Distinctive postprandial modulation of β cell function and insulin sensitivity by dietary fats: monounsaturated compared with saturated fatty acids

Sergio López, Beatriz Bermúdez, Yolanda M Pacheco, José Villar, Rocío Abia, and Francisco JG Muriana

ABSTRACT

Background: Exaggerated and prolonged postprandial triglyceride concentrations are associated with numerous conditions related to insulin resistance, including obesity, type 2 diabetes, and the metabolic syndrome. Although dietary fats profoundly affect postprandial hypertriglyceridemia, limited data exist regarding their effects on postprandial glucose homeostasis.

Objective: We sought to determine whether postprandial glucose homeostasis is modulated distinctly by high-fat meals enriched in saturated fatty acids (SFAs) or monounsaturated fatty acids (MUFAs).

Design: Normotriglyceridemic subjects with normal fasting glucose and normal glucose tolerance were studied. Blood samples were collected over the 8 h after ingestion of a glucose and triglyceride tolerance test meal (GTTTM) in which a panel of dietary fats with a gradual change in the ratio of MUFAs to SFAs was included. On 5 separate occasions, basal and postprandial concentrations of glucose, insulin, triglyceride, and free fatty acids (FFAs) were measured.

Results: High-fat meals increased the postprandial concentrations of insulin, triglycerides, and FFAs, and they enhanced postprandial β cell function while decreasing insulin sensitivity (as assessed with different model-based and empirical indexes: insulinogenic index, insulinogetic index/homeostasis model assessment of insulin resistance, area under the curve for insulin/area under the curve for glucose, homeostasis model assessment for β cell function, and GTTTM-determined insulin sensitivity, oral glucose insulin sensitivity, and the postprandial Belfiore indexes for glycemia and blood FFAs). These effects were significantly ameliorated, in a direct linear relation, when MUFAs were substituted for SFAs.

Conclusions: The data presented here suggest that β cell function and insulin sensitivity progressively improve in the postprandial state as the proportion of MUFAs with respect to SFAs in dietary fats increases. Am J Clin Nutr 2008;88:638–44.

INTRODUCTION

The loss of β cell function and insulin sensitivity is known to contribute to the development of diabetes. This metabolic disorder develops over a course of months to years, and a variety of methods have been used to determine its occurrence and to predict the onset of clinical symptoms. The homeostasis model assessment (HOMA) of β cell function (HOMA-B) and of insulin resistance (HOMA-IR) from basal plasma glucose and insulin concentrations is now a widely used clinical and epidemiologic tool. However, this only shows what is occurring with glucose homeostasis in the fasting state (1). Alternatively, euglycemic clamps or frequently sampled intravenous glucose tolerance tests (FSIVGTTs) are the reference methods used to determine β cell sensitivity to glucose and the sensitivity of body tissues to insulin (2). However, these tests are far from physiologic because insulin secretion or activity is only measured in the steady state. Empirical and model-based indexes based on the oral-glucose-tolerance test (OGTT) provide a reasonable approximation of postprandial β cell function and whole-body insulin sensitivity (3). However, an important caveat of the OGTT is that the events associated with the ingestion of a pure glucose solution are not wholly equivalent to the numerous metabolic events associated with eating a mixed meal when both carbohydrates and fats are ingested. It has been hypothesized that insulin resistance syndromes might be a postprandial phenomenon linked to acute dietary fat metabolism, as recently suggested from FSIVGTT data (4). Exaggerated postprandial hypertriglyceridemia is indeed an inherent feature of diabetic dyslipidemia and it is frequently found even in diabetic patients with normal fasting triglyceride concentrations (5–7). There is also strong evidence that saturated fatty acids (SFAs) selectively desensitize the response of peripheral tissue to insulin, whereas unsaturated fatty acids (including monounsaturated fatty acids; MUFAs) may counteract this effect (8, 9). Such phenomena would be in accordance with studies linking the nature of dietary fats to dysfunctions in insulin secretion and the frequency of type 2 diabetes (10, 11). However, it remains unclear to what extent the degree of unsaturation of dietary fatty acids influences the postprandial control of insulin secretion and resistance, even in healthy subjects. Therefore, we investigated whether the indexes of β cell function and insulin sensitivity could postprandially discriminate the influence of 1 From the Cellular and Molecular Nutrition, Instituto de la Grasa (CSIC), Seville, Spain (SL, BB, YMP, RA, and FJGM), and the Internal Medicine Service, University Hospital “Virgen del Rocío,” Seville, Spain (JV).

