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Maria Teresa Morujão Sarmento de Beires

Carotid Intima-Media Thickness in association with Lipoatrophy in HIV-infected patients treated with cART.

Associação entre a espessura da íntima-média carotídea e a lipoatrofia em indivíduos infectados por VIH, submetidos a terapia anti-retroviral conjugada.

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Carotid Intima-Media Thickness in association with Lipostrophy in HIV-infected Patients treated with cART.

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À minha família e ao João

CAROTID INTIMA-MEDIA THICKNESS IN ASSOCIATION WITH LIPOATROPHY IN HIV-INFECTED PATIENTS TREATED WITH CART

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ABSTRACT

Background: Combination antiretroviral therapy (cART) in HIV-infected patients has been associated with lipodystrophy, metabolic abnormalities and an increased risk for cardiovascular disease. Ultrasound measures of carotid artery intima-media thickness (cIMT) have been used as a valid measure of subclinical atherosclerosis and as tool to predict the risk for cardiovascular events. Our aim was to evaluate the progression of cIMT in HIV infected patients subjected to cART, with and without lipodystrophy, during one year.

Methods: We performed a one year prospective cohort study to compare changes in cIMT, metabolic and inflammation markers in HIV-infected patients under cART. Body composition was assessed by DXA and abdominal CT. Lipids, blood pressure, inflammatory markers and cIMT (evaluated by ultrasonoghaphy) were measured. Lipodystrophy defined by Fat Mass Ratio (L-FMR) was defined as the ratio of the percentage of trunk fat mass to the percentage of lower limb fat mass by DXA. Categorical variables were compared using the chi-square or Fisher's exact test. Wilcoxon ranks tests and the McNemar chi-square tests were used to compare results of selected variables, from the first to the second year of evaluation. Means of cIMT, adjusted for age, glucose, triglycerides levels, systolic blood pressure (SBP) and waist to hip ratio were calculated, using generalized linear models for repeated measures.

Results: L-FMR was present in 44.3% of patients and the mean of cIMT increased significantly in this group [0.82 (0.26) vs 0.92 (0.33); p=0.037], as well as in patients without lipodystrophy [0.73 (0.20) vs 0.84 (0.30); p=0.012]. In the overall sample, the progression of cIMT was statistically significant after the adjustment for age, glucose, triglycerides and SBP, but the significance of the progression ceased after the adjustment for waist-hip ratio [0.770 (0.737-0.803) vs 0.874 (0.815-0.933); p=0.514].

Conclusions: Carotid IMT progressed significantly in both groups of this HIV-infected cohort. No association between the progression of cIMT and the presence of lipodystrophy defined by

FMR was found. Visceral adipose tissue had an impact on the increment of cIMT, both in patients with and without lipodystrophy defined by FMR.

Key-words: *Lipodystrophy, HIV, Carotid Intima Media Thickness, Fat Mass Ratio, Body Composition.*

BACKGROUND

The use of combined antiretroviral therapy (cART) in HIV-infected patients has increased significantly the life expectancy of these subjects [1]. However, as a consequence, cardiovascular disease (CVD) has emerged as an important late concern in HIV-infected patients subjected to this treatment [2]. It has been proven that HIV-infected patients treated with cART have an increased risk of developing cardiovascular disease, and so it became essential to understand the underlying mechanism associated with this outcome. HIV-lipodystrophy is a well-established side effect of cART, specially associated with some specific regimens [3]. Patients presenting lipodystrophy may be at higher risk of developing atherosclerosis, since body fat redistribution is associated with the presence of several metabolic risk factors for cardiovascular disease [4].

The relative contributions of conventional cardiovascular risk factors, metabolic side effects of antiretroviral drugs and HIV infection itself on cardiovascular risk are difficult to identify, as these factors frequently occur simultaneously [5]. In this context, intima-media thickness of the carotid arteries (cIMT) has become a surrogate marker for atherosclerosis and it has been shown to be an advantageous and independent risk factor for the unfolding cardiovascular disease, on the grounds that it can be accurately and safely measured by ultrasound [6].

In our study previously published in 2014, it was shown that HIV-infected patients under cART with lipodystrophy defined by FMR had a significantly higher cIMT than those without lipodystrophy, which was also associated with classical cardiovascular risk factors, such as visceral adipose tissue and age. The purpose of this study was to evaluate the progression of atherosclerosis assessed by cIMT in the total of the HIV-infected patients under cART, in those with or without L-FMR, and evaluate the evolution of established cardiovascular risk factors during one year of follow-up.

METHODS

Subjects

We evaluated 115 HIV-infected patients under cART in this prospective longitudinal study. Only non-institutionalized Caucasian adults who were subjected to cART were evaluated and all patients were referred from the Infectious Diseases Outpatient Clinic. Participants were evaluated at baseline and after one year for each parameter (clinical assessment, evaluation of body composition, laboratory analysis and carotid IMT measurements). All patients were referred to the Nutrition consultation, motivated to comply with a structured diet plan, walk or exercise regularly and were advised to stop smoking. Patients with overweight or obesity were motivated to lose weight. Prediabetes, diabetes, hypertension and dyslipidemia were treated according to standard of care for HIV-population. This study was approved by the Ethics Committee for Health of the Hospital São João in Porto and each patient provided written, informed consent.

Clinical Assessment

For each patient, the following information was collected at both baseline and after the follow-up period (12 months), using a standardized protocol: age, gender, known duration of HIV infection and duration of cART exposure, HIV risk factor, characterization of the infection, smoking history, family history of cardiovascular diseases and use of anti-hypertensive, anti-diabetic, or lipid lowering drugs.

We used the "Centers for Disease Control and Prevention" (CDC) HIV staging classification [7]. Weight, height, circumference of neck, waist, hip, thigh and arm were measured, as previously described [8]. All measurements were performed by the same observer, using standard techniques [9].

Resting blood pressure (BP) taken whilst in a supine position was measured in a standardized fashion, as previously described [10].

Evaluation of body composition

Body composition was assessed with whole-body, dual-energy X-ray absorptiometry (DXA – Lunar Expert XL, 1999). DXA measurements were performed while the patient was in a supine position, with standard positioning of the arms and feet. Markers for the trunk and lower limbs that defined regions of interest were defined in accordance with the manufacturer's instructions. Regional fat mass values were grouped and analyzed for the following anatomical regions: arms, legs, trunk and total body. The fat mass ratio (FMR) was calculated as the ratio between the percentage of trunk fat mass and the percentage of lower limb fat mass (FMR=% of the trunk fat mass/% of the lower limb fat mass) [11]. We used a cut-off value for lipodystrophy defined by FMR for men of 1.961, and 1.329 for women [12].

