98¶	0.93¶	0.79¶
HDL cholesterol	–0.52‖	–0.50§	–0.43‡
FFAs	–0.04	–0.07	–0.09
Insulin	0.40†	0.50§	0.52‖
Glucose	0.15	0.12	0.11

*P < 0.05; †P < 0.01; ‡P < 0.005; §P < 0.001; ‖P < 0.0005; ¶P < 0.0001.

lated to PH-LPL activity in this subsample of 32 men (data not shown), men with high visceral AT tended to be characterized by lower PH-LPL activity compared with those with low visceral AT (29.6 ± 23.2 vs. 57.8 ± 40.1 nmol · min^{-1} · ml^{-1}, respectively). However, this difference did not reach statistical significance (P = 0.09).

DISCUSSION

Obesity, especially when associated with high levels of AT in the abdominal cavity, is recognized to have detrimental effects on the metabolic profile (1,2,11). In accordance with this notion, we found that men with high visceral AT accumulation (≥130 cm^2) were characterized by elevated insulin levels and also by increased TG and decreased HDL cholesterol concentrations, although, when compared with men with low visceral AT, this latter difference was not statistically significant. The metabolic abnormalities found among obese subjects are well known, particularly among subjects with high levels of visceral AT (1–11). In addition to the altered fasting metabolic profile, excess body fat was also associated with an increased postprandial TRL TG response to the meal. Such conclusions were also reached by Lewis et al. (20), who studied postprandial TG metabolism in obese individuals and reported an exaggerated postprandial TG response in obese patients compared with lean control subjects. However, they studied massively obese individuals as reflected by an average BMI of 44 kg/m^2. In our study, we also found associations between increased BMI and alterations of postprandial TRL metabolism. Furthermore, we found significant correlations between increased visceral AT accumulation and delayed postprandial TRL clearance. Similar observations were reported in a sample of middle-aged individuals (mean age ~62 years) (38). Alterations in postprandial lipemia were also reported in a small sample of men with increased WHR (39). However, in that study, abdominal obesity was measured only by anthropometry, and the importance of visceral AT in postprandial TG clearance disturbances was not investigated. The present study extends those previous observations to moderately obese and younger subjects with increased visceral AT accumulation.

In the present study, although significant associations were found between adiposity indexes and postprandial TRL TG concentrations, fasting plasma TG, insulin, and HDL cholesterol levels showed stronger correlations with postprandial TRL TG concentrations than body fatness and AT distribution variables, a finding that is concordant with previous observations. Indeed, high fasting TG and low HDL cholesterol concentrations have been reported to be associated with increased postprandial TRL levels (19,40–43). Moreover, alterations of postprandial TG metabolism have been observed in NIDDM patients who are insulin resistant and dyslipidemic in the fasting state (18,19,44).

We also found that features of the insulin resistance syndrome, namely fasting hypertriglyceridemia, hyperinsulinemia, and low HDL cholesterol concentrations as well as increased visceral AT accumulation were all significant correlates of an impaired postprandial TRL clearance. In this regard, we further examined the importance of visceral AT accumulation as a potential modulator of postprandial metabolic alterations. For that purpose, we compared two subgroups of men matched for their level of total body fat but with either a low or a high visceral AT accumulation. Comparison of postpran-

TABLE 4
Fasting metabolic profile of men matched on the basis of total body fat mass but with low versus high visceral adipose tissue accumulation

Variables	Low visceral AT	High visceral AT
Plasma cholesterol (mmol/l)	4.85 ± 0.90	5.59 ± 0.50*
Plasma triglycerides (mmol/l)	1.75 ± 0.87	2.39 ± 0.80
HDL cholesterol (mmol/l)	0.98 ± 0.28	0.85 ± 0.15
FFAs (mmol/l)	0.66 ± 0.39	0.58 ± 0.11
Insulin (pmol/l)	57 ± 18	105 ± 42 †
Glucose (mmol/l)	4.8 ± 0.6	5.2 ± 0.5

*P < 0.05 vs. low visceral AT subgroup; †P < 0.005 vs. low visceral AT subgroup.

