

# Metabolic Syndrome in Relation to Cardiorespiratory Fitness, Active and Sedentary Behavior in HIV+ Hispanics with and without Lipodystrophy

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**Objective:** Hispanics in Puerto Rico (PR) have a high prevalence of metabolic syndrome (met-syn), partially explained by low physical activity (PA) and possibly low cardiorespiratory fitness (VO<sub>2</sub>peak). Met-syn is also associated with lipodystrophy in HIV infected (HIV+) adults taking antiretroviral therapies. However, associations between met-syn, VO<sub>2</sub>peak, PA, sedentary behavior and lipodystrophy among HIV+ Hispanics have not been adequately reported. We tested the following hypotheses: 1) HIV+ Hispanics with lipodystrophy (HIV-Lipo) would have a higher prevalence of met-syn, lower VO<sub>2</sub>peak and PA, and higher sedentary behavior compared with those without lipodystrophy (HIV-no-Lipo) and without HIV infection (Non-HIV); and 2) met-syn would be inversely associated with VO<sub>2</sub>peak and PA, and directly associated with sedentary behavior.

**Methods:** Ninety Hispanic adults (32 HIV-Lipo, 28 HIV-no-Lipo, 30 Non-HIV) completed measurements of VO<sub>2</sub>peak, anthropometry, PA and sedentary behavior with accelerometry, blood pressure, fasting glucose, insulin, and lipids. ANOVA and chi-square tests were used to detect differences between groups, and regression analyses to test associations between variables.

**Results:** More HIV-Lipo (69%) had met-syn compared with HIV-no-Lipo (39%) and Non-HIV (37%) (P=0.002). Sedentary behavior and PA were not different, but VO<sub>2</sub>peak differed between all groups: lowest in HIV-Lipo and highest in non-HIV. PA and sedentary behavior were not associated with met-syn, but PA was directly associated with VO<sub>2</sub>peak (R<sup>2</sup>=0.26, p<0.01). Also, a lower odds ratio for met-syn was observed with higher VO<sub>2</sub>peak (0.87; 95% CI: 0.83-0.95).

**Conclusion:** Met-syn is related to lipodystrophy in HIV+ Hispanics in PR, and high VO<sub>2</sub>peak may protect against met-syn in this population. [*PR Health Sci J* 2014;33:163-169]

*Key words:* VO<sub>2</sub>peak, Physical activity, Sedentary time, Cardio-metabolic dysfunction, HIV

Increased prevalence of metabolic syndrome (met-syn) risk factors, including dyslipidemia, insulin resistance, central obesity, and elevated blood pressure have been reported in adults living with HIV (HIV+) treated with antiretroviral therapies (ART) (1). These met-syn risk factors, when analyzed individually or combined, are strongly associated with the development of cardiovascular diseases and all-cause mortality (2, 3). Central obesity is also one aspect of the lipodystrophy syndrome highlighted as significant in the development of met-syn among HIV+ adults (4). However, the association between lipodystrophy and met-syn in HIV+ adults is still controversial. For example, Estrada et al. reported 15.8% prevalence of met-syn among HIV+ adults, but no significant difference in the prevalence of met-syn by lipodystrophy status (18.2 vs. 10.6% in patients with and without lipodystrophy, respectively) (5). In another study, Freitas et al. observed a higher prevalence of met-syn (54%), but also no difference by lipodystrophy status (6).

A high prevalence of met-syn and its associated risk factors have been observed in the general population and among HIV+ adults in Puerto Rico (PR) compared with non-Hispanics in the US (7, 8); possibly influenced by low physical activity (PA), poor nutrition, and genetic factors. Physical inactivity is a significant health problem in PR, with less than 35% of the adult population reporting adequate levels of PA (<http://www.>

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cdc.gov/brfss, accessed 03/21/14). Low PA (less than 150 min/week of moderate to vigorous PA or less than 10,000 steps/day), low cardiorespiratory fitness ( $VO_{2peak}$  less than 50th percentile for age and sex), and sedentary behaviors (sitting or lying down for more than 6 hours/daytime) are factors directly associated with all-cause morbidity and mortality from chronic diseases (9) (10-12). Also, in the general population, good cardiorespiratory fitness ( $VO_{2peak}$ ) have been linked with a reduced prevalence of met-syn (13, 14), and sedentary time with an increased prevalence of met-syn (15, 16). HIV+ adults usually present low  $VO_{2peak}$  (17), and lower than recommended levels of PA (18). Therefore, it is possible that among HIV+ Hispanics, the combination of low PA, low  $VO_{2peak}$ , and lipodystrophy might increase even more the risk of met-syn and other health complications. However, the association between met-syn,  $VO_{2peak}$ , PA, sedentary behavior, and lipodystrophy among HIV+ adults in PR has not been adequately described.

