DOUGLAS EUGENIO BARBIERI

SÍNDROME METABÓLICA:
ASPECTOS RELACIONADOS AO TRATAMENTO ANTI-HIPERTENSIVO E À LIPEMIA PÓS-PRANDIAL

Tese apresentada à Universidade Federal de São Paulo – Escola Paulista de Medicina para obtenção do Título de Doutor em Ciências.

SÃO PAULO
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Orientadora:
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Prof. Dr. Clayton Luiz Dornelles Macedo

Profa. Dra. Sandra Roberta Gouvea Ferreira

Não fiz o melhor, mas fiz tudo
para que o melhor fosse feito.
Não sou o que deveria ser,
mas não sou o que era antes.

Martin Luther King

Esta tese é dedicada

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SUMÁRIO

1. CONSIDERAÇÕES INICIAIS

Com o aumento da prevalência de obesidade, uma entidade clínica heterogênea, associada à gordura visceral abdominal e à resistência à insulina, foi identificada como um fator de risco maior para diabetes mellitus do tipo 2 e morbidade e mortalidade por doença cardiovascular aterosclerótica.[1,2] Esta entidade, primeiramente descrita por Gerald Reaven em 1988 e denominada de "síndrome X" ou "síndrome de resistência à insulina",[3] é atualmente conhecida como síndrome metabólica. Trata-se de um conjunto de anormalidades metabólicas e hemodinâmicas que agrupa, classicamente, a obesidade abdominal, hipertensão arterial, hipertrigliceridemia, níveis diminuídos de colesterol HDL (lipoproteína de alta densidade) e/ou intolerância à glicose, refletindo, essencialmente, a condição de resistência à insulina.[3,4]

A prevalência da síndrome metabólica é estimada entre 20 e 25% da população geral, com comportamento crescente nas últimas décadas.[5,6] A partir de 2005, a International Diabetes Federation (IDF) reformulou o sistema de classificação da NCEP-ATP III,[7] apresentando critérios mais estritos para o diagnóstico da síndrome metabólica, valorizando a presença da obesidade central e diferenciando os valores de circunferência da cintura segundo a etnia.[8] As tentativas de se estabelecer critérios diagnósticos para esta síndrome são baseadas no princípio de que seus componentes podem agir de maneira sinérgica ou aditiva amplificando o risco cardiovascular.

A hipertensão arterial é uma condição de resistência à insulina, independente da obesidade ou de outras alterações metabólicas.[9,10] Nos pacientes hipertensos a ação da insulina de inibir a gliconeogênese hepática está preservada, contudo há menor captação periférica da glicose principalmente pelo músculo esquelético.[9] A ativação do sistema renina-angiotensina-aldosterona (SRAA) tem sido descrita como um dos mecanismos mais importantes responsável pela hipertensão arterial associada à obesidade. Ademais, identificou-se a expressão em

adipócitos de angiotensinogênio[11,12] e angiotensina II,[13] no entanto a contribuição do SRAA localizado no tecido adiposo para o aumento de seus componentes na circulação ainda vem sendo estudada.

A obesidade e a hipertensão arterial associadas levam à maior grau de resistência à insulina e hiperinsulinemia compensatória.[14] Portanto, os efeitos metabólicos dos anti-hipertensivos devem ser considerados no tratamento dos pacientes obesos ou com acúmulo de gordura abdominal. Os diuréticos tiazídicos, anti-hipertensivos freqüentemente utilizados na prática clínica, possuem efeitos deletérios sobre o metabolismo da glicose, com aumento no risco de desenvolvimento de diabetes do tipo 2.[15,16] A depleção de potássio induzida por tiazídicos, decorrente inclusive da ativação do SRAA,[17] é descrita como o principal fator que leva à alteração na homeostase da glicose.[18-20]

O acúmulo de adiposidade visceral, característico da síndrome metabólica, leva a alterações lipídicas caracterizadas por hipertrigliceridemia de jejum, diminuição das HDLs e produção das LDLs (lipoproteína de baixa densidade) pequenas e densas,[21,22] conferindo elevado risco cardiovascular.[23-25] A hiperlipemia pós-prandial (HLPP), possível marcador precoce de anormalidades metabólicas e da disfunção endotelial ainda não observadas no estado de jejum,[26,27] também tem sido sugerida como fator de risco para a doença arterial coronariana,[28,29] uma vez que as alterações decorrentes da HLPP contribuem para o processo de aterogênese.[30-32] De fato, a hipertrigliceridemia pós-prandial, mesmo com níveis plasmáticos de triglicérides normais no jejum, vem sendo associada com aumentos da glicemia e insulinemia[33] e foi identificada como um marcador de resistência à insulina, precedendo o estado de intolerância à glicose.[34] Por esta razão, propõem-se que a HLPP seja um novo componente da síndrome metabólica, estabelecendo uma nova esfera para o entendimento do processo aterosclerótico.[35-37]

Nos estados de resistência à insulina, a hipertrigliceridemia conseqüente a uma refeição hiperlipídica tem sido atribuída à diminuição da atividade da lipase lipoproteica (LPL),[38] enzima responsável pelo catabolismo de quilomícrons e das VLDLs (lipoproteínas de densidade muito baixa).[39]

A adiponectina, é uma proteína expressa exclusivamente nos adipócitos que, ao contrário das outras adipocitocinas, age como fator protetor para doenças cardiovasculares.[40] Ela possui a característica de melhorar a sensibilidade à insulina através do aumento da oxidação de ácidos graxos e da captação e utilização da glicose no músculo esquelético e tecido adiposo, além de reduzir a liberação da glicose hepática, levando ao melhor controle da glicemia e dos níveis séricos de ácidos graxos livres e triglicérides.[41] Também apresenta ações antiinflamatória e antiaterogênica[42] que ocorrem pela diminuição da expressão da molécula de adesão-1 (via redução da expressão do fator de necrose tumoral-α e atividade da resistina), diminuição da quimiotaxia ao macrófago para formação de células gordurosas e inibição da sinalização inflamatória no tecido endotelial.[43] Embora a adiponectina seja derivada do tecido adiposo, tem-se conhecimento que aumentos no peso corporal estão invariavelmente acompanhados de diminuição nos níveis plasmáticos desta adipocitocina.[44] A hipoadiponectinemia, por sua vez, contribui para as alterações observadas na síndrome metabólica, incluindo o desenvolvimento de resistência à insulina,[44,45] hipertensão arterial[46] e hipertrigliceridemia.[47]

A seguir, serão apresentados dois trabalhos originais que abordam aspectos relacionados à síndrome metabólica, particularmente ao tratamento anti-hipertensivo e à lipemia pós-prandial em indivíduos apresentando diferentes graus de resistência à insulina, conferidos pela presença de obesidade e/ou hipertensão arterial.

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2. OBJETIVOS

- Considerando que os pacientes hipertensos com a síndrome metabólica apresentam resistência à insulina e, supostamente, hiperatividade do SRAA, os objetivos do primeiro artigo foram os de avaliar se nestes pacientes, comparados aos hipertensos sem a síndrome metabólica, o tratamento com diurético tiazídico poderia induzir maior grau de depleção de potássio e, conseqüentemente, maior intolerância à glicose.

- No segundo artigo, objetivamos determinar a relação entre os níveis plasmáticos da adiponectina e dos triglicérides, antes e durante a realização de um teste de sobrecarga lipídica, em indivíduos apresentando diferentes graus de resistência à insulina dependentes da presença ou não de obesidade.

3. ARTIGO 1

DIURETIC-INDUCED POTASSIUM DEPLETION AND GLUCOSE INTOLERANCE ARE NOT RELATED TO HYPERACTIVITY OF THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM IN HYPERTENSIVE PATIENTS WITH THE METABOLIC SYNDROME

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Diuretic-Induced Potassium Depletion and Glucose Intolerance Are Not Related to Hyperactivity of the Renin-Angiotensin-Aldosterone System in Hypertensive Patients With the Metabolic Syndrome

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The metabolic syndrome (MS) has been associated with hyperactivity of the renin-angiotensin-aldosterone system (RAAS). To assess the hypothesis that diuretic therapy in MS patients through further stimulation of RAAS would elicit greater potassium (K) depletion, two groups of hypertensive patients with (MS group [MSG]; n=20) and without (control group [CG]; n=19) MS were studied. Plasma renin activity (PRA), aldosterone (PA), and K levels were determined and an oral glucose tolerance test with plasma insulin determinations for calculation of homeostasis model assessment of insulin resistance (HOMA-IR), sensitivity (ISI), and secretion (HOMA-β) was performed, both before and 12 weeks after hydrochlorothiazide (HCT; 25 mg/d) therapy. At baseline, higher HOMA IR and HOMA-β and lower ISI and plasma K were found in the MSG than in the CG, with no differences in PA and PRA between groups. With therapy, PRA increased similarly in both groups while PA increased only in the MSG. However, greater reduction in plasma K occurred in the CG, and the 2 groups reached similar final K values. Impairment in glucose tolerance occurred in both groups, with no change in HOMA-β in the CG and reduction in the MSG, suggesting that diuretic therapy increases insulin resistance and impairs insulin secretion independent of abdominal obesity. These alterations could not be attributed to hyperactivity of RAAS. J Clin Hypertens (Greenwich). *2009;11:549–554.* ©*2009 Wiley Periodicals, Inc*

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With the increase of obesity prevalence, several studies have identified the connection between abdominal visceral fat and insulin resistance.[1–3] From this relationship, a new clinical identity, currently known as the metabolic syndrome (MS),[3] has been shown to increase the risk of coronary artery disease and cardiovascular mortality.[4]

Arterial hypertension as part of MS, presents a strong connection with obesity and is associated with a greater risk of diabetes and glucose intolerance.[5,6] Therefore, when choosing the appropriate antihypertensive treatment for obese or MS patients, the metabolic effects of these drugs should be considered. Diuretic therapy, even in low doses, may induce the development of unwanted adverse

effects such as glucose intolerance with a subsequent increased risk of diabetes.[7–10]

Potassium depletion, induced by thiazide diuretics, is described as the main cause of alterations in glucose homeostasis.[10,11] Hypokalemia affects glucose metabolism through 2 different mechanisms: impairment in insulin secretion[11,12] and decrease in peripheral insulin sensitivity.[13] Thiazide diuretics lead to potassium depletion through the activation of the renin-angiotensin-aldosterone system (RAAS) in response to reductions in circulating blood volume, which increases urinary potassium excretion. In addition, the penetration of potassium in the cells, due to diuretic-induced alkalosis, contributes to decreased plasma potassium levels.[14]

Activation of the RAAS is one of the mechanisms responsible for arterial hypertension associated with obesity.[15,16] The increase of several circulating components of the RAAS, such as angiotensinogen, renin, angiotensin-converting enzyme, and aldosterone, have been observed in obese patients.[16] In addition, the presence of several RAAS components have been demonstrated in the adipose tissue of animals and humans.[17,18] However, the contribution of the adipose tissue RAAS in the increases of circulating RAAS components is still a matter of debate.

Assuming that patients with abdominal obesity/MS, compared with nonobese patients, present greater insulin resistance and activation of RAAS, diuretic therapy in these patients that promotes even greater activation of RAAS could potentially induce a higher degree of potassium depletion, thus increasing the risk of type 2 diabetes. The objective of the present study was to assess this hypothesis.

METHODS

This prospective clinical study (case control study) was conducted in 39 hypertensive patients assigned to 2 different groups: the case group (the MS group [MSG]), which was composed of 20 patients with MS; and the control group (CG), which included 19 patients without MS. The diagnostic criteria used to define MS were those defined by the International Diabetes Federation (IDF).[19] Participants were recruited from the hypertension and cardiovascular disease outpatient clinic at the Hospital do Rim e Hipertensão in Sao Paulo, Brazil.

The study protocol was approved by the ethics committee of the institution where the study was conducted. According to the research ethics criteria "*in anima nobili,*" patients were informed about the purposes of the study, all doubts were cleared in advance, and a written informed consent was obtained from each patient.

Male and female hypertensive patients, aged 30 to 60 years, were eligible. In both groups, sitting systolic and diastolic arterial blood pressure (BP) values, in the absence of antihypertensive treatment and after a 5-minute rest, were to be $\geq$140 mm Hg and 90 mm Hg but not >160 mm Hg and 100 mm Hg, respectively. Hypertensive patients taking antihypertensive therapy could have values <140/90 mm Hg. Thus, only patients with mild and moderate arterial hypertension were considered eligible.

In the MSG, waist circumference in men and women were $\geq$94 cm and 80 cm, respectively. In addition to this criterion (already added to the presence of arterial hypertension), at least 1 other condition needed to be present to characterize MS, such as triglyceride levels $\geq$150 mg/dL and/or high-density lipoprotein (HDL) cholesterol <40 mg/dL and 50 mg/dL in men and women respectively, and/or fasting glycemia $\geq$100 mg/dL. In the CG, waist circumference in men and women were <94 cm and 80 cm, respectively. In addition, except for arterial hypertension, patients could present only 1 more criterion of MS.

The exclusion criteria for this study were hypokalemia (plasma potassium <3.5 mEq/L), body mass index (BMI) >40 kg/m^2, fasting glycemia $\geq$110 mg/dL, glycemia at 120 minutes post-glucose load $\geq$200 mg/dL or diabetes while on treatment, triglycerides >400 mg/dL, congestive heart failure, chronic renal failure, hepatopathy, or severe psychiatric disease. Also, patients who presented with cardiovascular events (myocardial infarction or stroke) within the previous 6 months and women using oral contraceptives or who were pregnant did not take part in this study. In addition, patients who presented any evidence of secondary hypertension, malignant hypertension, or sitting systolic and diastolic BP levels >160 mm Hg and 100 mm Hg, respectively, were excluded.

The study protocol had a baseline period of 4 weeks for washout of antihypertensive drugs. After the first 2 weeks, patients were reevaluated and if their systolic and/or diastolic BPs were >160 mm Hg and 100 mm Hg respectively, alpha-methyldopa (maximum dosage of 500 mg twice a day) was introduced for the next 2 weeks to reduce BP, according to the ethics committee recommendation.

At the end of the baseline period, alpha-methyldopa was withdrawn and all patients received hydrochlorothiazide (HCT) 25 mg/d, maintaining their usual diet for a 12-week term. During HCT therapy, patients were evaluated every 4 weeks for BP, heart rate, and anthropometric determinations.

BP was measured 3 times after 5 minutes of rest in the sitting position and after 5 minutes in the upright position using a sphygmomanometer with an appropriate cuff size. The values presented correspond to the arithmetic average of each 3 determinations.

The BMI was calculated as weight in kilograms divided by height in squared meters. The waist circumference was determined in centimeters at the middle point between the costal margin and the iliac crest.

Fasting plasma potassium (K), uric acid, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides (TGs), creatinine, plasma aldosterone (PA), and plasma renin activity (PRA) after at least 2 hours of deambulation were determined and an oral glucose tolerance test (OGTT) was performed both after the washout period (baseline) and after a 12-week period of HCT therapy. During OGTT, glycemia and insulinemia were determined both after fasting and 120 minutes after an oral 75-g glucose load. Based on these parameters, homeostasis model assessment of insulin resistance (HOMA-IR),[20] insulin secretion (HOMA-β),[20] and insulin sensitivity (ISI)[21] were calculated. Urinary potassium excretion (mEq/24 h) was determined both before and after diuretic therapy.

PA was determined through Active DSL-8600 kit assay (Webster, TX), with analytical sensitivity of 7.64 pg/mL, intra-assay variability of 3.3% to 4.5%, and interassay variability of 5.9% to 9.9%. The kit assay used for PRA determination was GammaCoat, (Stillwater, Minnesota, MN), with analytical sensitivity of 0.018 ng per tube, intra-assay variability of 4.6% and 10.0%, and interassay variability of 5.6% and 7.6%. Plasma and urinary potassium values were determined by ion selective electrode method and expressed as mEq/L and mEq/24 h, respectively. Plasma glucose, uric acid, total cholesterol, and TGs were determined by enzymatic colorimetric method. HDL cholesterol was measured by homogeneous colorimetric enzymatic method and LDL cholesterol was calculated by the Friedwald formula: LDL cholesterol = total cholesterol − (HDL cholesterol + TG/5). The analyzer used was HITACHI 912 (Roche Diagnostics, Basel, Switzerland). Plasma creatinine was measured through alkaline picrate assay. Plasma insulin was determined by microparticle enzyme immunoassay.

