Insulin Resistance Is Independently Associated With Postprandial Alterations of Triglyceride-Rich Lipoproteins in Type 2 Diabetes Mellitus

Giovanni Annuzzi, Claudia De Natale, Ciro Iovine, Lidia Patti, Lucrezia Di Marino, Silvana Coppola, Stefano Del Prato, Gabriele Riccardi, Angela A. Rivellese

Objective—To evaluate the role of insulin resistance in development of postprandial dyslipidemia in type 2 diabetic patients in an experimental setting in which these patients were compared with nondiabetic subjects at similar glucose and insulin blood levels.

Methods and Results—Eight type 2 diabetic patients in optimal blood glucose control and 7 control subjects (aged 50.0±2.6 and 48.1±1.3 years; body mass index 28.3±1.2 and 25.6±1.1 kg/m²; fasting plasma triglycerides 1.12±0.13 and 0.87±0.08 mmol/L, respectively; mean±SEM; NS) consumed a mixed meal during an 8-hour hyperinsulinemic glyceic clamp. Mean blood glucose during clamp was ≈7.8 mmol/L, and plasma insulin during the preprandial steady state was ≈480 pmol/L in both groups, that differed for insulin sensitivity (M/I value lower in diabetic subjects [1.65±0.30 and 3.42±0.60; P<0.05]). Subjects with diabetes had higher postprandial levels of lipids and apolipoprotein B (apoB) in large very low-density lipoprotein (incremental area for triglycerides 1814±421 versus 549±153 μmol/L×6 hours; P<0.05; cholesterol 694±167 versus 226±41 μmol/L×6 hours; P<0.05; apoB-48 6.3±1.0 versus 2.6±0.7 mg/L×6 hours; P<0.05; apoB-100 56.5±14.9 versus 26.2±11.0 mg/L×6 hours; NS). Basal lipoprotein lipase (LPL) activity before and after meal was higher in diabetic subjects, whereas postheparin LPL activity 6 hours after the meal was similar.

Conclusions—Insulin resistance is also associated with postprandial lipoprotein abnormalities in type 2 diabetes after acute correction for hyperglycemia and hyperinsulinemia. (Arterioscler Thromb Vasc Biol. 2004;24:2397-2402.)

Key Words: postprandial lipemia ■ large VLDL ■ insulin resistance ■ type 2 diabetes ■ lipoprotein lipase

Patients with type 2 diabetes mellitus show abnormalities of the plasma lipoprotein profile in the postprandial state, mainly concerning triglyceride-rich lipoproteins.1 Because postprandial lipoprotein abnormalities have been consistently associated with an increased risk of coronary heart disease,2 they could be a major factor explaining the higher rate of cardiovascular diseases observed in these patients. The magnitude of postprandial lipemia is related to the fasting level of plasma triglycerides,3 and fasting hypertriglyceridemia is a main feature of diabetic dyslipidemia.4 However, we have shown recently in a group of patients with type 2 diabetes in very good blood glucose control that even with normal fasting triglyceridemia, these patients had higher postprandial levels of large very low-density lipoprotein (VLDL) particles of exogenous and endogenous origin.5

The factors responsible for these abnormalities, and the mechanisms through which they may influence postprandial lipid response in type 2 diabetic patients, are presently very much debated.4 Insulin resistance, or the compensatory hyperinsulinemia, as well as hyperglycemia (conditions characterizing type 2 diabetes) have been suggested as major determinants of postprandial lipemia. A possible role for insulin resistance was suggested by Jeppesen et al.,6 who showed in healthy nondiabetic individuals that resistance to insulin-mediated glucose disposal, determined by a modification of the insulin suppression test, was the only independent factor associated with postprandial lipid alterations, measured as triglycerides and retinyl palmitate concentrations. A higher triglyceride incremental area after a mixed meal has been reported in insulin-resistant (normoglycemic and normotriglyceridemic) first-degree relatives of patients with type 2 diabetes.7

As for the possible role of hyperglycemia, it has been shown that improved glycemic control, however achieved, in addition to decreasing fasting triglyceride levels,8 is able to decrease postprandial lipemia in type 2 diabetes.9

Compensatory hyperinsulinemia, which always accompanies insulin-resistant states, has been suggested as a possible
determinant of the postprandial lipemia on the basis of evidence that the higher the plasma insulin response to a meal, the greater the postprandial increase of triglyceride-rich lipoproteins of intestinal origin. The possibility that high insulin levels directly stimulate VLDL synthesis and secretion is also supported by some studies showing that hyperinsulinemia correlates with VLDL production rate in humans, and that the hypertriglycerideremia induced by a carbohydrate-rich diet was related to the increase in insulin levels.