In this study we compared met-syn,  $VO_{2peak}$ , PA, and sedentary behavior between HIV+ Hispanics with and without lipodystrophy and Non-HIV Hispanics. We hypothesized that: 1) HIV+ Hispanics with lipodystrophy (HIV-Lipo) would have a higher prevalence of met-syn, lower  $VO_{2peak}$ , lower PA, and higher sedentary behavior compared to those without lipodystrophy (HIV-no-Lipo) and without HIV infection (Non-HIV); and 2) met-syn would be inversely associated with  $VO_{2peak}$  and PA, and directly associated with sedentary behavior.

## Methods

Ninety Hispanic adults were recruited for this cross-sectional study: 32 HIV+ with lipodystrophy (HIV-Lipo), 28 HIV+ without lipodystrophy (HIV-no-Lipo), and 30 without HIV infection (Non-HIV). Sample size was estimated from previous studies in which data for cardio-metabolic risk factors in adults HIV-Lipo, HIV-n-Lipo, and Non-HIV were reported (19, 20). For example, to detect a difference of 6  $\mu$ U/ml of fasting insulin, 8 participants were needed per group; and to detect a difference of 15 mmHg in systolic blood pressure, 17-30 participants were needed per group (effect size = 0.50, power = 82-97%). Based on these calculations, 30 participants per group were deemed appropriate. However, at study completion when the database was revised against each participant's record, two HIV participants meeting the criteria for lipodystrophy were incorrectly placed in the HIV-no-Lipo group.

Lipodystrophy status was determined by at least two of these: 1) waist to hip ratios (WHR)  $\geq 1.00$  for males and  $\geq 0.85$  for females, 2) physician's diagnosis, and 3) self-reported changes in body size (fat accumulation in the abdomen, fat loss in the gluteal area and extremities, and changes in clothing size during the previous 5 years). HIV-Lipo participants were recruited first, and then, HIV-no-Lipo and Non-HIV participants of similar age and gender were recruited. All participants were

eligible if their age ranged from 30-65 years, were able to engage in ambulatory physical activities, free from drug or alcohol abuse, anemia, and diagnosed cardiac or kidney disease. For HIV+ participants eligibility also included: no current AIDS diagnosis and no uncontrolled diabetes, kidney or thyroid disease diagnosed previous to HIV infection. They were recruited from the AIDS Clinical Trials Unit at the University of Puerto Rico, Medical Sciences Campus; and "La Perla de Gran Precio" HIV/AIDS Community based program in San Juan, PR. To avoid possible selection bias, authorized personnel in each site informed potential participants about the study and referred those interested to the principal investigator for the evaluation of inclusion/exclusion criteria and recruitment. Healthy Non-HIV participants were recruited through personal contact at the University of Puerto Rico and the general community. The study was approved by the IRB of the University of Puerto Rico, Medical Sciences Campus, and participants signed the informed consent form after all their questions were answered.

A sociodemographic and general health questionnaire, and a food frequency questionnaire (21) were used to obtain general and nutritional characteristics of study participants, including smoking behavior and dietary fat intake as potential confounding variables. A digital scale (Tanita BF-522W, Tanita Corporation of America, Arlington Heights, Illinois, US) and a stadiometer (Seca 217, Seca Medical Scales and Measuring Systems, United Kingdom) were used to measure weight and height for the calculation of body mass index (BMI: kg/m<sup>2</sup>). Waist circumference at the level of the umbilicus and hip circumference at the level of the greatest protuberance of the gluteal muscles were measured with a Gulick anthropometric tape for the calculation of WHR.

Blood samples were obtained in the morning after a 10-12 hour overnight fast and sent to the Puerto Rico Clinical and Translational Research Consortium (PRCTRC) Bioanalytical Core Laboratory (fasting glucose and lipid panel) or Quest Diagnostics Laboratory (fasting insulin) for standard fluorometric analyses. Quest Diagnostics is certified by the College of American Pathologists (CAP) and the Clinical Laboratory Improvement Amendments (CLIA). Resting blood pressure was measured after participants rested for 30 min and before blood samples were collected. Insulin resistance was estimated from fasting blood glucose and insulin using the homeostasis model assessment for insulin resistance (HOMA-IR) (22). The proportion of participants meeting the criteria for met-syn and each individual component was determined based on the National Cholesterol Education Program - Adult Training Program III (NCEP-ATP III) (23).