Statistical Analysis

Statistical analyses were performed using SPSS version 13.0 software for Windows (SPSS, Inc, Chicago, IL). Paired *t* test for dependent measures and a *t* test for independent measures were used for comparison of variables within and between groups, respectively. Pearson coefficient was calculated to determine correlations between different variables. Data were expressed as mean ± SD and statistical significance was defined as $P<.05$.

RESULTS

Thirty-nine hypertensive patients of a miscigenated Brazilian population were included in this study. The Table shows the clinical and laboratory characteristics of all patients divided into the MSG (n=20) and the CG (n=19). There was no significant statistical difference in sex, age, smoking habit, or use of hormonal replacement therapy between the 2 study groups. Also, the number of participants who required alpha-methyldopa for BP control before HCT therapy (baseline) did not differ between the MSG (7 of 20) and the CG (7 of 19). Higher BMI (34.0±3.4 vs 24.6±2.6 kg/m^2; $P<.05$) and waist circumference (110.7±9.8 vs 82.9±6.6 cm; $P<.05$) were observed in the MSG than in the CG.

In the baseline period, compared with the CG, the MSG presented greater fasting insulinemia (9.3±3.3 vs 5.8±3.2 μU/mL; $P<.05$) and, at 120 minutes after glucose load, higher plasma glucose (117.0±16.2 vs 95.2±29.9 mg/dL; $P<.05$) and insulin levels (67.6±44.8 vs 35.1±30.1 μU/mL; $P<.05$). Thus, the MSG showed greater HOMA-IR (2.18±0.84 vs 1.29±0.74; $P<.05$) (Figure, A) and lower ISI (0.69±0.30 vs 1.05±0.29; $P<.05$) (Figure, B) than the CG.

Before diuretic therapy, no differences were observed between the MSG and CG in PRA (0.9±0.8 vs 1.1±1.0 ng/mL/h; *P*=not significant [NS]), PA (16.2±6.9 vs 15.4±7.5 ng/dL; NS), and 24-hour potassium urinary excretion (52.2±25.1 vs 51.1±28.9 mEq/24 h; NS), respectively. Baseline plasma K level, was lower in the MSG compared with the CG (4.24±0.31 vs 4.50±0.28 mEq/L; $P<.05$) and when the 2 groups were analyzed together, no correlation was found between baseline plasma K and PA (r=−0.17; *P*=.29). However, in the whole group, plasma K showed a negative and significant correlation with fasting plasma insulin (r=−0.46; *P*=.003) and HOMA-IR (r=−0.44; *P*=.005).

After 12 weeks of HCT therapy, a smaller fall in plasma K levels was observed in the MSG compared with the CG (−0.29±−0.27 vs −0.69±−0.35 mEq/L, respectively; $P<.05$), resulting in similar levels of final

Table. Clinical and Laboratory Findings in Patients With and Without the Metabolic Syndrome

Groups	Control Group		Metabolic Syndrome Group	
No.	19		20	
Age, y	49.32±8.69		47.10±9.81	
Women, %	47.4		50	
ΔK, mEq/L	−0.69±−0.35		−0.29±−0.27[a]	
Status	Baseline	Post-HCT	Baseline	Post-HCT
Body mass index, kg/m^2	24.58±2.58	24.54±2.60	34.01±3.39[a]	33.88±3.53[a]
Waist circumference, cm	82.89±6.64	82.42±6.84	110.65±9.78[a]	110.50±9.81[a]
Heart rate, bpm	73.84±8.45	71.05±8.91	76.65±8.72	77.65±5.62[a]
Systolic BP, mm Hg	141.89±10.70	132.16±12.66[b]	139.45±7.41	130.50±11.41[b]
Diastolic BP, mm Hg	93,42±3.02	88.42±7.43[b]	91.85±5.60	88.05±4.78[b]
Plasma K, mEq/L	4,50±0.28	3.80±0.31[b]	4.24±0.31[a]	3.95±0.38[b]
PA, ng/dL	15.44±7.53	20.90±12.12	16.25±6.87	28.67±15.00[b]
PRA, ng/mL/h	1.14±1.00	3.30±4.12[b]	0.90±0.85	2.35±1.72[b]
Glucose 0 min, mg/dL	91.26±13.25	100.53±24.04	94.70±11.22	101.20±10.77[b]
Glucose 120 min, mg/dL	95.21±29.90	107.74±34.43[b]	117.05±16.23[a]	130.40±27.11[a,b]
Insulin 0 min, μU/mL	5.78±3.17	6.74±4.31	9.31±3.30[a]	10.38±3.30[a]
Insulin 120 min, μU/mL	35.12±30.10	46.92±35.16	67.61±44.82[a]	69.54±43.21
Plasma creatinine, mg/dL	1.02±0.12	1.06±0.17	1.00±0.12	1.00±0.16
Total cholesterol, mg/dL	195.16±32.74	200.90±44.51	201.30±39.87	201.30±41.49
HDL cholesterol, mg/dL	58.42±12.35	58.32±17.07	49.90±15.58[a]	47.55±12.47[a]
LDL cholesterol, mg/dL	114.53±28.39	118.53±39.30	118.90±29.33	119.35±30.01
Triglycerides, mg/dL	100.32±38.93	120.42±48.89	156.55±74.01[a]	172.25±78.54[a]
Triglycerides/HDL ratio	1.84±1.00	2.30±1.39[b]	3.35±1.69[a]	3.80±2.00[a,b]
Uric acid, mg/dL	4.87±1.03	5.62±1.38[b]	5.48±1.35	6.13±1.57[b]
Urine volume, mL	1478.68±531.96	1401.58±668.04	1678.90±785.57	1337.25±498.75
Urinary K, mEq/24 h	51.07±28.89	40.62±26.58	52.23±25.10	39.51±14.80[b]

Abbreviations: 0 min, fasting on the oral glucose tolerance test; 120 min, 120 minutes after glucose load on the oral glucose tolerance test; BP, blood pressure; bpm, beats per minute; HCT, hydrochlorothiazide; HDL, high-density lipoprotein; K, potassium; LDL, low-density lipoprotein; PA, plasma aldosterone; PRA, plasma renin activity. Values are expressed as mean ± standard deviation. [a]$P<.05$ vs control group. [b]$P<.05$ vs baseline.

plasma K in MSG and CG (3.95±0.38 vs 3.80±0.31 mEq/L, respectively; NS). As shown in the Table, this was associated with similar increases in PRA in both groups, while a significant increase in PA was observed only in the MSG.

Following HCT therapy, increases in blood glucose occurred at fasting and 120 minutes after glucose load in both groups, reaching higher levels in the MSG. These increases in glycemia, however, were not followed by elevations in plasma insulin levels. Consequently, a significant increase in HOMA-IR was noted in the MSG (2.18±0.84 to 2.57±0.78; $P<.05$) (Figure, A) while ISI index decreased in the CG (1.05±0.29 to 0.89±0.33; $P<.05$) (Figure, B). Also, no significant change was observed in HOMA-β in the CG (83.5±42.3 to 86.9±74.0; NS) (Figure, C), while in the MSG, HOMA-β index decreased significantly (106.9± 43.8 to 99.8±46.3; $P<.05$) (Figure, C). These were associated with increases in TG/HDL ratio and uricemia in both groups, also indicating increases in insulin resistance.

DISCUSSION

In contrast to other studies, our results did not show evidence of hyperactivity of RAAS in patients with abdominal obesity and MS. Some published data suggest a direct association between higher levels of PA and MS, although this association has been demonstrated predominantly in black individuals.[22,23] Apart from differences in ethnicity, the reason for our different results is not known. Although we have studied a miscigenated population, our data are consistent with studies involving predominantly Caucasian individuals.[24,25] Kathiresan and colleagues[24] did not find any correlation between levels of PA and BMI values, while Egan and colleagues[25] did not find differences in mean PA levels between patients with and without MS.

In a previous study, our group also observed that plasma potassium levels in abdominal obese patients, even without diuretic therapy, were lower than in nonobese hypertensive patients.[26] This was attributed to a potential hyperactivity of the RAAS, not confirmed in the present study. Thus, the reasons for

the lower levels of plasma K in our abdominal obese patients are not clear. One could argue that aldosterone levels were relatively high for the levels of plasma potassium found in the MSG and that these lower plasma potassium levels would be masking a hyperactive RAAS by suppressing aldosterone levels. However, this possible mechanism has yet to be proven. The significant negative correlation found between baseline plasma insulin and plasma K in the present study could also suggest a role of hyperinsulinemia in the reduction of plasma potassium levels in abdominal obesity. This has been shown acutely during euglycemic glucose clamp[27] and OGTT,[28] but there is no report describing long-term hyperinsulinemia-inducing hypokalemia.

After HCT therapy, the mean plasma K level in the MSG, which was lower than in the CG at baseline, showed a drop that was smaller than in the CG, despite a significant increase in PA. This resulted in similar plasma K levels at the end of the study in the 2 study groups, suggesting that these lower final plasma K levels may have similarly limited the elevation of PA levels induced by HCT therapy, thereby hindering greater K depletion.

The increased risk of diabetes associated with the use of thiazides has been described in several studies.[7,29,30] In our study, HCT induced glucose intolerance not only in patients with MS but also in nonobese patients. Those patients with MS who were more insulin-resistant prior to HCT therapy showed more evident alterations, particularly in plasma glucose levels post-glucose overload. Our results suggest a worsening of insulin resistance associated with impairment in insulin secretion. In fact, in other studies, the changes that occurred in glucose metabolism after thiazide diuretic administration have been partially attributed to K depletion,[11] decrease in insulin secretion,[11,12] and reduction in peripheral insulin sensitivity.[13] Diuretic-induced increases in angiotensin II associated with hypokalemia may account for reductions in β-cell function and increases in insulin resistance.[11,12,31] Experimental studies have shown that angiotensin II interferes with both insulin action[32] and secretion.[33] Accordingly, it has been observed in clinical trials that angiotensin II blockade in hypertensive patients reduces the incidence of type 2 diabetes.[34]

The TG/HDL ratio showed significant increases in both groups, after HCT therapy, which, according to other studies, reflects a worsening in insulin resistance.[35,36] The increase in this ratio seems to be strongly associated with increase in the number of small LDL cholesterol particles, which are more atherogenic than normal-sized LDL particles, thereby predicting a greater risk of coronary arterial disease.[37]

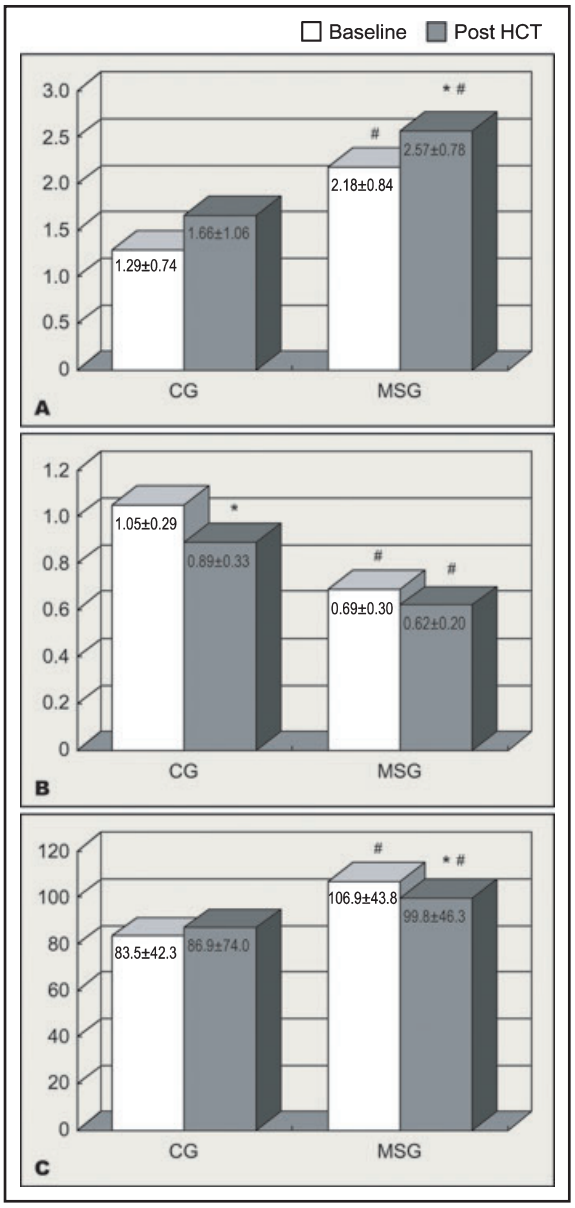

Figure. (A) Homeostasis model assessment of insulin resistance, (B) insulin sensitivity index, (C) and insulin secretion index in the control group (CG) and metabolic syndrome group (MSG). HCT indicates hydrochlorothiazide. *P<.05 *vs baseline* #P<.05 *vs CG.*

CONCLUSIONS

Our results indicate that patients with MS do not present systemic hyperactivity of the RAAS, which cannot explain the lower levels of plasma K found in abdominal obese patients. Although more pronounced in obese patients, the disturbances in glucose metabolism induced by thiazide diuretic therapy seem independent of the presence of MS

and can be attributed to worsening in both insulin resistance and secretion.

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4. ARTIGO 2

INSULIN RESISTANCE-INDUCED HYPOADIPONECTINEMIA AS A DETERMINANT CONDITION FOR POSTPRANDIAL HYPERLIPEMIA

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ABSTRACT

Postprandial hyperlipemia has been associated with insulin resistance while adiponectin plasma levels are inversely correlated with body mass index, and insulin resistance. In this study we determined the relationship between plasma adiponectin and triglyceride levels after an oral lipid overload in 64 subjects, aged 30-62 years, body mass index between 19.0 and 38.9 kg/m^2, showing different degrees of insulin resistance, depending on the degree of obesity. They were given a lipid-enriched meal with plasma triglyceride, adiponectin and insulin determinations at fasting and during 6 hours after the lipid overload. The homeostasis model assessment of insulin resistance (HOMA-IR) was also determined. Subjects were then paired according to body mass index and divided according to HOMA-IR in 2 groups: Low HOMA (n=32; HOMA-IR=1.04±0.63) and High HOMA (n=32; HOMA-IR=2.43±1.24). After lipid overload, triglyceride increased in both groups (P<0.05) showing higher levels in High HOMA than in Low HOMA group. Adiponectin levels also increased with lipid overload in both groups but, contrasting with triglyceride levels, were higher in Low HOMA than in High HOMA group (P<0.05). During lipid overload test, in all subjects triglyceride levels was inversely correlated with adiponectin levels and positively with insulin levels and body mass index. However, multivariate analyses identified only adiponectin levels as the major factor influencing triglyceride levels. In conclusion, independent on body mass index, insulin resistance-induced hypoadiponectinemia impairs plasma triglyceride clearance.

Key words: hypoadiponectinemia, postprandial hyperlipemia, insulin resistance, obesity.

INTRODUCTION

Accumulating clinical and experimental data suggest that postprandial hyperlipemia (PPHL) is related to the development of coronary artery disease, once PPHL is associated with several metabolic abnormalities that contribute to atherogenesis.[1-6] Postprandial hypertriglyceridemia, even in the absence of fasting triglyceride (TG) abnormalities, has been associated with increases in postprandial glucose and insulin levels,[7] and was identified as a marker of insulin resistance, preceding impaired glucose tolerance.[8] Therefore, PPHL has been proposed as a new component of metabolic syndrome and establishes a new experimental field in order to understand the atherosclerotic process.[9-11] In the insulin resistance state, increases in TG levels after a lipid-enriched meal has been attributed to decreases in lipoprotein lipase (LPL) activity[12] which is the key enzyme in the intravascular catabolism of chylomicrons and very low-density lipoprotein (VLDL).[13]

Adiponectin is an adipose tissue-specific collagen-like factor with insulin sensitizing,[14] anti-inflammatory, and antiatherogenic properties.[15] However, although adiponectin is produced by adipose tissue, it has been demonstrated that increases in body mass index are invariably accompanied by significant decreases in plasma adiponectin levels.[16,17] Hypoadiponectinemia contributes to the abnormalities of metabolic syndrome including increases in circulating free fat acids which, in turn, contribute to the development of insulin resistance,[18] hypertension,[19] and hypertriglyceridemia.[20]

In this study, we therefore evaluated the relationship between adiponectin levels and postprandial triglyceridemia in subjects showing different degrees of insulin resistance imposed by the presence of obesity.