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dietary fats supplied simultaneously to a single individual in conjunction with a relatively low carbohydrate load from a test meal similar to an OGTT, which we named the glucose and triglyceride tolerance test meal (GTTTM). This novel test was relatively low in carbohydrates to exclude the side effects of carbohydrates on dietary fat–derived postprandial events (12). The data were obtained each hour over the 8 h after the administration of the GTTTM to 14 normotriglyceridemic subjects with normal fasting glucose and normal glucose tolerance. Initially, 2 dietary fats rich in MUFAs or SFAs were included in the GTTTM, and, thereafter, a panel of different dietary fats with a gradual change in the ratio of MUFAs to SFAs was used.

SUBJECTS AND METHODS

Subjects

Studies were performed in 14 healthy men whose mean (± SD) age was 27 ± 7 y and BMI (in kg/m²) was 23.9 ± 1.9. All subjects had a normal blood count and serological measures, and they took no medication known to affect lipoprotein metabolism or insulin secretion or its activity. All protocols were approved by the local institutional review board (Ethics Committee of the University Hospital “Virgen del Rocío,” Seville, Spain), and written consent was obtained from each participant. The study was conducted according to the principles expressed in the Helsinki Declaration.

Experimental design

The study had a single-blind, randomized, within-subject crossover design in which the subjects attended a Research (Internal Medicine) unit at the University Hospital “Virgen del Rocío” on 5 separate occasions (13). Fasting (0 min) blood samples were collected at 0800 after the subjects had fasted overnight for 12 h. The subjects then ingested, within 15 min, a fat–rich meal consisting of dietary fat [50 g/m² body surface area of butter, refined olive oil (ROO), high-palmitic sunflower oil (HPSO) or a mixture of vegetable and fish oils (VEFO)] along with a portion of plain pasta (30 g/m² body surface area), one slice of brown bread, and one container of skim yogurt]. The fatty acid composition of the high-fat meals was as described previously (13), and the ratios of MUFAs to SFAs were 0.48 (Butter meal), 2.42 (HPSO meal), 5.43 (ROO meal), and 7.08 (VEFO meal). To avoid aberrant lipid metabolism that could interfere with postprandial triglyceride handling (12), the glycemic index of the carbohydrate-containing foods (14) and the glycemic load of the meals was low, ≈20 (25% of the glycemic load of 75-g OGTT; see details in “Supplemental data”). The average total energy provided by the meals was ≈800 kcal (≈10 kcal/kg), and the macronutrient profile was as follows: 72% fat, 22% carbohydrate, and 6% protein (see Table S1 under “Supplemental data” in the online issue). The subjects also consumed the same test meal containing no fat as a control meal.

After ingestion of the meal, blood samples were collected in tubes containing EDTA each hour to measure glucose, insulin, triglyceride, and FFA concentrations over 8 h. Thus, 9 blood samples were collected over a 480-min period after the ingestion of a mixed meal—a protocol that was named GTTTM. In this study, each participant served as his own control. For the terminology and definitions used and to show how some empirical indexes of β cell function and insulin sensitivity were calculated, see “Supplemental data.”

Biochemical determinations

Plasma glucose and triglyceride concentrations were measured on a Hitachi Modular Analytics D-2400 analyzer (Roche Diagnostics, Basel, Switzerland) using commercially available reagents and an enzyme-based kit. Plasma insulin was measured using a specific enzyme-linked immunosorbent assay (Dako, Cambridge, United Kingdom) on a Hitachi Modular Analytics E-170 analyzer. Plasma FFA concentrations were measured by using an ACS-ACOD assay (Wako Chemicals GmbH, Neuss, Germany) on a COBAS Mira-Plus analyzer (Roche Diagnostics, Basel, Switzerland).

