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PAPER

Relationships in women between body mass index and the intravascular metabolism of chylomicron-like emulsions

MRM Oliveira[1] and RC Maranhão[1]*

[1]*Faculty of Pharmaceutical Sciences, and Heart Institute of the Medical School Hospital (INCOR-HCFMUSP), University of São Paulo (USP), São Paulo, Brazil*

OBJECTIVE: To investigate whether increasing body mass index (BMI) produces increasingly intense disturbances in the metabolism of chylomicrons, the lipoproteins that carry the dietary lipids absorbed by the intestine in the circulation.
SUBJECTS: Four groups of 10 normolipidemic nondiabetic women at the normal (BMI $<25\,kg/m^2$), preobese (BMI 25–30), obese (BMI 30–40) and morbid obese (BMI >40).
METHODS: Chylomicron metabolism was studied using the method of triglyceride-rich emulsions that mimic chylomicrons. The chylomicron-like emulsion doubly labeled with ^{3}H-triolein (TO) and ^{14}C-cholesteryl-oleate (CO) was intravenously injected to calculate the plasma fractional clearance rates (FCR, in min^{-1}) by a compartmental analysis model. FCR-TO mirrors both the lipolysis from lipoprotein lipase that the emulsion suffers while still in the circulation, and the triglycerides portion that is not broken down and is removed from the plasma together with the remnant particles. Lipolysis index is calculated subtracting CO from TO areas under the curve.
RESULTS: FCR-TO did not differ among the four groups. The lipolysis index was positively correlated with BMI ($r=0.310$; $P=0.05$). On the other hand, FCR-CO progressively diminished from the normal to the morbid obese group (0.069 ± 0.01; 0.064 ± 0.01; 0.031 ± 0.003; $0.029\pm0.005\,min^{-1}$, respectively, $P=0.003$) and there was a negative correlation between FCR-CO and BMI ($r=-0.388$; $P=0.01$).
CONCLUSION: In obesity, the capacity to break down chylomicron triglycerides by lipoprotein lipase *in vivo* increases, but the ability of the organism to remove the resulting chylomicron remnants particles progressively diminishes as the BMI rises. Remnant accumulation most likely predisposes to coronary artery disease development.
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The increased risk of developing coronary artery diseases in obese subjects may be related, among other causes, to disturbances in the plasma lipoproteins elicited by the weight gain.[1,2] Fasting hypertriglyceridemia is the main dyslipidemia found in obesity. It reflects the plasma accumulation of very-low-density lipoprotein (VLDL), the triglyceride-rich lipoprotein produced by the liver.[3] Low plasma HDL cholesterol may also be found in obese subjects due to the seesaw effect, whereby VLDL and HDL plasma concentration are inversely correlated.[4,5] Owing to the action of transfer proteins, the cholesterol net mass transfer from HDL to VLDL occurs when VLDL concentration increases by mass action law, thus decreasing HDL cholesterol.[5] Furthermore, hepatic lipase is increased in obesity[6] and as this enzyme promotes HDL degradation by the liver, the lipoprotein concentration decreases.[7] Hypertriglyceridemia and low HDL are established risk factors for coronary artery disease. The status in obesity of low-density lipoprotein (LDL) cholesterol is less clear: in some studies it was found increased, while in others it was normal.[1,8] On the other hand, small, dense LDL, which is the LDL subfraction considered as more atherogenic, may be enhanced in obesity.[2]