METHODS

This cross-sectional study was carried out in Hypertension and Cardiovascular Disease Outpatient Clinic at *Hospital do Rim e Hipertensão*, Divisions of Endocrinology and Nephrology, Department of Medicine, Federal University of Sao Paulo (UNIFESP).

The study was approved by the Internal Ethics Committee of UNIFESP, and each patient gave informed consent.

Sixty-four male subjects of a admixtured multi-ethnic population, aged 30 to 62 years, body mass index (BMI) between 19.0 and 38.9 kg/m^2, were eligible, consisting thereafter of a sample of subjects with different degrees of insulin resistance, depending on the degree of obesity. Those who presented previous history of diabetes, showing a weight variation higher than 3 kg in the last 3 months, chronic renal failure, hepatopathy or cardiovascular failure, smoking, and alcoholism were excluded. Those who were on any type of antihypertensive or lipid lowering drug and/or insulin sensitizing agents had their medications interrupted for a period of 4 weeks. After 2 weeks of the medication withdrawn, subjects who presented fasting glucose levels ≥ 7 mmol/L, total cholesterol > 7.7 mmol/L, TG > 4.5 mmol/L or systolic blood pressure ≥ 160 mm Hg and/ or diastolic blood pressure ≥ 100 mm Hg were also not included.

After the washout period, all subjects were submitted to a physical examination, blood sample collection for lipid profile, and completed an oral glucose tolerance test ([OGTT], 75-gram glucose load), with plasma glucose and insulin levels determinations. Fasting plasma insulin was also determined for the homeostasis model assessment of insulin resistance (HOMA-IR) calculation.[21]

Blood pressure (BP) was measured using a sphygmomanometer (Tycos® 509 aneroid sphygmomanometer) and was taken as the mean of 3 readings measured 2 to 3 minutes apart on the right arm (with the forearm resting on the desk) after the subjects had been seated for ≥ 10 minutes. Systolic and diastolic (Korotkoff phase V) BP readings, measured by well-trained physician, were recorded to the nearest 2 mm Hg. Standard-sized cuffs were used. Hypertension was defined as sitting BP ≥ 140/90 mm Hg or regular antihypertensive drugs.[22] The BMI was calculated and classificated according the World Health Organization (WHO).[23] The waist circumference was determined in centimeters, at the midpoint between the lowest rib and the iliac crest at the end of a normal expiration in orthostatic position. The hip circumference, in centimeters, was determined in order to calculate the waist-hip ratio.[23]

On the next day of the OGTT, an oral lipid overload test was performed at fasting with a standard mixed meal consisting of 1 omelet (milk, egg, cheese, ham, and butter), 2 vienna sausages, and 1 milkshake (150 mL), which provided 1.300 kcal, was composed of 67% fat (35% saturated fat), 17% carbohydrate, and 16% protein. The meal was ingested in 15 minutes with no other food or beverage consumed through the 6-hour testing period. Plasma TG and glucose levels were determined at fasting and every hour, plasma insulin levels at fasting and every 2 hours, and adiponectin levels at fasting, 4 and, 6 hours after lipid overload. The blood samples were immediately centrifuged, and the plasma or serum portions were collected and frozen at -70 ºC.

Adiponectin samples were quantitated in duplicate by enzyme-linked immunosorbent assay (ELISA) (LINCO Research, St. Charles, MO), with the analytical sensitivity of 0.78 ng/mL, and both the intra- and interassay variability were <5%. Plasma glucose was determined by the oxidase method. Total cholesterol, high-density lipoprotein (HDL) cholesterol, and TG were measured

using the colorimetric enzymatic method. Low-density lipoprotein (LDL) cholesterol was calculated by the Friedwald's formula.[24] The analyzer used was HITACHI 912 (Roche Diagnostics, Basel, Switzerland). Plasma insulin was determined by chemiluminescent immunometric assay (Immulite – SIEMENS, Los Angeles, CA).

The magnitude of TG response was quantified as the total area under the curve (AUC), as well as the incremental area under the curve (IAUC) of TG calculated by the trapezoidal rule.

Statistical Analysis

Statistical analyses were performed using SPSS version 16.0 software for Windows (SPSS, Inc, Chicago, IL). The differences observed in the variables studied were analyzed through a paired *t* test for dependent measures and a *t* test for independent measures so as to allow the comparison of variables within and between groups, respectively. Repeated-measures ANOVA was performed to compare more than 2 values of a variable within a determined group. Pearson coefficient was calculated to determine correlations between different variables. Multivariate regression analysis was performed to evaluate the influence of BMI, adiponectin and insulin levels (independent variables) on the values of the fasting and postprandial TG levels (dependent variable). Data were expressed as mean ± SD and significant statistically differences were defined as $P < 0.05$.

RESULTS

The main clinical and laboratory characteristics of the 64 male subjects that were included in this study are presented in Table 1.

During the oral lipid overload, in all subjects the plasma TG levels increased significantly from the fasting value of 1.59 ± 0.82 mmol/L to 1.73 ± 0.92 ($P = 0.01$) at 60 minutes, reached the peak value of 2.68 ± 1.28 mmol/L ($P < 0.001$) at 240 minutes and then decreased to 2.23 ± 1.32 mmol/L at 360 minutes but remained higher than the fasting value ($P < 0.001$). It was also observed that the IAUC of TG strongly correlated with the levels obtained at 240 minutes after the lipid-enriched meal ($r = 0.973$; $P < 0.001$)

To assess the relationship of insulin resistance and adiponectin levels with postprandial TG levels, we divided all subjects in 2 groups, matched for BMI, and showing different degrees of insulin resistance, according to HOMA-IR named low HOMA ([L HOMA] n=32) and high HOMA ([H HOMA] n=32) groups. There was no significant statistical difference in age, BMI, waist circumference, waist-hip ratio, systolic and diastolic BP, and total and LDL-cholesterol values between the 2 study groups except for HDL-cholesterol values that were lower in the H HOMA than in L HOMA group (1.09 ± 0.26 vs 1.27 ± 0.38 mmol/L; $P < 0.05$) (Table 1).

During the oral lipid overload, the H HOMA group, compared with L HOMA group, presented higher plasma TG levels at 300 min (2.81 ± 1.33 vs 2.11 ± 1.16 mmol/L; $P< 0.05$) and at 360 min (2.62 ± 1.42 vs 1.83 ± 1.09 mmol/L; $P < 0.05$) (Figure 1, A), and, consequently, higher IAUC of TG (9.62 ± 4.25 mmol.h/L vs 7.63 ± 3.86 mmol.h/L; $P < 0.05$), respectively. It was observed that plasma TG at 360 minutes after lipid overload returned to the fasting values in L HOMA group (1.83 ± 1.09 to 1.53 ± 0.80 mmol/L; NS) but remained higher than

the fasting values in H HOMA group (2.62 ± 1.42 to 1.66 ± 0.84 mmol/L; $P < 0.001$). In both H HOMA and L HOMA groups, fasting adiponectin levels increased significantly in response to lipid overload at 360 minutes, from 4.36 ± 2.13 to 5.54 ± 3.35 ng/mL ($P < 0.05$) and from 6.12 ± 3.82 to 7.60 ± 5.03 ng/mL ($P < 0.05$), respectively (Figure 1, B). However, during lipid overload, adiponectin levels were lower in H HOMA group than in L HOMA group at fasting (4.36 ± 2.13 vs 6.12 ± 3.82 ng/mL; $P < 0.05$), at 240 min (4.61 ± 2.38 vs 6.70 ± 4.6 ng/mL; $P < 0.05$), and at 360 minutes (5.54 ± 3.35 vs 7.6 ± 5.03 ng/mL; $P < 0.05$).

As also shown in Figure 1, C, during OGTT, plasma glucose levels at fasting were not different between groups. After 2 hours of glucose load, the plasma glucose in the L HOMA group did not differ from the fasting values whereas in the H HOMA group it was higher than the fasting values of both groups. As expected, during OGTT, plasma insulin levels in the H HOMA group were higher than that observed in the L HOMA group (Figure 1, D).

In the whole group, adiponectin correlate negatively with TG (r = -0.313; $P < 0.001$) and plasma insulin levels (r = -0,368; $P < 0.001$), measured at fasting, 240, and 360 minutes after lipid overload. Significant positive correlations were also found both between BMI (r = 0.234; $P = 0.001$) and plasma insulin levels (r = 0.297; $P < 0.001$) and TG levels during lipid overload test. However, multivariate regression analyses with plasma TG as the dependent variable and BMI, plasma adiponectin, and insulin as the independent variables, considering all data obtained at fasting, 240, and 360 minutes during lipid overload (n=192), identified only adiponectin levels ($\beta = -0.264$; $P = 0.001$) as the major independent factor influencing the TG levels (Table 2).

DISCUSSION

In this study, the results obtained during an oral lipid overload test have shown that TG peak occurs at 4 hours after lipid overload returning to the basal levels after 6 hours in those subjects with low insulin resistance but not in those with higher insulin resistance. This pattern of response was similar to that observed for plasma glucose during OGTT, with those subjects with low insulin resistance, but not those insulin-resistant, showing 2 hours after glucose overload, plasma glucose levels not different from the basal values. These observations indicate that, not only plasma glucose uptake, but also plasma TG clearance is reduced in the insulin resistance state. The clinical importance of this finding lies, therefore, in the fact that lipid postprandial elevations persist all day long, once a new meal must be ingested within the period of 4-6 hours. In fact, Halkes et al,[7] evaluating the TG levels in obese patients during a 24-hour period, have showed that after breakfast the TG levels did not return to the fasting values, remaining high during all day. Consequently, TG levels determined after a 12-hour fasting period, according to what is done in clinical practice, may not be appropriated to adequately evaluate postprandial abnormalities in lipid metabolism associated to insulin resistance, since fasting plasma TG levels in this condition may be within the normal range. However, as already shown by Karamanos et al,[25] in our study, a strong correlation could be observed, between the TG peak values observed 4 hours after lipid overload and their incremental postprandial area under the curve. Thus, with a lipid-enriched meal, similar to that employed in this study, and just one post meal determination of plasma TG levels, it is possible to detect postprandial abnormalities in lipid metabolism.

The clinical regard of the maintenance of hypertriglyceridemia during all day long lies in the fact that this metabolic abnormality induces reductions in HDL-cholesterol levels[26,27] thereby predicting a greater risk of coronary heart

disease mortality.[28] These lipid alterations are characteristic of metabolic syndrome which is a state of insulin resistance.[29] Increases in TG levels in this condition have been attributed to increases in hepatic production and to the occurrence of reduced LPL activity.[30]

Previous reports suggest that adiponectin plays a role in mediating insulin sensitivity and fat oxidation.[31,32] Marked reductions in plasma TG levels were demonstrated in an experimental study in a mouse model showing high levels of adiponectin after Ad-mACRP30 adenovirus injection.[20] However, in this model, hepatic TG secretion rates were not altered by elevated adiponectin plasma levels whereas LPL activity showed a marked increase. The authors concluded that adiponectin increases TG catabolism without interfering on hepatic production. These findings suggest that adiponectin may be important to avoid marked increases in postprandial lipemia.

There are conflicting data concerning the influence that dietary fat content might have on adiponectin levels in humans. Berk et al,[33] studied lean and obese subjects maintained on an eucaloric diet with manipulations of carbohydrates and fat content for 1 week, detected that, within the obese group, the insulin-sensitive patients had significantly higher adiponectin during high-fat diet than did the insulin-resistant patients. Nevertheless, it has been shown that a single high fat meal either decreases[34] or has no effect[35] on postprandial adiponectin levels in normal and insulin-resistant subjects. In contrast, we demonstrated for the first time that plasma levels of adiponectin acutely increases after an oral lipid overload test. In all subjects, the significant inverse correlation observed between plasma adiponectin and TG levels during the lipid overload suggested a cause-effect relationship between these two variables, with insulin resistance interfering in this relationship. Those individuals showing higher degrees of insulin resistance also presenting higher plasma TG and lower adiponectin levels.

An association of decreased LPL activity with low adiponectin levels has been recently demonstrated.[36] It is known that TG clearance occurs as a two-step process: first, lipoproteins are hydrolyzed by LPL-releasing NEFA (non-esterified fatty acid); second, NEFA is taken up into the cell through a specific transport and re-esterefied to a storage TG molecule.[37] Excess generation and local accumulation of NEFA, however, inhibits LPL activity.[38] Thus, in a condition of increased of TG rich lipoprotein levels this mechanism would be responsible for the suppression of LPL activity. Adiponectin is known to enhance TG rich lipoprotein catabolism and fatty acid oxidation independently of insulin resistance.[39] However, adiponectin levels are reduced in central obesity,[16] a state of insulin resistance, and these low levels can contribute to increase free fat acid circulating levels and to decrease LPL activity,[36] which in turn would result in high TG lipoprotein levels, especially after a high fat meal. In our study, low LPL activity might be the factor linking the lower adiponectin to the high TG levels in the group showing higher insulin resistance.

Although produced only in adipocytes, it has been demonstrated that adiponectin correlates inversely with body mass index.[16] However, as shown in our study not only the amount of fat mass accounts for adiponectin production since we could observed in 2 groups, with similar body mass index, different amounts of adiponectin in the circulation in response to lipid overload test. The paradoxical down-regulation of adiponectin during obesity results from complex cross-regulatory interactions between adiponectin and inflammatory cytokines.[40] Oxidative stress has been suggested to inhibit the expression of adiponectin.[41] Also, it has been shown in experimental conditions that insulin controls adiponectin expression through an insulin-regulated secretory pathway in adipocytes.[42]

CONCLUSIONS

In conclusion, based on our results, we can raise the hypothesis that in insulin resistant states, insulin-induced adiponectin production is impaired, leading to delayed clearance of postprandial TG, possibly related to decreases in LPL activity.

The findings of this study would support a role for hypoadiponectinemia in the pathogenesis of postprandial hyperlipemia. These data have provided new insight into the mechanisms underlying the development of delayed clearance of postprandial TG. The findings of the current study need to be confirmed in larger population-based studies involving subjects of both sexes to further investigate the potential application of plasma adiponectin as a biomarker to identify subjects at higher cardiovascular risk. In addition, it would be of interest evaluate the effects of drugs which increase adiponectin on postprandial hyperlipemia.