The quantification of total, visceral, and subcutaneous fat was performed with a 64-slice, abdominal computed tomography (CT) scanner (Siemens Sensation 64 Cardiac), with the same technique as previously described [13, 14]. All values were expressed in cm^2, rounded to the nearest centesimal.

Laboratory analysis

Biological and inflammatory parameters

A venous blood sample was taken after a 12 hour overnight fast. All the samples were analyzed at the central laboratory of our hospital. The measurements of total cholesterol (TC), low density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, apolipoprotein A1 (Apo A1), apolipoprotein B (Apo B), lipoprotein (a) [Lp (a)], fibrinogen, high sensitivity C-reactive protein (hsCRP), homocysteine, uric acid, lactates, NT-proBNP, glucose, insulin and A1c serum levels were determined using commercial kits. Non HDL-C was defined as TC-HDL. Microalbuminuria was determined in a 24 hour urine sample. Patients without a previous diagnosis of diabetes were submitted to an oral glucose tolerance test (OGTT). This test was performed as instructed by the World Health Organization [15].

The CD4+ cell count ($x10^6$ cell/L) was determined by flow cytometry and plasma HIV-1 RNA loads were measured by a quantitate reverse transcriptase polymerase chain reaction (Roche Diagnostic Systems, Inc., Branchburg, NJ, USA), which had a lower limit of detection of 50 copies/mL.

Measurements of insulin resistance

Insulin resistance was defined by the homeostasis model assessment of insulin resistance (HOMA), using the following formula:

HOMA – IR index = (insulin 0 x glucose 0)/22.5 [16]

Carotid IMT measurements

High-resolution B-mode and Doppler ultrasonography of the carotid arteries was carried out with a Philips iU22 machine (Philips Medical, The Netherlands), equipped with a 17-5 MHz high-frequency linear-array transducer. Patients were examined in the supine position, with the head in a neutral position, or slightly turned away from the side that was being scanned. The left and right common carotid arteries (CCA) were examined in multiple directions and

measurements were performed using the images with the best wall definition. IMT was measured 3 cm below the carotid bulb in a longitudinal image. Three measurements were obtained on each side, and the mean IMT of these values was calculated. All studies were performed by the same radiologist, who had 12 years of experience in a vascular ultrasound, and were carried using the same machine.

The presence of subclinical carotid atherosclerosis was defined as IMT > 0.80 mm (70^{th} percentile of the IMT distribution), presence of plaque, or both [17-19].

Statistical analysis

Data was described as mean and standard deviation (SD) for quantitative variables, and was compared using Student-t or Mann-Whitney tests, as appropriate. Categorical variables were described as counts and proportions, and compared using the chi-square or Fisher's exact test. To study the association between cIMT and clinical and metabolic characteristics, Spearman correlation coefficients were estimated. Also, Wilcoxon ranks tests and the McNemar chi-square tests were used to compare results of selected variables from the baseline to the first follow up evaluation. Means of cIMT, were calculated, using generalized linear models for repeated measures, adjusted for age, glucose, triglycerides levels, systolic blood pressure and waist to hip ratio.

Statistical analysis was performed using SPSS version 24.0 software (SPSS Inc., Chicago, Illinois, USA). All probabilities were two tailed and p values of <0.05 were regarded as significant.

RESULTS

1) Baseline

Patient Characteristics

In 115 (91 male and 24 female) HIV-infected patients under cART, 51 (44.3%) presented lipodystrophy defined by FMR. The characteristics of the study sample according to the presence of lipodystrophy defined by FMR are illustrated in **Table 1.** Patients with lipodystrophy had been infected with HIV for a longer period of time (p=0.036) and were subjected to a greater length of cART (p=0.001). No differences in weight, height, BMI, waist, neck, and thigh and arm circumferences among patients with or without lipodystrophy were found.

Patients with lipodystrophy had a lower hip circumference and a higher waist/hip circumference ratio than those without lipodystrophy (p=0.006 and 0.003, respectively).

No differences were observed between patients with and without lipodystrophy regarding viral suppression rate, HIV risk factor, CDC classification and ART regime, smoking history, family history of cardiovascular disease and medication history (statins, fibrates, oral anti-diabetics, insulin and anti-hypertensive drugs), systolic blood pressure and CD4+ cell count.

Body Composition by DXA

In the evaluation of body composition by DXA, patients with lipodystrophy had a lower total and leg fat mass (p=0.017 and <0.001, respectively), both in terms of % and Kg. No differences were observed in trunk and arm fat mass (in % and Kg) between the two groups.

Patients with lipodystrophy had a higher visceral adipose tissue (VAT) value and VAT/SAT ratio (p=0.011 and 0.002, respectively), lower subcutaneous adipose tissue (SAT) (p=0.011) and no significant difference in total fat at abdominal level.

Metabolic Parameters

No significant differences were found in the levels of glucose, insulin, lipid profile (total cholesterol, LDL, HDL, non-HDL cholesterol and triglycerides), uric acid, lactates, HOMA, HbA1c, Apo A1, Apo B, ratio Apo B/Apo A1, Lp(a), homocysteine, CRP, hsCRP, NT-proBNP, fibrinogen, and microalbumin urinary excretion between patients with or without lipodystrophy.

Also, no significant differences regarding the prevalence of Metabolic Syndrome were observed between the two groups.

Carotid IMT measurements

Carotid IMT was higher in patients with lipodystrophy, compared to those without lipodystrophy [mean (SD) 0.82 (0.26) vs. 0.73 (0.20); p=0.050].

The cIMT was positively correlated with lipodystrophy evaluated by FMR, age, neck circumference, waist/hip ratio, systolic pressure, glucose at 0 and 120 minutes on OGTT, HbA1c, non HDL cholesterol, visceral obesity defined by total body fat mass by quantitative CT, VAT and VAT/SAT ratio, trunk fat mass evaluated by DXA, uric acid, CRP, hsCRP and homocysteine, as it is shown in **Table 2**. No significant correlations were found between cIMT and duration of HIV infection, length of cART, thigh circumference, total, leg and arm fat mass evaluated by DXA, CD4 cell count, leukocyte, insulin at 0 and 120 minutes on OGTT, HOMA, triglycerides and lactates.

2) After one year follow-up:

The progression of the study sample's characteristics throughout the period of follow-up (12 months) is illustrated in **Table 3**.