*Correspondence: Dr RC Maranhão, Laboratório de Lípides, Instituto do Coração do Hospital das Clínicas da FMUSP, Av. Enéas de Carvalho Aguiar, 44-CEP, 05403-000 São Paulo-SP, Brasil.
E-mail: ramarans@usp.br
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The metabolism of chylomicrons, which is much less studied than that of the other lipoproteins due to methodological difficulties, is also altered in obesity.[9–12] Chylomicrons are produced in the intestine from the absorbed dietary fats and undergo two major catabolic events in the blood stream. Firstly, chylomicron particles undergo the action of lipoprotein lipase on the endothelial surface of capillaries. This enzymic action is stimulated by apolipoprotein CII (apo CII), one of the apolipoproteins present on the surface of the lipoprotein particles. Apo CII binds the lipoprotein particle to the enzyme and also stimulates the lipase action. The products of triglyceride hydrolysis, glycerol and fatty acids, are absorbed in several body tissues, especially muscle and adipose tissue, where those compounds may be used immediately as a source of fuel or re-esterified and stored.[13,14] The second major event is the uptake, mainly by the liver cells of the smaller particles resulting from lipolysis, termed chylomicron remnants. After the lipolysis process, the remnants return to the circulation and are finally sequestered into the space of Disse and taken up by the liver cells by various receptors mechanisms, mainly the LDL receptors and the LDL receptor-related protein, LRP.[13–15] Apo E is the main ligand of chylomicron remnants to the hepatic receptors.[16]

The intravascular metabolism of chylomicrons has been related to coronary artery disease (CAD). Both slow lipolysis and slow removal from the plasma of remnants have been found in CAD patients as compared with their controls without the disease.[17]

In our recent study,[9] by using the method of chylomicron-like emulsions to assess this metabolism, it was shown that while the remnant removal was clearly diminished in obese patients comparatively with normal weight subjects, the lipolysis process was unexpectedly increased. In the current study, we evaluated the chylomicron catabolism in groups of normal weight, preobese, obese and morbid obese women, with body mass index (BMI) ranging from 22 to 50 kg/m^2. The chylomicron-like emulsion method was used. This method has been validated in several studies having unraveled chylomicron metabolism defects in disease states[18–20] and under drug treatment.[21] The emulsion is injected intravenously in minimal amounts and in a bolus after a 12 h fasting. By labeling the emulsion with radioactive triglycerides and cholesteryl esters, it is possible to determine *in vivo* and in an integrated manner the remnant removal process, followed by the kinetics of the emulsion cholesteryl esters and lipolysis that can be estimated by calculating a lipolysis index from both triglyceride and cholesteryl ester kinetics. The results showed that, with increasing weight gain, there is an increase in lipolysis and a decrease in remnant removal.

Subjects and methods

Subjects

A total of 40 women, aged from 30 to 40 y were divided into four groups of 10 according to their BMI(normal: BMI $<$ 25, preobese: 25 $<$ BMI $<$ 30, obese: 30 $<$ BMI $<$ 40, morbid obese: BMI $>$ 40 kg/m^2). Exclusion criteria were apparent or reported diseases, amenorrhea, pregnancy or breast-feeding, alcohol abuse, use of antihyperlipemia or antiobesity medications, as well as dietary regimen for weight loss for the last 6 months. All participants were sedentary, were not smokers and none had arterial hypertension.

The design and objective of the study were explained to each participant before the study, and an informed written consent was obtained from each of the individuals. The Scientific and Ethics Committee of the Medical School Heart Institute Hospital of São Paulo University (USP) approved the study.

Emulsion preparation

The emulsion was prepared as previously described,[22] with addition to the lipid mixtures of [1-^{14}C] cholesteryl-oleate (specific activity 2.07 Gbq/mmol) and [9,10-^{3}H] glycerol-trioleate (specific activity 518 GBq/mmol), supplied by Amersham International (UK). The emulsion was purified by two-step ultra centrifugation, as described previously,[23] sterilized by passage through a 0.2 μm filter and evaluated for sterility and pyrogenicity prior to injection into the patients.