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TABLES

Table 1. Clinical and Laboratorial Findings in Subjects When Divided in Low HOMA-IR (L HOMA) and High HOMA-IR (H HOMA) Groups

Parameter	**L HOMA**	**H HOMA**
N	32	32
Age, y	43.9 ± 8.1	42.3 ± 8.1
Body Mass Index, kg/m^2	29.3 ± 5.1	29.5 ± 5.0
Waist circumference, cm	96.6 ± 11.8	101.1 ± 14.2
Waist-hip ratio	0.95 ± 0.05	0.96 ± 0.07
Systolic blood pressure, mm Hg	129.8 ± 13.6	129.3 ± 14.5
Diastolic blood pressure, mm Hg	85.3 ± 8.6	85.7 ± 9.8
Glucose 0 min (OGTT), mmol/L	5.00 ± 0.67	5.18 ± 0.67
Glucose 120 min (OGTT), mmol/L	5.24 ± 1.50	6.05 ± 1.41*#
Insulin 0 min (OGTT), μU/mL	4.66 ± 2.70	10.58 ± 5.43*
Insulin 120 min (OGTT), μU/mL	39.71 ± 39.63	90.17 ± 72.58*
HOMA-IR	1.04 ± 0.63	2.43 ± 1.24*
Fasting triglycerides, mmol/L	1.53 ± 0.81	1.65 ± 0.84
Total cholesterol, mmol/L	5.12 ± 0.98	5.08 ± 1.03
LDL-cholesterol, mmol/L	3.12 ± 0.76	3.16 ± 0.86
HDL-cholesterol, mmol/L	1.27 ± 0.38	1.09 ± 0.26*

Data are mean ± SD. 0 min indicates fasting on the oral glucose tolerance test (OGTT); 120 min, 120 minutes after glucose load on the oral glucose tolerance test (OGTT); HOMA-IR, homeostasis assessment model of insulin resistance; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

* P< 0.05 vs L HOMA group # P< 0.05 vs Glucose 0 min

Table 2. Multivariate Regression Analyses Predicting Fasting and Postprandial Triglyceride Levels During the Oral Lipid Overload

	All Subjects		
Variable	**β**	**t**	***P***
Adiponectin levels	-0.264	-3.325	0.001*
Insulin levels	0.120	1.310	0.192
Body Mass Index	0.129	1.512	0.133

Dependent variable: fasting and postprandial triglyceride levels

Independent variable: body mass index, plasma adiponectin and insulin levels

* *P*= 0.001

FIGURE

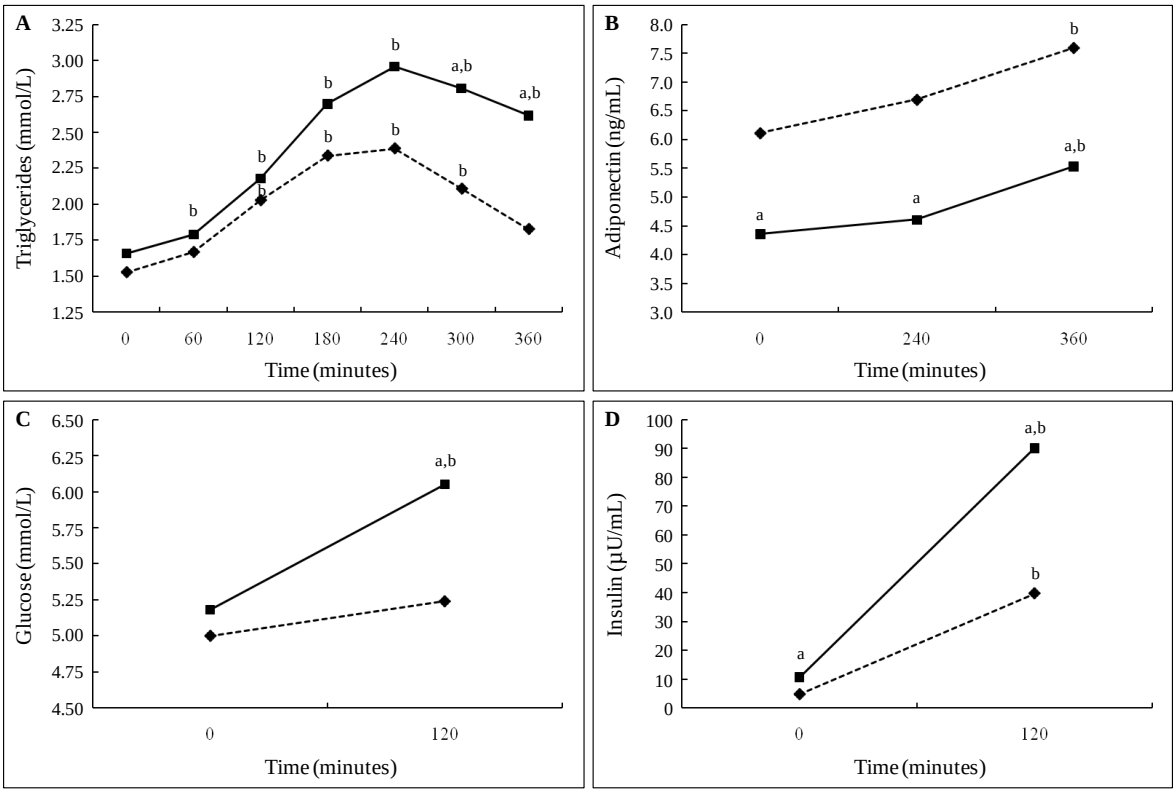

Figure 1. Plasma Triglyceride (A) and Adiponectin (B) Levels During the Oral Lipid Overload and Plasma Glucose (C) and Insulin (D) Levels During the Oral Glucose Tolerance Test in Low HOMA and High HOMA Groups

Figure Legend

High HOMA group Low HOMA group

a, $P < 0.05$ vs Low HOMA group; b, $P < 0.05$ vs 0 minute.

5. SUMÁRIO E CONCLUSÕES

ARTIGO 1

SUMÁRIO

Antes do tratamento com hidroclorotiazida

- O grupo de pacientes com a síndrome metabólica apresentou menores níveis plasmáticos de potássio não relacionados a maiores níveis de aldosterona.

- Ausência de diferenças na atividade sistêmica do sistema renina-angiotensina-aldosterona entre os dois grupos.

- Em todos os pacientes avaliados, se observou uma correlação negativa entre os níveis plasmáticos de potássio e a insulinemia de jejum.

Após o tratamento com hidroclorotiazida

- Os dois grupos de pacientes apresentaram níveis semelhantes de potássio plasmático, embora o aumento da aldosterona tenha sido mais acentuado nos pacienets com a síndrome metabólica.

- Nos dois grupos, as anormalidades no metabolismo da glicose se caracterizaram por:

- piora da sensibilidade à insulina;

- menor capacidade secretora de insulina;

- elevações dos níveis glicêmicos consequentes à redução (pacientes com a síndrome metabólica) ou elevação insuficiente (pacientes sem a síndrome metabólica) na secreção de insulina.

- As diferenças encontradas no metabolismo da glicose entre os dois grupos de pacientes não se mostraram dependentes dos níveis plasmáticos de potássio, mas do grau inicial de resistência à insulina.

CONCLUSÕES

- Os menores níveis plasmáticos de potássio encontrados nos pacientes com obesidade abdominal não decorrem de hiperatividade sistêmica do sistema renina-angiotensina-aldosterona.

- Os distúrbios no metabolismo da glicose induzidos pelo tratamento com diurético tiazídico podem ser observados mesmo em condições de baixa resistência à insulina. Entretanto, a magnitude das alterações observadas se mostram dependentes das condições basais de resistência à insulina, conferidas pelo acúmulo de gordura abdominal.

- Embora após a administração de hidroclorotiazida os níveis plasmáticos de potássio tivessem se mostrado semelhantes nos dois grupos, o impacto da terapia diurética na ação e secreção de insulina, ainda que associada a menor redução da calemia, mostrou-se maior em condições de maior resistência à insulina.

ARTIGO 2

SUMÁRIO

- Durante o teste de sobrecarga lipídica o pico dos triglicérides ocorreu aos 240 minutos e retornaram aos níveis de jejum aos 360 minutos, apenas nos indivíduos com menor resistência à insulina.

- Em todos os indivíduos avaliados, ocorreu um aumento agudo da adiponectinemia, primeira vez demonstrado na literatura, em resposta ao teste oral de sobrecarga lipídica.

- O maior grau de resistência à insulina se associou a menor produção de adiponectina e a maiores níveis de triglicérides após a ingestão de uma dieta hiperlipídica.

- No teste oral de sobrecarga lipídica, menores níveis de adiponectina se correlacionaram a maiores níveis de triglicérides.

CONCLUSÕES

- Os resultados do nosso estudo nos permitem levantar a hipótese de que os níveis plasmáticos mais baixos de adiponectina decorrem não só de elevações no índice de massa corporal, mas também da ocorrência de maior grau de resistência à insulina, o que resulta em retardo na depuração dos triglicérides circulantes, possivelmente relacionado à diminuição da atividade da lipase lipoprotéica.

6. ANEXOS

Anexo 1: Dados individuais dos pacientes do Artigo 1

NOME	Nº	GRUPO	GÊNERO	IDADE	TABAGISMO	USO TRH	IMC PRÉ-HCT	IMC PÓS-HCT	CIRC. CINT. PRÉ-HCT	CIRC. CINT. PÓS-HCT	CIRC. QUA PRÉ-HCT	CIRC. QUA PÓS-HCT
MAS	1	NÃO SM	FEM	58	NÃO	NÃO	24,76	23,16	79	76	99	98
BEM	2	NÃO SM	FEM	45	SIM	NÃO	20,99	20,61	79	79	88	88
MLMB	3	NÃO SM	FEM	51	NÃO	NÃO	22,75	22,75	79	78	87	88
IFS	4	NÃO SM	FEM	50	SIM	NÃO	22,81	23,55	75	75	93	93
NK	5	NÃO SM	FEM	59	NÃO	NÃO	24,17	22,88	77	74	97	98
EMCP	6	NÃO SM	FEM	36	NÃO	NÃO	25	25,19	80	79	97	99
AMJ	7	NÃO SM	FEM	46	SIM	NÃO	24,25	25,58	79	79	100	101
AMPS	8	NÃO SM	FEM	53	NÃO	NÃO	25,3	23,95	79	77	102	103
MFMS	9	NÃO SM	FEM	53	SIM	NÃO	23,91	24,35	77	77	91	92
JJP	10	NÃO SM	MASC	58	NÃO	NÃO	21,87	21,79	78	78	84	85
MADS	11	NÃO SM	MASC	55	NÃO	NÃO	23,04	22,41	84	84	93	92
NB	12	NÃO SM	MASC	57	SIM	NÃO	21,98	22,7	84	86	94	96
BDP	13	NÃO SM	MASC	56	NÃO	NÃO	20,34	20,89	75	76	93	94
JFLS	14	NÃO SM	MASC	40	NÃO	NÃO	28,77	28,16	92	91	104	102
AMS	15	NÃO SM	MASC	54	NÃO	NÃO	27,2	27,57	93	92	102	102
JBS	16	NÃO SM	MASC	43	NÃO	NÃO	28,88	29,4	87	89	94	96
JPO	17	NÃO SM	MASC	57	NÃO	NÃO	25,55	26,78	92	93	104	106
SOE	18	NÃO SM	MASC	34	NÃO	NÃO	28,22	27,65	93	92	105	105
LFC	19	NÃO SM	MASC	32	NÃO	NÃO	27,31	26,95	93	91	103	104
CPA	20	SM	FEM	50	NÃO	NÃO	35,83	35,4	113	113	122	121
TBM	21	SM	FEM	59	NÃO	SIM	35	34,35	99	98	107	109
HW	22	SM	FEM	52	NÃO	SIM	29,79	31,08	98	99	105	107
AMDS	23	SM	FEM	51	NÃO	NÃO	31,56	31,04	98	99	108	108
IMP	24	SM	FEM	60	NÃO	NÃO	28,6	28,43	100	99	113	111
CCB	25	SM	FEM	54	NÃO	NÃO	36	35,24	110	107	129	129
LDSR	26	SM	FEM	56	NÃO	NÃO	38,08	38,41	114	113	113	116
LDCS	27	SM	FEM	31	NÃO	NÃO	35,73	35,18	114	114	126	126
EMLV	28	SM	FEM	58	NÃO	NÃO	28,82	28	92	92	106	106
MCMM	29	SM	FEM	59	NÃO	NÃO	29,83	28,86	101	100	107	106
LPDS	30	SM	MASC	48	SIM	NÃO	31,83	31,61	110	110	102	104
JAAS	31	SM	MASC	39	SIM	NÃO	31,67	32,06	114	116	111	111
FLSJ	32	SM	MASC	34	NÃO	NÃO	31,15	30,9	113	114	105	106
EPDS	33	SM	MASC	30	NÃO	NÃO	38,58	38,58	123	123	119	120
DJDF	34	SM	MASC	56	NÃO	NÃO	37,23	37,58	111	113	114	114
RDSB	35	SM	MASC	43	SIM	NÃO	36,56	37,34	123	124	115	114
MHS	36	SM	MASC	44	NÃO	NÃO	33,4	32,87	123	120	110	111
AFDS	37	SM	MASC	42	NÃO	NÃO	38,62	39,23	115	116	110	111
JPDS	38	SM	MASC	38	NÃO	NÃO	35,39	34,53	115	113	109	110
JLF	39	SM	MASC	38	NÃO	NÃO	36,6	36,98	127	127	121	123

NOME	Nº	GRUPO	RCQ PRÉ-HCT	RCQ PÓS-HCT	FC PRÉ-HCT	FC PÓS-HCT	PAS PRÉ-HCT	PAS PÓS-HCT	PAD PRÉ-HCT	PAD PÓS-HCT	USO METILDOPA	ALD PRÉ-HCT	ALD PÓS-HCT
MAS	1	NÃO SM	0,79	0,77	73	77	156	135	93	86	SIM	12,5	33,0
BEM	2	NÃO SM	0,89	0,89	80	68	136	109	91	81	NÃO	7,0	19,7
MLMB	3	NÃO SM	0,9	0,88	77	84	143	136	91	97	NÃO	12,7	5,5
IFS	4	NÃO SM	0,8	0,8	71	63	153	152	91	85	SIM	25,8	11,0
NK	5	NÃO SM	0,79	0,75	84	81	145	155	95	93	SIM	15,1	18,8
EMCP	6	NÃO SM	0,82	0,79	79	74	123	128	96	96	NÃO	15,2	14,8
AMJ	7	NÃO SM	0,79	0,78	71	70	155	146	99	96	NÃO	11,0	24,5
AMPS	8	NÃO SM	0,77	0,74	64	65	146	130	93	89	SIM	10,2	14,8
MFMS	9	NÃO SM	0,84	0,83	77	71	125	126	85	81	NÃO	20,0	45,9
JJP	10	NÃO SM	0,92	0,91	64	56	153	129	97	79	NÃO	5,3	7,5
MADS	11	NÃO SM	0,9	0,91	91	79	157	140	95	97	NÃO	10,4	17,6
NB	12	NÃO SM	0,89	0,89	56	55	132	113	94	72	NÃO	12,5	8,8
BDP	13	NÃO SM	0,8	0,8	75	69	140	124	95	83	NÃO	20,1	38,7
JFLS	14	NÃO SM	0,88	0,89	72	71	139	123	95	80	NÃO	12,2	7,4
AMS	15	NÃO SM	0,92	0,9	61	56	143	135	95	90	NÃO	30,6	31,7
JBS	16	NÃO SM	0,92	0,92	74	80	153	145	93	95	SIM	27,6	24,4
JPO	17	NÃO SM	0,88	0,87	72	82	133	135	94	93	SIM	12,1	40,9
SOE	18	NÃO SM	0,88	0,87	81	76	133	113	90	92	SIM	6,6	12,0
LFC	19	NÃO SM	0,9	0,87	81	73	131	137	93	95	NÃO	26,5	20,1
CPA	20	SM	0,92	0,93	75	82	137	123	89	85	SIM	11,2	13,6
TBM	21	SM	0,92	0,9	89	81	140	113	97	92	NÃO	14,9	61,2
HW	22	SM	0,93	0,92	58	75	131	111	83	81	NÃO	22,9	42,9
AMDS	23	SM	0,9	0,91	77	82	139	134	95	91	NÃO	8,0	41,2
IMP	24	SM	0,88	0,89	61	67	149	134	73	87	NÃO	20,0	25,4
CCB	25	SM	0,85	0,83	88	73	129	134	91	85	SIM	12,2	16,4
LDSR	26	SM	1	0,97	79	83	147	142	93	90	NÃO	13,3	18,2
LDCS	27	SM	0,9	0,9	79	76	127	121	97	90	NÃO	21,0	18,2
EMLV	28	SM	0,86	0,86	76	74	155	156	95	95	NÃO	15,5	37,9
MCMM	29	SM	0,94	0,94	79	76	139	117	92	86	NÃO	5,6	29,3
LPDS	30	SM	1,07	1,05	87	83	141	120	93	75	NÃO	5,6	33,7
JAAS	31	SM	1,02	1,04	76	74	138	133	91	87	SIM	13,1	8,8
FLSJ	32	SM	1,07	1,07	67	71	141	123	96	85	SIM	14,0	46,0
EPDS	33	SM	1,03	1,02	86	85	142	135	92	93	SIM	18,7	43,1
DJDF	34	SM	0,97	0,99	71	75	143	141	95	89	SIM	13,8	11,8
RDSB	35	SM	1,06	1,08	72	72	136	135	92	89	NÃO	26,2	30,6
MHS	36	SM	1,11	1,08	82	84	129	121	89	95	SIM	17,6	21,5
AFDS	37	SM	1,04	1,04	78	83	134	137	94	85	NÃO	15,4	18,1
JPDS	38	SM	1,05	1,02	67	71	141	139	92	89	NÃO	33,6	8,0
JLF	39	SM	1,04	1,03	86	86	151	141	98	92	NÃO	22,4	47,6