PA and sedentary time were objectively measured for seven consecutive days using the ActiGraph GT1M accelerometer attached to an elastic belt around the waist. Participants were asked to wear the instrument during all day and take it off only

during showering or sleeping at night. The accelerometer's activity counts were used to determine hr/day of sedentary time (<100 activity counts/min), min/week of moderate to vigorous PA (MVPA:  $\geq 1952$  activity counts/min) and number of steps/day using the ActiLife Data Analysis Software (Version 5, 2011, ActiGraph, Pensacola, Florida, US). Participants also completed a graded exercise test on a motorized treadmill until volitional fatigue during which breath by breath respiratory gases were analyzed (Schiller CS200 Ergo Spirometer, Surgo Surgical Supply, Ontario, Canada) for the measurement of  $VO_{2peak}$  using the modified Bruce protocol.

Data analyses were conducted with STATA for Windows (Version 11, SataCorp LP, College Station, Texas). Continuous variables are presented as mean $\pm$ se. Significant differences between groups were determined with ANOVA and Bonferroni post-hoc analyses for continuous variables, and chi-square tests for categorical variables. Linear and logistic regressions were used to test for associations between met-syn, the individual components of met-syn, and  $VO_{2peak}$ . Another logistic regression analysis was conducted in which other potential factors in the prediction of met-syn were added (smoking, PA, sedentary time, education, and dietary fat intake). An alpha level of 0.05 was determined a priori to test for significance.

## Results

The HIV-Lipo and HIV-no-Lipo groups had similar viral profiles (proportion of participants with  $CD4 > 500 = 63$  and  $62\%$ , and undetected viral load [ $< 50$  copies] =  $93$  and  $79\%$ , respectively,  $P > 0.05$ ), and were taking ART for an average of  $9.7 \pm 1.2$  and  $11.0 \pm 1.1$  years, respectively ( $P > 0.05$ ). A higher level of education was observed in the Non-HIV group with  $70\%$  having completed education beyond high school compared with  $24$  and  $18\%$  in the HIV-Lipo and HIV-no-Lipo groups ( $P < 0.05$ ). The percentage of participants perceiving their health as good or excellent was similar between groups ( $86$ ,  $76$ , and  $90\%$ ), but more HIV-no-lipo were smokers compared with HIV-lipo and Non-HIV groups ( $55$ ,  $19$ ,  $7\%$ , respectively). Some participants in the HIV-Lipo group ( $25\%$  [ $8/32$ ]) and none in the other two groups had diabetes ( $P = 0.02$ ). No participant in the no-HIV but about the same proportion of HIV-Lipo and HIV-no-Lipo had hypertension ( $21\%$  [ $7/32$ ] and  $24\%$  [ $7/28$ ], respectively). Both

diabetes and hypertension were controlled and diagnosed after the onset of HIV infection.

Other general, PA,  $VO_{2peak}$ , and met-syn characteristics by study groups are presented in Table 1. By study design, age and gender distributions were similar between groups. BMI was not different between groups, and also by study design, WHR was higher in the HIV-lipo group. No differences between groups were observed for total dietary fat, trans fat intake, or total dietary energy intake.  $VO_{2peak}$  was significantly lower in the HIV-Lipo group, but sedentary time and physical activity behavior was not different between the groups. Compared with HIV-no-Lipo and Non-HIV, the HIV-Lipo group had lower HDL and higher waist circumference, fasting glucose, fasting insulin, HOMA-IR, triglycerides, and VLDL. No significant differences between groups were observed for systolic and diastolic blood pressures, cholesterol, and LDL; with average values considered within normal levels. However, average values considered at risk for metabolic and cardiovascular disease were observed in the HIV-Lipo in the following variables: triglycerides, HDL, VLDL, glucose, insulin, and HOMA-IR. Physical activity recommendations for MVPA or steps/day were not met, and sedentary time was considered high for all groups.