Kinetics of the emulsion

Determination of chylomicron-like emulsion plasma kinetics was performed in four women groups. The fraction of the emulsion preparation that was injected into each subject contained approximately 3.0 mg total lipid mass in 500 μl volume. [^{14}C] and [^{3}H] radioactivity of the labeled lipids were 74 kBq (2 μCi) and 148 kBq (4.0 μCi), respectively. The emulsion was injected intravenously in a bolus, after 12 h fasting. Blood samples were collected from another peripheral vein at pre-established intervals during 45 min. Blood was centrifuged and the radioactivity contained in 1.0 ml of plasma was measured by '*Liquid Scintillation Counting*' (Packard 1.660 TR, Meridien, CT, USA). The safety of the radioactive dose injected into the subjects was warranted according to radioprotection regulations[24] as described elsewhere.[17]

Compartmental analysis

Emulsion removal from the plasma was evaluated by compartmental analysis according to a modification of the model proposed by Redgrave *et al*.[25] Briefly, four compartments were employed to estimate the kinetic parameters for both ^{14}C-Cholesteryl-oleate (CO) and ^{3}H-Triolein (TO) tracers. Plasma hydrolysis and removal of native chylomicrons, as well as chylomicron-like emulsions, displayed a rapid initial decay followed by a slow removal phase.[9,17,26] The $k_{x,y}$ constants represent the transfer or fractional catabolic rates (FCR) from compartment $_x$ to compartment $_y$. Compartments 1–4 and 5–8 represent the kinetics of cholesterol and triglycerides metabolism, respectively. The rapid and slow decay phases evaluated by the CO and TO

tracers are represented, respectively, by $k_{1,3}$ and $k_{2,3}$ and by $k_{5,7}$ and $k_{6,7}$. The model also takes into account the recirculation of the radioactive tracers in plasma on the form of newly synthesized VLDL (expressed by $k_{3,4}$ and $k_{7,8}$ for the ^{14}C and ^{3}H, respectively). The lipolysis index, which estimates the percentage of TO removed by lipoprotein lipase action, was calculated from the differences between the areas under the curve (AUC) for the removal of CO and TO. All calculations were performed using a computer software.[27] Details of the compartmental analysis calculations were published previously.[28]

Biochemical analysis

Serum triglycerides, total, LDL and HDL cholesterol, apolipoprotein A1 (apo A1) and apoliprotein B (apo B) and glucose were determined from blood samples taken after 12 h fasting using an automatic instrument (Cobas Mira Plus—Roche). Total cholesterol and triglycerides were determined with the aid of enzymatic test kits (CHO-PAD, Boehringer and Abbott, respectively). HDL cholesterol was determined by the same method, after precipitation of LDL and VLDL with $MgCl_2$, phosphotungstic acid and LDL cholesterol were calculated using the Friedewald equation.[29] An oral glucose tolerance test was performed over 2 h after the ingestion of a 75 g glucose load.

Statistical analysis

All recorded variables were tabulated as means ± s.d. or s.e.m. The differences in the obtained data were evaluated by one-way ANOVA. When the ANOVA showed significant differences, median values were compared by Kruskal–Wallis nonparametric test. The level of significance was set at $P<0.05$ for all comparisons. The Pearson product–moment correlation coefficients were used to quantify associations among variables.

Results

Plasma, lipids, apolipoproteins and glucose

Table 1 shows the physical characteristics and the plasma lipid and apoliprotein profile of the four women groups. Total cholesterol values were not different among the groups. HDL cholesterol, however, was progressively lower from normal weight to preobese, obese and morbid obese groups ($P<0.05$). ApoA1 was lower in morbid obese and preobese compared to the normal weight group. In the obese, this trend did not attain statistical significance. Apolipoprotein B values were greater than the normal weight group in the preobese and morbid obese groups, but not in the obese group. Fasting triglycerides were greater in the obese and morbid obese. All the women groups had fasting glucose plasma concentrations within the normal range. The oral glucose test was performed in the groups of the obese and morbid obese women, but not in the normal weight and preobese groups. The 2 h post 75 g glucose load glycemia was 4.8 ± 1.04 mmol/l in the obese and 4.32 ± 1.01 mmol/l in the morbid obese group. No subjects of the obese group and only one of the morbid obese group had 2 h glycemia above the 7.0 mmol/l cutoff level for glucose intolerance.[30]

Emulsion plasma kinetics

Figure 1 shows the plasma decay curves of the emulsion radioactive lipids obtained from the four study groups. It is apparent that the triolein decay curves of the four groups was not different, but the curves of the cholesteryl oleate were progressively slower in the preobese, obese and morbid obese groups, taking the normal weight curve as reference.