NOME	Nº	GRUPO	REN PRÉ-HCT	REN PÓS-HCT	CREAT PRÉ-HCT	CREAT PÓS-HCT	K PRÉ-HCT	K PÓS-HCT	DELTA K	NA PRÉ-HCT	NA PÓS-HCT	GLI (0MIN) PRÉ-HCT	GLI (0MIN) PÓS-HCT
MAS	1	NÃO SM	1,7	6,6	1,0	1,1	4,4	3,7	-0,7	142	140	98	111
BEM	2	NÃO SM	3,0	7,0	1,0	1,1	4,9	4,1	-0,8	134	136	104	109
MLMB	3	NÃO SM	1,2	1,5	1,0	1,1	4,9	3,8	-1,1	136	140	81	88
IFS	4	NÃO SM	0,2	0,4	0,9	0,9	4,1	4,0	-0,1	138	138	84	96
NK	5	NÃO SM	2,3	4,4	1,0	1,0	4,4	3,5	-0,9	139	142	113	123
EMCP	6	NÃO SM	1,1	1,8	0,9	0,9	4,7	4,0	-0,7	138	138	86	85
AMJ	7	NÃO SM	1,6	3,3	0,8	0,8	4,3	3,5	-0,8	138	135	88	83
AMPS	8	NÃO SM	0,6	18,5	0,9	1,1	4,3	4,2	-0,1	136	140	85	97
MFMS	9	NÃO SM	0,2	2,7	1,0	1,3	4,2	3,3	-0,9	137	140	87	93
JJP	10	NÃO SM	0,2	2,1	1,2	1,3	4,5	4,3	-0,2	138	134	91	90
MADS	11	NÃO SM	0,2	0,7	0,9	1,0	4,5	3,7	-0,8	138	138	94	116
NB	12	NÃO SM	1,1	1,8	1,0	0,9	4,9	3,5	-1,4	141	139	86	176
BDP	13	NÃO SM	1,3	2,7	1,2	1,2	5,0	4,3	-0,7	134	134	119	133
JFLS	14	NÃO SM	0,2	1,5	1,2	1,1	4,5	3,7	-0,8	137	142	87	79
AMS	15	NÃO SM	0,2	1,7	1,2	1,1	4,3	3,4	-0,9	138	139	86	90
JBS	16	NÃO SM	2,5	2,2	1,2	1,3	4,6	3,7	-0,9	137	136	88	97
JPO	17	NÃO SM	0,7	0,6	1,1	1,1	4,0	3,7	-0,3	136	139	81	87
SOE	18	NÃO SM	0,2	0,2	1,0	1,2	4,6	3,7	-0,9	136	140	72	72
LFC	19	NÃO SM	3,1	3,0	1,0	0,8	4,4	4,2	-0,2	139	136	91	85
CPA	20	SM	0,5	1,6	0,9	0,7	3,7	3,1	-0,6	138	139	102	105
TBM	21	SM	2,5	3,5	0,9	1,1	4,1	3,7	-0,4	136	141	82	97
HW	22	SM	0,2	2,1	1,0	1,0	4,7	4,3	-0,4	136	140	95	103
AMDS	23	SM	0,9	1,7	0,8	0,9	4,4	4,1	-0,3	137	137	96	107
IMP	24	SM	1,8	2,0	0,9	0,9	4,5	4,4	-0,1	141	138	100	114
CCB	25	SM	0,3	1,3	0,9	0,9	4,2	4,1	-0,1	135	141	73	88
LDSR	26	SM	0,2	0,2	0,9	0,9	4,6	4,4	-0,2	134	140	83	88
LDCS	27	SM	0,2	2,0	0,9	0,9	4,5	4,4	-0,1	135	138	98	104
EMLV	28	SM	0,2	0,4	1,0	1,0	4,3	4,5	0,2	136	141	104	112
MCMM	29	SM	1,4	4,0	0,9	1,0	5,0	4,2	-0,8	136	138	104	114
LPDS	30	SM	2,9	4,3	1,2	1,3	4,1	3,8	-0,3	137	138	116	118
JAAS	31	SM	0,2	1,2	1,1	0,9	4,0	3,7	-0,3	139	141	92	88
FLSJ	32	SM	0,7	3,2	1,1	1,1	4,2	3,9	-0,3	138	139	88	93
EPDS	33	SM	1,2	7,4	1,1	0,9	4,3	3,7	-0,6	135	141	70	83
DJDF	34	SM	2,2	1,4	1,0	0,9	3,9	3,6	-0,3	135	140	92	110
RDSB	35	SM	1,1	1,4	1,2	1,2	4,1	4,3	0,2	136	135	95	114
MHS	36	SM	0,2	4,5	1,1	1,0	4,2	4,0	-0,2	138	143	102	92
AFDS	37	SM	0,7	2,7	1,2	1,4	3,8	3,8	0,0	138	143	94	89
JPDS	38	SM	0,2	1,2	1,0	0,9	4,0	3,4	-0,6	134	142	106	101
JLF	39	SM	0,5	0,9	1,2	1,2	4,2	3,6	-0,6	137	141	102	104

NOME	Nº	GRUPO	GLI (120MIN) PRÉ-HCT	GLI (120MIN) PÓS-HCT	INS (0MIN) PRÉ-HCT	INS (0MIN) PÓS-HCT	INS (120MIN) PRÉ-HCT	INS (120MIN) PÓS-HCT	ISI PRÉ-HCT	ISI PÓS-HCT	HOMA IR PRÉ-HCT	HOMA IR PÓS-HCT
MAS	1	NÃO SM	164	174	9,6	7,8	152,9	119,4	0,28	0,32	2,3	2,1
BEM	2	NÃO SM	117	122	9,8	8,7	60,7	51,7	0,61	0,66	2,5	2,3
MLMB	3	NÃO SM	106	105	4,0	4,2	24,5	36,7	1,13	0,93	0,8	0,9
IFS	4	NÃO SM	111	117	4,5	4,7	8,9	20,7	1,45	1,12	0,9	1,1
NK	5	NÃO SM	138	171	2,8	2,9	37,9	26,3	0,80	0,89	0,8	0,9
EMCP	6	NÃO SM	87	88	5,5	7,4	30,6	110,9	1,05	0,50	1,2	1,6
AMJ	7	NÃO SM	83	78	6,5	2,1	41,4	21,8	0,91	1,28	1,4	0,4
AMPS	8	NÃO SM	82	125	7,7	5,4	34,0	103,1	0,99	0,44	1,6	1,3
MFMS	9	NÃO SM	74	74	5,8	2,3	36,9	53,2	1,00	0,85	1,2	0,5
JJP	10	NÃO SM	91	82	2,4	5,4	18,1	14,7	1,30	1,33	0,5	1,2
MADS	11	NÃO SM	121	131	2,7	4,2	28,8	20,8	1,01	1,05	0,6	1,2
NB	12	NÃO SM	70	171	3,0	4,3	27,8	39,2	1,18	0,63	0,6	1,9
BDP	13	NÃO SM	71	62	2,7	12,2	18,0	3,9	1,27	1,37	0,8	4,0
JFLS	14	NÃO SM	54	86	7,0	7,3	16,0	34,5	1,36	1,00	1,5	1,4
AMS	15	NÃO SM	79	99	7,3	4,8	30,5	26,7	1,05	1,07	1,6	1,1
JBS	16	NÃO SM	46	76	7,1	12,9	14,9	38,7	1,40	0,87	1,5	3,1
JPO	17	NÃO SM	112	107	3,8	7,4	42,0	97,9	0,88	0,50	0,8	1,6
SOE	18	NÃO SM	77	75	3,1	4,4	21,1	16,6	1,31	1,38	0,6	0,8
LFC	19	NÃO SM	126	104	14,6	19,7	22,2	54,7	0,93	0,66	3,3	4,1
CPA	20	SM	100	90	14,4	10,1	76,4	29,6	0,55	0,94	3,6	2,6
TBM	21	SM	109	154	6,3	7,3	86,2	98,3	0,56	0,41	1,3	1,7
HW	22	SM	137	122	6,4	8,2	38,6	56,7	0,79	0,64	1,5	2,1
AMDS	23	SM	124	133	7,5	12,6	78,0	45,6	0,54	0,66	1,8	3,3
IMP	24	SM	125	187	7,4	9,2	197,1	162,1	0,26	0,24	1,8	2,6
CCB	25	SM	85	134	6,3	6,3	8,4	46,9	1,50	0,74	1,1	1,4
LDSR	26	SM	110	124	6,8	10,4	100,8	56,0	0,50	0,66	1,4	2,3
LDCS	27	SM	104	148	12,2	12,2	63,2	171,7	0,62	0,26	3,0	3,1
EMLV	28	SM	138	175	7,5	6,3	41,8	62,4	0,73	0,52	1,9	1,7
MCMM	29	SM	137	155	4,5	6,8	30,8	31,1	0,89	0,81	1,2	1,9
LPDS	30	SM	122	130	11,8	12,0	59,3	51,7	0,58	0,61	3,4	3,5
JAAS	31	SM	128	134	8,0	7,2	48,2	45,7	0,71	0,74	1,8	1,6
FLSJ	32	SM	125	95	9,4	12,6	138,4	87,7	0,36	0,53	2,0	2,9
EPDS	33	SM	104	123	14,6	16,6	47,4	82,5	0,78	0,50	2,5	3,4
DJDF	34	SM	119	113	8,9	9,1	47,5	42,7	0,73	0,75	2,0	2,5
RDSB	35	SM	124	163	10,1	14,5	57,4	16,1	0,63	0,90	2,4	4,1
MHS	36	SM	126	124	15,9	11,3	60,7	141,2	0,56	0,35	4,0	2,6
AFDS	37	SM	134	106	13,6	17,7	121,9	68,3	0,36	0,58	3,2	3,9
JPDS	38	SM	107	110	7,1	9,4	39,1	46,5	0,82	0,74	1,9	2,3
JLF	39	SM	83	88	7,6	7,8	11,0	48,0	1,33	0,78	1,9	2,0

NOME	Nº	GRUPO	HOMA β PRÉ-HCT	HOMA β PÓS-HCT	COLES TOTAL PRÉ-HCT	COLES TOTAL PÓS-HCT	HDL PRÉ-HCT	HDL PÓS-HCT	LDL PRÉ-HCT	LDL PÓS-HCT	TG PRÉ-HCT	TG PÓS-HCT
MAS	1	NÃO SM	98,7	58,5	196	205	70	68	98	111	139	132
BEM	2	NÃO SM	86,0	68,1	237	188	56	50	164	116	84	111
MLMB	3	NÃO SM	80,0	60,5	209	191	81	58	111	108	87	125
IFS	4	NÃO SM	77,1	51,3	188	215	54	56	119	139	77	100
NK	5	NÃO SM	20,2	17,4	154	171	72	80	65	71	83	102
EMCP	6	NÃO SM	86,1	121,1	180	185	45	51	122	117	64	86
AMJ	7	NÃO SM	93,6	37,8	194	222	60	64	126	143	41	75
AMPS	8	NÃO SM	126,0	57,2	152	171	62	67	76	90	72	68
MFMS	9	NÃO SM	87,0	27,6	204	343	72	57	115	244	84	210
JJP	10	NÃO SM	30,9	72,0	208	164	54	48	126	93	138	115
MADS	11	NÃO SM	31,4	28,5	140	141	46	39	76	82	91	99
NB	12	NÃO SM	47,0	13,7	190	172	55	61	122	76	63	176
BDP	13	NÃO SM	17,4	62,7	196	225	76	110	105	103	73	62
JFLS	14	NÃO SM	105,0	164,3	222	195	50	47	136	131	180	83
AMS	15	NÃO SM	114,3	64,0	265	267	69	71	174	172	112	120
JBS	16	NÃO SM	102,2	136,6	150	162	37	36	91	98	109	138
JPO	17	NÃO SM	76,0	111,0	173	188	60	56	91	107	111	126
SOE	18	NÃO SM	124,0	176,0	213	204	50	52	142	132	107	102
LFC	19	NÃO SM	187,7	322,4	237	208	41	37	117	119	191	258
CPA	20	SM	132,9	86,6	208	216	41	40	132	144	177	161
TBM	21	SM	119,4	77,3	214	211	56	55	129	112	152	218
HW	22	SM	72,0	73,8	148	181	49	45	81	101	83	173
AMDS	23	SM	81,8	103,1	236	230	42	49	160	141	99	200
IMP	24	SM	72,0	64,9	168	192	49	52	90	111	147	146
CCB	25	SM	226,8	90,7	234	301	66	64	123	183	227	272
LDSR	26	SM	122,4	149,8	244	192	70	69	139	85	175	190
LDCS	27	SM	125,5	107,1	195	221	47	59	113	107	176	277
EMLV	28	SM	65,9	46,3	219	245	56	63	138	156	123	131
MCMM	29	SM	39,5	48,0	182	188	42	48	101	114	194	130
LPDS	30	SM	80,2	78,5	189	178	50	46	96	92	215	201
JAAS	31	SM	99,3	103,7	114	107	38	34	57	52	94	106
FLSJ	32	SM	135,4	151,2	186	158	38	32	125	102	101	119
EPDS	33	SM	750,9	298,8	279	251	46	41	177	154	280	282
DJDF	34	SM	110,5	69,7	169	163	39	37	103	107	104	96
RDSB	35	SM	113,6	102,4	245	229	42	40	166	156	184	164
MHS	36	SM	146,8	140,3	160	155	42	37	103	105	75	63
AFDS	37	SM	157,9	245,1	244	211	43	34	131	107	348	351
JPDS	38	SM	59,4	89,1	178	186	38	34	112	128	138	120
JLF	39	SM	70,2	68,5	214	211	104	72	102	130	39	45

NOME	Nº	GRUPO	REL TG/HDL PRÉ-HCT	REL TG/HDL PÓS-HCT	ÁC. ÚRI PRÉ-HCT	ÁC. ÚRI PÓS-HCT	VOL URI PRÉ-HCT	VOL URI PÓS-HCT	K URI (24H) PRÉ-HCT	K URI (24H) PÓS-HCT
MAS	1	NÃO SM	1,99	1,94	4,5	6,4	1220	1320	34	40
BEM	2	NÃO SM	1,50	2,22	4,1	4,6	2180	2200	57	35
MLMB	3	NÃO SM	1,07	2,16	4,3	6,2	935	470	32	12
IFS	4	NÃO SM	1,43	1,79	4,2	4	1800	1830	230	16
NK	5	NÃO SM	1,15	1,28	4,1	4	1480	1030	53	30
EMCP	6	NÃO SM	1,42	1,69	4,2	3,9	1080	1250	46	19
AMJ	7	NÃO SM	0,68	1,17	4,2	4,4	720	880	35	37
AMPS	8	NÃO SM	1,16	1,01	3,8	7,1	1220	1030	45	25
MFMS	9	NÃO SM	1,17	3,68	4,9	7,5	1560	1450	34	46
JJP	10	NÃO SM	2,56	2,40	5,4	6,5	1420	1240	23	21
MADS	11	NÃO SM	1,98	2,54	4,6	5,6	1470	2275	44	55
NB	12	NÃO SM	1,15	2,89	3,7	3,9	800	750	46	34
BDP	13	NÃO SM	0,96	0,56	4,3	4,3	2200	2200	66	86
JFLS	14	NÃO SM	3,60	1,77	5,9	5,2	2830	2330	150	28
AMS	15	NÃO SM	1,62	1,69	6,2	6,6	1500	1510	84	89
JBS	16	NÃO SM	2,95	3,83	7	8,1	2020	2530	198	172
JPO	17	NÃO SM	1,85	2,25	6,3	6,7	1100	1410	47	47
SOE	18	NÃO SM	2,14	1,96	4,3	4,6	1310	495	29	29
LFC	19	NÃO SM	4,66	6,97	6,7	7,1	1250	430	35	18
CPA	20	SM	4,32	4,03	4,3	6,6	2315	1020	39	31
TBM	21	SM	2,71	3,96	4,2	4,3	1530	1665	112	100
HW	22	SM	1,69	3,84	3,2	3,8	1840	1175	57	43
AMDS	23	SM	2,36	4,08	5	5,8	1400	2235	29	54
IMP	24	SM	3,00	2,81	5	5,5	1090	1630	44	44
CCB	25	SM	3,44	4,25	6,2	7	2900	1190	46	38
LDSR	26	SM	2,50	2,75	4,7	5,1	930	1330	45	41
LDCS	27	SM	3,74	4,69	4,2	4,8	780	1090	43	27
EMLV	28	SM	2,20	2,08	5,5	5,3	1720	1280	46	47
MCMM	29	SM	4,62	2,71	3,5	3,8	800	920	58	47
LPDS	30	SM	4,30	4,37	5,9	4,9	3530	1330	102	64
JAAS	31	SM	2,47	3,12	8,1	9,3	2170	1240	69	73
FLSJ	32	SM	2,66	3,72	5,9	6,9	2700	1980	57	24
EPDS	33	SM	6,09	6,88	6,8	8,2	2260	1230	72	55
DJDF	34	SM	2,67	2,59	6,3	5,8	1430	1070	77	43
RDSB	35	SM	4,38	4,10	6,2	5,7	2120	2390	394	112
MHS	36	SM	1,79	1,70	5,7	7,3	725	520	86	31
AFDS	37	SM	8,09	10,32	8,5	9	1270	1405	67	67
JPDS	38	SM	3,63	3,53	5,6	7,2	1048	465	42	24
JLF	39	SM	0,38	0,63	4,9	6,4	1020	980	35	31