**Table 1.** General, Physical Activity (PA), Cardiorespiratory Fitness ( $VO_{2peak}$ ), and Metabolic Syndrome (Met-Syn) characteristics of study participants by group (N, means  $\pm$  se)

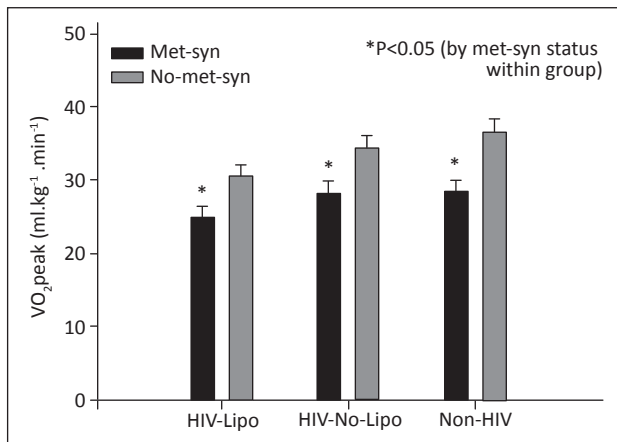
Variable	HIV-Lipo	HIV-no-Lipo	Non-HIV	P
<i>General Characteristics</i>				
N (females, males)	32 (19, 13)	28 (13, 15)	30 (15, 15)	0.51
Age (years)	50.3 $\pm$ 1.2	48.1 $\pm$ 1.3	50.2 $\pm$ 1.4	0.42
BMI (kg/m <sup>2</sup> )	29.0 $\pm$ 0.8	26.4 $\pm$ 1.4	28.1 $\pm$ 0.8	0.18
Waist to Hip Ratio	0.97 $\pm$ 0.01*	0.90 $\pm$ 0.01†	0.89 $\pm$ 0.01‡	<0.0001
Dietary Energy Intake (Kcal/day)	1799.8 $\pm$ 95.1	1938.7 $\pm$ 174.1	1765.5 $\pm$ 142.4	0.79
Saturated Fat Intake (g)	21.7 $\pm$ 1.4	23.0 $\pm$ 2.6	20.4 $\pm$ 1.8	0.70
Trans Fat Intake (g)	2.0 $\pm$ 0.2	2.3 $\pm$ 0.3	2.1 $\pm$ 0.2	0.89
<i>Physical Activity, Sedentary Time, and Cardiorespiratory Fitness</i>				
MVPA (min/week)	59.3 $\pm$ 13.8	82.5 $\pm$ 32.5	101.7 $\pm$ 25.6	0.49
Steps/day (number)	6602 $\pm$ 414	6759 $\pm$ 509	8148 $\pm$ 3513	0.07
Sedentary Time (hr/day)	8.5 $\pm$ 0.4	8.0 $\pm$ 0.5	8.8 $\pm$ 0.4	0.42
$VO_{2peak}$ (ml $\cdot$ kg <sup>-1</sup> $\cdot$ min <sup>-1</sup> )	26.8 $\pm$ 1.3*	32.2 $\pm$ 1.5	33.8 $\pm$ 1.7	0.004
<i>Met-Syn Characteristics</i>				
Waist Circumference (cm)	100.5 $\pm$ 2.0*	88.7 $\pm$ 2.3	92.4 $\pm$ 1.9	<0.001
Systolic BP (mm Hg)	121.1 $\pm$ 2.4	127.1 $\pm$ 2.9	126.9 $\pm$ 2.9	0.17
Diastolic BP (mmHg)	75.9 $\pm$ 1.2	80.2 $\pm$ 1.7	79.2 $\pm$ 1.7	0.10
Triglycerides (mg/dL)	217.1 $\pm$ 21.2*	170.7 $\pm$ 15.9	122.6 $\pm$ 11.7‡	<0.001
Cholesterol (mg/dL)	194.8 $\pm$ 7.5	193.3 $\pm$ 7.3	189.2 $\pm$ 8.1	0.86
HDL (mg/dL)	39.3 $\pm$ 2.1*	41.3 $\pm$ 2.7	50.4 $\pm$ 3.5‡	0.01
LDL (mg/dL)	112.5 $\pm$ 6.4	117.6 $\pm$ 7.1	114.1 $\pm$ 6.6	0.85
VLDL (mg/dL)	43.4 $\pm$ 4.4*	34.2 $\pm$ 3.2	24.6 $\pm$ 2.4‡	<0.001
Fasting glucose (mg/dL)	104.9 $\pm$ 5.4*	94.3 $\pm$ 1.7	91.6 $\pm$ 2.1‡	0.03
Insulin ( $\mu$ U/L)	28.2 $\pm$ 5.4*	15.0 $\pm$ 2.1	8.9 $\pm$ 1.2	<0.001
HOMA-IR	7.4 $\pm$ 1.5*	3.6 $\pm$ 0.5	2.1 $\pm$ 0.3‡	<0.001

N=number, BMI=body mass index, MVPA=moderate to vigorous physical activity (in 10-min bouts),  $VO_{2peak}$ = peak oxygen consumption (cardiorespiratory fitness), BP = blood pressure, HDL= high density lipoprotein, LDL=low density lipoprotein, VLDL=very low density lipoprotein, HOMA-IR = homeostatic model assessment for insulin resistance. Values with different symbols are significantly different from each other.