β Cell function

Of the empirical indexes of β cell function, the insulinogenic index (IGI) is a surrogate measure of first-phase insulin secretion (15), and it was calculated as the difference between the postprandial insulin peak (measured at 60 min) and basal insulin in relation to the difference in glucose (IGI = ∆I₁₀–₆₀/∆G₁₀–₆₀). We also calculated the ratio of the IGI to the HOMA-IR, which gives an adjusted measure of β cell function that accounts for variations in insulin sensitivity (16). The ratio of the insulin to glucose areas under the curve (AUC₁₀/AUC₆₀) is significantly correlated with glucose sensitivity (P < 0.0001) and it is a sophisticated parameter that describes the secretory process of β cells (17). Finally, the HOMA-B as I₀ × 3.33/(G₀ – 3.5) was also used (17), and we assessed β cell function during the GTTTM by extending the values of HOMA-B to those at 60 min.

Basal insulin resistance and sensitivity measurements

We used 3 surrogate measures of insulin-mediated glucose disposal: 1) HOMA-IR (I₀ × G₀/22.5, 18), 2) the revised-quantitative insulin sensitivity check index (rQUICKI = 1/[log I₀ + log G₀ + log FFA₀]) (19), and 3) the basal insulin sensitivity (IS) index (IS₀) for glycemia and blood FFAs proposed by Belfiore et al (20; see details in “Supplemental data”).

Postprandial insulin sensitivity

We used 3 surrogate indexes of IS during the GTTTM: 1) an IS index (IS₁₀–₆₀) according to an integral equation model proposed by Caumo et al (21), 2) an oral glucose IS index (OGIS₁₀–₆₀) proposed by Mari et al (17), and 3) the postprandial IS index (ISI₀–₆₀) for glycemia and blood FFAs proposed by Belfiore et al (20). Such indexes were denoted as IS₁₀–₆₀, OGIS₁₀–₆₀, and ISI₀–₆₀, respectively (see details in “Supplemental data”).

Statistical analysis

The summary data (the fasting and postprandial response) for glucose, insulin, triglycerides, and FFAs were analyzed by using one-factor repeated-measures analysis of variance. The postprandial time courses after the test meals were analyzed by using 2-factor repeated-measures analysis of variance with interaction, and a Bonferroni correction was applied for the post hoc detection of significant pairwise differences. The AUCs were calculated for glucose, insulin, triglycerides, and FFAs with the trapezoidal rule (22). A Pearson correlation was used to explore the strength of the association between postprandial estimates of β cell function and insulin sensitivity with the ratio of MUFAs to SFAs in dietary fats.
RESULTS

Basal characteristics of the study subjects

There were no differences in the mean plasma glucose, insulin, triglyceride, and FFA concentrations between the subjects at fasting (see Table S2 under “Supplemental data” in the online issue). Likewise, we found no significant differences in the basal values for HOMA-B (Figure 1), HOMA-IR, rQUICKI, and the basal Belfiore indexes for glycemia and blood FFAs (see Figure S1 under “Supplemental data” in the online issue). These data indicated that the subjects had a similar basal β cell function and insulin sensitivity before ingesting the GTTMM.

