Fasting and Daylong Triglycerides in Obesity With and Without Type 2 Diabetes

J.P.H. van Wijk, C.J.M. Halkes, D.W. Erkelens, and M. Castro Cabezas

Postprandial hypertriglyceridemia associated with insulin resistance is one of the cardiovascular risk factors in obesity and type 2 diabetes. It is not known whether diabetics have a more pronounced postprandial hypertriglyceridemia than obese subjects. Daylong triglyceridemia, representing postprandial lipemia, was determined in obese subjects with and without type 2 diabetes and in lean subjects. Nineteen type 2 diabetics (F/M: 7/12, body mass index [BMI]: 30.6 ± 5.4 kg/m^2), 45 obese nondiabetics (F/M: 16/29, BMI: 29.5 ± 2.6 kg/m^2) and 78 lean subjects (F/M: 28/50, BMI: 23.7 ± 2.2 kg/m^2) measured capillary triglycerides (TGc) during 3 days on 6 fixed time-points each day in an out-of-hospital situation. Daylong TGc profiles were calculated as mean integrated area under the TGc-curve (TGc-AUC). Fasting plasma TG were higher in diabetics and obese nondiabetics (1.81 ± 0.79 and 1.77 ± 0.80 mmol/L) compared with lean subjects (1.23 ± 0.67 mmol/L, $P < .001$). TGc-AUC was similarly increased in both diabetics and obese nondiabetics (35.0 ± 12.1 and 35.2 ± 10.6 mmol · h/L) compared with lean controls (25.5 ± 12.0 mmol · h/L, $P < .001$). Self-reported energy intake was not significantly different between the groups. Fasting TGc ($r = .87$, $P < .001$) and waist circumference ($r = .51$, $P < .001$) were the parameters best associated with TGc-AUC. Using stepwise multiple regression analysis, fasting TGc, BMI, total cholesterol, and high-density lipoprotein (HDL) cholesterol were the best predictors of TGc-AUC, explaining 77% of the variation. The cut-off level for "normal" TGc-AUC, calculated as the 75th percentile of TGc-AUC in lean subjects, was 30.7 mmol · h/L and corresponded with a fasting TGc of 1.8 mmol/L (eg, 1.6 mmol/L in plasma), calculated using univariate regression analysis. In conclusion, daylong triglyceridemia is similarly increased in diabetics and obese nondiabetics compared with lean subjects. Fasting TG and central obesity largely determine daylong triglyceridemia, independent of the presence of type 2 diabetes. Decreasing fasting plasma TG below 1.6 mmol/L could lead to a normalization of postprandial lipemia in obese subjects with and without diabetes.

FASTING PLASMA hypertriglyceridemia is a risk factor for cardiovascular disease (CVD), even in a range previously considered to be normal (between 1.00 and 1.84 mmol/L).[1-3] However, fasting triglycerides (TG) are not invariably increased in the fasting state and exaggerated and prolonged postprandial hyperlipidemia with accumulation of atherogenic chylomicron remnants may be a concealed risk factor in some patients.[4-6] It has been demonstrated in an in vivo animal model that chylomicron remnants easily migrate through the vessel wall.[7,8] Accumulation of chylomicron remnants in the subendothelial space may initiate the process of atherosclerosis by formation of fatty streaks.

Obesity is associated with increased mortality, largely due to CVD.[9-11] Cardiovascular risk factors in obesity are hyperinsulinemia, abdominal obesity, high blood pressure, high clotting activity, decreased high-density lipoprotein (HDL) cholesterol, small dense low-density lipoprotein (LDL) particles and increased TG levels.[10,12-14] The clustering of these risk factors in an individual patient is often referred to as the "insulin resistance syndrome." Furthermore, obesity and insulin resistance are essential to the development of the majority of cases of type 2 diabetes.[15,16] Both type 2 diabetes and obesity have been associated with exaggerated postprandial lipemia.[17-20] However, direct comparisons between groups matched for body mass index (BMI), with and without diabetes, are scarce.