The proportion of participants in each group meeting the criteria for met-syn and its individual components are presented in Table 2. A higher proportion of participants in the HIV-Lipo (22/32) met the criteria for met-syn, compared with the HIV-no-Lipo (11/28) and Non-HIV group (11/30). Also, compared with Non-HIV and HIV-no-Lipo, a higher proportion of HIV-Lipo met the criteria for elevated fasting glucose, triglycerides, and waist circumference. The three met-syn components with the highest prevalence among HIV-Lipo were: low HDL (81%), high waist circumference (71%), and elevated triglycerides (69%); among HIV-no-Lipo were: low HDL (66%), elevated blood pressure (55%), and elevated triglycerides (53%); and among Non-HIV were: elevated blood pressure (63%), low HDL (55%), and high waist circumference (43%). A higher proportion of women met the criteria for met-syn (27/47 = 57%) compared with men (17/43 = 40%) (P=0.04) for all groups combined, and also within HIV+ only (64% vs. 36%). Waist circumference was the only individual component of the met-syn where a higher proportion of women met the criteria compared to men (70% vs. 32%, respectively, P<0.001).

**Table 2.** Proportion (%) of participants by group meeting the criteria for metabolic syndrome (met-syn) and its individual components.

Variable	HIV-Lipo	HIV-no-Lipo	Non-HIV	P
Met-Syn	69*	38	37	0.016
Glucose	28*	7	10	0.044
Triglycerides	69	53	37*	0.041
HDL	81	66	55	0.089
Waist Circumference	71*	38	43	0.022
Blood Pressure	47	55	63	0.428



**Figure 1.** Cardiorespiratory fitness (VO<sub>2</sub>peak) among study participants by group and metabolic syndrome (met-syn) status

For all groups combined, VO<sub>2</sub>peak was inversely correlated with individual components of the met-syn including waist circumference (r= -0.54, P<0.0001), glucose (r= -0.23, P=0.04), and systolic blood pressure (r= -0.22, P=0.04). To test if

VO<sub>2</sub>peak was a significant factor in the prediction of met-syn, a logistic regression was obtained including VO<sub>2</sub>peak and all individual met-syn components. In this model, VO<sub>2</sub>peak (OR [95% CI]: 0.87 [0.80-0.97], P=0.01), waist circumference (OR [95% CI]: 1.1 [1.01-1.16, P=0.03]), and fasting glucose (OR [95% CI]: 1.10 [1.01-1.20], P=0.02) were significant factors in the prediction of met-syn among all participants. Also, when physical and behavioral characteristics (age, sex, education, smoking, steps/day, sedentary time, and dietary fat) were added as potential factors influencing met-syn in the logistic regression model, VO<sub>2</sub>peak was the only factor reaching statistical significance (OR [95% CI]: 0.83; 0.76 - 0.91, P<0.001). VO<sub>2</sub>peak was significantly associated with steps/day for all groups combined (R<sup>2</sup>= 0.26, P<0.001) and also for each individual group, but VO<sub>2</sub>peak was not associated with sedentary time.

The analysis of VO<sub>2</sub>peak by group and met-syn status (3 x 2 ANOVA) revealed a significant effect of both factors, and no interaction. VO<sub>2</sub>peak was lower for those with met-syn in each group (Figure 1). Other comparisons by met-syn status in each group are presented in Table 3. Those with met-syn in the HIV-Lipo group had higher waist circumference, higher systolic and diastolic blood pressures, and higher glucose levels compared with those without met-syn. HIV-no-Lipo with met-syn had higher waist circumference, BMI, and insulin levels compared with those without met-syn. Non-HIV with met-syn had lower steps/day and HDL levels, and higher BMI, waist circumference, triglycerides, VLDL, glucose, and insulin levels. We noticed that BMI was similar among those with met-syn in each group, but HIV-Lipo with met-syn appear to have poorer met-syn profile than HIV-no-Lipo and Non-HIV with met-syn including elevated triglycerides, glucose, insulin, and HOMA-IR.