The controversies on this issue are mainly attributable to the strong interrelationships among insulin resistance, hyperinsulinemia, and hyperglyceremia that make it difficult to assess these factors independently of each other. In fact, no study has tried to evaluate their distinctive effects, and, in particular, the role of insulin resistance per se has not been evaluated.

Therefore, our aims were first to evaluate the possible role of insulin resistance per se on development of the postprandial lipid abnormalities generally found in patients with type 2 diabetes, particularly those without fasting hypertriglycerideremia, and second to evaluate whether the effect of insulin resistance was mediated by changes in the activity of lipoprotein lipase (LPL). We tried to unravel these issues comparing the lipemic postprandial response of type 2 diabetic subjects and nondiabetic control subjects in the absence of differences between these 2 groups in glucose and insulin plasma levels. This was obtained by keeping these variables at similar levels through a prolonged hyperinsulinemic glycemic clamp.

Methods

Subjects

Eight patients with type 2 diabetes mellitus, 6 males and 2 females, treated with diet (n = 5) or diet + sulfonylurea (n = 3), and 7 nondiabetic controls, 3 males and 4 females, participated in the study. The 2 groups were comparable regarding: age (50.0 ± 2.6 and 48.1 ± 1.3 years), body mass index (28.3 ± 1.2 and 25.6 ± 1.1 kg/m²), plasma cholesterol (4.8 ± 0.3 and 4.9 ± 0.2 mmol/L), and plasma triglycerides (1.12 ± 0.13 and 0.87 ± 0.08 mmol/L), respectively, for diabetic and control subjects (mean ± SEM; differences not statistically significant). All subjects had normal fasting plasma concentration of triglyceride (<1.7 mmol/L) and cholesterol (<5.5 mmol/L). The diabetic subjects had higher fasting plasma glucose levels (7.7 ± 0.8 versus 4.8 ± 0.2 mmol/L; P < 0.005) and were in optimal blood glucose control (hemoglobin A1c 6.2 ± 0.3%).

Subjects had no history or symptoms of any known disease, apart from diabetes, nor were they vegetarians or engaged in intensive physical activity. The study protocol was approved by the Federico II University ethics committee and informed consent by participants was obtained.

Experimental Procedures

In the morning after at least a 12-hour fast, subjects underwent an 8-hour hyperinsulinemic glycemic clamp. Two hours after the beginning of the clamp, a standard meal was administered. Before and during the clamp, serial blood samples were taken for determination of plasma levels of glucose, insulin, plasma lipids and lipoproteins, apolipoprotein B-48 (apoB-48) and apoB-100, free fatty acid (FFA), and LPL activity. At the end of the clamp, heparin (100 U/kg body weight) was injected intravenously and a blood sample was obtained after 15 minutes for LPL and hepatic lipase (HL) activity measurement. Blood was collected in EDTA tubes kept in ice, and plasma was separated within 15 minutes by low-speed centrifugation at 4°C.

Hyperinsulinemic Glycemic Clamp

A polyethylene cannula was inserted into a cubital vein for infusions. A second cannula was placed retrogradely into a forearm vein for blood sampling; the forearm was kept warm in a heated box (∼60°C) to ensure arterialization of venous blood. Regular human insulin was administered intravenously at a constant rate of 1.5 mU/kg body weight per minute for 8 hours. At the same time, a variable amount of a 33% glucose solution was also infused to maintain blood glucose concentration ~7.8 mmol/L. This was achieved by adjusting the glucose infusion rate according to blood glucose measurements, which were performed at 5- to 10-minute intervals on an Accutrend glucose analyzer (Roche). This glycemic target was chosen to better match usual blood glucose levels of diabetic patients in the postprandial state. Moreover, at these blood levels of glucose and insulin, hepatic glucose production is expected to be completely inhibited. The glucose infusion rate (mg/kg body weight per minute) during the 30 minutes before the meal divided by the concomitant plasma insulin concentrations (pmol/L) multiplied by 100 was calculated as a measure of insulin sensitivity (M/I value).