Anexo 2: Dados individuais dos pacientes do Artigo 2

NOME	Nº	GRUPO	GRUPO HOMA	GÊNERO	IDADE (anos)	PESO (kg)	ALT (m)	IMC (kg/m^2)	CIRC. CINT (cm)	CIRC. QUA (cm)	RCQ	FC (bpm)	PAS (mmHg)	PAD (mmHg)
SDOE	1	NO-HT	LOW	MASC	34	80	1,68	28,34	93	106	0,88	78	121	87
JJP	2	NO-HT	LOW	MASC	58	56	1,6	21,88	78	83	0,94	61	148	89
AMDS	3	NO-HT	LOW	MASC	54	74	1,65	27,18	93	101	0,92	61	127	91
RDSB	4	OB-HT	HIGH	MASC	43	118	1,79	36,83	125	114	1,1	72	134	86
LFDC	5	NO-HT	HIGH	MASC	32	84,2	1,76	27,18	93	104	0,89	72	125	73
MCC	6	NO-NT	HIGH	MASC	46	63	1,66	22,86	84	91	0,92	82	112	74
EPDS	7	OB-HT	HIGH	MASC	30	124,5	1,8	38,43	121	119	1,02	79	129	88
FLDSJ	8	OB-HT	HIGH	MASC	34	95	1,77	30,32	110	105	1,05	88	138	95
DJDF	9	OB-HT	LOW	MASC	56	104	1,68	36,85	109	114	0,96	96	154	96
ABM	10	NO-HT	HIGH	MASC	60	65	1,72	21,97	83	90	0,92	81	150	96
RAS	11	NO-HT	LOW	MASC	60	87	1,77	27,77	86	92	0,93	71	138	91
MHDS	12	OB-HT	HIGH	MASC	44	105,6	1,79	32,96	120	109	1,1	89	138	93
WLF	13	OB-HT	HIGH	MASC	33	120,4	1,82	36,35	120	117	1,03	75	141	84
JPDDS	14	OB-HT	LOW	MASC	38	101,4	1,7	35,09	112	108	1,04	75	131	89
JLF	15	OB-HT	LOW	MASC	38	124	1,85	36,23	125	120	1,04	82	151	104
JADS	16	NO-HT	HIGH	MASC	47	85,6	1,74	28,27	94	100	0,94	72	131	95
LDBF	17	NO-HT	HIGH	MASC	36	86,2	1,79	26,90	91	97	0,94	78	143	98
AADS	18	NO-NT	LOW	MASC	43	69,2	1,71	23,80	88	89	0,99	65	126	80
MA	19	NO-NT	HIGH	MASC	37	82,1	1,75	26,81	94	103	0,91	64	130	79
GDS	20	NO-NT	LOW	MASC	38	78,7	1,66	28,56	90	99	0,91	69	111	81
GMDS	21	OB-NT	LOW	MASC	47	96,1	1,7	33,25	98	97	1,01	75	130	78
AAS	22	NO-HT	HIGH	MASC	62	81,5	1,69	28,54	100	104	0,96	75	182	120
JJMDS	23	NO-NT	HIGH	MASC	42	59,8	1,67	21,44	84	93	0,9	74	120	78
JRTDA	24	NO-NT	LOW	MASC	34	80,1	1,68	28,38	92	97	0,95	63	128	82
MDSF	25	NO-NT	HIGH	MASC	42	69,4	1,64	25,80	95	115	0,83	80	116	74
EADL	26	OB-HT	HIGH	MASC	46	104	1,74	34,35	124	120	1,03	78	144	93
MVDS	27	NO-NT	LOW	MASC	47	67,3	1,63	25,33	90	93	0,97	64	118	74
SVDS	28	NO-NT	HIGH	MASC	36	70,9	1,75	23,15	88	99	0,89	78	114	80
RJR	29	OB-NT	HIGH	MASC	44	77,8	1,61	30,01	93	96	0,97	73	120	81
LSF	30	OB-HT	LOW	MASC	47	100,6	1,7	34,81	109	105	1,04	85	152	103
JBDS	31	OB-HT	LOW	MASC	49	82,5	1,64	30,67	99	100	0,99	76	129	92
WEW	32	NO-NT	LOW	MASC	35	96,9	1,84	28,62	97	104	0,93	69	112	73

NO-NT: não-obeso e normotenso; NO-HT: não-obeso e hipertenso; OB-NT: obeso e normotenso; OB-HT: obeso e hipertenso; TOTG: teste oral de tolerância à glicose; TSL: teste de sobrecarga lipídica

NOME	Nº	GRUPO	GRUPO HOMA	GÊNERO	IDADE (anos)	PESO (kg)	ALT (m)	IMC (kg/m^2)	CIRC. CINT (cm)	CIRC. QUA (cm)	RCQ	FC (bpm)	PAS (mmHg)	PAD (mmHg)
JSF	33	OB-NT	HIGH	MASC	55	108,1	1,72	36,54	123	130	0,95	73	123	81
AM	34	OB-NT	HIGH	MASC	40	101,7	1,72	34,38	109	107	1,02	73	128	82
CRDS	35	OB-NT	HIGH	MASC	38	89,9	1,73	30,04	104	103	1,01	73	136	84
MBC	36	OB-NT	LOW	MASC	48	103,8	1,83	31,00	115	114	1,01	74	133	80
CAM	37	OB-NT	LOW	MASC	42	114,1	1,84	33,70	99	103	0,96	77	130	80
ALDS	38	OB-NT	LOW	MASC	41	102,2	1,62	38,94	109	124	0,88	69	123	78
LADS	39	OB-NT	HIGH	MASC	43	81,3	1,6	31,76	102	107	0,95	68	130	81
AM	40	OB-NT	HIGH	MASC	35	92,4	1,72	31,23	109	107	1,02	73	118	81
MAF	41	OB-HT	LOW	MASC	52	88,9	1,62	33,87	105	110	0,95	89	143	84
AVSDS	42	OB-NT	LOW	MASC	45	97,1	1,72	32,82	104	114	0,91	77	124	83
ADJG	43	NO-NT	HIGH	MASC	43	77,9	1,65	28,61	98	104	0,94	66	126	83
AVDS	44	NO-HT	LOW	MASC	39	82	1,78	25,88	93	99	0,94	69	121	89
CHMR	45	NO-NT	LOW	MASC	38	92,4	1,85	27,00	96	103	0,93	73	123	82
OLR	46	OB-NT	HIGH	MASC	46	81,4	1,63	30,64	95	97	0,98	71	103	81
VAC	47	NO-HT	LOW	MASC	46	65,1	1,76	21,02	73	88	0,83	67	129	82
VAM	48	OB-NT	HIGH	MASC	47	94,7	1,69	33,35	105	104	1,01	77	121	82
BDDP	49	NO-HT	HIGH	MASC	57	60,2	1,7	20,83	73	93	0,78	71	121	77
AMNDR	50	NO-HT	HIGH	MASC	31	87	1,76	28,09	96	107	0,9	71	141	100
FATMP	51	NO-HT	HIGH	MASC	45	85,8	1,88	24,28	90	98	0,92	78	130	91
JUDS	52	OB-HT	LOW	MASC	52	86,8	1,7	30,03	105	102	1,03	81	162	104
AFFN	53	NO-NT	LOW	MASC	38	73,5	1,72	24,84	84	93	0,9	67	111	72
ECBA	54	OB-HT	LOW	MASC	30	102,5	1,77	32,72	98	105	0,93	89	121	84
SRP	55	NO-HT	LOW	MASC	45	91	1,84	26,88	97	105	0,92	67	132	84
VN	56	NO-HT	LOW	MASC	49	63,5	1,72	21,46	84	92	0,91	74	141	93
RIF	57	OB-NT	HIGH	MASC	35	114,7	1,8	35,40	124	118	1,05	73	128	77
AABDC	58	OB-NT	HIGH	MASC	50	104,9	1,72	35,46	110	106	1,04	84	121	79
LAS	59	NO-HT	HIGH	MASC	38	69	1,66	25,04	92	94	0,98	81	133	94
ACDMR	60	NO-NT	LOW	MASC	46	63,6	1,64	23,65	83	87	0,95	64	119	79
ADADS	61	OB-HT	LOW	MASC	36	95,2	1,74	31,44	105	107	0,98	81	129	88
WRFJ	62	OB-NT	LOW	MASC	27	100,2	1,67	35,93	104	112	0,93	73	102	71
JBAR	63	NO-HT	LOW	MASC	53	50,1	1,62	19,09	77	81	0,95	91	133	88
SLDS	64	NO-NT	HIGH	MASC	38	77,9	1,77	24,87	87	94	0,93	64	110	81

NO-NT: não-obeso e normotenso; NO-HT: não-obeso e hipertenso; OB-NT: obeso e normotenso; OB-HT: obeso e hipertenso; TOTG: teste oral de tolerância à glicose; TSL: teste de sobrecarga lipídica

NOME	Nº	GRUPO	COLES TOTAL (mg/dL)	COLES TOTAL (mmol/L)	HDL (mg/dL)	HDL (mmol/L)	LDL (mg/dL)	LDL (mmol/L)	GLI (0 MIN) TOTG (mg/dL)	GLI (0 MIN) TOTG (mmol/L)	GLI (120 MIN) TOTG (mg/dL)	GLI (120 MIN) TOTG (mmol/L)
SDOE	1	NO-HT	213	5,51	50	1,29	142	3,67	72	4	77	4,28
JJP	2	NO-HT	208	5,38	48	1,24	126	3,26	91	5,06	91	5,06
AMDS	3	NO-HT	265	6,85	69	1,78	174	4,50	86	4,78	79	4,39
RDSB	4	OB-HT	245	6,34	42	1,09	166	4,29	96	5,33	124	6,89
LFDC	5	NO-HT	237	6,13	41	1,06	117	3,03	91	5,06	126	7,00
MCC	6	NO-NT	220	5,69	47	1,22	152	3,93	83	4,61	91	5,06
EPDS	7	OB-HT	279	7,21	46	1,19	177	4,58	70	3,89	104	5,78
FLDSJ	8	OB-HT	186	4,81	38	0,98	125	3,23	88	4,89	125	6,94
DJDF	9	OB-HT	169	4,37	45	1,16	103	2,66	92	5,11	119	6,61
ABM	10	NO-HT	170	4,40	55	1,42	100	2,59	109	6,06	49	2,72
RAS	11	NO-HT	256	6,62	74	1,91	157	4,06	79	4,39	59	3,28
MHDS	12	OB-HT	160	4,14	42	1,09	103	2,66	97	5,39	126	7,00
WLF	13	OB-HT	154	3,98	25	0,65	97	2,51	97	5,39	90	5,00
JPDDS	14	OB-HT	178	4,60	38	0,98	112	2,90	106	5,89	107	5,94
JLF	15	OB-HT	214	5,53	72	1,86	102	2,64	92	5,11	83	4,61
JADS	16	NO-HT	197	5,09	43	1,11	114	2,95	89	4,94	110	6,11
LDBF	17	NO-HT	94	2,43	36	0,93	33	0,85	94	5,22	133	7,39
AADS	18	NO-NT	189	4,89	66	1,71	112	2,90	85	4,72	65	3,61
MA	19	NO-NT	196	5,07	64	1,66	115	2,97	81	4,50	94	5,22
GDS	20	NO-NT	198	5,12	53	1,37	130	3,36	81	4,50	51	2,83
GMDS	21	OB-NT	206	5,33	45	1,16	118	3,05	91	5,06	125	6,94
AAS	22	NO-HT	211	5,46	44	1,14	105	2,72	95	5,28	108	6,00
JJMDS	23	NO-NT	177	4,58	43	1,11	114	2,95	92	5,11	101	5,61
JRTDA	24	NO-NT	217	5,61	56	1,45	126	3,26	120	6,67	86	4,78
MDSF	25	NO-NT	141	3,65	47	1,22	80	2,07	129	7,17	86	4,78
EADL	26	OB-HT	217	5,61	53	1,37	133	3,44	107	5,94	99	5,50
MVDS	27	NO-NT	243	6,28	79	2,04	130	3,36	96	5,33	83	4,61
SVDS	28	NO-NT	219	5,66	50	1,29	122	3,15	83	4,61	96	5,33
RJR	29	OB-NT	176	4,55	30	0,78	96	2,48	104	5,78	75	4,17
LSF	30	OB-HT	137	3,54	34	0,88	56	1,45	73	4,06	103	5,72
JBDS	31	OB-HT	172	4,45	39	1,01	105	2,72	67	3,72	85	4,72
WEW	32	NO-NT	181	4,68	57	1,47	101	2,61	75	4,17	60	3,33

NO-NT: não-obeso e normotenso; NO-HT: não-obeso e hipertenso; OB-NT: obeso e normotenso; OB-HT: obeso e hipertenso; TOTG: teste oral de tolerância à glicose; TSL: teste de sobrecarga lipídica