## Discussion

The main findings of this study are: 1) A higher proportion of HIV-Lipo met the criteria for met-syn and had lower VO<sub>2</sub>peak compared with HIV-no-Lipo and Non-HIV participants. However, PA and sedentary time was not different between the groups; and 2) Met-syn was inversely associated with VO<sub>2</sub>peak but not associated with PA or sedentary behavior. However, PA (steps/day) was directly and significantly associated with VO<sub>2</sub>peak. These results suggest that: 1) lipodystrophy might be a factor to consider in the risk of met-syn among HIV+ Hispanics, 2) improvements in VO<sub>2</sub>peak might help protect against met-syn, and 3) higher levels of PA might help improve VO<sub>2</sub>peak in this population.

The prevalence of met-syn in our HIV-no-Lipo (39%) and Non-HIV (37%) participants was similar to previous reports among the HIV+ (35%) (8) and the general population (43%) in PR (7). However, the prevalence of met-syn in the HIV-Lipo was higher than expected (69%), and higher than previously

**Table 3.** Physical, metabolic and lifestyle behavior characteristics by metabolic syndrome (met-syn) status in each study group (N, means±se).

Variable	HIV-Lipo			HIV-no-Lipo			Non-HIV		
	Met-Syn	No Met-Syn	P	Met-Syn	No Met-Syn	P	Met-Syn	No Met-Syn	P
N	22	10		11	17		11	19	
(females, males)	(14, 8)	(5, 5)	0.47	(7, 4)	(6, 11)	0.11	(6, 5)	(9, 10)	0.71
Age (yrs)	50.3±1.6	50.0±2.2	0.92	45.2±2.3	50.3±1.4	0.06	50.6±2.2	50.0±1.6	0.81
BMI (kg/m <sup>2</sup> )	30.4±1.3	26.3±1.0	0.06	30.1±2.4	24.2±0.7	0.01	30.2±0.4	26.9±0.9	0.04
Waist (cm)	103.7±2.6	94.2±1.9	0.02	94.1±4.8	85.5±2.0	0.07	99.1±3.1	88.5±2.0	0.01
SBP (mmHg)	121.4±2.1	102.3±10.6	0.02	122.1±5.5	120.4±3.9	0.81	125.0±3.2	121.5±3.7	0.52
DBP (mmHg)	79.7±1.6	72.6±2.0	0.02	76.4±3.2	77.2±2.1	0.83	78.3±1.8	77.9±1.9	0.89
Cholesterol (mg/dL)	200.7±8.5	181.9±13.9	0.24	177.0±12.4	203.2±8.4	0.08	195.7±10.5	185.4±11.2	0.54
Triglycerides (mg/dL)	219.5±19.8	189.8±53.7	0.40	182.6±17.9	163.4±23.4	0.57	179.2±19.7	89.8±8.0	<0.01
HDL (mg/dL)	37.1±1.7	43.9±5.8	0.15	34.9±3.0	45.2±3.7	0.06	39.5±3.5	56.7±4.6	0.01
LDL (mg/dL)	117.7±8.0	101.0±9.0	0.22	105.4±11.8	125.1±8.8	0.19	120.1±10.1	110.6±8.5	0.49
VLDL (mg/dL)	45.9±4.0	38.0±10.8	0.40	36.5±3.6	32.7±4.7	0.57	36.0±3.9	18.0±1.6	<0.01
Glucose (mg/dL)	113.0±7.2	87.1±3.3	0.02	98.4±3.2	91.8±1.9	0.07	99.8±3.7	86.8±1.9	<0.01
Insulin (mg/dL)	26.4±4.2	32.2±15.6	0.64	20.3±2.4	11.8±2.8	0.04	13.0±2.4	6.6±0.8	<0.01
HOMA-IR	7.4±1.4	7.5±3.9	0.98	5.0±0.7	2.7±0.6	0.02	3.3±0.7	1.4±0.2	<0.01
Energy intake (kcal/day)	1840.9 ±131.6	1709.4±148.0	0.55	2079.7±154.6	1852.5±245.8	0.51	1580.0±271.9	1872.9±145.3	0.31
Saturated fat intake (g)	22.7±1.9	19.6±2.2	0.33	24.3±2.2	22.1±3.8	0.67	19.2±4.1	21.1±1.4	0.60
Sedentary time (hrs/day)	8.4±0.6	8.7±0.6	0.80	7.9±0.8	8.1±0.5	0.80	8.8±0.6	8.8±0.4	0.90
Steps/day (number)	6814±505	6157±740	0.46	5766±641	7311±705	0.16	6274±516	9234±884	0.02