Postprandial lipid metabolism has been investigated in metabolic ward studies under standardized circumstances, which may not reflect the free-living daylong situation. In addition, metabolic ward studies are complex and time consuming and cannot be applied in clinical practice in large populations. Recently, a novel method has been developed to study TG metabolism in the free-living situation using serial capillary self-measurements in an out-of-hospital setting.[21-26] Daylong capillary TG (TGc) profiles are closely related to postprandial lipemia as assessed by standardized oral fat loading tests.[21,25] Daylong TGc profiles are increased in overweight insulin-resistant subjects compared with lean subjects.[22] This study was performed to compare daylong TGc profiles between type 2 diabetics, obese nondiabetics and healthy lean subjects. In addition, we evaluated the determinants of daylong TGc profiles and aimed to define a cut-off level for "normal" daylong TGc profiles.

SUBJECTS AND METHODS

Subjects

Data were analyzed from 142 subjects who participated in a study aimed to evaluate daylong TG changes in an out-of-hospital situation. Inclusion criteria were age 35 to 65 years and fasting cholesterol < 7 mmol/L. Type 2 diabetic subjects were included from the department of Internal Medicine from the University Medical Center Utrecht and fulfilled the criteria as described by the American Diabetes Association.[27] Exclusion criteria for diabetic patients were glycosylated hemoglobin (HbA_{1c}) > 9%, BMI > 40 kg/m^2, alcohol intake > 3 U/d, the use of lipid-lowering medication, and renal, thyroid, and/or liver disease. Nondiabetic subjects were recruited by advertisement and subdivided into either obese (BMI ≥27 kg/m^2) or lean (BMI <27 kg/m^2). Exclusion criteria were the presence of type 2 diabetes, BMI >40 kg/m^2, alcohol intake >3 U/d, the use of lipid-lowering medication, and renal, thyroid, and/or liver disease. Participants visited our department after a 12-hour fast. A fasting blood sample was obtained, and

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length, weight, blood pressure, and waist circumference were measured. All subjects gave written informed consent before participating. The study was approved by the Medical Ethical Committee of the University Medical Center Utrecht.

TG Self-Measurements

Self-measurement of TGc was performed with a TG-specific point-of-care testing device (Accutrend GCT, Roche Diagnostics, Mannheim, Germany).[21-26] The TGc-analyzer detects TG reliably, regardless of the nature of the TG-carrying lipoprotein species, indicating that it is suitable for determination of both fasting and postprandial TG.[23] Subjects were instructed to wash and dry their hands thoroughly before each measurement. With a lancing device, a drop of blood (30 μL) from the finger was obtained, which was applied to the TG test strip in the TGc-analyzer. Subsequently, the TG concentration from the capillary blood sample was measured by a process of dry chemistry and colorimetry. If there was not enough blood on the TGc test strip, subjects were advised to repeat the measurement. Each subject was instructed by the same investigator. The measurement range for TGc is 0.80 to 6.86 mmol/L. In a previous study, variation coefficients for different TGc concentrations were 3.3% to 5.3%.[24] The correlation coefficient between TGc measurements with the TGc-analyzer and plasma measurements according to enzymatic methods is 0.94.[24] Similar results have been obtained in our laboratory.[21,25] TGc concentrations are generally 0.2 to 0.3 mmol/L higher than TG concentrations in venous plasma,[21-26] which may reflect differences between capillary and venous samples. Furthermore, daylong TGc profiles correlate with postprandial lipemia as assessed by a standardized oral fat loading test.[21] Daylong triglyceridemia estimated with 6 measurements was not different compared with hourly measurements, suggesting that these time-points are representative for the daylong study period.[25]

Subjects were instructed to measure TGc on 3 different days (preferably Monday, Wednesday, and Friday; not on the weekends) at the following time-points: fasting, before and 3 hours after lunch and dinner, and at bedtime. The 3-hour postprandial measurements were performed exactly 3 hours after the meals, regardless of intake of snacks. The results were recorded in a diary. Subjects were requested to refrain from heavy physical activity, although normal daily activities, such as riding the bike to work, were allowed. In cases where there were 1 or more missing measurements during a day, the data for that particular day were not used for construction of an average daylong TGc profile. The mean daylong TGc profile was used for statistical analysis.