Standard Test Meal

Two hours after the beginning of the clamp, a standard mixed meal consisting of a potato gateau (a pie made of mashed potato, whole milk, egg, cheese, ham, and butter) was ingested in 15 minutes. The meal, which provided 944 kcal, was composed of 31% carbohydrates, 57% fat (34% saturated fat), and 12% protein.

Laboratory Procedures

Lipoprotein Separation

Samples were kept at 4°C before, during, and after centrifugation and adequately treated to minimize proteolytic degradation of apoB. Fasting and postprandial lipoprotein subfractions were isolated by discontinuous density gradient ultracentrifugation, as slightly modified from Redgrave and Carlson. Ultracentrifugation was performed in a Beckman SW 40 Ti rotor on a Beckman Optima L-90K ultracentrifuge (Beckman Instruments). Briefly, 3 consecutive runs were performed at 15°C and at 4000 rpm to float: chylomicrons (Svedberg flotation unit [SF] > 400), large VLDL (SF 60 to 400), and small VLDL (SF 20 to 60). Intermediate-density lipoprotein (IDL; SF 12 to 20) and low-density lipoprotein (LDL; SF 0 to 12) were collected from the gradient after the SF 20 to 60 particles had been collected. HDLs were isolated by the phosphotungstic acid/magnesium chloride precipitation method.

ApoB-48 and ApoB-100

Concentrations of apoB-48 and apoB-100 were analyzed in chylomicrons, large VLDL, and small VLDL fractions by SDS-PAGE on self-made 3.5% to 20% gel gradient. The intragel and intergel coefficients of variation (CVs) were 15.7% and 12.6% for apoB-48 and 7.8% and 11.4% for apoB-100, respectively. The detection limits for apoB-48 and apoB-100 ranged between 0.01 and 0.02 mg/L.

Plasma Lipolytic Activities

Postheparin blood samples for LPL and HL activities were obtained at the end of the clamp, whereas serial samples for preheparin LPL were obtained before and during the clamp. Samples were collected into tubes containing EDTA, and plasma was immediately separated by centrifugation at 4°C and stored at −80°C until analysis. Lipase activities were determined according to Nilsson-Ehle and Ekman, using as substrate a (H) trioleoylglycerol emulsion stabilized by dioleoyl phosphatidyl choline. LPL activity in preheparin plasma was measured after separation by sephadex column chromatography according to a modified procedure. Main modifications were the use of lower amounts of heparin–Sepharose gel (1 mL) and plasma sample (0.5 mL), and elution of LPL with 3 mL 1% heparin buffer. The free fatty acid (FFA) activity measurement was 11.0% intra-assay and 20.6% interassay. Because of the high interassay variability, data were corrected by a standard control sample.
Other Measurements
Total cholesterol and triglyceride concentrations were assayed in plasma and isolated lipoprotein fractions by enzymatic colorimetric methods (Roche Molecular Biochemicals) on an autoanalyzer Cobas Mira (ABX Diagnostics). Plasma nonesterified fatty acid concentrations were analyzed by the enzymatic colorimetric method (Wako Chemicals). Plasma insulin and C-peptide concentrations were measured by radioimmunoassay (Technogenetics).

Statistical Analysis
Data are expressed as mean±SEM, unless otherwise stated. Postprandial incremental area was calculated by the trapezoidal method as the area under the curve above the baseline value. Differences between diabetic and control subjects were evaluated by Student t test for independent samples. Differences between the 2 groups at single time points after the meal were first evaluated by ANOVA for repeated measures. Two-tailed tests were used, and a P<0.05 was considered statistically significant. Variables not normally distributed were analyzed after logarithmic transformation or by nonparametric tests (ie, the Mann–Whitney for independent samples). Statistical analysis was performed according to standard methods using the Statistical Package for Social Sciences software (SPSS/PC; SPSS).