Total Population

Concerning the progression of body composition and metabolic parameters during one year in the totality of the sample, the values of thigh and arm circumference are lower than those obtained at baseline ($p<0.001$ and 0.049, respectively). The systolic and diastolic blood pressure also decreased significantly in the follow-up period ($p=0.005$ and <0.001), as well as total cholesterol, non-HDL cholesterol and triglycerides levels ($p=0.012$ and <0.001, for both non-HDL cholesterol and triglycerides). The values of HDL, LDL and Apo A1 show increments since baseline ($p=0.012$, 0.001 and <0.001, respectively), and the values of Apo B and the ratio apo B/ apo A1 decreased ($p<0.001$ for both variables).

Lastly, values of homocysteine and lactates are higher ($p=0.05$ and 0.002), compared with baseline, and the values of hsCRP and uric acid are lower ($p=0.030$ and 0.022).

Patients with Lipodystrophy

Patients with lipodystrophy presented lower thigh circumference, when compared with baseline ($p=0.023$), but higher values of leg fat mass, both in terms of Kg and % ($p=0.008$ and 0.007, respectively). The analysis according to quantitative CT showed a decreased value of VAT and VAT/SAT ratio ($p=0.049$ and 0.019). Diastolic blood pressure, total cholesterol, non-HDL cholesterol and triglycerides levels are lower compared with baseline values ($p=0.001$, 0.007, and <0.001 for both non HDL-cholesterol and triglycerides levels). Furthermore, HDL and Apo A1 levels increased ($p= 0.018$ and 0.001) and the Apo B/Apo A1 ratio has decreased

(p=0.001). The values of homocysteine are higher, while uric acid levels are lower than the ones obtained at baseline (p=0.008 and 0.005, respectively).

Patients without Lipodystrophy

Patients without lipodystrophy presented lower thigh circumference and leg fat mass (kg) compared with baseline (p<0.001 and 0.047). The value of VAT increased in this group during the follow-up period (p=0.024). In addition to the decline of systolic and diastolic blood pressure (p=0.027 and <0.001, respectively), CRP and hsCRP levels also decreased (p=0.038 and 0.066). The values of LDL, Apo A1 and lactates increased (p=0.001, 0.002 and 0.001), while triglycerides levels and Apo B/Apo A1 ratio decreased (p=0.001 and 0.02, respectively).

Carotid IMT measurements

During the one year of follow-up there was an increase in carotid IMT in the total of HIV-infected patients and in those with and without lipodystrophy, **when** compared with baseline (p=0.001, 0.037 and 0.012, respectively). After the follow-up period, the cIMT value of the patients presenting lipodystrophy was still higher than those without lipodystrophy, but the difference between them is no longer statistical significant (p=0.178).

Table 2 shows the variables that were positively correlated with carotid IMT at baseline. The one year evolution of these variables during follow-up in the total population can be observed in **Table 4**. During the follow-up period, the cIMT increased in the totality of the sample, despite the significant decreasing in the values of systolic blood pressure, non-HDL cholesterol, hsCRP and uric acid. The only variable positively correlated with cIMT that increased significantly in the total population was homocysteine.

Using generalized linear models for repeated measures, means of cIMT between baseline and 1 year follow up were calculated and adjusted for age, glucose, triglycerides levels, systolic

blood pressure and waist to hip ratio (**Table 5**). In the total population, the progression cIMT was significant after the adjustment for age, glucose, triglycerides and systolic blood pressure, but the significance of the cIMT progression ceased after the adjustment for waist-hip ratio.

The same analysis was performed for the group of patients presenting lipodystrophy, and the cIMT progression was significant after the adjustments for age, glucose, triglycerides, but not after the adjustment for systolic blood pressure and waist-hip ratio. The same result was obtained after the analysis of the group of patients without lipodystrophy.

DISCUSSION

Atherosclerosis is a progressive disease, whose contribution to the increase of the cardiovascular risk is well-known. This conventional CVD risk factor, as well as body fat redistribution, is associated with the progression of cIMT [20]. The intervention in cardiometabolic risk factors through the introduction of changes in terms of diet, exercise, smoking cessation and drug therapy (antidiabetic, antihypertensive and anti-dyslipidemic) may regress or delay the progression of atherosclerosis [21]. We evaluated the progression of cIMT during one year of follow-up, in a cohort of HIV-infected patients under cART, treated for the conventional risk factors. Indeed, after a year of follow up, patients improved some lipid profile items, blood pressure levels and showed decreased VAT values. Despite this improvement, the means of cIMT increased during this period of time. In fact, during one year, both groups of HIV-infected patients (with and without lipodystrophy) had a significant progression of cIMT, even after adjustment for some conventional cardiovascular risk factors (age, glucose and triglycerides). However, during the follow-up we observed an increased in LDL in the total of the population and in those without lipodystrophy, which could impact in the progression of cIMT.

Furthermore, the presence of lipodystrophy defined by FMR was not associated with the progression of cIMT. Our data suggests that the increment of cIMT is associated with body fat abnormalities, particularly visceral body fat, as the cIMT adjustment for waist-hip ratio ceased the significance of the progression. It is well known that cART can induce a large spectrum of metabolic disturbances and abnormal body fat distribution, and its contributions to an increased risk of premature and accelerated atherosclerosis in HIV infection are well recognized [10, 22, 23]. Since our goal was to evaluate if the presence of lipodystrophy influences the progression of cIMT, only patients under cART were included in our study. The overall progression of cIMT in both groups (with and without lipodystrophy) may reflect the fact that all the patients were subjected to cART and were under a low grade chronic state of inflammation associated with the HIV disease *per se*.

The values of cIMT increased significantly in both fractions of the population, despite the fact that, at baseline, lipodystrophic patients had higher waist/hip circumference, VAT and VAT/SAT ratio. At follow-up, on the other hand, this group had lower WHR values but showed equivalent results for cardiometabolic markers, when compared with patients without lipodystrophy. During the one year of follow-up, the values for VAT, VAT/SAT ratio and WHR did not change significantly in the total of the population, and in those with and without lipodystrophy. Analyses from large observational cohorts have demonstrated that increments in cIMT ranging from 0.03 to 0.2 mm are associated with 33% to 300% higher risk for coronary heart disease and stroke [24-26]. In our study, the progression of cIMT was over 0.1 mm in both groups, thus reflecting an increased cardiovascular risk in HIV infected patients under cART. The values of systolic and diastolic blood pressure decreased in this period of time, in both groups.

