ORIGINAL RESEARCH

Cardiorespiratory Fitness Relative to Lean Body Mass in HIV+ and HIV- Women

Farah A. Ramírez-Marrero, PhD[1], Valerie Wojna, MD[1],
Jorge Santana-Bagur, MD[1], Walter R. Frontera, MD, PhD[1]

ABSTRACT

Background: Cardiorespiratory fitness (CRF) influences mortality from chronic diseases and is commonly expressed relative to body weight. However, CRF relative to lean body mass (LBM) is more informative because of its energy demand; this is relevant in chronic diseases such as HIV infection. The primary aims of this study were to compare CRF (1) in absolute terms, (2) relative to body weight, and (3) relative to LBM in HIV positive (HIV+) and HIV negative (HIV-) women; and to determine the percent variance explained by body weight vs. LBM.
Methods: Measures of total mass, LBM, and fat were conducted with dual-energy x-ray absorptiometry (DEXA); and body weight, and fat also with bio-impedance analysis (BIA) in 32 HIV+ and 15 HIV- Hispanic women. CRF was measured on a cycle ergometer using 25W increments until volitional fatigue. Independent *t* tests were conducted to detect between group differences, and linear regressions to determine the percent variance in CRF explained by body weight and LBM.
Results: No between group differences were observed for age (45.1 ± 10.4 vs. 41.1 ± 14.2 y), BMI (28.8 ± 5.9 vs. 28.0 ± 6.3 $kg \cdot m^{-2}$), BIA fat (43.0% ± 8.6% vs. 44.1% ± 6.7%), DEXA fat (41.1% ± 7.2% vs. 43.3% ± 4.8%), LBM (41.6 ± 5.7 vs. 39.6 ± 6.7 kg), absolute CRF (1.40 ± 0.34 vs. 1.53 ± 0.34 $L \cdot min^{-1}$), or CRF relative to body weight (19.3 ± 3.6 vs. 21.4 ± 4.2 $mL \cdot kg^{-1} \cdot min^{-1}$). A lower CRF relative to LBM was observed among HIV+ compared with HIV- women (33.4 ± 5.3 vs. 38.6 ± 6.3 $mL \cdot kg^{-1} \cdot min^{-1}$, $P = 0.006$). Body weight and LBM explained 38% and 50% of the variance in CRF in men and women, respectively.
Conclusion: These results suggest that LBM might be considered for CRF comparison between various population groups, particularly HIV+ women. *Journal of Clinical Exercise Physiology*. 2019;8(4):138–143.

Keywords: VO_2peak, DEXA, bioelectrical impedance

INTRODUCTION

Low risks of morbidity and mortality from chronic diseases have been consistently observed among adults with high cardiorespiratory fitness (CRF) or high capacity for maximal or peak oxygen transport, delivery, and consumption (VO_2max or VO_2peak) (1). Because CRF helps improve prediction of adverse health outcomes, its inclusion as a *vital sign* has been recently encouraged for routine clinical practice (2).

Expression of CRF relative to body weight ($ml \cdot kg^{-1} \cdot min^{-1}$) is common, and available sex and age reference standards for CRF classification present higher average values for men compared with women, and for younger compared with older adults (3,4). However, body weight is the combination of body fat mass (FM) plus lean body mass (LBM), and the method of expressing CRF could influence its interpretation in people with different body composition characteristics (5). Previous studies show no association between FM and CRF (6,7). Different from FM, LBM is a high energy demanding tissue strongly associated with CRF (6–8); therefore, expressing CRF relative to LBM could be a better representation of the cardiorespiratory system's capacity to meet the oxygen demand of metabolically active tissue (5,9).

[1]University of Puerto Rico School of Medicine, San Juan, PR 00936-5067 USA

Address for correspondence: Farah A. Ramírez-Marrero, PhD, 165 Hostos Avenue #428, San Juan, PR 00918; (787) 602 0088; e-mail: Farah.ramirez1@upr.edu.