N=number, BMI = body mass index, Waist = waist circumference, SBP = systolic blood pressure, DBP = diastolic blood pressure, HDL= high density lipoprotein, LDL=low density lipoprotein, VLDL=very low density lipoprotein, HOMA-IR = homeostatic model assessment for insulin resistance. P = within each group (HIV-Lipo, HIV-no-Lipo, Non-HIV, respectively).

reported among HIV+ adults with or without lipodystrophy (5, 6). Similar to Estrada et al. (5), and different from Freitas et al. (6), we found that HIV-related lipodystrophy influences met-syn in our Hispanic group. Our results also support these two previous studies in that impaired glucose metabolism, abdominal adiposity, and dyslipidemia are risk factors that greatly affect HIV+ adults with lipodystrophy; thus, likely increasing their risk of met-syn.

The higher prevalence of met-syn among HIV+ Hispanic women compared with men previously reported in PR using data from clinical records (8), was confirmed in the present study. We also confirmed that central adiposity is the most influencing factor explaining this difference. Freitas et al. (6) reported no difference in the prevalence of met-syn among HIV+ women and men; but similar to our study, waist circumference was the individual criteria affecting more women than men (58% vs. 18%). These observations highlight the importance of considering sex differences when testing and treating metabolic and cardiovascular risk factors among HIV+ adults.

To reduce the risk of met-syn and cardiovascular disease it is important to increase physical activity, reduce sedentary behaviors, and incorporate sound nutritional habits (12, 15, 16, 24, 25). Nutritional guidelines recommend dietary intake of saturated fat to be less than 10% of the total daily caloric intake or less than 20 gm for a 2,000 kcal diet; and for trans-fat less than 1.3 gm or less than 0.6% of energy intake (<http://www.cdc.gov/nutrition/everyone/basics/fat/index.html>, accessed 07/08/12). Our study participants consumed on average more than 20 gm of saturated fat with a caloric intake less than 2,000

kcal. These nutritional characteristics were similar between the HIV-Lipo, HIV-no-Lipo, and Non-HIV groups; and were not associated with the metabolic syndrome or its individual components.

For sedentary behavior, although no specific recommendations are available, recent studies suggest that 7-9 hr/day is significantly associated with all cause mortality independent of PA behavior (26, 27). The average sedentary time in the present study was 8 hr/day, with no differences between groups or by met-syn status; and no association with VO<sub>2</sub>peak. It is possible that the lack of variability in sedentary behavior obscured the association between sedentary time and met-syn reported by others (15, 16).

The current PA recommendation in steps/day for adults suggests the accumulation of at least 8,000-10,000 steps/day (28, 29), which translates to approximately 150 min/week of MVPA (29-31). On average, only the Non-HIV, particularly those without met-syn, complied with this recommendation. Steps/day was not associated with met-syn, but steps/day was directly associated with VO<sub>2</sub>peak.

Previous studies have reported significant associations between VO<sub>2</sub>peak and met-syn in the general population (13, 14). The present study is the first to report a significant association between VO<sub>2</sub>peak and met-syn among Hispanic adults in Puerto Rico, a population at a disproportionately high risk of met-syn and cardiovascular disease. Participants with met-syn were more likely to have low VO<sub>2</sub>peak, elevated fasting glucose and waist circumference; suggesting that VO<sub>2</sub>peak is also a factor to be considered in the evaluation and control of

met-syn in this population. Moreover, the inverse association between  $VO_{2peak}$ , waist circumference, glucose, and systolic blood pressure highlights even further the importance of including  $VO_{2peak}$  or cardiorespiratory fitness as an outcome measure in any intervention designed to reduce the risk of met-syn among Hispanic adults in general and HIV+ Hispanic adults. Also, because  $VO_{2peak}$  was directly associated with steps/day, improving PA behavior must also be considered as a non-pharmacological treatment to help improve metabolic and cardiovascular health.