Dietary Intake

Dietary intake and time of intake were accurately recorded in a diary. Subjects did not receive recommendations concerning the frequency and composition of the meals and were requested to use their regular diet during the study. Quantities of intake were estimated according to instructions given by a dietician and according to a table with standardized portion sizes.[21,26] Particularities, such as illness, were also recorded. The diaries were evaluated by a trained physician together with each subject individually. Foods consumed were converted into nutrients with a release of the Dutch Nutrient Data Base.[21,26] Dietary intake was calculated as an average of 3 days. Mean absolute intake and intake as percentage of total energy intake were used for statistical analysis.

Analytical Determinations

Fasting blood was collected at inclusion after a 12-hour fast for measurement of lipids, apolipoproteins, insulin, and glucose from plasma. Cholesterol and TG in plasma and HDL cholesterol (obtained after precipitation with dextransulphate/$MgCl_2$) were determined using a Vitros 250 analyzer (Johnson & Johnson, Rochester, NY). Plasma apolipoprotein B (apo B) was measured by nephelometry using apo B monoclonal antibodies (Behring Diagnostics NV, OSAN 14/15). Plasma apo AI was measured by nephelometry using apo AI monoclonal antibodies (Behring Diagnostics NV, OUED 14/15). Plasma glucose was measured by glucose oxidase dry chemistry (Vitros GLU slides) and colorimetry, and insulin was measured by competitive radioimmunoassay with polyclonal antibodies. For estimation of insulin sensitivity in nondiabetic subjects, homeostasis model assessment (HOMA) (= glucose * insulin/22.5) was calculated.[28] LDL cholesterol was calculated using the Friedewald formula. In cases of hypertriglyceridemia (fasting TG $>$ 4.6 mmol/L), LDL cholesterol was measured by ultracentrifuge.

Statistics

Our primary end point was daylong triglyceridemia in type 2 diabetics, obese nondiabetics, and healthy lean subjects. Secondary end points were the determinants of daylong triglyceridemia and the cut-off level for "normal" daylong triglyceridemia.

Data are given as means ($\pm$SD). Daylong TGc profiles were calculated as mean integrated area under the TGc-curve (total daylong triglyceridemia; TGc-AUC). Incremental triglyceridemia (dTGc-AUC) was calculated as mean integrated area under the TGc-curve, after correction for fasting TGc. Differences in diet or TGc-AUC between the 3 separate days were tested by paired *t* test. Comparisons between the 3 groups were performed with repeated measures analysis of variance (ANOVA) with least significance difference test as post hoc analysis test, with Bonferroni correction to the *P* value. Differences between 2 groups were tested by Student's *t* test. Bivariate correlations were calculated using Pearson's correlation coefficients. These calculations were performed for the total group and for the 3 groups separately. All significantly correlated variables were used as independent variables in stepwise multiple regression analysis with TGc-AUC as dependent variable. For this analysis, fasting TGc was used as baseline TG instead of fasting plasma TG. In the case of TG, insulin, and HOMA index, calculations were performed after logarithmic transformation. The cut-off level for "normal" daylong triglyceridemia was defined as the 75th percentile of TGc-AUC in lean subjects. The corresponding fasting TGc concentration was calculated using univariate regression analysis.

For statistical analysis, the SPSS software package (version 10.0; SPSS, Chicago, IL) was used. Calculations of TGc-AUC's were performed with Graph Pad Prism version 3.0 (Graph Pad Software, San Diego, CA) using nonlogarithmic transformed TG concentrations. Statistical significance was reached when $P < .05$ (2-sided).

RESULTS

General Characteristics

Nine-teen type 2 diabetics, 45 obese nondiabetics and 78 lean subjects were included in this study. Group-wise general characteristics of the participants are listed in Table 1. Fasting plasma TG was higher in diabetics and obese nondiabetics than in lean subjects. Obese nondiabetics had elevated HOMA compared with lean subjects. Body composition and fasting plasma lipids and apolipoproteins were comparable between diabetics and obese nondiabetics. Three diabetic subjects were on insulin therapy, 3 were taking metformin.