The degree to which cART therapy contributes to the increased cardiovascular risk of HIV patients is not clear yet. Even though there is a great body of evidence in the literature pointing to a moderate association between HIV infection and increased cIMT, in both cross-sectional settings and prospective studies, the results are still controversial [27-29]. A prospective study that evaluated the progression of cIMT in HIV-infected patients, during 6

years, found that HIV-infected patients accumulate CVD risk over time, beyond that experienced in the general population [30]. A recent large prospective cohort study that evaluated the progression of subclinical atherosclerosis in HIV-infected patients, over seven years, concluded that HIV infection is associated with increased cardiovascular risk, and that this elevated risk persisted among ART-treated individuals with persistent HIV viral suppression [31]. Hanna et al. shown that HIV infection is associated with greater increases in focal plaque formation, even when the patients are subjected to antiretroviral therapy, but HIV infection itself was not associated with increased cIMT over time, and no associations were found between persistent virulogic suppression and cIMT progression, compared with uninfected individuals [31]. These findings contradict several other studies that reported an association between HIV infection and cIMT progression over time [5, 30, 32-35]. Although van Vonderen et al. reported an independent association between HIV infection and increased cIMT, the ART use was only associated with increased stiffness of the femoral artery, not cIMT [5]. The same study also didn't find an independent association between lipodystrophy and cIMT, which is consistent with our study. Volpe et al. found that changes in cIMT over time were associated not only with tradition risk factors but also with HIV-related factors, and that these associations vary with the type of surrogate marker evaluated [29]. In fact, some studies have suggested that traditional risk factors overshadow the role of HIV infection and cART use, and that they are the major influences of cIMT progression [6, 35-37]. Visceral obesity is a well-known independent risk factor for CVD in the background population [38] and independent associations between carotid intima-media thickness and abdominal adiposity were already demonstrated [39]. Although the physiologic mechanisms by which obesity is linked to an early carotid atherosclerosis are not clearly described, some theories regarding the importance of metabolic factors, such as changes in plasma adiponectin levels and insulin resistance, have been proposed [6]. In our study, we found a higher prevalence of visceral adiposity among patients with lipodystrophy. We expected that the visceral adiposity present in patients with lipodystrophy would contribute to the progression of cIMT, which was not the case. We can speculate that the high frequency of visceral adiposity in patients without

lipodystrophy defined by FMR may contribute to the absence of differences in the progression of cIMT between patients with and without lipodystrophy. In contrast with the results obtained at baseline, the means of cIMT remained significant after the adjustment for age. In fact, the progression of cIMT was significant after the adjustment for age, glucose, triglycerides and systolic blood pressure, but the significance of the progression ceased after the adjustment for waist-hip ratio. This indicates that although cIMT is known to be affected by age, a well-established cardiovascular risk factor, the progression of cIMT that occurred in our study was not due to the age of the patients. It was, instead, mostly affected by the presence of visceral adiposity.

Additional research, with a large sample size, is needed to better characterize the underlying proatherogenic mechanisms of HIV infection and cART, as well as to evaluate the impact body composition, namely lipodystrophy, on long term cardiovascular risk in HIV-infected patients.

STUDY LIMITATIONS

The limitations of this study are mainly related to the small size of the sample. Therefore, this study might have been underpowered to detect small differences in cIMT progression, between the two groups. Due to the fact that the design of this study did not include an HIV-uninfected control group, it remains unclear whether the observed increased cardiovascular risk can be fully explained by the effects of antiretroviral drugs and their metabolic side effects, body composition or whether chronic HIV infection itself may play a role.

Highlights of this study

This study emphasizes the role of body composition, namely VAT, in addition to other traditional risk factors in the progression of CIMT. Moreover, it was performed in a highly experienced unit in the assessment of metabolic and body fat abnormalities in HIV-infected patients. All clinical evaluations were executed by the same practitioner, and an objective definition of lipodystrophy was used (fat mass ratio by DEXA).

CONCLUSIONS

Carotid IMT progressed significantly in HIV-infected patients under cART, both in those with or without lipodystrophy. Although patients with lipodystrophy defined by FMR had a higher cIMT when compared with those without lipodystrophy, there is no association between the progression of cIMT and the presence of lipodystrophy defined by FMR. Visceral adipose tissue had an impact on the increment of cIMT during the follow-up period (both in patients with and without lipodystrophy defined by FMR), which suggests an independent association between VAT and the increasing of subclinical carotid atherosclerosis.

List of Abbreviations

cART - combination antiretroviral therapy; FMR – Fat Mass Ratio; cIMT – carotid intima-media thickness; WHR – waist-hip ratio, SPB – systolic blood pressure; VAT – visceral adipose tissue; SAT – subcutaneous adipose tissue; L-FMR – lipodystrophy defined by FMR; CVD – cardiovascular disease; OGTT – Oral glucose tolerance test.

Competing interests

The authors declare that they have no competing interests

Authors' contributions

MTB participated in the acquisition of data and drafted the manuscript; ASP participated in the acquisition of data and revised the manuscript; ACS performed the statistical analysis and critically revised the manuscript; AJM performed the CT scans and reviewed the data; JP performed DXA scans and reviewed the data; DC conceived the study and participated in its design; AS critically revised the manuscript; PF conceived the study, participated in its design, in the acquisition of data and critically revised the manuscript. All authors read and approved the final manuscript.

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Table 1: Basal sample characteristics according to the presence of lipodystrophy defined by FMR

	Without Lipodystrophy defined by FMR	With Lipodystrophy defined by FMR	*P*
n (%)	64	51	-
Gender [n(%)] Male Female	 49 (76.6%) 15(23.4%)	 42(82.4%) 9(17.6%)	 0.448
Age [years, mean (sd)]	45 (12.2)	49(9.9)	0.052
Duration of HIV infection [years, mean (sd)]	7.2 (3.8)	8.5(3.7)	**0.036**
cART [years, mean (sd)]	5.9 (3.6)	7.9 (3.5)	**0.001**
Weight [Kg, mean (sd)]	69.5 (13.5)	67.8 (9.6)	0.410
Height [m, mean (sd)]	1.66 (0.09)	1.64 (0.08)	0.188
BMI [(Kg/m^2), mean (sd)]	25.2 (4.7)	25.2 (3.8)	0.976
Waist circumference [cm, mean (sd)]	91.3 (12.7)	91.6 (9.9)	0.877
Hip circumference [cm, mean (sd)]	95.7(8.5)	91.9(6.4)	**0.006**
Thigh circumference [cm, mean (sd)]	48,7 (5.1)	47.1(5.2)	0.113
Arm circumference [cm, mean (sd)]	26.9 (3.0)	27.0 (2.7)	0.939
Neck circumference [cm, mean (sd)]	37.8 (3.6)	37.6 (3.3)	0.829