NOME	Nº	GRUPO	COLES TOTAL (mg/dL)	COLES TOTAL (mmol/L)	HDL (mg/dL)	HDL (mmol/L)	LDL (mg/dL)	LDL (mmol/L)	GLI (0 MIN) TOTG (mg/dL)	GLI (0 MIN) TOTG (mmol/L)	GLI (120 MIN) TOTG (mg/dL)	GLI (120 MIN) TOTG (mmol/L)
JSF	33	OB-NT	247	6,39	31	0,80	145	3,75	99	5,50	132	7,33
AM	34	OB-NT	224	5,79	43	1,11	164	4,24	91	5,06	127	7,06
CRDS	35	OB-NT	211	5,46	54	1,40	141	3,65	96	5,33	137	7,61
MBC	36	OB-NT	242	6,26	34	0,88	182	4,71	108	6,00	102	5,67
CAM	37	OB-NT	181	4,68	43	1,11	123	3,18	92	5,11	63	3,50
ALDS	38	OB-NT	97	2,51	25	0,65	58	1,50	92	5,11	78	4,33
LADS	39	OB-NT	224	5,79	34	0,88	171	4,42	69	3,83	137	7,61
AM	40	OB-NT	122	3,15	34	0,88	75	1,94	96	5,33	115	6,39
MAF	41	OB-HT	237	6,13	27	0,70	132	3,41	103	5,72	132	7,33
AVSDS	42	OB-NT	160	4,14	33	0,85	94	2,43	113	6,28	139	7,72
ADJG	43	NO-NT	143	3,70	30	0,78	81	2,09	107	5,94	88	4,89
AVDS	44	NO-HT	219	5,66	46	1,19	155	4,01	87	4,83	108	6,00
CHMR	45	NO-NT	210	5,43	41	1,06	152	3,93	90	5,00	127	7,06
OLR	46	OB-NT	226	5,84	40	1,03	154	3,98	94	5,22	104	5,78
VAC	47	NO-HT	189	4,89	41	1,06	103	2,66	84	4,67	137	7,61
VAM	48	OB-NT	171	4,42	34	0,88	98	2,53	109	6,06	187	10,39
BDDP	49	NO-HT	196	5,07	72	1,86	114	2,95	104	5,78	98	5,44
AMNDR	50	NO-HT	201	5,20	35	0,91	133	3,44	77	4,28	87	4,83
FATMP	51	NO-HT	169	4,37	41	1,06	109	2,82	84	4,67	133	7,39
JUDS	52	OB-HT	176	4,55	34	0,88	114	2,95	90	5,00	153	8,50
AFFN	53	NO-NT	153	3,96	49	1,27	87	2,25	70	3,89	53	2,94
ECBA	54	OB-HT	225	5,82	39	1,01	159	4,11	98	5,44	72	4,00
SRP	55	NO-HT	158	4,09	53	1,37	91	2,35	85	4,72	85	4,72
VN	56	NO-HT	218	5,64	58	1,50	124	3,21	97	5,39	86	4,78
RIF	57	OB-NT	232	6,00	32	0,83	170	4,40	84	4,67	92	5,11
AABDC	58	OB-NT	221	5,72	37	0,96	139	3,59	86	4,78	132	7,33
LAS	59	NO-HT	235	6,08	50	1,29	169	4,37	95	5,28	92	5,11
ACDMR	60	NO-NT	185	4,78	50	1,29	115	2,97	94	5,22	121	6,72
ADADS	61	OB-HT	219	5,66	44	1,14	136	3,52	84	4,67	113	6,28
WRFJ	62	OB-NT	165	4,27	43	1,11	94	2,43	96	5,33	83	4,61
JBAR	63	NO-HT	264	6,83	86	2,22	157	4,06	91	5,06	96	5,33
SLDS	64	NO-NT	181	4,68	35	0,91	107	2,77	93	5,17	89	4,94

NO-NT: não-obeso e normotenso; NO-HT: não-obeso e hipertenso; OB-NT: obeso e normotenso; OB-HT: obeso e hipertenso; TOTG: teste oral de tolerância à glicose; TSL: teste de sobrecarga lipídica

NOME	Nº	GRUPO	INS (0 MIN) TOTG	INS (120 MIN) TOTG	HOMA IR	TG (0 MIN) TSL (mg/dL)	TG (0 MIN) TSL (mmol/L)	TG (60 MIN) TSL (mg/dL)	TG (60 MIN) TSL (mmol/L)	TG (120 MIN) TSL (mg/dL)	TG (120 MIN) TSL (mmol/L)
SDOE	1	NO-HT	3,10	21,10	0,55	113,00	1,28	127,00	1,43	177,00	2,00
JJP	2	NO-HT	2,40	18,10	0,54	120,00	1,35	134,00	1,51	183,00	2,07
AMDS	3	NO-HT	7,30	30,50	1,55	74,00	0,84	79,00	0,89	107,00	1,21
RDSB	4	OB-HT	10,10	57,40	2,39	129,00	1,46	159,00	1,80	208,00	2,35
LFDC	5	NO-HT	14,60	222,20	3,28	191,00	2,16	196,00	2,21	207,00	2,34
MCC	6	NO-NT	4,40	36,20	0,90	68,00	0,77	73,00	0,82	99,00	1,12
EPDS	7	OB-HT	14,60	47,40	2,52	253,00	2,86	224,00	2,53	232,00	2,62
FLDSJ	8	OB-HT	9,40	138,40	2,04	71,00	0,80	73,00	0,82	85,00	0,96
DJDF	9	OB-HT	8,90	47,50	2,02	88,00	0,99	139,00	1,57	138,00	1,56
ABM	10	NO-HT	5,90	18,00	1,59	78,00	0,88	74,00	0,84	92,00	1,04
RAS	11	NO-HT	2,00	78,30	0,39	138,00	1,56	162,00	1,83	204,00	2,30
MHDS	12	OB-HT	15,90	60,70	3,81	86,00	0,97	84,00	0,95	94,00	1,06
WLF	13	OB-HT	8,50	255,00	2,04	177,00	2,00	182,00	2,05	212,00	2,39
JPDDS	14	OB-HT	7,10	39,10	1,86	150,00	1,69	149,00	1,68	164,00	1,85
JLF	15	OB-HT	7,60	11,00	1,73	43,00	0,49	42,00	0,47	68,00	0,77
JADS	16	NO-HT	5,20	65,90	1,14	174,00	1,96	178,00	2,01	233,00	2,63
LDBF	17	NO-HT	10,80	66,00	2,51	65,00	0,73	104,00	1,17	131,00	1,48
AADS	18	NO-NT	2,40	11,10	0,50	102,00	1,15	93,00	1,05	104,00	1,17
MA	19	NO-NT	4,80	30,30	0,96	131,00	1,48	123,00	1,39	142,00	1,60
GDS	20	NO-NT	3,40	5,60	0,68	73,00	0,82	88,00	0,99	144,00	1,63
GMDS	21	OB-NT	9,90	89,70	2,22	218,00	2,46	216,00	2,44	248,00	2,80
AAS	22	NO-HT	17,50	15,80	4,10	171,00	1,93	175,00	1,98	178,00	2,01
JJMDS	23	NO-NT	3,70	33,20	0,84	95,00	1,07	87,00	0,98	99,00	1,12
JRTDA	24	NO-NT	3,80	17,20	1,13	218,00	2,46	213,00	2,40	307,00	3,47
MDSF	25	NO-NT	6,60	49,00	2,10	109,00	1,23	115,00	1,30	177,00	2,00
EADL	26	OB-HT	13,70	19,90	3,62	175,00	1,98	193,00	2,18	249,00	2,81
MVDS	27	NO-NT	2,80	6,70	0,66	138,00	1,56	137,00	1,55	166,00	1,87
SVDS	28	NO-NT	5,10	79,20	1,05	202,00	2,28	223,00	2,52	319,00	3,60
RJR	29	OB-NT	13,00	58,10	3,34	251,00	2,83	259,00	2,92	321,00	3,62
LSF	30	OB-HT	9,50	164,00	1,71	263,00	2,97	300,00	3,39	394,00	4,45
JBDS	31	OB-HT	7,70	144,00	1,27	169,00	1,91	242,00	2,73	294,00	3,32
WEW	32	NO-NT	3,00	20,00	0,56	123,00	1,39	114,00	1,29	148,00	1,67

NO-NT: não-obeso e normotenso; NO-HT: não-obeso e hipertenso; OB-NT: obeso e normotenso; OB-HT: obeso e hipertenso; TOTG: teste oral de tolerância à glicose; TSL: teste de sobrecarga lipídica

NOME	Nº	GRUPO	INS (0 MIN) TOTG	INS (120 MIN) TOTG	HOMA IR	TG (0 MIN) TSL (mg/dL)	TG (0 MIN) TSL (mmol/L)	TG (60 MIN) TSL (mg/dL)	TG (60 MIN) TSL (mmol/L)	TG (120 MIN) TSL (mg/dL)	TG (120 MIN) TSL (mmol/L)
JSF	33	OB-NT	18,30	100,20	4,47	315,00	3,56	339,00	3,83	387,00	4,37
AM	34	OB-NT	14,10	144,50	3,17	72,00	0,81	119,00	1,34	131,00	1,48
CRDS	35	OB-NT	17,70	293,50	4,20	86,00	0,97	105,00	1,19	130,00	1,47
MBC	36	OB-NT	5,50	34,80	1,47	134,00	1,51	133,00	1,50	208,00	2,35
CAM	37	OB-NT	7,60	6,70	1,73	63,00	0,71	69,00	0,78	104,00	1,17
ALDS	38	OB-NT	4,20	5,20	0,95	66,00	0,75	62,00	0,70	58,00	0,65
LADS	39	OB-NT	13,40	195,00	2,28	85,00	0,96	111,00	1,25	148,00	1,67
AM	40	OB-NT	8,30	42,90	1,97	64,00	0,72	79,00	0,89	78,00	0,88
MAF	41	OB-HT	9,80	116,40	2,49	391,00	4,41	535,00	6,04	456,00	5,15
AVSDS	42	OB-NT	7,20	50,10	2,01	188,00	2,12	179,00	2,02	200,00	2,26
ADJG	43	NO-NT	12,60	130,00	3,33	138,00	1,56	141,00	1,59	198,00	2,24
AVDS	44	NO-HT	3,00	24,70	0,64	123,00	1,39	141,00	1,59	191,00	2,16
CHMR	45	NO-NT	3,90	34,10	0,87	128,00	1,45	149,00	1,68	204,00	2,30
OLR	46	OB-NT	12,90	182,00	2,99	204,00	2,30	222,00	2,51	297,00	3,35
VAC	47	NO-HT	2,00	21,10	0,41	81,00	0,91	95,00	1,07	114,00	1,29
VAM	48	OB-NT	12,20	110,00	3,28	333,00	3,76	321,00	3,62	372,00	4,20
BDDP	49	NO-HT	2,40	23,70	0,62	56,00	0,63	73,00	0,82	150,00	1,69
AMNDR	50	NO-HT	8,40	94,30	1,60	162,00	1,83	219,00	2,47	213,00	2,40
FATMP	51	NO-HT	42,70	3,80	8,86	96,00	1,08	138,00	1,56	150,00	1,69
JUDS	52	OB-HT	5,40	33,40	1,20	153,00	1,73	178,00	2,01	175,00	1,98
AFFN	53	NO-NT	2,00	72,20	0,35	73,00	0,82	82,00	0,93	114,00	1,29
ECBA	54	OB-HT	2,10	25,80	0,51	139,00	1,57	155,00	1,75	195,00	2,20
SRP	55	NO-HT	2,00	19,40	0,42	49,00	0,55	65,00	0,73	74,00	0,84
VN	56	NO-HT	2,30	19,50	0,55	240,00	2,71	175,00	1,98	207,00	2,34
RIF	57	OB-NT	24,80	73,50	5,14	187,00	2,11	191,00	2,16	245,00	2,77
AABDC	58	OB-NT	16,20	133,00	3,44	176,00	1,99	182,00	2,05	216,00	2,44
LAS	59	NO-HT	3,50	34,60	0,82	76,00	0,86	79,00	0,89	100,00	1,13
ACDMR	60	NO-NT	2,50	35,50	0,58	101,00	1,14	113,00	1,28	182,00	2,05
ADADS	61	OB-HT	4,40	44,50	0,91	134,00	1,51	135,00	1,52	161,00	1,82
WRFJ	62	OB-NT	2,20	13,70	0,52	150,00	1,69	147,00	1,66	183,00	2,07
JBAR	63	NO-HT	2,00	9,80	0,45	101,00	1,14	85,00	0,96	82,00	0,93
SLDS	64	NO-NT	6,10	33,00	1,40	219,00	2,47	246,00	2,78	302,00	3,41

NO-NT: não-obeso e normotenso; NO-HT: não-obeso e hipertenso; OB-NT: obeso e normotenso; OB-HT: obeso e hipertenso; TOTG: teste oral de tolerância à glicose; TSL: teste de sobrecarga lipídica

NOME	Nº	GRUPO	TG (180 MIN) TSL (mg/dL)	TG (180 MIN) TSL (mmol/L)	TG (240 MIN) TSL (mg/dL)	TG (240 MIN) TSL (mmol/L)	TG (300 MIN) TSL (mg/dL)	TG (300 MIN) TSL (mmol/L)	TG (360 MIN) TSL (mg/dL)	TG (360 MIN) TSL (mmol/L)
SDOE	1	NO-HT	227,00	2,56	307,00	3,47	293,00	3,31	252,00	2,85
JJP	2	NO-HT	186,00	2,10	174,00	1,96	134,00	1,51	100,00	1,13
AMDS	3	NO-HT	125,00	1,41	117,00	1,32	124,00	1,40	85,00	0,96
RDSB	4	OB-HT	249,00	2,81	243,00	2,74	211,00	2,38	189,00	2,13
LFDC	5	NO-HT	252,00	2,85	284,00	3,21	261,00	2,95	291,00	3,29
MCC	6	NO-NT	135,00	1,52	151,00	1,70	166,00	1,87	174,00	1,96
EPDS	7	OB-HT	255,00	2,88	278,00	3,14	291,00	3,29	313,00	3,53
FLDSJ	8	OB-HT	81,00	0,91	110,00	1,24	118,00	1,33	98,00	1,11
DJDF	9	OB-HT	168,00	1,90	195,00	2,20	173,00	1,95	120,00	1,35
ABM	10	NO-HT	127,00	1,43	110,00	1,24	119,00	1,34	72,00	0,81
RAS	11	NO-HT	217,00	2,45	177,00	2,00	135,00	1,52	116,00	1,31
MHDS	12	OB-HT	131,00	1,48	149,00	1,68	156,00	1,76	107,00	1,21
WLF	13	OB-HT	235,00	2,65	252,00	2,85	228,00	2,57	216,00	2,44
JPDDS	14	OB-HT	226,00	2,55	244,00	2,75	212,00	2,39	136,00	1,54
JLF	15	OB-HT	78,00	0,88	78,00	0,88	51,00	0,58	63,00	0,71
JADS	16	NO-HT	257,00	2,90	306,00	3,45	241,00	2,72	236,00	2,66
LDBF	17	NO-HT	163,00	1,84	140,00	1,58	100,00	1,13	82,00	0,93
AADS	18	NO-NT	118,00	1,33	170,00	1,92	162,00	1,83	169,00	1,91
MA	19	NO-NT	193,00	2,18	296,00	3,34	221,00	2,50	161,00	1,82
GDS	20	NO-NT	191,00	2,16	158,00	1,78	116,00	1,31	93,00	1,05
GMDS	21	OB-NT	280,00	3,16	400,00	4,52	340,00	3,84	333,00	3,76
AAS	22	NO-HT	228,00	2,57	276,00	3,12	257,00	2,90	254,00	2,87
JJMDS	23	NO-NT	136,00	1,54	230,00	2,60	163,00	1,84	169,00	1,91
JRTDA	24	NO-NT	439,00	4,96	413,00	4,66	288,00	3,25	234,00	2,64
MDSF	25	NO-NT	209,00	2,36	203,00	2,29	201,00	2,27	197,00	2,22
EADL	26	OB-HT	334,00	3,77	319,00	3,60	249,00	2,81	202,00	2,28
MVDS	27	NO-NT	200,00	2,26	192,00	2,17	167,00	1,89	150,00	1,69
SVDS	28	NO-NT	357,00	4,03	412,00	4,65	338,00	3,82	321,00	3,62
RJR	29	OB-NT	397,00	4,48	466,00	5,26	470,00	5,31	458,00	5,17
LSF	30	OB-HT	380,00	4,29	349,00	3,94	300,00	3,39	249,00	2,81
JBDS	31	OB-HT	321,00	3,62	257,00	2,90	201,00	2,27	300,00	3,39
WEW	32	NO-NT	143,00	1,61	141,00	1,59	117,00	1,32	106,00	1,20

NO-NT: não-obeso e normotenso; NO-HT: não-obeso e hipertenso; OB-NT: obeso e normotenso; OB-HT: obeso e hipertenso; TOTG: teste oral de tolerância à glicose; TSL: teste de sobrecarga lipídica