Table 2 shows the plasma kinetic data calculated from the decay curves. There was no difference among the study groups with regard to the FCR-TO. However, the FCR-CO was smaller in the obese and morbid obese groups compared to the normal weight groups, while preobese values were not different.

Table 1 Individual physical characteristics, plasma lipid and apolipoprotein profiles (mean ± s.d.) in women groups according to BMI

	Normal (n = 10)	*Preobese (n = 10)*	*Obese (n = 10)*	*Morbid obese (n = 10)*	P[a]
Age (y)	34 ± 3	36 ± 3	37 ± 3	33 ± 4	0.227
BMI (kg/m^2)	22.7 ± 1.2	27.1 ± 0.5*	33.2 ± 2.4*,**	42.5 ± 3.0*,**,***	0.001
Waist (cm)	72 ± 5	80 ± 5	91 ± 6*,**	110 ± 13*,**,***	0.001
Fasting glycemia (mmol/l)	3.55 ± 1.16	3.60 ± 1.05	4.27 ± 0.88	3.83 ± 0.94	0.352
Triglycerides (mmol/l)	1.12 ± 0.57	1.04 ± 0.49	1.38 ± 0.51	1.73 ± 0.23*,**	0.001
Cholesterol					
Total (mmol/l)	4.1 ± 0.57	4.57 ± 0.65	4.58 ± 0.36	4.37 ± 0.60	0.570
VLDL	0.51 ± 0.26	0.48 ± 0.22	0.63 ± 0.23	0.79 ± 0.11*,**	0.001
LDL	2.46 ± 0.54	2.92 ± 0.52	3.00 ± 0.23	1.91 ± 0.57**,***	0.001
HDL	1.26 ± 0.25	1.07 ± 0.17	0.91 ± 0.07	0.71 ± 0.31*,**	0.001
Apo A1 (g/l)	1.71 ± 0.15	1.41 ± 0.14*	1.43 ± 0.36	1.33 ± 0.40*	0.004
Apo B (g/l)	1.03 ± 0.25	1.20 ± 0.32	1.06 ± 0.33	1.22 ± 0.30	0.001

[a]Probabilities for ANOVA; *$P \leq 0.05$ *vs* normal; **$P \leq 0.05$ *vs* preobese and ***$P \leq 0.05$ *vs* obese groups.