Daylong TGc Profiles

Mean fasting TGc were not significantly different between diabetics (2.02 $\pm$ 0.78 mmol/L) and obese nondiabetics (2.04 $\pm$ 0.75 mmol/L), but increased in both compared with

Table 1. General Characteristics and Fasting Metabolic Profile of the Study Group

	Diabetic Subjects (n = 19)	Obese Subjects (n = 45)	Lean Subjects (n = 78)	*P* Value From ANOVA
Age (yr)	57.0 (6.3)*	52.5 (9.2)	51.6 (6.3)	<.05
Females/males	7/12	16/29	28/50	NS
Postmenopausal females	6	12	20	NS
Females using OAC	1	0	2	NS
BMI (kg/m^2)	30.6 (5.4)*	29.5 (2.6)*	23.7 (2.2)	<.001
Waist (m)	1.09 (0.14)*	1.03 (0.10)*	0.87 (0.09)	<.001
Systolic BP (mm Hg)	143 (16)*	140 (17)*	127 (17)	<.001
Diastolic BP (mm Hg)	90 (12)	89 (11)	84 (13)	NS
Glucose (mmol/L)	10.74 (3.29)*†	5.62 (0.52)	5.37 (0.56)	<.001
HbA_{1c} (%)	7.52 (0.88)	ND	ND	
Insulin (mU/L)	ND	13.7 (9.7)*	8.4 (4.3)	<.05‡
HOMA	ND	3.40(2.47)*	2.04 (1.23)	<.05‡
Plasma TG (mmol/L)	1.81 (0.79)*	1.77 (0.80)*	1.23 (0.67)	<.001
Cholesterol (mmol/L)	5.38 (1.07)	5.79 (1.20)	5.46 (1.02)	NS
LDL-C (mmol/L)	3.48 (1.13)	3.85 (1.07)	3.66 (0.92)	NS
HDL-C (mmol/L)	1.18 (0.35)	1.09 (0.32)	1.25 (0.31)†	<.05
Apo AI (g/L)	1.39 (0.27)	1.30 (0.26)	1.40 (0.22)	NS
Apo B (g/L)	1.01 (0.24)	1.08 (0.26)	0.96 (0.25)	*P* = .07

NOTE. N = 142; data are mean (±SD).

Abbreviations: NS, not significant; ND, not determined; OAC, oral anticontraceptive drug.

*$P < .05$ *v* lean subjects.

†$P < .05$ *v* obese subjects.

‡Analyzed by Student's *t* test.

lean subjects (1.46 ± 0.76 mmol/L, $P < .001$ for each). In 11 subjects, mean daylong TGc profiles were based on 2 instead of 3 days, due to missing TGc values on 1 day. The distribution of these missing days occurred equally among all groups. TGc increased after each eating occasion during the day (Fig 1). The largest TGc increase in diabetics and obese nondiabetics was seen after lunch (from 2.18 ± 0.85 to 2.74 ± 1.04 mmol/L and from 2.18 ± 0.81 to 2.67 ± 0.89 mmol/L, respectively, $P <$ .001 for both) and in lean subjects after dinner (from 1.89 ± 1.01 to 2.27 ± 1.06 mmol/L, $P < .001$). All TGc concentrations during the day were significantly higher than the fasting concentrations in each group. Diabetics and obese nondiabetics had a significantly higher TGc-AUC (35.0 ± 12.1 and 35.2 ± 10.6 mmol · h/L, respectively) than lean subjects (25.5 ± 12.0 mmol · h/L, $P < .001$ for each). There was no significant difference in TGc-AUC between diabetics and obese nondiabetics. dTGc-AUC was not significantly different between diabetics, obese nondiabetics, and lean subjects (6.7 ± 5.2, 6.8 ± 6.8, and 5.1 ± 5.9 mmol · h/L, respectively). The cut-off level for "normal" TGc-AUC was 30.7 mmol · h/L and corresponded with fasting TGc of 1.8 mmol/L (eg, 1.6 mmol/L in plasma), calculated using univariate regression analysis.