NOME	Nº	GRUPO	TG (180 MIN) TSL (mg/dL)	TG (180 MIN) TSL (mmol/L)	TG (240 MIN) TSL (mg/dL)	TG (240 MIN) TSL (mmol/L)	TG (300 MIN) TSL (mg/dL)	TG (300 MIN) TSL (mmol/L)	TG (360 MIN) TSL (mg/dL)	TG (360 MIN) TSL (mmol/L)
JSF	33	OB-NT	464,00	5,24	561,00	6,33	554,00	6,25	542,00	6,12
AM	34	OB-NT	142,00	1,60	147,00	1,66	166,00	1,87	136,00	1,54
CRDS	35	OB-NT	245,00	2,77	199,00	2,25	182,00	2,05	156,00	1,76
MBC	36	OB-NT	202,00	2,28	168,00	1,90	198,00	2,24	153,00	1,73
CAM	37	OB-NT	94,00	1,06	80,00	0,90	80,00	0,90	56,00	0,63
ALDS	38	OB-NT	62,00	0,70	69,00	0,78	71,00	0,80	69,00	0,78
LADS	39	OB-NT	231,00	2,61	219,00	2,47	237,00	2,68	181,00	2,04
AM	40	OB-NT	74,00	0,84	69,00	0,78	76,00	0,86	72,00	0,81
MAF	41	OB-HT	460,00	5,19	527,00	5,95	577,00	6,51	533,00	6,02
AVSDS	42	OB-NT	226,00	2,55	243,00	2,74	240,00	2,71	224,00	2,53
ADJG	43	NO-NT	330,00	3,73	374,00	4,22	325,00	3,67	239,00	2,70
AVDS	44	NO-HT	245,00	2,77	250,00	2,82	212,00	2,39	150,00	1,69
CHMR	45	NO-NT	254,00	2,87	235,00	2,65	192,00	2,17	150,00	1,69
OLR	46	OB-NT	356,00	4,02	373,00	4,21	373,00	4,21	384,00	4,34
VAC	47	NO-HT	130,00	1,47	137,00	1,55	86,00	0,97	120,00	1,35
VAM	48	OB-NT	468,00	5,28	475,00	5,36	493,00	5,57	509,00	5,75
BDDP	49	NO-HT	145,00	1,64	90,00	1,02	63,00	0,71	53,00	0,60
AMNDR	50	NO-HT	257,00	2,90	276,00	3,12	310,00	3,50	300,00	3,39
FATMP	51	NO-HT	173,00	1,95	235,00	2,65	277,00	3,13	303,00	3,42
JUDS	52	OB-HT	217,00	2,45	222,00	2,51	239,00	2,70	181,00	2,04
AFFN	53	NO-NT	168,00	1,90	122,00	1,38	108,00	1,22	86,00	0,97
ECBA	54	OB-HT	221,00	2,50	221,00	2,50	164,00	1,85	147,00	1,66
SRP	55	NO-HT	90,00	1,02	96,00	1,08	83,00	0,94	65,00	0,73
VN	56	NO-HT	262,00	2,96	272,00	3,07	230,00	2,60	184,00	2,08
RIF	57	OB-NT	300,00	3,39	312,00	3,52	320,00	3,61	282,00	3,18
AABDC	58	OB-NT	265,00	2,99	295,00	3,33	294,00	3,32	267,00	3,01
LAS	59	NO-HT	120,00	1,35	168,00	1,90	131,00	1,48	98,00	1,11
ACDMR	60	NO-NT	219,00	2,47	209,00	2,36	141,00	1,59	126,00	1,42
ADADS	61	OB-HT	204,00	2,30	243,00	2,74	223,00	2,52	183,00	2,07
WRFJ	62	OB-NT	191,00	2,16	224,00	2,53	245,00	2,77	198,00	2,24
JBAR	63	NO-HT	88,00	0,99	92,00	1,04	77,00	0,87	82,00	0,93
SLDS	64	NO-NT	356,00	4,02	395,00	4,46	364,00	4,11	371,00	4,19

NO-NT: não-obeso e normotenso; NO-HT: não-obeso e hipertenso; OB-NT: obeso e normotenso; OB-HT: obeso e hipertenso; TOTG: teste oral de tolerância à glicose; TSL: teste de sobrecarga lipídica

NOME	Nº	GRUPO	ÁREA CURVA TG (mg/dL)	ÁREA CURVA TG (mmol/L)	ÁREA CURVA INCREMENTAL TG (mg/dL)	ÁREA CURVA INCREMENTAL TG (mmol/L)
SDOE	1	NO-HT	1313,50	14,83	974,50	11,00
JJP	2	NO-HT	921,00	10,40	561,00	6,33
AMDS	3	NO-HT	631,50	7,13	409,50	4,62
RDSB	4	OB-HT	1229,00	13,88	842,00	9,51
LFDC	5	NO-HT	1441,00	16,27	868,00	9,80
MCC	6	NO-NT	745,00	8,41	541,00	6,11
EPDS	7	OB-HT	1563,00	17,65	804,00	9,08
FLDSJ	8	OB-HT	551,50	6,23	338,50	3,82
DJDF	9	OB-HT	917,00	10,35	653,00	7,37
ABM	10	NO-HT	597,00	6,74	363,00	4,10
RAS	11	NO-HT	1022,00	11,54	608,00	6,86
MHDS	12	OB-HT	710,50	8,02	452,50	5,11
WLF	13	OB-HT	1305,50	14,74	774,50	8,74
JPDDS	14	OB-HT	1138,00	12,85	688,00	7,77
JLF	15	OB-HT	370,00	4,18	241,00	2,72
JADS	16	NO-HT	1420,00	16,03	898,00	10,14
LDBF	17	NO-HT	711,50	8,03	516,50	5,83
AADS	18	NO-NT	782,50	8,83	476,50	5,38
MA	19	NO-NT	1121,00	12,66	728,00	8,22
GDS	20	NO-NT	780,00	8,81	561,00	6,33
GMDS	21	OB-NT	1759,50	19,86	1105,50	12,48
AAS	22	NO-HT	1326,50	14,98	813,50	9,18
JJMDS	23	NO-NT	847,00	9,56	562,00	6,34
JRTDA	24	NO-NT	1886,00	21,29	1232,00	13,91
MDSF	25	NO-NT	1058,00	11,94	731,00	8,25
EADL	26	OB-HT	1532,50	17,30	1007,50	11,37
MVDS	27	NO-NT	1006,00	11,36	592,00	6,68
SVDS	28	NO-NT	1910,50	21,57	1304,50	14,73
RJR	29	OB-NT	2267,50	25,60	1514,50	17,10
LSF	30	OB-HT	1979,00	22,34	1190,00	13,44
JBDS	31	OB-HT	1549,50	17,49	1042,50	11,77
WEW	32	NO-NT	777,50	8,78	408,50	4,61

NO-NT: não-obeso e normotenso; NO-HT: não-obeso e hipertenso; OB-NT: obeso e normotenso; OB-HT: obeso e hipertenso; TOTG: teste oral de tolerância à glicose; TSL: teste de sobrecarga lipídica

NOME	Nº	GRUPO	ÁREA CURVA TG (mg/dL)	ÁREA CURVA TG (mmol/L)	ÁREA CURVA INCREMENTAL TG (mg/dL)	ÁREA CURVA INCREMENTAL TG (mmol/L)
JSF	33	OB-NT	2733,50	30,86	1788,50	20,19
AM	34	OB-NT	809,00	9,13	593,00	6,69
CRDS	35	OB-NT	982,00	11,09	724,00	8,17
MBC	36	OB-NT	1052,50	11,88	650,50	7,34
CAM	37	OB-NT	486,50	5,49	297,50	3,36
ALDS	38	OB-NT	389,50	4,40	191,50	2,16
LADS	39	OB-NT	1079,00	12,18	824,00	9,30
AM	40	OB-NT	444,00	5,01	252,00	2,85
MAF	41	OB-HT	3017,00	34,06	1844,00	20,82
AVSDS	42	OB-NT	1294,00	14,61	730,00	8,24
ADJG	43	NO-NT	1556,50	17,57	1142,50	12,90
AVDS	44	NO-HT	1175,50	13,27	806,50	9,11
CHMR	45	NO-NT	1173,00	13,24	789,00	8,91
OLR	46	OB-NT	1915,00	21,62	1303,00	14,71
VAC	47	NO-HT	662,50	7,48	419,50	4,74
VAM	48	OB-NT	2550,00	28,79	1551,00	17,51
BDDP	49	NO-HT	575,50	6,50	407,50	4,60
AMNDR	50	NO-HT	1506,00	17,00	1020,00	11,52
FATMP	51	NO-HT	1172,50	13,24	884,50	9,99
JUDS	52	OB-HT	1198,00	13,53	739,00	8,34
AFFN	53	NO-NT	673,50	7,60	454,50	5,13
ECBA	54	OB-HT	1099,00	12,41	682,00	7,70
SRP	55	NO-HT	465,00	5,25	318,00	3,59
VN	56	NO-HT	1358,00	15,33	638,00	7,20
RIF	57	OB-NT	1602,50	18,09	1041,50	11,76
AABDC	58	OB-NT	1473,50	16,64	945,50	10,67
LAS	59	NO-HT	685,00	7,73	457,00	5,16
ACDMR	60	NO-NT	977,50	11,04	674,50	7,62
ADADS	61	OB-HT	1124,50	12,70	722,50	8,16
WRFJ	62	OB-NT	1164,00	13,14	714,00	8,06
JBAR	63	NO-HT	515,50	5,82	212,50	2,40
SLDS	64	NO-NT	1958,00	22,11	1301,00	14,69

NO-NT: não-obeso e normotenso; NO-HT: não-obeso e hipertenso; OB-NT: obeso e normotenso; OB-HT: obeso e hipertenso; TOTG: teste oral de tolerância à glicose; TSL: teste de sobrecarga lipídica

NOME	Nº	GRUPO	INS (0 MIN) TSL	INS (120 MIN) TSL	INS (240 MIN) TSL	INS (360 MIN) TSL	ADIPO (0 MIN) TSL	ADIPO (240 MIN) TSL	ADIPO (360 MIN) TSL
SDOE	1	NO-HT	7,10	5,40	3,50	2,00	4,40	4,40	
JJP	2	NO-HT	5,30	4,90	3,90	2,10	8,40	7,80	
AMDS	3	NO-HT	2,00	8,50	2,80	2,20	5,10	5,50	
RDSB	4	OB-HT	16,60	19,30	10,70	9,70	4,80	4,40	
LFDC	5	NO-HT	14,90	16,80	10,60	10,30	2,10	1,80	
MCC	6	NO-NT	2,80	5,40	2,70	2,00	5,30	4,50	
EPDS	7	OB-HT	10,80	21,40	15,30	10,00	2,20	1,50	
FLDSJ	8	OB-HT	8,50	10,40	10,20	6,40	4,90	6,80	6,50
DJDF	9	OB-HT	7,30	17,90	8,10	4,20	1,60	1,10	2,10
ABM	10	NO-HT	4,80	9,40	6,30	2,00	4,70	4,10	6,10
RAS	11	NO-HT	4,10	9,00	5,30	2,00	12,70	12,60	16,70
MHDS	12	OB-HT	9,80	15,90	9,70	5,90	7,10	4,60	13,20
WLF	13	OB-HT	37,20	45,90	19,40	17,90	2,60	3,20	5,60
JPDDS	14	OB-HT	7,50	10,60	10,20	5,20	5,90	5,20	7,90
JLF	15	OB-HT	6,90	10,70	9,90	3,90	9,90	12,40	11,20
JADS	16	NO-HT	3,90	12,30	5,40	2,00	2,30	3,00	4,60
LDBF	17	NO-HT	7,40	16,00	2,20	3,70	3,10	3,00	2,20
AADS	18	NO-NT	3,50	7,70	4,60	2,60	7,50	9,80	6,20
MA	19	NO-NT	5,90	7,00	6,80	2,00	10,30	10,90	13,10
GDS	20	NO-NT	2,70	6,70	4,70	2,00	6,60	8,40	9,30
GMDS	21	OB-NT	4,80	11,60	6,00	2,10	2,70	4,20	5,70
AAS	22	NO-HT	9,30	10,80	9,80	7,50	4,80	5,60	6,10
JJMDS	23	NO-NT	3,40	6,40	3,70	2,00	8,60	9,40	8,90
JRTDA	24	NO-NT	2,00	6,20	2,20	2,00	3,70	3,40	4,30
MDSF	25	NO-NT	4,90	6,70	3,10	2,00	4,00	3,10	3,40
EADL	26	OB-HT	16,30	25,40	10,70	8,30	5,60	7,80	6,40
MVDS	27	NO-NT	2,80	2,50	2,20	2,00	10,40	12,40	9,70
SVDS	28	NO-NT	11,10	14,30	10,90	5,60	6,60	1,70	1,00
RJR	29	OB-NT	5,70	18,50	10,50	5,10	1,30	6,80	7,20
LSF	30	OB-HT	13,60	31,90	16,10	7,80	2,50	4,00	1,70
JBDS	31	OB-HT	8,00	17,80	9,90	4,10	3,40	4,00	2,60
WEW	32	NO-NT	4,10	5,50	3,10	2,00	15,20	14,40	11,40

NO-NT: não-obeso e normotenso; NO-HT: não-obeso e hipertenso; OB-NT: obeso e normotenso; OB-HT: obeso e hipertenso; TOTG: teste oral de tolerância à glicose; TSL: teste de sobrecarga lipídica

NOME	Nº	GRUPO	INS (0 MIN) TSL	INS (120 MIN) TSL	INS (240 MIN) TSL	INS (360 MIN) TSL	ADIPO (0 MIN) TSL	ADIPO (240 MIN) TSL	ADIPO (360 MIN) TSL
JSF	33	OB-NT	20,10	23,80	12,30	7,10	3,80	4,90	5,50
AM	34	OB-NT	20,00	32,70	24,30	11,20	3,60	5,50	5,70
CRDS	35	OB-NT	12,50	22,30	11,70	6,70	4,10	5,00	3,10
MBC	36	OB-NT	5,10	8,70	4,70	2,00	6,70	7,50	8,80
CAM	37	OB-NT	8,90	11,60	8,40	2,80	6,10	4,00	6,70
ALDS	38	OB-NT	4,00	3,40	2,30	2,00	16,90	23,10	21,00
LADS	39	OB-NT	14,80	36,50	19,70	10,00	3,10	2,10	2,50
AM	40	OB-NT	8,20	9,60	12,90	10,40	2,60	3,30	2,70
MAF	41	OB-HT	15,70	19,60	19,70	10,50	2,80	3,20	2,40
AVSDS	42	OB-NT	6,40	17,20	8,50	3,40	6,70	7,70	7,10
ADJG	43	NO-NT	12,20	38,10	15,90	8,00	3,60	2,20	6,10
AVDS	44	NO-HT	6,60	9,00	2,90	2,00	2,50	3,70	3,10
CHMR	45	NO-NT	5,80	5,50	3,30	2,00	6,10	4,50	6,50
OLR	46	OB-NT	12,10	32,90	21,90	9,70	1,40	1,20	1,00
VAC	47	NO-HT	2,20	3,80	2,40	2,00	2,30	6,60	
VAM	48	OB-NT	11,70	40,60	12,90	9,30	4,70	5,20	
BDDP	49	NO-HT	2,20	6,80	2,40	2,00	8,50	6,60	
AMNDR	50	NO-HT	13,70	4,00	5,10	5,70	3,20	3,20	
FATMP	51	NO-HT	8,60	8,00	6,40	3,20	6,30	8,00	
JUDS	52	OB-HT	11,50	35,00	11,40	6,00	4,40	3,00	
AFFN	53	NO-NT	2,00	7,00	2,20	2,00	9,00	10,30	
ECBA	54	OB-HT	6,20	6,10	2,10	2,00	3,20	3,70	
SRP	55	NO-HT	4,10	10,00	3,20	2,00	8,80	6,10	
VN	56	NO-HT	2,30	7,60	4,70	2,00	2,80	1,70	
RIF	57	OB-NT	23,60	40,00	18,00	16,20	2,80	3,30	
AABDC	58	OB-NT	14,50	23,30	15,90	9,20	2,60	2,60	
LAS	59	NO-HT	3,40	5,40	2,90	2,00	4,10	4,90	
ACDMR	60	NO-NT	5,10	6,70	3,70	3,40	2,40	2,10	
ADADS	61	OB-HT	3,90	11,70	4,90	2,10	4,60	6,40	
WRFJ	62	OB-NT	3,60	9,60	5,60	5,40	2,70	2,10	
JBAR	63	NO-HT	2,80	2,90	2,30	2,00	7,90	9,00	
SLDS	64	NO-NT	4,20	7,30	2,40	2,00	5,00	7,30	

NO-NT: não-obeso e normotenso; NO-HT: não-obeso e hipertenso; OB-NT: obeso e normotenso; OB-HT: obeso e hipertenso; TOTG: teste oral de tolerância à glicose; TSL: teste de sobrecarga lipídica

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