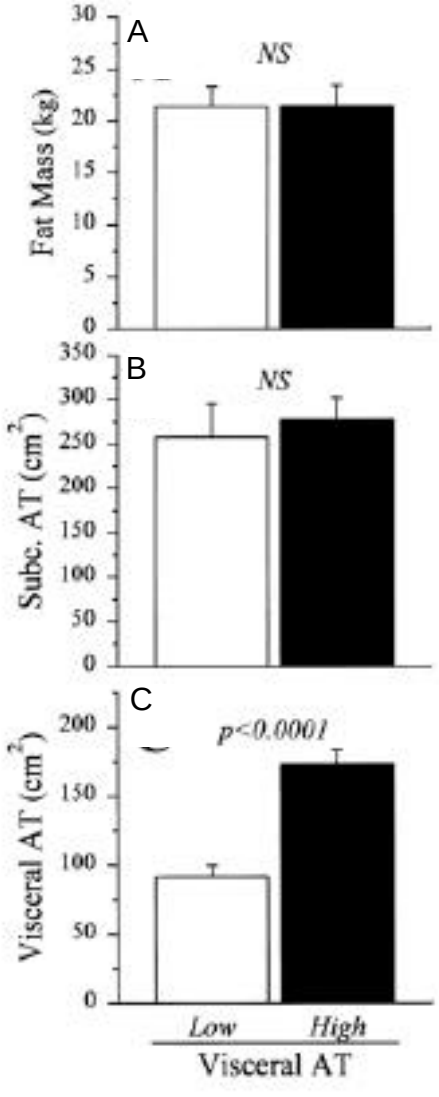

FIG. 1. Body fat mass (*A*) and abdominal subcutaneous (*B*) and visceral AT (*C*) accumulation in two subgroups of men matched for fat mass (within a 1-kg difference) but with visceral AT <130 cm² (low AT; □; 91 ± 8 cm²; *n* = 10) and >130 cm² (high AT; ■; 173 ± 10 cm²; *n* = 10). Data are means ± SE. In *C*, *P* < 0.0001 vs. men with low levels of visceral AT.

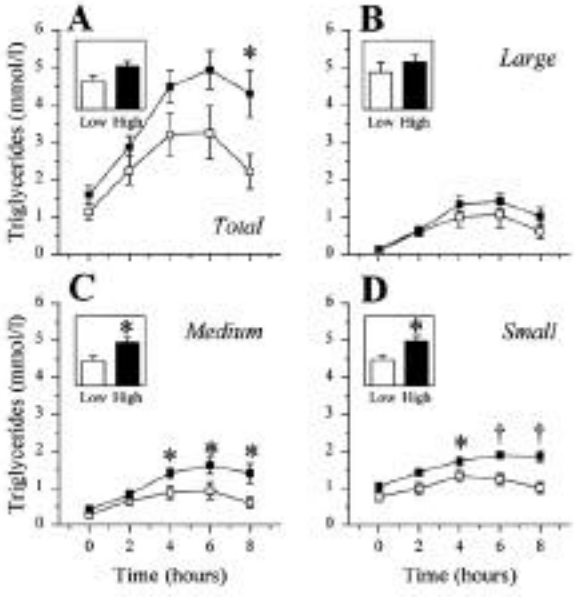

FIG. 2. Postprandial triglyceride responses of total (*A*), large (*B*), medium (*C*), and small (*D*) TRLs in two subgroups of men matched for total body fat mass (within a 1 kg difference) but with low (□; *n* = 10) versus high (■; *n* = 10) levels of visceral AT. Bars represent the AUIC responses of each subgroup. Data are means ± SE. **P* < 0.05; †*P* < 0.005 vs. men with low levels of visceral AT.

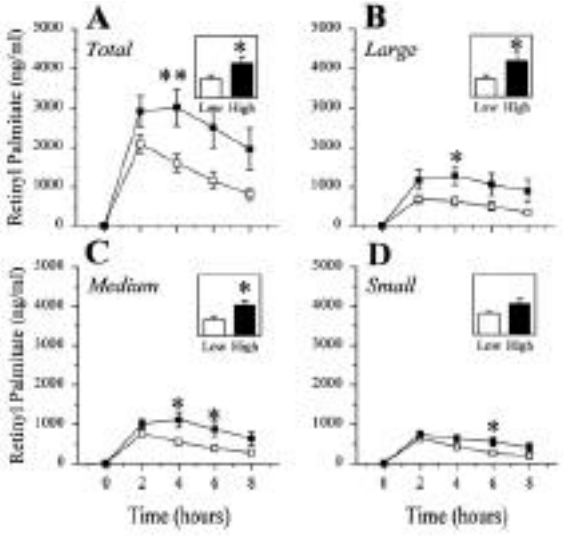

FIG. 3. Postprandial RP responses of total (*A*), large (*B*), medium (*C*), and small (*D*) TRLs in two subgroups of men matched for total body fat mass (within a 1 kg difference) but with low (□; *n* = 10) versus high (■; *n* = 10) levels of visceral AT. Bars represent the AUIC responses of each subgroup. Data are means ± SE. **P* < 0.05 vs. men with low levels of visceral AT.