Waist/ hip circumference ratio [mean (sd)]	0.95 (0.09)	0.99 (0.07)	**0.003**
CD4 cell count [cells/mm3, mean (sd)]	522.9 (288.7)	584.6 (331.9)	0.289
HIV RNA (<50) [n (%)]	52 (81.3%)	47 (92.92%)	0.093
HIV risk factor [n (%)]			
Injecting drug user	19 (29.7%)	11 (21.6%)	0.073
Homosexual contact	39 (60.9%)	27 (52.9%)	
Heterosexual contact	4 (6.3%)	11 (21.6%)	
Others	1(1.6%)	2 (3.9%)	
CDC [n (%)]			
A	32 (50.0%)	31(60.8%)	0.248
B	-	-	
C	32 (50.0)	20 (39.2)	
ART [n (%)]			
PI	32 (50.0%)	30 (58.8%)	0.346
NNRTI	31 (48.4%)	23 (45.1%)	0.721
NRTI	60 (93.8%)	50 (98.0%)	0.380

Smoking history [n (%)]			
Never	19 (30.2%)	20 (39.2)	0.556
Current	33 (52.4%)	22 (43.1%)	
Former	11 (17.5%)	9 (17.6%)	
Familial history of CVD [n (%)]	23 (35.9%)	21 (41.2%)	0.566
Taking medications [n (%)]			
Statins	14 (22.2%)	15 (29.4%)	0.381
Fibrates	29 (46.0%)	27 (52.9%)	0.463
Oral anti-diabetics	9 (14.3%)	12 (23.5%)	0.306
Insulin	4 (6.3%)	4 (7.8%)	0.999
Anti-hypertensive drugs	13 (20.3%)	12 (24.0%)	0.637
Fat mass [%, mean (sd)] DXA			
Total	22.6 (13.1)	17.8 (8.0)	**0.017**
Trunk	24.1 (13.5)	22.7 (8.6)	0.508
Leg	22.3 (15.4)	9.7 (6.7)	**<0.001**
Arm	23.4 (16.3)	18.7 (13.3)	0.095
Fat mass [Kg, mean (sd)] DXA			

Total	16.4 (11.0)	12.1 (6.6)	**0.012**
Trunk	9.1 (6.2)	8.4 (4.3)	0.470
Leg	4.7 (3.4)	1.8 (1.3)	**<0.001**
Arm	1.9 (1.7)	13.8 (1.2)	0.063
Body Fat Mass by Quantitative CT**			
Total fat [cm^2, mean (sd)]	272.6 (188.1)	259.6 (112.9)	0.651
VAT [cm^2, mean (sd)]	116.8 (95.4)	154.8 (59.7)	**0.011**
SAT [cm^2, mean (sd)]	155.8 (123.2)	104.8 (85.2)	**0.011**
VAT/SAT ratio [cm^2, mean (sd)]	1.3 (1.8)	2.4 (1.7)	**0.002**
Systolic blood pressure [mmHg, mean (sd)]	122.0 (19.4)	124.0 (16.0)	0.558
Diastolic blood pressure [mmHg, mean (sd)]	78.5 (12.1)	79.2 (11.1)	0.750
Leukocytes [10^9/L, mean (sd)]	5.7 (1.7)	6.5 (1.9)	**0.034**
Glucose 0 min [mg/dL, mean (sd)]	106.4 (47.1)	119.1 (52.1)	0.175
Glucose 2 hours [mg/dL, mean (sd)]	122.3 (46.3)	138.5 (47.7)	0.126
Insulin 0 min [μU/mL, mean (sd)]	10.5 (12.8)	10.9 (6.5)	0.863
Insulin 2 hours [μU/mL, mean (sd)]	53.1 (49.2)	105.9 (186.8)	0.072

HOMA [mean (sd)]	2.9 (3.6)	3.2 (2.6)	0.601
A1c [% mean (sd)]	5.6 (1.2)	6.0 (1.1)	0.123
Total cholesterol [mg/dL, mean (sd)]	213.6 (56.0)	226.9 (57.6)	0.216
LDL-cholesterol [mg/dL, mean (sd)]	113.5 (49.2)	123.7 (49.2)	0.270
HDL-cholesterol [mg/dL, mean (sd)]	43.9 (12.1)	43.6 (11.3)	0.911
Non-HDL cholesterol [mg/dL, mean (sd)]	169.8 (52.0)	183.2 (52.2)	0.170
Triglycerides[mg/dL, mean (sd)]	284.4 (191.7)	298.9 (186.9)	0.683
Apo A1 [mg/dL, mean (sd)]	110.4 (24.0)	111.6 (16.6)	0.763
Apo B [mg/dL, mean (sd)]	104.7 (24.4)	104.8 (26.7)	0.975
Ratio apo B/apo A1 [mean (sd)]	0.98 (0.3)	0.95 (0.3)	0.604
Lp (a) [mg/dL, mean (sd)]	28.9 (31.0)	27.5 (33.5)	0.821
Homocysteine [μmol/L, mean (sd)]	9.4 (4.1)	9.7 (3.5)	0.701
CRP [mg/L, mean (sd)]	6.6 (16.6)	4.3 (4.7)	0.496
hsCRP [mg/dL, mean (sd)]	0.83 (1.5)	0.34 (0.31)	0.496
Lactates [mmol/L, mean (sd)]	1.1 (0.5)	1.3 (0.6)	0.056
NT-ProBNP [pg/mL, mean (sd)]	41.2 (74.8)	31.6 (31.9)	0.450

Fibrinogen [mg/dL, mean (sd)]	350.8 (103.8)	342.9 (105.9)	0.696
Microalbumin [mg/L, mean (sd)]	76.7 (196.6)	40.6 (91.3)	0.441
Uric acid [mg/L, mean (sd)]	46.0 (14.6)	49.8 (12.8)	0.140
Carotid IMT [mm, mean (sd)]	0.73 (0.196)	0.82 (0.257)	**0.050**
Metabolic Syndrome (%)	31 (49.2%)	27 (54.0%)	0.705

(L- Lipodystrophy FMR defined; CDC - Centers for Disease Control and Prevention criteria for staging of HIV infection; cART- combined antiretroviral therapy; BMI- body mass index; FMR – fat mass ratio; CVD – cardiovascular disease; DXA – dual-energy X-ray absorptiometry; CT – computed tomography; PI – protease inhibitor; NNRTI –non-nucleoside reverse transcriptase inhibitor; NRTI – nucleoside reverse transcriptase inhibitor; VAT- visceral adipose tissue; SAT – subcutaneous adipose tissue; HOMA – the homeostasis model assessment of insulin resistance; HDL-high density cholesterol; LDL – low density cholesterol; Apo A1 – apolipoprotein A1; Apo B – apolipoprotein B; Lp(a) – lipoprotein (a); CPR – C protein reactive; hsCRP – high sensitivity C protein reactive; NT-ProBNP - N-terminal prohormone of brain natriuretic peptide; IMT – intima-media thickness).