Results
Blood Glucose, Plasma Insulin, Plasma C-Peptide, and Glucose Infusion Rate
As expected, fasting blood glucose was higher in diabetic subjects (Figure 1A). Mean blood glucose concentration during the 8-hour clamp was instead similar in diabetic subjects (7.83±0.06 mmol/L) and in controls (7.89±0.06 mmol/L; Figure 1A), with an average CV of 8.6% and 9.6% in the 2 groups (NS), respectively.

Plasma insulin levels at fasting were 60.6±13.1 pmol/L in diabetic subjects and 56.5±15.6 pmol/L in controls (NS) and reached a similar plateau during the insulin infusion during the 30 minutes before the meal (467±47 pmol/L and 466±100 pmol/L, respectively; NS). After the meal, a slight increase in plasma insulin levels was observed in both groups, with a tendency to steadily higher levels in control subjects (P>0.05 by repeated-measures ANOVA; Figure 1B).

Plasma C-peptide concentrations were not significantly different in the 2 groups, either in the fasting basal state (0.96±0.26 and 0.59±0.13 nmol/L; NS) or during insulin infusion during the 60 minutes before the meal (1.4±0.4 and 1.6±1.3 nmol/L; NS). A greater postprandial increase was observed in control subjects compared with diabetic subjects, with significant differences in the first 2 hours after the meal (Figure 1C).

Glucose infusion rate during the 30 minutes before the meal was 7.0±0.7 mg/kg body weight per minute in diabetic subjects and 12.8±1.6 mg/kg body weight per minute in controls (P<0.01) and remained similarly lower in diabetic subjects during the postprandial period (Figure 1D). The M/I value during the premeal steady state was 1.65±0.30 and 3.42±0.60 in the diabetic and control subjects, respectively (P<0.05).

Lipids and ApoB Concentrations in Whole Plasma and in Plasma Lipoproteins
Whole Plasma
The postprandial incremental area for plasma triglycerides was higher, albeit nonsignificantly, in diabetic subjects (4281±695 versus 2843±648 μmol/L×6 hours). A slight but constant decrease in cholesterol levels over the postprandial phase was observed in diabetic and control subjects, without significant differences between the 2 groups (Table I, available online at http://atvb.ahajournals.org).

Chylomicrons
Patients with diabetes had significantly higher levels of chylomicron lipids in the fasting state (triglycerides 26.7±4.7 versus 11.3±1.9 μmol/L, P<0.05; cholesterol 3.3±0.8 versus 1.3±0.3 μmol/L, P<0.05) and 2 hours after insulin infusion (triglycerides 16.3±4.6 versus 4.7±0.8 μmol/L, P<0.05; cholesterol 2.7±0.8 versus 0.8±0.3 μmol/L, P<0.05). After the meal, triglyceride and cholesterol concentrations increased more, although not significantly, in diabetic subjects than in controls (incremental area for triglycerides 2357±524 versus 1915±388 μmol/L×6 hours; and for cholesterol 206±40 versus 140±31 μmol/L×6 hours) (Fig-
ure 2). Postprandial apoB-48 levels increased almost similarly in both groups (Figure 2). Negligible amounts of apoB-100 were measured in this lipoprotein fraction before and after the meal (Figure 2; Table I).

**Large VLDL**

Hyperinsulinemia before the meal induced a decrease in triglycerides, cholesterol, and apoB-100 concentrations in this fraction in the control subjects, whereas no changes were observed in diabetic subjects. After the meal, there was a greater increase in large VLDL particles in diabetic subjects in triglycerides ([incremental area 1814±421 versus 549±153 μmol/L×6 hours; *P*<0.05]) and cholesterol ([incremental area 694±167 versus 226±41 μmol/L×6 hours; *P*<0.05]), which was more evident in the late postprandial phase (Figure 3; Table I). In diabetic subjects, these particles were also richer in apoB-48 ([incremental area 6.3±1.0 versus 2.6±0.7 mg/L×6 hours; *P*<0.05]). ApoB-48 concentrations 6 hours after the meal were inversely correlated with the M-value (γ=0.61; *P*<0.05). Although the postprandial increase in apoB-100 was more than double in diabetic subjects compared with controls, the difference was not statistically significant (*P*>0.05 by ANOVA for repeated measures).