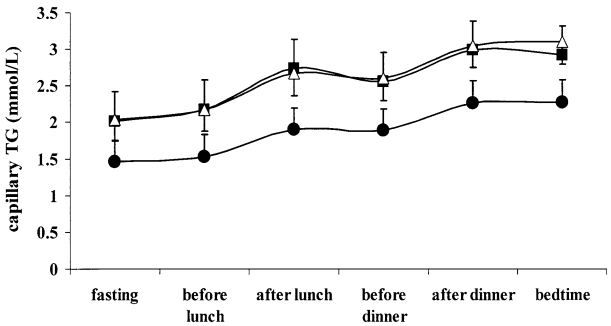

Fig 1. Mean daylong capillary triglyceride profiles in diabetic subjects (■), obese nondiabetic subjects (△), and lean subjects (●). Data are mean ± SD. All TGc concentrations were significantly higher in diabetic and nondiabetic subjects compared with lean subjects.

Dietary Intake

The mean absolute food intake and intake as percentage of total energy intake are shown in Table 2. Total energy intake was not significantly different between diabetics, obese nondiabetics, and lean subjects. Lean subjects reported a higher absolute carbohydrate intake compared with diabetic subjects. There were no significant differences in intake of other nutrients between the groups. All subjects reported 3 eating occasions; breakfast, lunch, and dinner. There was little variation in the intake of snacks. In each group, there were no significant differences in dietary intake between the 3 different measurement days (data not shown).

Determinants of Daylong Triglyceridemia

Pearson's correlation coefficients between TGc-AUC and other variables are shown in Table 3. In each group, fasting TGc was the variable best related to TGc-AUC. When the whole group was taken together, this association persisted.

Using stepwise multiple regression analysis, fasting TGc (standardized $\beta = 0.73$), BMI ($\beta = 0.14$), total cholesterol ($\beta = 0.15$), and HDL cholesterol ($\beta = -0.11$) were the parameters included in the model, explaining 77% of the variation (Fig 2). Stepwise multiple regression analysis with exclusion of fasting TG showed that systolic blood pressure ($\beta =$

Table 2. Dietary Intake of the Study Group (n = 142)

	Diabetic Subjects (n = 19)	Obese Subjects (n = 45)	Lean Subjects (n = 78)	*P* Value From ANOVA
Total energy (kJ/d)	7,829 (1,297)	8,307 (2,016)	9,014 (2,200)	NS
Total fat (g/d)	74.5 (15.8)	73.5 (23.3)	80.4 (22.1)	NS
% TEI	36.1 (4.8)	33.4 (6.1)	34.1 (6.3)	NS
Saturated fat (g/d)	26.7 (5.4)	28.4 (9.5)	29.6 (8.9)	NS
% TEI	13.0 (2.1)	13.1 (3.4)	12.6 (3.1)	NS
Monounsaturated fat (g/d)	28.4 (6.9)	27.4 (9.6)	30.2 (9.6)	NS
% TEI	13.7 (2.4)	12.4 (2.7)	12.7 (3.0)	NS
Polyunsaturated fat (g/d)	13.7 (5.0)	12.6 (5.6)	14.0 (5.5)	NS
% TEI	6.6 (1.9)	5.7 (2.2)	5.9 (2.0)	NS
Carbohydrates (g/d)	195 (37)*	217 (66)	244 (66)	<.01
% TEI	42.4 (4.7)	43.9 (8.8)	46.1 (6.5)	NS
Protein (g/d)	88.1 (16.4)	92.5 (22.5)	89.2 (18.4)	NS
% TEI	19.3 (2.9)	20.0 (8.7)	17.5 (3.7)	NS
Alcohol (g/d)	8.3 (12.6)	12.1 (17.2)	15.6 (19.1)	NS
Cholesterol (mg/d)	178 (67)	186 (80)	174 (82)	NS

NOTE. N = 142; data are mean (SD).
Abbreviation: % TEI, intake as percentage of total energy intake.
*$P < .05$ *v* lean men.