Table 2 – Correlations between cIMT and body composition and metabolic parameters.

Correlations between cIMT and:	**R**	**P**
Age	0.709	**<0.001**
Waist/Hip Ratio	0.387	**<0.001**
Neck circumference	0.202	**0.007**
Systolic Blood Pressure	0.419	**<0.001**
Glucose 0 min	0.284	**<0.001**
Glucose 2 hours OGTT	0.220	**0.006**
A1c	0.285	**<0.001**
Non-HDL cholesterol	0.254	**<0.001**
CRP	0.196	**0.005**

hsCRP	0.334	**0.003**
Homocysteine	0.150	**0.032**
Uric Acid	0.146	**0.034**
Trunk Fat Mass by DXA (g)	0.168	**0.0018**
Total fat on Abdominal CT scan	0.218	**0.002**
VAT on abdominal CT scan	0.418	**<0.001**
VAT/SAT on abdominal CT scan	0.290	**<0.001**
FMR	0.250	**<0.001**
Duration of HIV infection	-0.019	0.779
Leg Fat Mass by DXA (g)	-0.037	0.604
Thigh Circumference	-0.095	0.169
CD4 cell count	-0.027	0.701
Leukocytes	-0.049	0.478
SAT on abdominal CT scan	-0.009	0.901
Insulin 2 hours OGTT	-0.089	0.271
HOMA	0.094	0.185
Insulin 0 min	0.026	0.711
Lactates	0.081	0.253
Triglycerides	0.109	0.113
Total Fat Mass by DXA (g)	0.084	0.236
Arm Fat Mass by DXA (g)	0.029	0.686
cART	0.024	0.727

(FMR – fat mass ratio; OGTT – oral glucose tolerance test: CT – computed tomography; VAT- visceral adipose tissue; SAT – subcutaneous adipose tissue; HDL-high density cholesterol; CPR – C protein reactive; hsCRP – high sensitivity C protein reactive; HOMA – the homeostasis model assessment of insulin resistance; DXA – dual-energy X-ray absorptiometry; cART- combined antiretroviral therapy; IMT – intima-media thickness).

Table 3 – Progression of sample characteristics during follow-up.

Total Population	With Lipodystrophy	Without Lipodystrophy

	Baseline	**1 year after**	**p**	**Baseline**	**1 year after**	**p**	**Baseline**	**1 year after**	**p**
Weight [Kg, mean (sd)]	68.7 (11.9)	67.8 (11.8)	0.474	67.8 (9.6)	65.7 (12.0)	0.360	69.5 (13.5)	69.5 (13.5)	0.977
Height [m, mean (sd)]	1.65 (0.1)	1.65 (0.1)	-	1.64 (0.08)	1.64 (0.08)	-	1.66 (0.09)	1.66 (0.09)	-
BMI [(Kg/m^2), mean (sd)]	25.2 (4.3)	25.0 (4.9)	0.547	25.2 (3.8)	24.5 (4.7)	0.359	25.2 (4.7)	25.4 (5.1)	0.849
Waist circumference [cm, mean (sd)]	91.4 (11.5)	90.9 (10.8)	0.654	91.6 (9.9)	89.7 (11.2)	0.402	91.4 (12.8)	92.0 (10.4)	0.804
Hip circumference [cm, mean (sd)]	94.0 (7.8)	93.2 (6.8)	0.496	91.9(6.4)	92.6 (7.0)	0.561	95.7(8.6)	93.6 (6.7)	0.120
Thigh circumference [cm, mean (sd)]	48.0 (5.2)	45.3 (4.2)	**<0.001**	47.2 (5.2)	45.0 (4.14)	**0.023**	48,7 (5.1)	45.5 (4.4)	**<0.001**
Arm circumference [cm, mean (sd)]	27.0 (2.9)	26.1 (2.8)	**0.049**	27.0 (2.7)	25.9 (2.9)	0.082	27.0 (3.1)	26.5 (2.8)	0.353
Neck circumference [cm, mean (sd)]	37.7 (3.5)	36.9 (3.5)	0.143	37.6 (3.3)	36.8 (3.9)	0.327	37.8 (3.6)	37.1 (3.2)	0.322
Waist/ hip circumference ratio [mean (sd)]	0.97 (0.08)	0.97 (0.08)	0.786	1.00 (0.07)	0.97 (0.09)	0.086	0.95 (0.09)	0.98 (0.08)	0.066
Fat mass [%, mean (sd)] DXA									
Total	20.5 (11.4)	21.6 (10.4)	0.554	17.8 (8.0)	19.9 (10.5)	0.264	22.6 (13.1)	22.9 (10.1)	0.941
Trunk	23.5 (11.6)	24.8 (10.8)	0.561	22.7 (8.6)	22.7 (11.2)	0.980	24.1 (13.5)	26.5 (10.2)	0.418
Leg	16.7 (13.8)	16.2 (11.0)	0.898	9.7 (6.7)	15.0 (10.4)	**0.007**	22.3 (15.4)	17.2 (11.5)	0.088
Arm	21.3 (15.2)	23.8 (15.0)	0.267	18.7(13.3)	22.4 (15.8)	0.232	23.4 (16.3)	24.9 (14.4)	0.631
Fat mass [Kg, mean (sd)] DXA									
Total	14.5 (9.5)	14.7 (8.3)	0.867	12.1 (6.7)	13.1 (7.7)	0.406	16.4 (11.0)	16.0 (8.6)	0.736
Trunk	8.7 (5.4)	9.0 (5.0)	0.897	8.4 (4.3)	8.0 (4.9)	0.766	9.1 (6.2)	9.8 (5.1)	0.641
Leg	3.5 (3.0)	3.3 (2.5)	0.810	1.8 (1.3)	2.8 (2.0)	**0.008**	4.7 (3.4)	3.6 (2.8)	**0.047**
Arm	1.7 (1.5)	1.8 (1.3)	0.293	1.4 (1.2)	1.7 (1.3)	0.238	1.9 (1.7)	1.9 (1.3)	0.744
Body Fat Mass by Quantitative CT**									
Total fat [cm^2, mean (sd)]	266.8 (158.4)	274.5 (146.0)	0.625	259.6 (112.9)	249.6 (160.5)	0.708	272.6 (188.1)	295.3 (130.4)	0.361
VAT [cm^2, mean (sd)]	133.8 (83.2)	136.0 (85.1)	0.670	154.8 (59.7)	126.2 (97.2)	**0.049**	116.8 (95.4)	144.2 (73.3)	**0.024**
SAT [cm^2, mean (sd)]	133.0 (110.4)	139.3 (95.7)	0.314	104.9 (85.2)	125.2 (95.8)	0.180	155.8 (123.2)	151.1 (94.8)	0.848
VAT/SAT ratio [cm^2, mean (sd)]	1.8 (1.8)	1.6 (1.8)	0.298	2.4 (1.7)	1.6 (1.6)	**0.019**	1.3 (1.8)	1.6 (1.9)	0.185
Systolic blood pressure	122.9 (18.0)	117.2 (18.1)	**0.005**	124.0	119.3	0.072	122.0 (19.4)	115.6	**0.027**