GTTMM

The mean plasma glucose, insulin, triglyceride, and FFA concentrations during the GTTMM were measured (Figure 2), and, as expected, the control meal did not induce any postprandial lipemic response. The postprandial glucose response was similar after ingestion of the control, ROO, Butter, HPSO, and VEFO meals. However, the fat-enriched meals significantly increased the AUC for insulin from 19 960 ± 2766 pmol · min⁻¹ · L⁻¹ after the control meal, to 29 619 ± 4975 pmol · min⁻¹ · L⁻¹ after the MUFA-enriched (ROO) meal, and to 37 582 ± 4364 pmol · min⁻¹ · L⁻¹ after the SFA-enriched (Butter) meal (P < 0.01). Similarly, triglycerides increased from 390 ± 54 mmol · min⁻¹ · L⁻¹ after the control meal, to 593 ± 69 mmol · min⁻¹ · L⁻¹ after the MUFA-enriched (ROO) meal, and to 757 ± 78 mmol · min⁻¹ · L⁻¹ after the SFA-enriched (Butter) meal (P < 0.001). FFAs also increased, from 160 800 ± 24 971 μmol · min⁻¹ · L⁻¹ after the control meal, to 205 200 ± 22 793 μmol · min⁻¹ · L⁻¹ after the MUFA-enriched (ROO) meal, and to 276 600 ± 19 574 μmol · min⁻¹ · L⁻¹ after the SFA-enriched (Butter) meal (P < 0.001); see Table S1 under “Supplemental data” in the online issue. After the VEFO meal, the AUC for insulin was 27 970 ± 2107 pmol · min⁻¹ · L⁻¹ (P < 0.01 compared with the HPSO and Butter meals), for triglycerides was 609 ± 76 mmol · min⁻¹ · L⁻¹ (P < 0.01 compared with the HPSO and Butter meals), and for FFAs was 200 400 ± 17 050 μmol · min⁻¹ · L⁻¹ (P < 0.01 compared with the HPSO and Butter meals). Similarly, the AUC for insulin after the HPSO meal was 34 749 ± 1167 pmol · min⁻¹ · L⁻¹ (P < 0.01 compared with the ROO meal), while it was 556 ± 38 mmol · min⁻¹ · L⁻¹ for triglycerides (P < 0.001 compared with the Butter meal), and 231 222 ± 11 007 μmol · min⁻¹ · L⁻¹ for FFAs (P < 0.001 compared with the Butter meal). All of these effects were proportional to the ratio of MUFAs to SFAs in the dietary fats. Accordingly, the AUC for insulin and FFAs were positively and well correlated (P < 0.001) with the AUC for triglycerides (Figure 3).

When the empirical indexes of postprandial β cell function were assessed (Figure 1), all of these indexes were significantly higher after the high-fat meals than after the control meal (P < 0.01), including the IGI, IGI/HOMA-IR, and AUC₁/AUCₐ during the 0–120- and 0–480-min GTTMM and the HOMA-B at the 60-min GTTMM. These indexes increased in conjunction with the increase in the proportion of SFAs in the dietary fats.

When estimates of postprandial insulin sensitivity were analyzed (Figure 4), we found significantly lower values (P < 0.001) for iSGTTTM, OGTTGTTMM, and the postprandial Belfiore indexes for glycemia and blood FFAs after the high-fat meals than after the control meal. These estimates decreased in conjunction with the amount of SFAs in the dietary fats.

All of the indexes calculated for β cell function and insulin sensitivity during the GTTMM (Table 1) showed a strong and significant correlation with the ratio of MUFAs to SFAs in the dietary fats (P < 0.001; Table 2).

FIGURE 1. Indexes of β cell function reported as means ± SDs. A: insulinogenic index (IGI = Δ[Insulin]/Δ[Glucose]) and IGI/homoeostasis model assessment (HOMA) of insulin resistance (IR) (× 5⁻¹) at 0–60 min; B: ratio of the area under the curve (AUC) for insulin to the AUC for glucose at 0–120 and 0–480 min; and C: HOMA for β cell function (HOMA-B) at 0 and 60 min. The data were collected before and after the ingestion of a glucose and triglyceride tolerance test meal (GTTMM) with no fat (control meal), enriched in monounsaturated fatty acids (MUFAs) from refined olive oil (ROO meal), or enriched in saturated fatty acids (SFA; Butter meal). a: 14. Statistical differences are based on repeated-measures ANOVA with Bonferroni correction. Lowercase letters in a box are equally used for black or gray bars. Bars with a different lowercase letter are significantly different at P < 0.05. There were no significant differences between groups at 0 min for HOMA-B.
DISCUSSION