0.35), waist circumference ($\beta = 0.26$), HDL cholesterol ($\beta = -0.34$), and total cholesterol ($\beta = 0.29$) were included in the model, predicting 65% of the variation. Similar results were found when lean subjects were not included in this analysis. Stepwise multiple regression analysis with fasting plasma TG as dependent variable revealed that systolic blood pressure ($\beta = 0.15$), HDL-cholesterol ($\beta = -0.86$), total cholesterol ($\beta = 0.27$), and LDL-cholesterol ($\beta = 0.22$) predicted 90% of the variation.

DISCUSSION

Metabolic ward studies have shown that both type 2 diabetics and obese nondiabetics are characterized by postprandial hyperlipidemia compared with healthy subjects.[17-20] However, direct comparisons between groups matched for BMI, with and without diabetes, are scarce. In our study, daylong triglyceridemia was similarly disturbed in diabetic and nondiabetic obese subjects compared with lean controls, suggesting that obesity largely determines postprandial lipemia in both disorders, probably by its effect on fasting TG, which were similarly elevated in both groups.

Fasting plasma hypertriglyceridemia is a risk factor for CVD, even in a range previously considered to be normal (between 1.00 and 1.84 mmol/L).[1-3] However, humans are nonfasting most of the day, and there is emerging evidence that enhanced postprandial lipemia may result in accelerated atherosclerosis. In the Physicians Health Study, plasma TG levels 3 to 4 hours after a meal distinguished better between cases with future myocardial infarction and controls than fasting plasma TG levels.[29] In agreement with the postulate of Zilversmit[30] that atherogenesis is a postprandial phenomenon, risk assessment using nonfasting TG could be useful in clinical practice. A possible mechanism leading to atherosclerosis in hypertriglyceridemic patients may be exaggerated and prolonged post-

Table 3. Pearson's Correlation Coefficients Between Total Daylong Triglyceridemia (TGc-AUC) and Other Variables

	Total Group (n = 142)	Diabetic Subjects (n = 19)	Obese Subjects (n = 45)	Lean Subjects (n = 78)
Fasting plasma TG	0.74*	0.73*	0.79*	0.65*
Fasting capillary TG	0.87*	0.87*	0.79*	0.87*
Cholesterol	0.24†	0.13	0.23	0.34†
LDL cholesterol	0.16	0.04	0.09	0.27‡
HDL cholesterol	−0.41*	−0.73*	−0.31‡	−0.31†
Apo AI	−0.35*	−0.40‡	−0.40‡	−0.26‡
Apo B	0.41*	0.04	0.26 ($P = .1$)	0.47†
BMI	0.45*	0.39‡	0.15	0.32†
Waist circumference	0.51*	0.50‡	0.27 ($P = .09$)	0.41*
Systolic blood pressure	0.50*	0.25	0.65*	0.33†
Diastolic blood pressure	0.43*	0.65†	0.54*	0.24‡
Insulin	0.38*	–	0.30‡	0.30†
HOMA	0.32*	–	0.31‡	0.28†
HbA_{1c}	–	0.22	–	–

NOTE. Fasting insulin and HOMA were determined in nondiabetic subjects only.
*$P < .001$; †$P < .01$; ‡$P < .05$.