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HIV infection and antiretroviral treatment are known to influence body composition, particularly the long-term accumulation of fat in the abdominal area and fat loss in the periphery (10), loss of bone mineral density (11,12), and loss of LBM (13). These body composition characteristics might influence the interpretation of CRF levels when expressed relative to body weight. CRF expressed relative to body weight in adults living with HIV infection (HIV+) tends to be lower compared with their non-HIV (HIV-) counterparts (14,15). In a previous study we compared CRF relative to body weight between HIV+ adults with central fat accumulation, HIV+ adults without central fat accumulation, and HIV- adults; and reported no CRF difference between the last 2 groups but lower CRF in the HIV+ adults with central fat accumulation, suggesting that body composition characteristics and their associated metabolic complications (i.e., insulin resistance, dyslipidemia, metabolic syndrome) may influence CRF (15). However, the association between body weight, LBM, and CRF was not explored, and no other published study has demonstrated these associations in HIV+ adults, particularly among HIV+ women, who often have more body composition disease-based effects compared with their male counterparts (16,17).

Therefore, the primary aims of this study were: (1) to compare VO_2peak expressed in absolute terms ($L \cdot min^{-1}$), relative to body weight ($mL \cdot kg^{-1} \cdot min^{-1}$), and relative to LBM ($ml \cdot kg\ LBM^{-1} \cdot min^{-1}$) among HIV+ and HIV- Hispanic women in Puerto Rico; and (2) to determine the percent variance in VO_2peak ($L \cdot min^{-1}$) explained by body weight, and LBM. These participants were part of a larger study evaluating CRF, cognition, and metabolism among HIV+ Hispanic women in Puerto Rico (15). In a secondary analysis, we compared FM measured with bio-electrical impedance analysis (BIA) and dual-energy x-ray absorptiometry (DEXA).

METHODS

Participants

A group of 32 HIV+ and 15 HIV- community-dwelling Hispanic women in Puerto Rico volunteered to participate and signed an informed consent form previously approved by the University of Puerto Rico Medical Sciences Campus' Institutional Review Board. Inclusion criteria were: 21 years of age or older, CD4 higher than 500 $cells \cdot mm^{-3}$ or viral load lower than 1,000 $cells \cdot mm^{-3}$, education level of at least 9th grade, no diagnosed dementia, no opportunistic disease of the central nervous system, no active systemic infection, no neurodegenerative diseases, no uncontrolled hypertension or diabetes.

Body Composition

Full body DEXA scan (HOLOGIC Discovery system, Analysis software version 13.4:7, Toronto, Canada), BIA, and body weight (OMRON full body sensor body composition monitor and scale, Model HBF-510, Kioto, Japan) were obtained on the same day. Body weight was measured with participants stepping barefoot on the scale, and holding the arm sensor with arms raised, elbows extended, and shoulders at 90° angle. Height was measured with a SECA 213 stadiometer (SECA, Hanover, Maryland) with participants without shoes, chin slightly bent (Frankfurt horizontal plane), and at normal inhalation. Waist circumference was measured with a Gulick anthropometric tape (Creative Health Products, Ann Arbor, Michigan) midway between last rib and iliac crest, and at normal exhalation.

Cardiorespiratory Fitness

Cardiorespiratory fitness was measured on a Monark cycle-ergometer 928E (Vansbro, Sweden) at 50 $r \cdot m^{-1}$, with an initial resistance of 25 W, and increasing 25 W every 2 min until volitional fatigue. Oxygen consumption and ventilation was measured with a COSMED FitMate Med metabolic system (Concord, California). Heart rate (HR) was monitored with a Garmin band (Garmin LTD, Olathe, Kansas) interacting with the COSMED system, and a 12-lead ECG (Edan SE-12 Express, Edan Instruments, Shenzhen, China).

Statistical Analysis

Statistical analyses included independent *t* tests (Kruskal-Wallis test when appropriate) to detect between group differences in CRF expressed in absolute terms, relative to body weight and relative to LBM. Linear regression was used to determine the percent variance in CRF explained by body weight and LBM. The Bland-Altman concordance and limits of agreement analysis was conducted to compare LBM and FM measured with DEXA and BIA.

RESULTS

HIV+ participants were all on combined antiretroviral therapy (cART), had an average CD4 count of $788.3 \pm 317.8\ cells \cdot mm^{-3}$, and 75% had nondetectable viral loads. For those with detectable viral loads, counts were less than 200 $cells \cdot mm^{-3}$.

From the general, anthropometric, and body composition characteristics of HIV+ and HIV- participants presented in Table 1, significant differences were observed for waist circumference and waist to hip ratio, with higher values in the HIV+ participants. Because of the average body mass index (BMI) value of 28.8 $kg \cdot m^{-2}$ combined with an average waist circumference of 97.3 cm (38 inches), these HIV+ women are in a high-risk category (18). Body weight or body mass, FM, and LBM were not different between groups. Percent fat estimated with both DEXA and BIA classified study participants, on average, as obese (>40% fat).