dial TRL TG concentrations in these two groups revealed that men characterized by high levels of visceral AT presented increased medium- and small-TRL TG responses after the meal compared with those with a low visceral AT accumulation. These increased postprandial medium- and small-TRL TG responses in subjects with high levels of visceral AT did not appear to be influenced by the quantity of larger TRL particles, as no difference was found in large-TRL TGs between both subgroups of men. Competition for LPL between chylomicrons, chylomicron remnants, and VLDL during the postprandial period could be responsible, at least in part, for the delayed clearance of TRLs (45). Delayed uptake of lipoproteins by the liver could also be a cause of the retarded clearance of TRL particles. In our study, postprandial small-TRL TG concentrations were higher in visceral obese men. This observation is in accordance with previously published results that

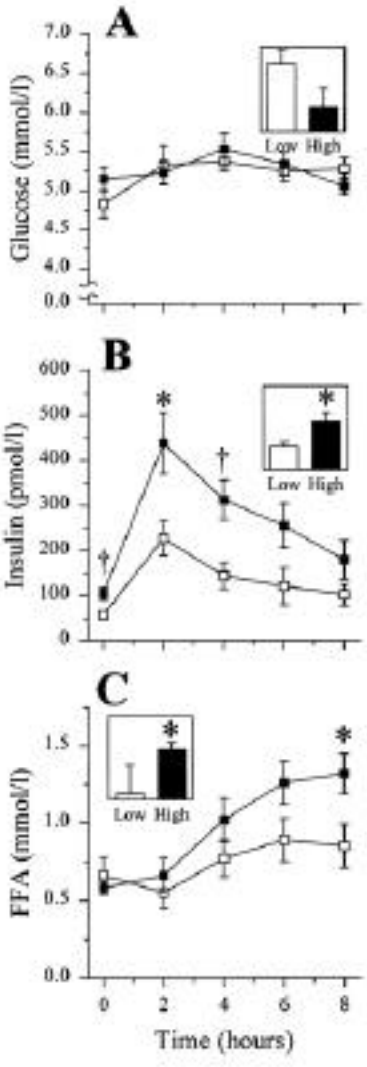

FIG. 4. Postprandial plasma glucose (*A*), insulin (*B*), and FFA (*C*) responses in two subgroups of men matched for total body fat mass (within a 1 kg difference) but with low (□; *n* = 10) versus high (■; *n* = 10) levels of visceral AT. Bars represent the AUIC responses of each subgroup. Data are means ± SE. **P* < 0.05; †*P* < 0.01 vs. men with low levels of visceral AT.

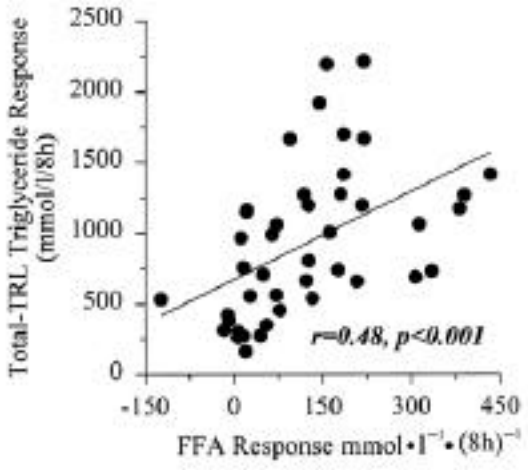

FIG. 5. Association between postprandial FFA and total-TRL TG responses in the whole sample of 43 men.