**Small VLDL**

No significant differences in fasting levels and postprandial response of triglyceride, cholesterol, apoB-48, and apoB-100 concentrations in the smaller VLDL particles were observed between diabetic and control subjects (supplemental Table I).

**IDL, LDL, and HDL**

The fasting lipid concentrations and the changes induced by the meal in the IDL, LDL, and HDL fractions did not significantly differ between diabetic and control subjects, the total postprandial incremental areas of cholesterol and triglycerides being negative in both groups (supplemental Table I).

**Plasma FFA**

Fasting plasma FFA levels were not significantly different between diabetic subjects and controls (511±71 and 480±82 μmol/L, respectively; Figure 4). Insulin infusion before the meal induced a lower suppression of plasma FFA in diabetic subjects (70±6 μmol/L) than in control subjects (37±4 μmol/L; *P*<0.001). After the meal, FFA levels gradually increased in the 2 groups during the first 3 hours. In the late postprandial phase, significantly higher levels were observed in diabetic subjects compared with controls at 4, 5,
and 6 hours. Plasma FFA concentrations 6 hours after the meal were directly correlated with the changes in the triglyceride content of large VLDL (6-hour value – fasting value; $r=0.88; P<0.001$).

**LPL and HL**

LPL activity in plasma obtained without heparin stimulation was constantly higher in diabetic subjects ($P<0.05$) in the fasting state as well as during hyperinsulinemia before and after the meal (Figure I, available online at http://atvb.ahajournals.org). LPL activity in the postheparin plasma obtained 6 hours after the meal was similar in the 2 groups (64.6 ± 6.9 and 64.4 ± 14.7 nmol FA/mL per minute, in the diabetic and the control group, respectively; NS). HL activity in the postheparin plasma obtained 6 hours after the meal was instead significantly higher in diabetic subjects compared with controls (226 ± 30 versus 113 ± 21 nmol FA/mL per minute; $P<0.05$).

**Discussion**

In this study, the postprandial lipid alterations of type 2 diabetic patients were also observed in the absence of higher blood levels of glucose and insulin in these patients compared with control nondiabetic subjects. Therefore, because the 2 groups only differed for the level of insulin sensitivity, these data indicate that insulin resistance, more than hyperglycemia and hyperinsulinemia, plays a determinant role in development of postprandial lipid abnormalities. It is noteworthy that these results were observed in type 2 diabetic patients with optimal fasting triglyceride values and satisfactory blood glucose control. It is likely that in patients with higher fasting triglyceride or nonoptimal blood glucose control (thus also more insulin resistant than our diabetic subjects), the differences in postprandial abnormalities would have been more evident.

As to the possible role of hyperglycemia, in the time frame of this experiment, hyperglycemia could not be responsible for the postprandial lipid abnormalities observed in diabetic subjects because similar blood glucose levels were maintained over the whole study in both groups. In addition, it should be considered that because of their higher insulin sensitivity, controls were given a greater amount of glucose during the clamp. This higher caloric load providing an increased substrate supply to the liver, together with the higher plasma insulin levels, may have induced in these subjects an increased hepatic VLDL production, possibly hampering the assessment of the true differences between diabetic patients and controls.

This study also showed that postprandial lipid abnormalities were not related to the presence of hyperinsulinemia in diabetic patients. Plasma insulin and C-peptide levels were in fact similar in the 2 groups before the meal and even higher in the control subjects in the postprandial state. As mentioned above, this may have influenced postprandial lipid response but clearly argues against a direct role of hyperinsulinemia in diabetic patients, at least in this acute experimental setting.

Concerning the type of lipid abnormalities induced by the meal, this study shows that postprandial hypertriglyceridemia in diabetic subjects was mainly attributable to an increase of the large VLDL fraction (Sf 60 to 400). In the absorptive state, this fraction represents lipoproteins of intestinal and hepatic origin, as confirmed in our study by the concomitant increase in apoB-48 and apoB-100 concentrations. As discussed above, the experimentally induced increased substrate supply in controls may have lessened the difference in hepatic VLDL. Anyhow, apoB-48 increase in diabetic subjects was more distinct and statistically significant, indicating that the postprandial change observed in the Sf 60 to 400 fraction was mainly attributable to a higher presence of chylomicron remnants. It must be considered that in the postprandial phase, on the basis of the apoB-48 and apoB-100 concentrations measured in the large VLDL fraction, ~20% of particles contained apoB-48 and 80% apoB-100 in both groups. Therefore, the almost doubled amount of apoB-100 in subjects with type 2 diabetes may, in any case, have a relevant pathophysiological role.