Based on CRF expressed relative to body weight, our study participants were in the 10th to 20th percentile (very poor to poor). HIV+ and HIV- women participants were not different in their CRF when expressed in absolute terms ($L \cdot min^{-1}$), and relative to body weight ($mL \cdot kg^{-1} \cdot min^{-1}$). However, HIV+ women had a lower CRF when expressed relative to LBM, suggesting a lower capacity of their metabolically active tissue to obtain and consume oxygen. For both groups combined, body weight explained 38% of the variance in CRF ($L \cdot min^{-1}$) (44% in HIV+, 34% in HIV-; Figure 1a) while LBM explained 50% of the variance (63%

TABLE 1. General, anthropometric, and body composition characteristics of study participants (mean±SD).

Variable	HIV+ (n=32)	HIV- (n=15)	*P* Value
Age (y)	45.1±10.4	41.1±14.2	0.54
Weight (kg)	73.6±15.2	72.0±12.3	0.79
Height (cm)	160.0±6.4	158.6±6.4	0.49
BMI ($kg \cdot m^{-2}$)	28.8±5.9	28.6±4.5	0.68
Waist Circumference (cm)	97.3±12.9	88.6±8.7	**0.02**
Waist to Hip ratio	0.92±0.06	0.84±0.08	**<0.01**
Total Mass – DEXA (kg)	72.0±15.2	70.3±12.4	0.73
FM – DEXA (kg)	30.4±10.5	30.6±7.7	0.95
LBM – DEXA (kg)	41.6±5.7	39.6±6.7	0.17
LBM – BIA (kg)	41.1±4.4	39.9±3.8	0.40
Fat – BIA (%)	43.0±8.6	44.1±6.7	0.90
Fat – DEXA (%)	41.1±7.2	43.3±4.8	0.47
VO_2peak ($L \cdot min^{-1}$)	1.4±0.3	1.5±0.3	0.19
VO_2peak ($mL \cdot kg^{-1} \cdot min^{-1}$)	19.3±3.6	21.4±4.2	0.11
VO_2peak ($mL \cdot kg\ LBM^{-1} \cdot min^{-1}$)	33.4±5.3	38.6±6.3	**0.01**

BMI = body mass index; DEXA = dual-energy x-ray absorptiometry; FM = fat mass; LBM = lean body mass; BIA = bio-electrical impedance analysis

in HIV+, 47% in HIV-; Figure 1b). The steeper slope in the regression line for the HIV+ group (Figure 1b, second line), suggests LBM is a strong predictor of CRF. Interestingly, Figure 1b also shows regression lines converging with higher LBM, suggesting that the CRF difference between HIV+ and HIV- women is higher with lower LBM and vice versa. FM was associated with CRF only in the HIV+ group (HIV+: $R^2=0.29$, $P=0.001$; HIV-: $R^2=0.14$, $P=0.18$).

In a secondary analysis we compared body composition measures, specifically LBM and %Fat, obtained with BIA and DEXA in our study participants. Percent FM estimated with BIA and DEXA were significantly different only in the HIV+ ($t=2.40$, $P=0.02$), while LBM estimates with these 2 methods were not significantly different (HIV+ [$P=0.73$]) and HIV- [$P=0.87$]). However, the regression analysis revealed a significant association between BIA and DEXA for %Fat in both groups (HIV+: $R^2=0.73$, $P<0.0001$; HIV-: $R^2=0.56$, $P=0.001$) but not for LBM (HIV+: $R^2=0.09$, $P=0.09$; HIV-: $R^2=0.0009$, $P=0.92$). Bland-Altman limits of agreement analysis further demonstrated the strong agreement between BIA and DEXA %Fat (Figure 2) with an interval of agreement of 1.58 (95% CI: -7.2 to 10.4), and a concordance correlation coefficient of 0.79 ($P=0.004$).