[mmHg, mean (sd)]				(16.1)	(20.9)			(15.5)	
Diastolic blood pressure [mmHg, mean (sd)]	78.8 (11.6)	71.8 (8.9)	**<0.001**	79.2 (11.1)	72.2 (8.6)	**0.001**	78.5 (12.1)	71.6 (9.2)	**<0.001**
Glucose 0 min [mg/dL, mean (sd)]	112.0 (49.6)	101.2 (25.6)	0.481	119.1 (52.1)	104.6 (28.7)	0.307	106.4 (47.1)	99.4 (22.8)	0.992
Glucose 2 hours [mg/dL, mean (sd)]	129.5 (47.4)	137.3 (47.6)	0.445	138.5 (47.7)	137.7 (47.5)	0.819	122.3 (46.3)	136.9 (48.2)	0.451
Insulin 0 min [µU/mL, mean (sd)]	10.7 (10.4)	13.3 (14.8)	0.166	10.9 (6.5)	12.1 (9.9)	0.419	10.5 (12.8)	14.1 (17.7)	0.227
Insulin 2 hours [µU/mL, mean (sd)]	76.5 (131.5)	71.8 (60)	0.886	105.9 (186.8)	69.9 (60.4)	0.220	53.1 (49.2)	73.3 (59.9)	0.307
HOMA [mean (sd)]	3.1 (3.2)	3.5 (4.8)	0.552	3.2 (2.5)	3.2 (2.9)	0.857	2.9 (3.6)	3.8 (5.8)	0.369
A1c [% mean (sd)]	5.8 (1.2)	5.5 (0.8)	0.095	5.9 (1.1)	5.5 (0.9)	0.096	5.6 (1.2)	5.4 (0.7)	0.556
Total cholesterol [mg/dL, mean (sd)]	219.5 (56.8)	204.7 (41.4)	**0.012**	226 (57.6)	203.8 (41.9)	**0.007**	213.6 (56.0)	205.4 (41.2)	0.396
LDL-cholesterol [mg/dL, mean (sd)]	118.0 (49.2)	135.7 (31.3)	**0.001**	123.7 (49.2)	133.9 (28.4)	0.153	113.5 (49.2)	137.2 (33.6)	**0.001**
HDL-cholesterol [mg/dL, mean (sd)]	43.8 (11.7)	48.6 (13.3)	**0.012**	43.6 (11.3)	50.6 (14.6)	**0.018**	43.9 (12.1)	46.9 (12.0)	0.280
Non-HDL cholesterol [mg/dL, mean (sd)]	175.7 (52.3)	156.2 (37.6)	**<0.001**	183.2 (52.2)	153.2 (37.6)	**<0.001**	169.8 (52.0)	158.5 (37.6)	0.192
Triglycerides [mg/dL, mean (sd)]	290.8 (189.0)	180.5 (110.5)	**<0.001**	298.9 (186.9)	165.6 (107.2)	**<0.001**	284.4 (191.7)	192.3 (112.5)	**0.001**
Apo A1 [mg/dL, mean (sd)]	111 (21)	126.4 (24.0)	**<0.001**	111.6 (16.6)	130.0 (25.2)	**0.001**	110.4 (23.9	123.7 (22.8)	**0.002**
Apo B [mg/dL, mean (sd)]	104.7 (25.3)	101.4 (21.7)	**<0.001**	104.8 (26.7)	100.0 (21.6)	0.126	104.7 (24.4)	102.4 (22.0)	0.706
Ratio apo B/apo A1 [mean (sd)]	0.97 (0.3)	0.83 (0.3)	**<0.001**	0.95 (0.3)	0.79 (0.2)	**0.001**	0.98 (0.3)	0.87 (0.3)	**0.02**
Lp (a) [mg/dL, mean (sd)]	28.3 (32.0)	36.3 (43.3)	0.289	27.5 (33.5	44.4 (47.8)	0.102	28.9 (30.9)	30.1 (38.7)	0.906
Homocysteine [µmol/L, mean (sd)]	9.5 (3.8)	11.1 (4.8)	**0.005**	9.7 (3.5)	12.1 (5.2)	**0.008**	9.4 (4.1)	10.3 (4.3)	0.179