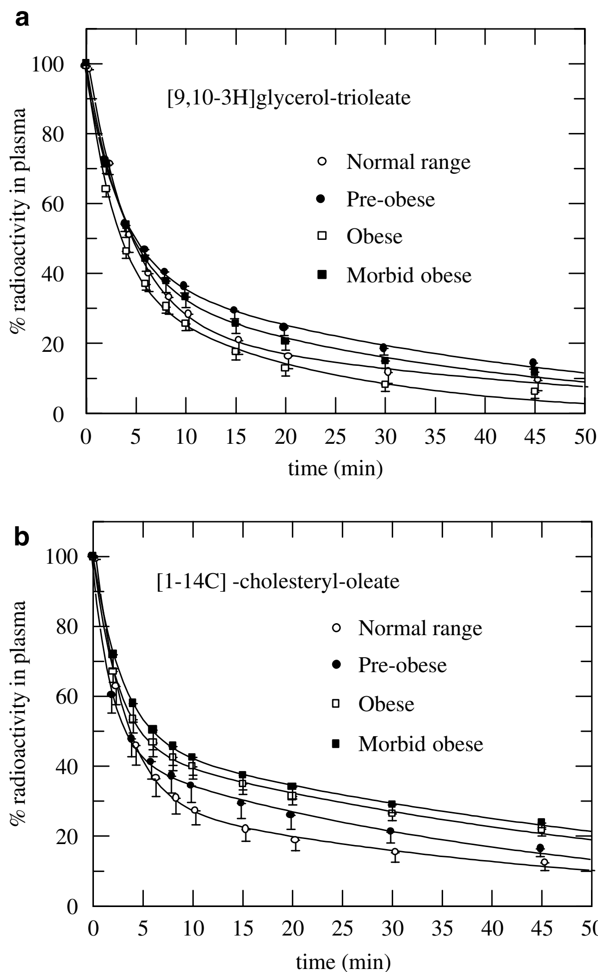

Figure 1 Removal from the plasma of the emulsion (a) [^{3}H] glycerol trioleate (NS by ANOVA) and (b) [^{14}C] Cholesteryl-oleate ($P<0.003$ by ANOVA) in women groups according to BMI.

Figure 2 and Table 3 show that the FCR-CO negatively correlates with the BMI of the subjects ($r=-0.388$; $P=0.01$). Figure 2 also shows that the FCR-TO of the emulsion did not correlate with BMI, but, nonetheless, there is a positive correlation between the lipolysis index and BMI.

There was also a positive correlation between the FCR-CO with HDL cholesterol ($r=0.345$; $P=0.03$), and negative with fast triglycerides ($r=-0.428$; $P=0.005$). Correlations between glycemia or plasma tryglyceride and waist circumference with the kinetics of the emulsion-labeled lipids were not found.

Classical correlations of blood lipids and BMI were confirmed in this study, such as the positive correlations of the BMI with fast triglycerides ($r=0.496$; $P=0.001$), the negative correlation of the BMI with HDL cholesterol ($r=0.683$; $P=0.0001$) and positive correlation of waist circumference with fast triglycerides ($r=0.518$; $P=0.001$). Plasma glucose values did not correlate with BMI and waist circumference.

The difference in FCR-CO was largely due to the $k_{1\text{-}3}$ constant. According to the compartmental model used to analyze data, the $k_{1\text{-}3}$ constant is related with the first exponential of the decay curve.

The lipolysis index was greater in the two obese women groups compared with the normal weight and preobese groups ($P<0.001$).

Discussion

In this study, it is shown in normotriglyceridemic women with normal fasting plasma glucose that the FCR of the emulsion cholesteryl oleate correlates negatively with the BMI. There is no correlation between the FCR of the emulsion triglycerides and the BMI, but a positive correlation was found between the lipolysis index and BMI. Those results were obtained in women with a wide BMI range, spanning from 22 to 50 kg/m^2.

It is noteworthy that the triglyceride values were positively correlated with the BMI, whereas the HDL values correlated negatively with the BMI. Both increase in triglycerides and decrease in HDL levels are considered markers of insulin resistance,[31] which implies that insulin resistance tends to increase as the BMI increases. This is important because the

Table 2 Plasma kinetic parameters of the emulsion (mean±s.e.m.) in women groups according to BMI

	Normal (n = *10*)	*Preobese* (n = *10*)	*Obese* (n = *10*)	*Morbid obese* (n = *10*)	P[a]
FCR-TO (min^{-1})	0.126±0.017	0.120±0.030	0.139±0.015	0.096±0.008	0.175
$K_{5.6}$	0.095±0.017	0.258±0.077	0.203±0.027	0.193±0.027	0.087
$K_{5.7}$	0.268±0.063	0.402±0.127	0.394±0.110	0.249±0.033	0.682
$K_{6.7}$	0.074±0.019	0.042±0.006	0.057±0.007	0.059±0.010	0.282
$K_{7.8}$	0.002±0.009	0.001±0.001	0.1010±0.100	0.002±0.001	0.921
Lipolysis (%)	25.0±4.3	21.3±5.8	65.7±3.9*,**	35.4±5.8***	0.001
FCR-CO (min^{-1})	0.069±0.009	0.064±0.010	0.031±0.003*,**	0.029±0.005*,**	0.003
$K_{1.2}$	0.095±0.017	0.258±0.027	0.203±0.027	0.193±0.027	0.087
$K_{1.3}$	0.270±0.042	0.370±0.085	0.137±0.070**	0.132±0.030	0.011
$K_{2.3}$	0.023±0.005	0.0268±0.005	0.028±0.007	0.023±0.003	0.795
$K_{3.4}$	0.001±0.001	0.001±0.000	0.009±0.001	0.001±0.001	0.125