DISCUSSION

To our knowledge, this is the first study to report a significant influence of LBM on CRF (63% of variance explained) among HIV+ Hispanic women, a population with distinct body composition changes primarily attributed to the antiretroviral therapies. Our findings support previous studies suggesting that LBM is a stronger predictor of CRF than body weight (5–9,19,20), and should be considered as the standard

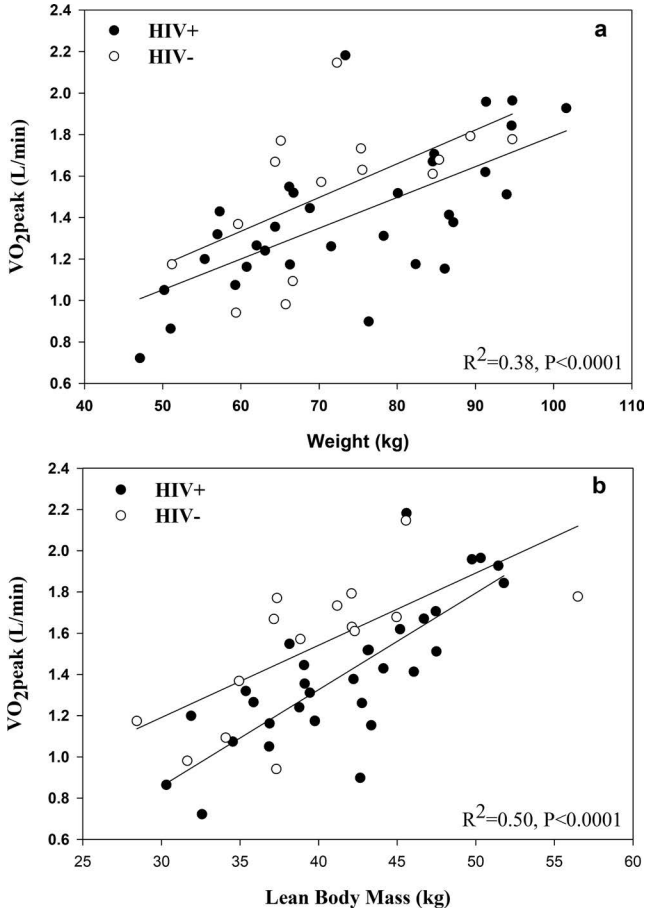

FIGURE 1. Cardiorespiratory fitness (CRF) association with body weight (a) and lean body mass (b) in HIV+ (second line) and HIV- (first line) Hispanic women. Combined R^2 shown.

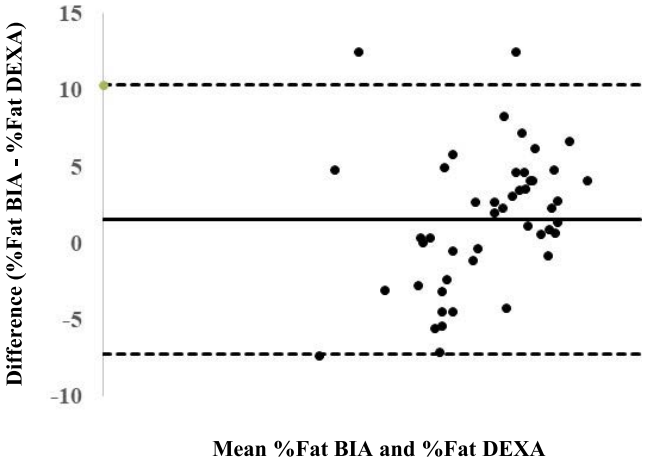

FIGURE 2. Bland-Altman limits of agreement plot between %Fat with bio-electrical impedance analysis (BIA) and dual-energy x-ray absorptiometry (DEXA) in HIV+ and HIV- Hispanic women. Interval of agreement = 1.58 (95% CI: -7.2 to 10.4), and concordance correlation coefficient = 0.79 ($P = 0.004$).

for CRF comparison between various population groups with different body compositions characteristics.

Goran et al. (6) reported that while FM was not related to CRF, LBM was strongly and significantly correlated with CRF *(r* = 0.87) in a group of 129 children; and no difference in CRF between obese and lean children were observed when it was expressed relative to LBM (57.9 ± 5.8 vs. 59.2 ± 4.9 mL·kgLBM^{-1}·min^{-1}). For obese individuals, Königstein et al. (5) and Krachler et al. (9) suggested that CRF is more accurate when expressed relative to LBM or muscle mass (56% of the variance explained); therefore, having a considerably higher impact on oxygen demand. In an early study comparing untrained young and older adults (22-87 years of age), Fleg and Lakatta (19) reported that the age-associated decline in CRF was explained by loss of muscle mass based on creatinine excretion. Another early study by Proctor and Joyner (20) evaluated young and older (< 30 and > 60 years of age, respectively) chronically endurance-trained adults, and observed that older males and females had a 13% and 14% lower CRF difference, respectively, compared with their younger counterparts when CRF was expressed relative to muscle mass. The authors attributed the remaining difference to age-related reductions in oxygen delivery capacity. More recently, Kim et al. (8) also reported a strong and significant association between CRF and lean muscle mass in old and young adults ($R^2 = 0.76$ and 0.61, respectively, $P < 0.05$), and attributed the remaining difference in CRF relative to muscle mass between older and younger adults to age-associated declines in maximal HR and cardiac output.