Our results also showed that  $VO_{2peak}$  was similar between the HIV-no-Lipo and Non-HIV groups, but lower in the HIV-Lipo group; thus, suggesting that lipodystrophy status might influence cardiorespiratory fitness. Chapplain et al. (32) reported a tendency for a lower cardiorespiratory fitness in HIV-Lipo vs. HIV-no-Lipo participants, and Roge et al. (33) also reported a tendency towards a reduced cardiorespiratory fitness in HIV-Lipo vs. Non-HIV participants, and suggested mitochondrial dysfunction as a potential explanation. Mitochondrial DNA content is known to be reduced with the use of nucleoside reverse transcriptase inhibitors, with potential side effects such as lipodystrophy, dyslipidemia, and insulin resistance (34). However, Sutinen et al. (35) reported no differences in the amount of mitochondrial DNA (mtDNA) in skeletal muscle of HIV-Lipo and HIV-no-Lipo participants, but lower mtDNA in the subcutaneous adipose tissue of HIV-Lipo compared to HIV-no-Lipo participants. These investigators also reported no difference between HIV-Lipo and HIV-no-Lipo in the quadriceps femoris muscle perfusion and oxygen uptake measured with PET scanning during two 12-min dynamic knee-extension exercises performed at 70% of the maximum voluntary contraction. They concluded that muscle aerobic exercise metabolism is not affected by HIV-related lipodystrophy. HIV+ adults with and without lipodystrophy appear to be capable of improving muscle oxygen uptake and cardiorespiratory fitness (36-38); thus suggesting that the physiological capacity of skeletal and cardiac muscle to extract and utilize oxygen is unaltered by lipodystrophy status. However, the integration of cardiovascular, pulmonary, neuromuscular, and metabolic functions contributing to changes in cardiorespiratory fitness might still differ with lipodystrophy status and remains to be clarified.

In conclusion, the results from this study suggest that among HIV+ Hispanics: 1) met-syn is influenced by lipodystrophy status, 2)  $VO_{2peak}$  (cardiorespiratory fitness) is an important factor that might protect against met-syn, and 3) cardiorespiratory fitness is influenced by PA but not sedentary behavior. Because of the cross-sectional nature of this study, a cause-effect relationship between PA, sedentary behavior, cardiorespiratory fitness, and met-syn in HIV+ Hispanic adults can not be determined. Therefore, there is a need for randomized controlled trials evaluating the interaction between cardiovascular, pulmonary, neuromuscular, and metabolic

outcomes resulting from different PA interventions in the clinical care of HIV patients.

## Resumen

**Objetivo:** Los hispanos en Puerto Rico (PR) tienen alta prevalencia de síndrome metabólico (sin-met) en parte por la baja actividad física (AF) y probable baja aptitud cardiorespiratoria ( $VO_{2pico}$ ). El sin-met también se asocia con lipodistrofia en pacientes con VIH (VIH+) en tratamiento antiretroviral. Sin embargo, la relación entre sin-met,  $VO_{2pico}$ , AF, sedentarismo y lipodistrofia entre hispanos VIH+ no se ha reportado adecuadamente. Se probaron las hipótesis: 1) Hispanos VIH+ con lipodistrofia (VIH-Lipo) tendrán mayor prevalencia de sin-met, menor  $VO_{2pico}$  y AF, y mayor comportamiento sedentario comparados con aquellos sin lipodistrofia (VIH-no-Lipo) y sin VIH (No-VIH); y 2) sin-met se relacionará inversamente con  $VO_{2pico}$  y AF, y directamente con sedentarismo. **Método:** Noventa adultos hispanos (32 VIH-Lipo, 28 VIH-no-Lipo, 30 No-VIH) completaron medidas de  $VO_{2pico}$ , antropométricas, AF y sedentarismo con acelerometría, presión arterial, glucosa, insulina y lípidos. Se utilizó ANOVA y ji cuadrado para detectar diferencias entre grupos, y análisis de regresión para detectar asociaciones entre variables. **Resultados:** Más VIH-Lipo tuvo sin-met (69%) comparados con VIH-no-Lipo (39%) y No-VIH (37%) ( $P=0.002$ ). No hubo diferencias en AF y sedentarismo, pero  $VO_{2pico}$  fue diferente ( $p<0.05$ ) entre grupos: No-VIH con el mayor y VIH-Lipo con el menor valor. No hubo asociación entre AF, sedentarismo y sin-met, pero hubo asociación directa entre AF y  $VO_{2pico}$  ( $R^2=0.26$ ,  $p<0.01$ ). Además, la razón de probabilidad de sin-met fue menor con mayor  $VO_{2pico}$  (OR: 0.87; 95% CI: 0.83-0.95). **CONCLUSIÓN:** Sin-met se asocia con lipodistrofia en hispanos VIH+ en PR, y un mayor  $VO_{2pico}$  puede proteger contra sin-met en esta población.

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