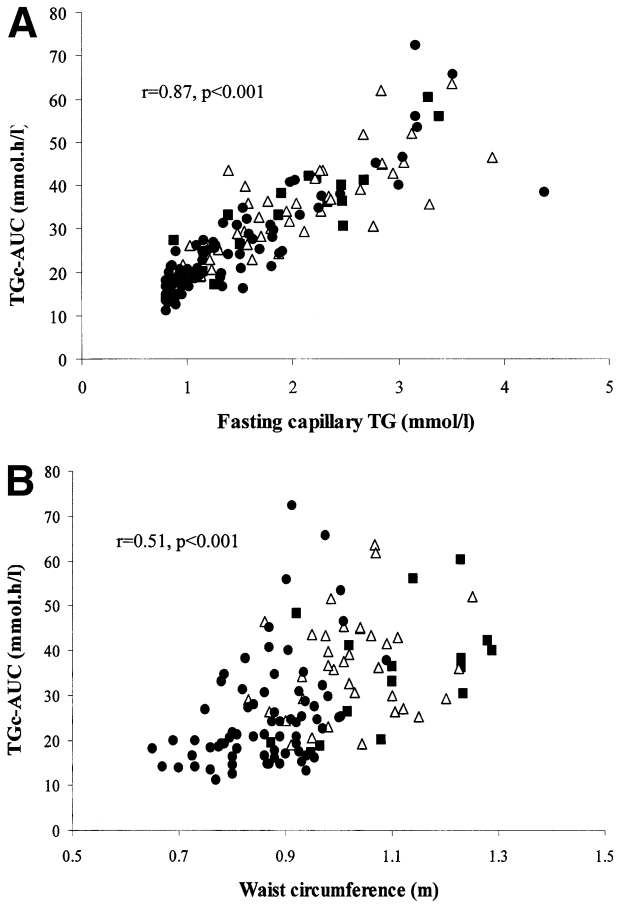

Fig 2. Association between daylong triglyceridemia and (A) fasting TGc and (B) waist circumference diabetic subjects (■), obese nondiabetic subjects (△), and lean subjects (●). Pearson's correlation coefficients (*r*) are given.

prandial hyperlipidemia with accumulation of remnants of TG-rich particles. It has been shown that both, apo B48- and apo B100-containing particles penetrate the vessel wall.[31] Accumulation of these particles in the subendothelial space may promote atherosclerosis by the formation of fatty streaks.[7,8,31]

Recently, a novel method has been introduced for the evaluation of TG changes during the day using serial capillary self-measurements with a TGc-analyzer in an outpatient, uncontrolled setting.[21-26] Daylong TGc profiles are closely related to postprandial lipemia as assessed by standardized oral fat loading tests and can easily be applied in clinical practice for routine screening of populations.[21,25] Daylong TGc profiles may help to detect groups at risk for atherosclerosis on the basis of disturbed TG metabolism. Repeated measurements of daylong triglyceridemia were less variable than repeated measurements of fasting and postprandial capillary TG in normolipidemic subjects and in subjects with familial combined hyperlipidemia.[21,32] In healthy normolipidemic males, daylong TGc profiles were associated with insulin sensitivity, body composition, and diet, but age was not a major determinant.[25] Therefore, we believe that the small difference in age between diabetics and lean subjects in our study may not have led to an overestimation of TGc-AUC in diabetic subjects. In this study, mean fasting TGc was slightly higher than mean fasting plasma TG, which is in concordance with previous reports. One of the explanations is that fasting TGc was measured on different days than plasma TG. Additionally, fasting plasma TG was measured after a 12-hour overnight fast, whereas fasting TGc was measured after waking up, without dietary restrictions on the previous evening. Finally, different groups have found that simultaneous plasma and TGc measurements differ by 0.2 to 0.3 mmol/L.[21-26,32]

TG concentrations vary considerably throughout the day, mainly because of food intake. The effects of different nutritional components on postprandial TG have been widely investigated in metabolic ward studies using meals with different nutritional compositions. When tested after oral fat loads, the magnitude of postprandial lipemia increases stepwise with the fat content of the meal.[33] However, food intake usually consists of a mixture of different nutritional components, and acute oral tests with mixed meals have shown that the degree of postprandial lipemia is also significantly influenced by the carbohydrate content of the meal.[34,35] Moreover, both fasting and postprandial TG concentrations in healthy volunteers were significantly higher 2 weeks after consumption of high-carbohydrate, low-fat diets than after consumption of low-carbohydrate, high-fat diets.[36] These results have been confirmed by our group, showing that incremental daylong triglyceridemia was best associated with the carbohydrate content of the diet in healthy, free-living males.[26]