By which mechanisms could insulin resistance induce the lipoprotein abnormalities found in our diabetic subjects? It is possible that the increase in large VLDL was attributable to an increased hepatic VLDL synthesis during the postprandial period. This could be a consequence of the higher flux of FFA to the liver, as suggested by the higher FFA plasma levels in diabetic subjects compared with controls in the late postprandial period, and the strong direct correlation between FFA levels and changes in large VLDL triglyceride concentration 6 hours after the meal. However, it is also possible that VLDL abnormalities were induced by a decrease in the direct inhibitory effects of insulin on the synthesis of these particles.

We investigated the possibility that reduced activity of LPL, the key enzyme in the intravascular catabolism of chylomicrons and VLDL, could be responsible for the postprandial lipid alterations observed in diabetic subjects. LPL activity in postheparin plasma obtained 6 hours after the meal was not different between the 2 groups, whereas preheparin LPL activity was, if anything, higher in diabetic subjects, before and after the meal. This is in line with the higher postprandial preheparin LPL levels shown previously in a group of coronary heart disease patients compared with normotriglyceridemic controls.20 The behavior of LPL of different source/tissue in insulin resistance states is
Indeed controversial. In nondiabetic individuals, Panarotto et al. found that insulin resistance was negatively correlated to adipose tissue LPL mRNA and activity but not to postheparin LPL activity or mass. Eriksson et al. showed instead that adipose tissue LPL activity and mass were enhanced by a fat-rich meal to a similar degree in patients with type 2 diabetes and in healthy control subjects. As a whole, our results do not suggest a relevant role of a deficit in LPL activity in development of postprandial lipid abnormalities, at least in this group of diabetic patients, without fasting hypertriglyceridemia. However, we cannot rule out the possibility of a “relative” deficit of LPL activity in type 2 diabetic patients, considering the increased substrate in the circulation resulting from the higher postprandial flux of chylomicrons remnants and hepatic VLDL in these patients.

HL activity in postheparin plasma 6 hours after meal was higher in diabetic subjects, confirming our observation in normal “nonclamp” conditions. An increased activity of this enzyme in the fasting condition has been shown in type 2 diabetic patients, as well as in other states of insulin resistance, and it has been related to an excess of small, dense LDL particles. In the postprandial state, HL could promote the clearance of chylomicron remnants through its ligand activity. If this mechanism was operating in our study, because we observed higher levels of HL in the diabetic patients with a concomitant increase in chylomicron remnants, it would indicate that either this mechanism was not relevant in clearance of remnants or it was in line with an increased production rate of remnants. It must be considered that an increased clearance of remnants enhances FFA availability in the liver, eventually leading to an augmented VLDL secretion.

In conclusion, this study shows that in type 2 diabetic patients, insulin resistance, independently of hyperglycemia and hyperinsulinemia, is associated with an increase in the large VLDL/chylomicron remnant particles during the postprandial period. This increase is probably the consequence of a higher production of chylomicron remnants (the lipolysis of chylomicrons is substantially effective because of the preferential choice of larger particles by LPL) and a concomitant lack of inhibition by insulin of the hepatic synthesis of large VLDL, which compete with chylomicron remnants for their removal.

The results of this study strengthen the importance of targeting insulin resistance in the effort to correct postprandial hyperlipemia and, therefore, reduce cardiovascular risk in type 2 diabetes and the metabolic syndrome.

Acknowledgments
This work was supported in part by funds from the Italian Ministry of University, Research, and Technology (COFIN 1998 to 2000). The excellent technical laboratory assistance of Paola Cipriano and the work of the Diabetes Unit dietitians are gratefully acknowledged.