[a]Probabilities for ANOVA; *$P\leq0.05$ *vs* normal; **$P\leq0.05$ *vs* preobese and ***$P\leq0.05$ *vs* obese groups.

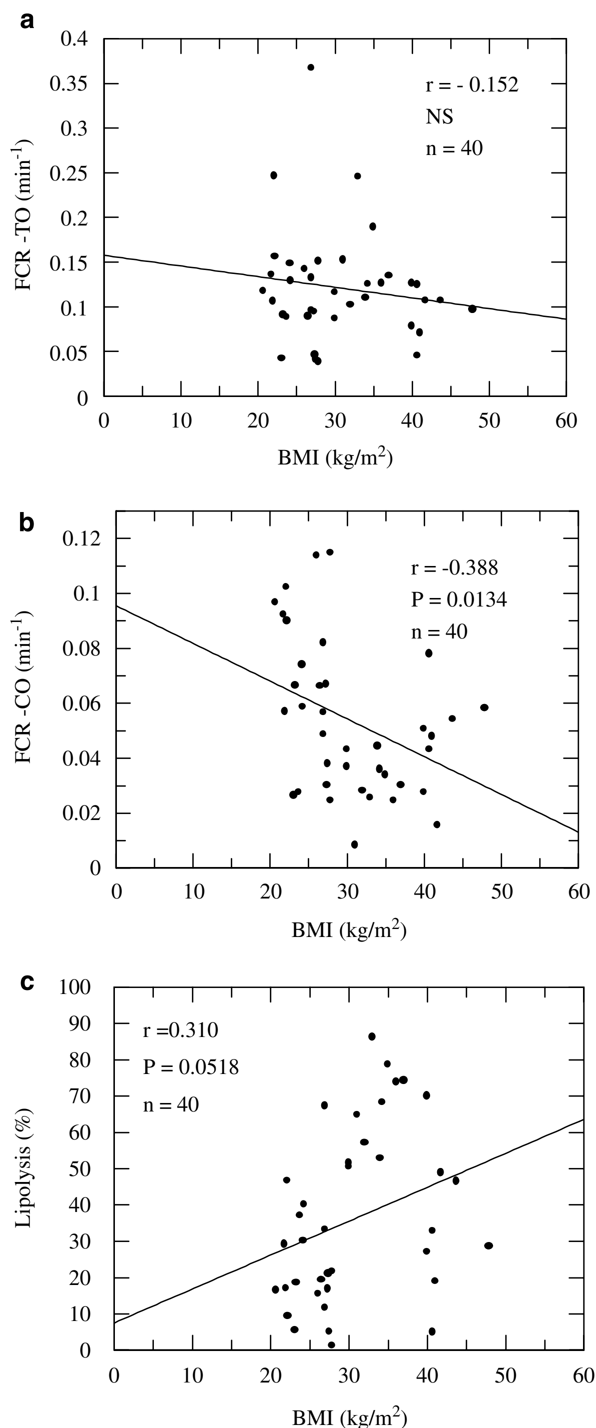

Figure 2 Correlation between BMI and (a) FCR-TO, (b) FCR-CO and (c) lipolysis.

action of lipoprotein lipase is insulin dependent. Nonetheless, all participant subjects had normal fasting glucose levels and in the group of obese and morbid obese women, wherein the test was performed, the results of the oral glucose tolerance test were normal, except for just one woman in the morbid obese group. As a remark, HDL cholesterol values in the normal weight women group (1.26 mmol/l) could be considered somewhat low for the female sex at this age range.