Our study used mixed meals containing common foods, which provided the same relative but low amount of carbohydrates to circumvent the confounding and masking effects of adding carbohydrates to a high-fat meal (12). These meals were administered in the presence or absence of dietary fats after an oral challenge (GTTTM). More importantly, we compared isocaloric mixed meals with the same nutrient distribution but with different proportions of MUFAs and SFAs. Subjects showed similar fasting insulin sensitivities on the basis of HOMA-IR, rQUICKI, and basal Belfiore indexes for glycemia and blood FFAs, and all of the meals elicited superimposable postprandial glucose responses. However, we found that 1) a high-fat meal increased postprandial cell function when assessed on the basis of the IGI, IGI/HOMA-IR, AUCI/AUCG, and HOMA-B; 2) a high-fat meal decreased postprandial insulin sensitivity as assessed on the basis of the ISGTTTM, OGISGTTTM, and the postprandial Belfiore indexes for glycemia and blood FFAs; and 3) subjects became less insulin resistant postprandially as the proportion of MUFAs compared with SFAs in dietary fats increased (VEFO/L50140 ROO/L50140 HPSO/L50140 Butter), and this effect was linear. Similarly, we discovered that when the early postprandial insulin response was used as a measure of cell function, it decreased as the ratio of dietary MUFAs to SFAs increased.

Dietary fats, particularly those containing SFAs, are known to potentiate insulin secretion (23) and insulin resistance (24). Indeed, β cells are particularly sensitive to the degree of unsaturation of the fatty acids (8, 25). Here, we show for the first time that the degree of unsaturation of dietary fats modulates cell function and insulin sensitivity acutely, in a situation of low-carbohydrate intake and of lipid-induced β cell compensation for insulin resistance. We found a significant correlation between the AUC for triglycerides and insulin, but there were differences

FIGURE 2. Mean (± SD) plasma glucose, insulin, triglyceride, and free fatty acid (FFA) concentrations during the glucose and triglyceride tolerance test meal (GTTTM) with no fat (control), enriched in monounsaturated fatty acids (MUFAs) from refined olive oil (ROO meal), or enriched in saturated fatty acids (SFA; Butter meal). n = 14. The data were analyzed by simple linear regression, and a Pearson correlation coefficient (r) was determined.

FIGURE 3. Plots and correlations of the mean (± SD) area under the curve (AUC) for triglycerides with the AUC for glucose, insulin (× 50⁻¹), and free fatty acids (FFA; × 5⁻¹) in mmol · min⁻¹ · L⁻¹ after the glucose and triglyceride tolerance test meal (GTTTM) with no fat (control), enriched in monounsaturated fatty acids (MUFAs) from refined olive oil (ROO meal), or enriched in saturated fatty acids (SFA; Butter meal). n = 14. The data were analyzed by simple linear regression, and a Pearson correlation coefficient (r) was determined.

TABLE 1. Slopes and r values for the correlation between the AUC for triglycerides with the AUC for glucose, insulin, and FFA in mmol · L⁻¹ · min⁻¹ after the glucose and triglyceride tolerance test meal (GTTTM) with no fat (control), enriched in monounsaturated fatty acids (MUFAs) from refined olive oil (ROO meal), or enriched in saturated fatty acids (SFA; Butter meal).