CRP [mg/L, mean (sd)]	5.6 (12.8)	5.1 (11.3)	0.147	4.3 (4.7)	6.1 (14.4)	0.857	6.6 (16.6)	4.3 (8.0)	**0.038**
hsCRP [mg/dL, mean (sd)]	0.6 (1.2)	0.5 (1.2)	**0.030**	0.34 (0.31)	0.65 (1.6)	0.225	0.83 (1.5)	0.43 (0.8)	**0.066**
Lactates [mmol/L, mean (sd)]	1.2 (0.5)	1.4 (0.6)	**0.002**	1.3 (0.6)	1.4 (0.6)	0.307	1.1 (0.48)	1.4 (0.5)	**0.001**
NT-ProBNP [pg/mL, mean (sd)]	36.8 (59.0)	39.0 (63.0)	0.241	31.6 (31.9)	35.9 (33.2)	0.177	41.2 (74.8)	41.3 (79.0)	0.769
Fibrinogen [mg/dL, mean (sd)]	347.3 (104.4)	332.6 (79,0)	0.611	342.9 (105.9)	333.8 (80.1)	0.841	350.8 (103.8)	331.6 (78.8)	0.370
Microalbumin [mg/L, mean (sd)]	58.2 (151.4)	36.0 (159.8)	0.527	40.6 (91.3)	20.5 (35.6)	0.551	76.7 (196.6)	47.7 (209.3)	0.852
Uric acid [mg/L, mean (sd)]	47.7 (14.0)	44.1 (14.6)	**0.022**	49.8 (12.8)	43.7 (13.0)	**0.005**	45.9 (14.6)	474.3 (15.8)	0.470
Carotid IMT [mm, mean (sd)]	0.77 (0.23)	0.87 (0.32)	**0.001**	0.82 (0.26)	0.92 (0.33)	**0.037**	0.73 (0.20)	0.84 (0.30)	**0.012**
Metabolic Syndrome (%)	58 (51.3)	48 (43.2)	0.203	27 (54.0)	19 (38.8)	0.134	31 (49.2)	29 (46.8)	0.851

(L- Lipodystrophy FMR defined; BMI- body mass index; FMR – fat mass ratio; DXA – dual-energy X-ray absorptiometry ; CT – computed tomography; VAT- visceral adipose tissue; SAT – subcutaneous adipose tissue; HOMA – the homeostasis model assessment of insulin resistance; HDL-high density cholesterol; LDL – low density cholesterol; ; Apo A1 – apolipoprotein A1; Apo B – apolipoprotein B; Lp(a) – lipoprotein (a); CPR – C protein reactive; hsCRP – high sensitivity C protein reactive; NT-ProBNP - N-terminal prohormone of brain natriuretic peptide; IMT – intima-media thickness).

Table 4 - Evolution of the variables positively correlated with cIMT during follow-up in the total sample.

	Baseline	**One Year follow-up**	**P**
Waist/Hip Ratio	0.97 (0.08)	0.97 (0.08)	0.786
Neck circumference	37.7 (3.5)	36.9 (3.5)	0.143
Systolic Blood Pressure	122.9 (18.0)	117.2 (18.1)	**0.005**
Glucose 0 min	112.0 (49.6)	101.7 (25.6)	0.481
Glucose 2 hours OGTT	129.5 (47.4)	137.3 (47.6)	0.445
A1c	5.8 (1.2)	5.5 (0.8)	0.095
Non-HDL cholesterol	175.7 (52.3)	156.2 (37.6)	**<0.001**
CRP	5.6 (12.8)	5.1 (11.3)	0.147

hsCRP	0.6 (1.2)	0.5 (1.2)	**0.030**
Homocysteine	9.5 (3.8)	11.1 (4.8)	**0.005**
Uric Acid	47.7 (14.0)	44.1 (14.6)	**0.022**
Trunk Fat Mass by DXA (kg)	8.7 (5.4)	9.0 (5.0)	0.897
Total fat on Abdominal CT scan	266.8 (158.4)	274.5 (146.0)	0.625
VAT on abdominal CT scan	133.8 (83.2)	136.0 (85.1)	0.670
VAT/SAT on abdominal CT scan	1.8 (1.8)	1.6 (1.8)	0.298

OGTT – oral glucose tolerance test: CT – computed tomography; VAT- visceral adipose tissue; SAT – subcutaneous adipose tissue; HDL-high density cholesterol; CPR – C protein reactive; hsCRP – high sensitivity C protein reactive;DXA – dual-energy X-ray absorptiometry; IMT – intima-media thickness).

Table 5 – Crude and adjusted means of cIMT at baseline and at 1 year follow up.

Total Sample	**cIMT baseline**	**cIMT 1year follow up**	**P**
Crude model	0.770 (0.728 – 0.812)	0.874 (0.815 – 0.932)	**<0.001**
Model adjusted for age	0.770 (0.738-0.802)	0.874 (0.816-0.932)	**<0.001**
Model adjusted for age and glucose	0.770 (0.737-0.803)	0.874 (0.816-0.932)	**<0.001**
Model adjusted for age, glucose and Triglycerides	0.770 (0.737-0.803)	0.874 (0.815-0.933)	**0.001**
Model adjusted for age, glucose, triglycerides and Systolic Pressure	0.770 (0.738-0.802)	0.874 (0.815-0.932)	**0.050**
Model adjusted for age, glucose, triglycerides, Systolic Pressure and WHR	0.770 (0.737-0.803)	0.874 (0.815-0.933)	0.514
Patients with Lipodystrophy			
Crude model	0.817 (0.744-0.889)	0.919 (0.825-1.01)	**0.030**
Model adjusted for age	0.817 (0.757-0.876)	0.919 (0.826-1.01)	**0.027**

Model adjusted for age and glucose	0.817 (0.756-0.877)	0.919 (0.825-1.01)	**0.018**
Model adjusted for age, glucose and triglycerides	0.817 (0.756-0.877)	0.919 (0.825-1.01)	0.053
Model adjusted for age, glucose, triglycerides and Systolic Pressure	0.817 (0.756-0.878)	0.919 (0.825-1.01)	0.401
Model adjusted for age, glucose, triglycerides, Systolic Pressure and WHR	0.817 (0.755-0.878)	0.919 (0.823-1.01)	0.644
Patients Without Lipodystrophy			
Crude model	0.733 (0.684-0.784)	0.838 (0.763 – 0.914)	**0.020**
Model adjusted for age	0.733 (0.698-0.767)	0.838 (0.763 – 0.914)	**0.003**
Model adjusted for age and glucose	0.733 (0.698-0.768)	0.838 (0.763 – 0.914)	**0.015**
Model adjusted for age, glucose and triglycerides	0.733 (0.698-0.768)	0.838 (0.762 – 0.915)	**0.017**
Model adjusted for age, glucose, triglycerides and Systolic Pressure	0.733 (0.698-0.768)	0.838 (0.762 – 0.915)	0.130
Model adjusted for age, glucose, triglycerides, Systolic Pressure and WHR	0.733 (0.698-0.768)	0.838 (0.761 – 0.915)	0.676

(L- Lipodystrophy FMR defined; FMR – fat mass ratio; SBP – systolic blood pressure; WHR – waist/hip ratio; IMT – intima-media thickness)

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ANEXOS

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