In our study, self-reported energy intake tended to be higher in lean subjects than in the other groups, despite a lower weight in the former. This could be explained by several factors, such as differences in genetic predisposition to obesity and physical (in)activity.[37-39] In addition, all diabetic subjects received dietary recommendations from the practitioner, which may have influenced the reported energy intake. Finally, it is known that obese subjects are more likely than normal-weight subjects to underreport their food intake.[40] Selective underreporting of fat intake has also been observed in obese individuals.[40] Lean subjects reported a higher carbohydrate intake than diabetics. Because incremental triglyceridemia is associated with carbohydrate intake and not with fat intake in healthy non-obese men,[26] possible underreporting of fat intake in obese subjects was probably not a major confounding factor. Nevertheless, we cannot fully exclude that underreporting has been a confounding factor in our study.

Metabolic ward studies have demonstrated increased fasting and postprandial TG in both, diabetics and obese nondiabetics compared with healthy lean controls.[17-20] The results of the present study are in line with those observations and extend those results showing that daylong triglyceridemia is similarly disturbed in diabetic and nondiabetic obese subjects in an uncontrolled, real life situation. It is known that cardiovascular risk factors are present before the onset of clinical diabetes, especially increased TG levels and decreased HDL cholesterol.[12,13,41] The existence of a possible atherogenic prediabetic state suggests a common metabolic disorder in both type 2 diabetes and obesity. Most investigators believe that insulin resistance may be the common metabolic disorder, and this may largely determine daylong triglyceridemia in both disor-

ders. In insulin resistance, reduced inhibition of adipose tissue hormone sensitive lipase (HSL) results in increased flux of free fatty acids (FFA) to the liver.[42] Increased substrate availability and reduced inhibition of very–low-density lipoprotein (VLDL) secretion causes overproduction of VLDL-TG-rich particles.[43] Increased competition of VLDL-TG with dietary TG (transported in chylomicrons) for the same clearance mechanism (eg, endothelium-bound lipoprotein lipase [LPL]) may result in exaggerated and prolonged postprandial hypertriglyceridemia. In a previous study, we found a significant association between insulin sensitivity and daylong triglyceridemia in healthy men.[25] The association in the present study between HOMA and TGc-AUC in nondiabetic subjects supports those results. Visceral adiposity may be an especially important factor linking insulin resistance with postprandial hyperlipidemia, as suggested by the strong correlation between the waist circumference and daylong triglyceridemia. Excessive FFA flux from intra-abdominal fat into the liver may cause overproduction of VLDL particles.[43-45] Furthermore, LPL activity and mass in plasma are inversely associated with intra-abdominal fat accumulation.[46]

Fasting TG were the variable best associated with postprandial lipemia, which is in agreement with other reports.[21,25] Fasting TG were similarly increased in diabetics and obese nondiabetics compared with lean subjects. This was also the case for daylong triglyceridemia. Clearly, elevated daylong triglyceridemia in both diabetics and obese nondiabetics could have been predicted by fasting plasma TG levels. However, the cut-off level for "normal" TG remains a matter of debate. The National Cholesterol Education Program (NCEP) has endorsed a cut-off level for "normal" fasting plasma TG (1.7 mmol/L), which corresponds more or less with the 75th percentile of the American population aged 20 years and older.[47] We defined a cut-off level for "normal" daylong triglyceridemia by calculating the 75th percentile of TGc-AUC in healthy lean subjects. This cut-off level (30.7 mmol · h/L) corresponded with fasting TGc of 1.8 mmol/L (eg, 1.6 mmol/L in plasma, taking the known difference between plasma and capillary TG concentrations into account), calculated using univariate regression analysis. Our data suggest that decreasing fasting TG below this concentration may normalize postprandial lipemia.

In conclusion, the present study provides information on fasting and daylong TG concentrations in diabetics, obese nondiabetics, and lean subjects in a physiologic, real life situation. Daylong triglyceridemia is similarly increased in diabetic and nondiabetic obese subjects compared with lean subjects. Fasting TG and central obesity largely determine daylong triglyceridemia, independent of the presence of type 2 diabetes. Reducing fasting plasma TG below 1.6 mmol/L may lead to a normalization of postprandial lipemia.

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