With HIV+ adults commonly experiencing body composition changes such as central fat accumulation, reduced lean mass and bone density (10–13), and cardiovascular abnormalities such as a reduced capacity for maximal heart rate (i.e., chronotropic incompetence) (21), it would be expected that their CRF is also impaired even when their capacity to improve CRF with exercise training is not impaired (22). It has been suggested that CRF in HIV+ adults is among the lowest (mean = 26.4 mL·kg^{-1}·min^{-1}) in vulnerable populations, but that not enough data is available to compare with HIV- adults (14). We previously showed that CRF in HIV+ adults without lipodystrophy is not different compared with HIV- adults (32.2 ± 1.5 vs. 33.8 ± 1.7 mL·kg^{-1}·min^{-1}, $P > 0.05$) but higher compared with HIV+ with lipodystrophy (26.8 ± 1.3 mL·kg^{-1}·min^{-1}, $P = 0.004$) (15). In the present study, we again observed no difference in CRF between our HIV+ and HIV- Hispanic women when measured relative to body weight; but lower CRF among HIV+ when measured relative to LBM, even when average LBM was not different between groups, therefore suggested a metabolically active tissue with lower capacity for oxygen delivery, extraction, and/or consumption. Fleishman et al. (23) showed that cART, including nucleoside reverse transcriptase inhibitors, impair muscle mitochondrial DNA and function in HIV+ adults. Tran et al. (24) demonstrated a reduced mitochondrial bioenergetic capacity and functional limitations in asymptomatic HIV+ adults possibly associated with their persistent immune activation and inflammation. These observations support the idea that, although the quantity of muscle mass or LBM is an important factor influencing oxygen consumption and energy production, muscle or LBM *quality* for energy production is perhaps a stronger explanation for the observed differences between groups in the present study. Moreover, it also appears that the *quality* for oxygen consumption and energy production is influenced by the *quantity* of LBM (Figure 1b). In other words, in the HIV+ group particularly, the metabolic *quality* appears lower with a lower LBM and higher with a higher LBM. Nevertheless, with no available standards of CRF relative to LBM, it is difficult to determine if the results observed are within an expected range for healthy and chronic disease populations.

An unexpected difference observed between our HIV+ and HIV- women was the significant influence of FM on CRF in our HIV+ participants, which contradicts previous reports on healthy individuals (6) but supports others (25) who have reported in healthy men that both FM and LBM's influence on body weight also influence CRF. Nonetheless, different from healthy adults, it is possible that the chronic immune activation and antiretroviral treatment among HIV+ adults could also influence metabolic characteristics of adipose tissue, which needs further clarification.

The strong association between BIA and DEXA measures of percent body fat in our HIV+ (73% variance explained) and HIV- (56% variance explained) women participants supports previous research. BIA measures of fat mass and fat free mass using the RJL-systems (Detroit, Michigan) in HIV+ adults have been compared with ^{2}H dilution technique (26), and DEXA (27,28), showing important correlations and agreements. We also show important correlation and agreement between DEXA and BIA measures of %Fat using a relatively inexpensive scale (OMRON HBF-510, Kioto, Japan) in our HIV+ and HIV- Hispanic women.

From a practical, clinical standpoint, confidence in BIA fat percentage estimates would allow a less expensive body composition assessment tool for clinical studies among HIV+ adults; therefore, future studies must test the consistency of our findings.

CONCLUSIONS AND CLINICAL IMPLICATIONS

LBM was the best predictor of CRF among HIV+ and HIV- Hispanic women in Puerto Rico. HIV- showed higher CRF than HIV+ only when expressed relative to LBM; therefore, LBM might be considered for CRF comparison between various population groups, particularly HIV+ women. However, standardized CRF relative to LBM must be developed for healthy and chronic disease populations to determine values that are clinically relevant. Also, the validity of BIA estimate of body fat percentage in HIV+ adults must be further evaluated in future studies.

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