References
3. Annuzzi G, Holmquist L, Carlson LA. Concentrations of apolipoproteins B, C-I, C-II, C-III, E, and lipids in serum and serum lipoproteins of normal

Insulin Resistance Is Independently Associated With Postprandial Alterations of Triglyceride-Rich Lipoproteins in Type 2 Diabetes Mellitus
Giovanni Annuzzi, Claudia De Natale, Ciro Iovine, Lidia Patti, Lucrezia Di Marino, Silvana Coppola, Stefano Del Prato, Gabriele Riccardi and Angela A. Rivellese

Arterioscler Thromb Vasc Biol. 2004;24:2397-2402; originally published online September 30, 2004;
doi: 10.1161/01.ATV.0000146267.71816.30

Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 1079-5642. Online ISSN: 1524-4636

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://atvb.ahajournals.org/content/24/12/2397

Data Supplement (unedited) at:
http://atvb.ahajournals.org/content/suppl/2004/12/03/01.ATV.0000146267.71816.30.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Arteriosclerosis, Thrombosis, and Vascular Biology can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Arteriosclerosis, Thrombosis, and Vascular Biology is online at:
http://atvb.ahajournals.org//subscriptions/
Figure I

LPL activity (nmol FA/ml/min)

- Controls
- Diabetes

* Significant difference
Figure I. Plasma lipoprotein lipase activity before and after a standard meal consumed during a hyperinsulinemic glycemic clamp in subjects with type 2 diabetes and in nondiabetic controls. Values are means ± SEM; by ANOVA for repeated measures, p<0.05; by t-test, * p<0.05 vs. controls.
<table>
<thead>
<tr>
<th></th>
<th>Type 2 Diabetes</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole plasma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG</td>
<td>4281 ± 695</td>
<td>2843 ± 648</td>
</tr>
<tr>
<td>Chol</td>
<td>-1979 ± 386</td>
<td>-2195 ± 260</td>
</tr>
<tr>
<td>Chylomicrons</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG</td>
<td>2357 ± 524</td>
<td>1915 ± 388</td>
</tr>
<tr>
<td>Chol</td>
<td>206 ± 40</td>
<td>140 ± 31</td>
</tr>
<tr>
<td>B-48</td>
<td>0.26 ± 0.10</td>
<td>1.12 ± 0.71</td>
</tr>
<tr>
<td>B-100</td>
<td>0.03 ± 0.02</td>
<td>-0.04 ± 0.03</td>
</tr>
<tr>
<td>Large VLDL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG</td>
<td>1814 ± 421 *</td>
<td>549 ± 153</td>
</tr>
<tr>
<td>Chol</td>
<td>694 ± 167 *</td>
<td>226 ± 41</td>
</tr>
<tr>
<td>B-48</td>
<td>6.31 ± 1.02 *</td>
<td>2.66 ± 0.72</td>
</tr>
<tr>
<td>B-100</td>
<td>56.5 ± 14.9</td>
<td>26.2 ± 11.0</td>
</tr>
<tr>
<td>Small VLDL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG</td>
<td>-12 ± 150</td>
<td>95 ± 95</td>
</tr>
<tr>
<td>Chol</td>
<td>-143 ± 235</td>
<td>-67 ± 86</td>
</tr>
<tr>
<td>B-48</td>
<td>1.73 ± 0.87</td>
<td>1.19 ± 0.58</td>
</tr>
<tr>
<td>B-100</td>
<td>-21.1 ± 23.6</td>
<td>-22.2 ± 20.4</td>
</tr>
<tr>
<td>IDL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG</td>
<td>-56 ± 79</td>
<td>-11 ± 31</td>
</tr>
<tr>
<td>Chol</td>
<td>-196 ± 80</td>
<td>-148 ± 87</td>
</tr>
<tr>
<td>B-48</td>
<td>1.24 ± 0.27</td>
<td>0.61 ± 0.57</td>
</tr>
<tr>
<td>B-100</td>
<td>3.3 ± 12.9</td>
<td>-7.0 ± 18.6</td>
</tr>
<tr>
<td>LDL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG</td>
<td>-123 ± 29</td>
<td>-108 ± 24</td>
</tr>
<tr>
<td>Chol</td>
<td>-1158 ± 426</td>
<td>-1403 ± 244</td>
</tr>
<tr>
<td>HDL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG</td>
<td>-43 ± 27</td>
<td>-81 ± 53</td>
</tr>
<tr>
<td>Chol</td>
<td>-894 ± 93</td>
<td>-855 ± 126</td>
</tr>
</tbody>
</table>