<table>
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<td>0.11</td>
<td>NS</td>
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<tr>
<td>Insulin</td>
<td>2.40</td>
<td>0.99</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>FFA</td>
<td>1.56</td>
<td>0.98</td>
<td>&lt; 0.01</td>
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in the hyperinsulinemic postprandial peak to GTTTM when MUFAs and SFAs elicited similar postprandial triglyceride concentrations. It is likely that MUFAs and SFAs could compete at the level of the β cell, in line with a previous model to explain the capacity of fatty acids to trigger insulin secretion by glucose-responsive triglyceride/FFA cycling (26). The islet tissue, which expresses lipoprotein lipase (27), could access postprandial triglycerides as a source of FFAs, such that the FFA type and concentration in the immediate vicinity of the β cells is likely to be dependent on the nature of dietary fats. This system could be linked to the local promotion of both intracellular triglyceride lipolysis (28) and fatty acid esterification (29). FFA deprivation in islet tissue has indeed been reported to impede glucose-stimulated insulin secretion, a process rapidly reversed by replacement with exogenous FFAs (30). There was no temporal relation between the rise in postprandial insulin and FFAs, consistent with the absence of a relation between FFAs and the impairment of early postprandial insulin sensitivity (4). These data emphasize the potential role of postprandial triglycerides to acutely partition FFAs in β cells. The insulinoceptive potential of individual FFAs was previously shown in the perfused pancreas from fasted rats (31). Oleic acid was found to elicit half the insulinoceptive potency of palmitic or stearic acids. Thus, we hypothesize that, when compared with SFAs, MUFAs might moderate the postprandial hyperactivity of β cells, although whether this maintenance of glucose tolerance during feeding periods could prevent or delay the development of overt type 2 diabetes needs to be elucidated.

It is probable that while postprandial insulin sensitivity remains at a peak without the appearance of a prediabetic phase, a less extensive weakening of β cells by the insulin-sparing action of MUFAs would be expected as long as β cell compensation remains adequate. It is also conceivable that the incretin hormones glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinoceptive polypeptide (GIP) may participate in these effects. When compared with SFAs, MUFAs were shown to increase postprandial concentrations of GLP-1 and GIP in healthy subjects and diabetic patients (32, 33). Here, the time course of the glucose response to the MUFA- and SFA-enriched meals did not differ, although the SFA-enriched meal was more insulinotropic than was the MUFA meal. This discrepancy may be at least partially explained by the low carbohydrate content of our novel meal, whereas SFAs and MUFAs might express lipoprotein lipase (27), could access postprandial triglycerides as a source of FFAs, such that the FFA type and concentration in the immediate vicinity of the β cells is likely to be dependent on the nature of dietary fats. This system could be linked to the local promotion of both intracellular triglyceride lipolysis (28) and fatty acid esterification (29). FFA deprivation in islet tissue has indeed been reported to impede glucose-stimulated insulin secretion, a process rapidly reversed by replacement with exogenous FFAs (30). There was no temporal relation between the rise in postprandial insulin and FFAs, consistent with the absence of a relation between FFAs and the impairment of early postprandial insulin sensitivity (4). These data emphasize the potential role of postprandial triglycerides to acutely partition FFAs in β cells. The insulinoceptive potential of individual FFAs was previously shown in the perfused pancreas from fasted rats (31). Oleic acid was found to elicit half the insulinoceptive potency of palmitic or stearic acids. Thus, we hypothesize that, when compared with SFAs, MUFAs might moderate the postprandial hyperactivity of β cells, although whether this maintenance of glucose tolerance during feeding periods could prevent or delay the development of overt type 2 diabetes needs to be elucidated.

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In a setting of early postprandial hyperinsulinemia, the suppression of peripheral lipolysis reduces FFA concentrations (34). However, a serious breakdown in lipid dynamics, often reflected by elevated concentrations of triglycerides and FFAs, can have devastating consequences on glucose homeostasis at a later postprandial stage. It has been shown that artificial elevation of plasma triglycerides and FFAs in healthy humans induces adverse structural (35) and functional (36) changes in muscles and significant suppression of insulin-mediated glucose disposal (37) 4–5 h after lipid or heparin infusion. Through the GTTTM, we found a significant increase in the postprandial values for triglycerides and FFAs several hours after ingestion of the SFA-enriched meal, as shown previously (38, 39). These increases raise the possibility of primary defects in muscle and other organs.