Oral fat load tests are usually employed to evaluate post-prandial lipidemia status. In those tests, the ingestion of a standard fatty meal is followed by determination in sequential plasma samples of triglycerides and chylomicron labels such as retinyl palmitate[12] and apo B48.[11] In some studies, those determinations are made after plasma ultracentrifugation to separate the 'chylomicron' from 'nonchylomicron' fractions.[32] However, the post-prandial lipidemia is made up of lipids of both intestinal and hepatic origin. Since both chylomicrons and VLDL undergo the same catabolic processes, both lipoproteins compete for lipoprotein lipase and thus VLDL also accumulates in the plasma in the post-prandial period.[33] Owing to this and other factors, such as the long period of fat intestinal absorption, the great interindividual variation in absorption rates and the short (~10 min) half-lives of chylomicrons and remnants of the oral fat load test are difficult to interpret and may not be specific for chylomicron catabolism. In this regard, substantial amounts of apo B48, which is the apo B form present in chylomicrons, are found in the 'nonchylomicron' fraction and, conversely, apo B100, which is the VLDL apo B form, is found in the 'chylomicron' fraction.

The chylomicron-like emulsion method used in this study specifically tests the chylomicron metabolic pathway. In the plasma, the emulsions gain apolipoproteins from the circulating lipoproteins. The acquired apo CII stimulates lipoprotein lipase and apo E allows binding to the cell receptors that remove remnants from the plasma, similar to chylomicron metabolism. The emulsion shows plasma half-lives of cholesteryl esters and triglycerides that are equivalent to those of lymph chylomicrons in rats and subjects.[17,25] Since only minimal amounts of cholesteryl esters shift from the emulsion particles, this moiety is indeed a marker of the removal of the remnant particles.[17,25] Since the emulsions are injected intravenously, the gastrointestinal component is bypassed allowing straightforward calculation of the plasma kinetic data. Injected in minimal lipid amounts after a 12 h fasting, the emulsion does not disturb the VLDL metabolism. The injection into subjects of the double-labeled emulsion after the intake of the fatty meal resulted in diminution of the lipolysis index.[22] In fact, the absorption of the meal lipids had a greater impact on the plasma clearance of the emulsion triglycerides than on the cholesterol ester clearance. In the fed subjects, there was a six-fold post-prandial decrease in the FCR of triglycerides, while the cholesteryl ester FCR was reduced by two-fold. Therefore, when challenged by the massive entry of chylomicron lipids into the circulation, the lipoprotein lipase function appears more readily saturable than the hepatic receptors that take up remnants.

Table 3 Correlation between plasma kinetic parameters, BMI and plasma lipid in women ($n=40$)

	BMI (kg/m²)		*FCR (min⁻¹)*		*FCR (min⁻¹)*		*Lipolysis (%)*	
	r	P	r	P	r	P	r	P
BMI (kg/m²)	–	–	−0.388	0.01	0.152	0.348	0.310	0.05
Triglycerides (mmol/l)	0.496	0.001	−0.428	0.005	−0.238	0.140	0.059	0.714
HDL – cholesterol (mmol/l)	−0.683	0.001	0.345	0.029	0.132	0.418	−0.175	0.281

In fat load tests, Couillard *et al*[34,35] and Guerci *et al*[32] reported that obese subjects with normal fasting triglycerides display the AUC of post-prandial triglycerides of the 'chylomicron fraction' similar to the nonobese controls and accumulation of triglycerides of the nonchylomicron fraction, suggesting that VLDL triglycerides, and not those of chylomicrons, accumulate in plasma of the obese after a fatty meal. Jensen *et al*[36] and Mekki *et al*[37] found increased triglyceride AUC in the chylomicron fraction, but in both studies the obese had higher fasting triglycerides than their controls. In our previous study,[9] the emulsion triglycerides were normally removed in normotriglyceridemic obese women and the lipolysis index was increased.