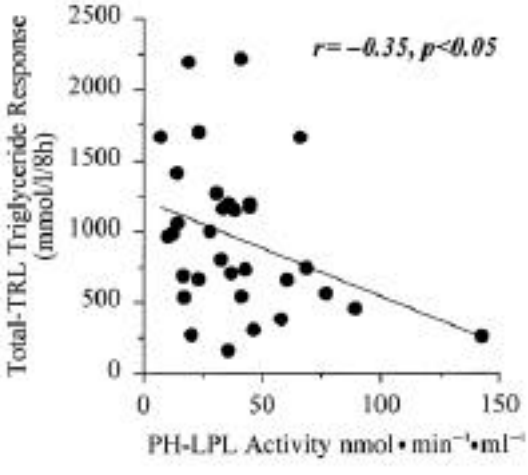

FIG. 6. Association between PH-LPL activity and total-TRL TG response in a subsample of 32 men.

underlined the importance of hepatic TG-rich particles in altered postprandial TG clearance (40).

Fasting hypertriglyceridemia is a common feature of visceral obesity (1,2). This metabolic alteration is believed to result from an increased flux of FFAs to the liver. Indeed, visceral adipocytes are characterized by lively lipolytic activity that is poorly inhibited by insulin, resulting in the elevation of FFAs in the portal circulation and in plasma (46). In response to this increased FFA availability, an increased esterification of FFAs and a reduced hepatic degradation of apolipoprotein B lead to an increased synthesis and secretion of VLDL particles. In the present study, the two subgroups of subjects classified on the basis of visceral AT accumulation showed different FFA response patterns to the fat load. Indeed, we noted a slight but nonsignificant decrease in FFA levels 2 h after the test meal in men with low levels of visceral AT, which also corresponded to the peak in postprandial insulin concentrations, a finding largely explained by the antilipolytic effect of insulin on AT (47,48). In fact, our results indicated that postprandial FFA levels did not differ from fasting concentrations in men with a low visceral AT accumulation. However, the decrease in FFA concentrations at peak insulin levels and the maintenance of FFA concentrations throughout the postprandial period were not observed in men with high levels of visceral AT. Indeed, plasma FFA levels increased progressively throughout the entire postprandial period, which resulted in a significantly increased FFA response in viscerally obese subjects, even in the presence of a marked postprandial hyperinsulinemic state in these individuals. These results agree with previously published observations of impaired postprandial plasma FFA metabolism associated with upper-body obesity (49). Furthermore, although FFA concentrations measured at the end of the test returned to near-fasting values in men with low levels of visceral AT, men with excess visceral AT had FFA concentrations that were significantly higher than fasting values, even 8 h after meal ingestion.

These altered postprandial FFA levels in individuals with visceral obesity may contribute to the elevation of fasting TGs through the stimulation of hepatic VLDL-TG secretion long after meal ingestion. This interpretation is supported by results obtained from the measurement of TRL RP concentrations. Indeed, the increased TG response in small TRLs noted among men with high levels of visceral AT was not accompanied by a higher RP response in that TRL fraction in comparison with obese men with lower levels of visceral AT. This observation supports the notion that TGs from endogenous TRLs, presumably VLDL particles, account for most of the increase in small-TRL TG levels observed late through the postprandial period. A possible contribution of the raised postprandial FFA levels to the increased production of VLDL in visceral obesity is also supported by the positive correlation that we found between postprandial FFA levels and the total-TRL TG response to the meal. Furthermore, when we compared subgroups of subjects matched on the basis of visceral AT but showing low versus high body fat mass, no difference was found in postprandial TRL metabolism (data not shown).

Other factors, such as decreased LPL activity, are thought to play a major role in an altered postprandial TRL metabolism (50,51). In the present study, PH-LPL activity was measured in 32 men. We found a negative relationship between PH-LPL and total-TRL TG response, but not between PH-LPL and visceral AT accumulation. However, men with high visceral AT levels were characterized by lower PH-LPL activity compared with men matched for body fat mass but showing low visceral AT levels. Although this difference was not significant ($P < 0.09$), it suggests that reduced PH-LPL activity may be implicated in the altered postprandial TRL metabolism among viscerally obese subjects. Further studies are required to validate this observation.

In summary, the present results indicate that excess visceral AT accumulation is associated with an impaired postprandial TRL TG clearance that is largely determined by phenomena that can also lead, to some extent, to fasting hypertriglyceridemia. Results of the present study also suggest that increased visceral AT accumulation might contribute to this fasting hypertriglyceridemic state by altering FFA metabolism, particularly in the postprandial state.

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