**FIGURE 4.** Indexes of insulin sensitivity reported as means ± SDs. A: insulin sensitivity (IS); B: oral glucose IS index (OGIS) determined by using the 3-h OGIS equation; C: postprandial insulin sensitivity index (ISI) for glycemia; D: postprandial ISI for blood free fatty acids (FFAs). The data were collected after the glucose and triglyceride tolerance test meal (GTTTM) with no fat (control), enriched in monounsaturated fatty acids (MUFAs) from refined olive oil (ROO meal), or enriched in saturated fatty acids (SFA; Butter meal); n = 14. Statistical differences are based on repeated-measures ANOVA with Bonferroni correction. Bars with a different lowercase letters are significantly different at P < 0.05. See Table 1 for units.
TABLE 1
Mean data from the VEFO, ROO, HPSO, and Butter meals for different estimates of postprandial β cell function and insulin sensitivity

<table>
<thead>
<tr>
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<th>VEFO</th>
<th>ROO</th>
<th>HPSO</th>
<th>Butter</th>
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<tbody>
<tr>
<td>IGI (pmol/mmol)</td>
<td>90.2 ± 0.4a</td>
<td>154.5 ± 19.1c</td>
<td>311.6 ± 21.8a</td>
<td>281.3 ± 14.5b</td>
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<td>IGI/HOMA-IR (L/mmol)</td>
<td>7.5 ± 0.6c</td>
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<td>AUC/AUCG 0–120 min (pmol/mmol)</td>
<td>20.1 ± 1.1c</td>
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<td>AUC/AUCG 0–480 min (pmol/mmol)</td>
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<td>HOMA-B 60 min (pmol/mmol)</td>
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<td>ISI(GTTTM) (min−1 × dL × kg−1 μU/mL)</td>
<td>167.2 ± 11.2c</td>
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<td>154.6 ± 8.9d</td>
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<td>OGIS(GTTTM) (mL × m−3 × min−1)</td>
<td>311.1 ± 15.6c</td>
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<td>287.0 ± 18.4b</td>
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<td>ISI(GTTTM)</td>
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TABLE 2
Correlation coefficients obtained by a simple linear regression analyses between the ratio of MUFAs to SFAs during the GTTTM (7.08, 5.43, 2.42, and 0.48 for the VEFO, ROO, HPSO, and Butter meals, respectively) and different estimates of postprandial β cell function and insulin sensitivity

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REFERENCES
7. Schaefer EJ, McNamara JR, Shah PK, et al. Framingham Offspring Study: elevated remnant-like particle cholesterol and triglyceride levels by postprandial metabolic handling of triglyceride-rich lipoproteins. In our study, the postprandial FFA concentrations in the late postprandial phase were similar to the usual fasting FFA concentrations observed in obese and type 2 diabetic subjects (40). They are also similar to those reached artificially and shown to significantly impair insulin receptor and insulin receptor substrate (IRS)-1 tyrosine phosphorylation, phosphatidylinositol 3-kinase activity associated with IRS-1, and Akt serine phosphorylation in skeletal muscle (36). When compared with MUFAs, our data showed that SFAs dramatically decreased postprandial insulin sensitivity toward blood FFAs, ie, they reduce postprandial ISI(FFA)GTTTM, which suggests that lower ratios of MUFAs to SFAs in dietary fats could profoundly affect the antilipolytic action of insulin. Nevertheless, the rise in the postprandial FFA concentration could also reflect the slower clearance of apolipoprotein B-48–containing triglyceride-rich lipoproteins in the late postprandial phase (38, 39), which strikingly is associated with the degree of unsaturation of the dietary fats (41).

Thus, our data highlight the need to study the mechanisms and pathways that might account for transient but repetitive (daily) dietary fat–induced postprandial hyperinsulinemia. Such a phenomenon would imply a greater propensity toward new onset diabetes as the insulinemic and lipemic postprandial responses become more pronounced (exaggerated and prolonged). This largely subclinical and silent condition further suggests a new role for lifestyle as a diabetes risk factor and links postprandial metabolism of (saturated) dietary fats and diabetogenic disorders. We conclude that the ratio of MUFAs to SFAs is useful when designing optimal dietary fat intake to reduce postprandial insulin concentrations.