The finding in this study that the lipolysis index increases as the BMI increases does not necessarily imply that the activity of lipoprotein lipase is increased. As the clearance of the emulsion particles, expressed by the cholesteryl ester FCR, is inversely correlated with BMI, whereas the triglyceride FCR is unchanged, it can be assumed that the lipolysis of the particles continues for longer periods as the particles remain longer in the circulation than in normal weight subjects. Consequently, less triglycerides are removed by the liver together with the emulsion remnant particles and greater amounts are degraded by lipoprotein lipase. This results in increase in the lipolysis index that is calculated from the differences between the areas under the decay curves of the emulsion-labeled cholesteryl oleate and triglycerides. In this condition, remnants more depleted in triglycerides, conceivably of smaller size that offers greater potential for entry in the artery wall, and remaining in the blood stream for longer periods can become more atherogenic.[38] Regarding the activity of the enzyme, as measured *in vitro* in post-heparin plasma in obese *vs* nonobese subjects, the results from the literature are somewhat controversial. Some authors found alterations in the lipoprotein lipase activity in the obese,[39–42] whereas others did not[11,43,44] and this may be related to several variables such as type of obesity, the plasma triglyceride levels and alterations in the insulin action.[45]

Most studies found decreased removal of remnants in obesity, as evaluated by the B48[11,37] or retinyl palmitate[12,34,35] measurement in the plasma after a test fatty meal or by chylomicron-like emulsion tests.[9,10,46] However, Vansant *et al*[47] and Lewis *et al*[12] did not find obese *vs* control differences in retinyl palmitate AUC. Fat accumulation in visceral region, which is frequently associated to insulin resistance, has also been associated to decreased chylomicron remnant removal from circulation.[10,37,47,48] The decrease in remnant removal from the plasma may be consequent to the greater VLDL production by the liver in the obese, leading to competition between both lipoprotein classes and saturation of the removal mechanisms (Riches *et al*.[11,49] Increase in the VLDL hepatic production is consequent to the greater caloric intake by the obese.

Efficiency in the lipolysis process is a precondition for efficient removal of remnants from the circulation and it is expected that when the emulsion and for extension the chylomicron lipolysis is impaired, the plasma clearance of the particles is diminished.[15] However, this is not the case of our study subjects, since the emulsion triglyceride FCR did not correlate with BMI and the lipolysis index was even increased as BMI increased. The negative correlation between remnant removal, expressed by the emulsion cholesteryl oleate, and the BMI of the study subjects found here can be ascribed to decrease in the function of the mechanisms that remove remnants. In this regard, Mamo[11] found decreased uptake of LDL by mononuclear cells of obese subjects, indicating reduction in the expression of the LDL receptors. LDL receptors in the liver are a major mechanism for remnant removal.[15,50]

Since apo E is the ligand for the remnants of the chylomicron-like emulsion to the receptor mechanisms that remove them from the circulation, it would be expected that the apo E isoforms might influence the emulsion clearance.[51,52] Apo E4/4 tends to increase remnant removal, whereas in the case of apo E2/2, the removal is the slowest. However, the frequency in the population of apo E4 and mainly E2 in the homozygous form, which is less than 1%, is too low to influence the results, as we documented in our previous study.[28]

In concluding, in obesity the capacity to break down the chylomicron-like emulsion triglycerides is preserved and the lipolysis even increases as the BMI increases. However, the ability of the organism to remove remnants formed during this process decreases proportionally to the increase in BMI. Previously, it was shown that decreased removal of emulsion remnants[17] or chylomicron markers in oral fat load tests[38,53,54] is associated with CAD. Therefore, our results imply that remnant retention may be an important link between weight gain and atherogenesis.

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