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Development of predictive equations for total and segmental body fat in HIV-seropositive patients

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ABSTRACT

Objectives: The central point of the HIV lipodystrophy syndrome is changes in body composition that mainly involve the loss of fat in the limbs and face (lipoatrophy) and/or fat gain in the abdominal region and back neck (lipohypertrophy). Currently, the determination of fat per body segment in this group can be obtained by imaging methods such as dual-energy X-ray absorptiometry (DXA) but not by methods that would be more feasible in the practical clinics. The aim of this study was to develop equations to estimate total body fat and fat in each segment using anthropometric and bioelectrical impedance analysis (BIA) variables in HIV-seropositive patients.
Methods: We measured circumferences (arm, waist, hip, thigh, calf), skinfolds (biceps, triceps, subscapular, suprailiac) and conducted examinations of BIA, segmental BIA, and DXA in 100 HIV-seropositive men on highly active antiretroviral therapy. Equations were developed by linear regression from these variables to estimate total and segmental fat (arm, leg, and trunk).
Results: We developed a model for estimation of total body fat with BIA variables and a model based on anthropometric variables. To estimate segmental fat, we developed one model for each segment using anthropometric variables. The coefficients of determination for models of total fat-free mass (BIA and anthopometry), arm fat, trunk fat, and leg fat were 0.87, 0.84, 0.66, 0.76, and 0.5, respectively.
Conclusions: The equations proposed in this study allow the assessment of total body fat and fat per body segment with data obtained from accessible, accurate, and reliable methods used in clinical practice.

Introduction

HIV infection has changed from an inexorably fatal disease to a condition of a chronic nature, where infected individuals with adequate treatment, can be asymptomatic, enjoying a good quality of life [1,2]. Notably, recent scientific advances on highly active antiretroviral therapy (HAART) have provided unquestionable benefits and significant improvement in the management of these patients [3]. However, the therapy has specific types of toxicity including morphologic changes and modifications in lipid and glucose metabolism [4].

The morphologic changes include redistribution of body fat [5], whereas metabolic changes include elevation of serum total cholesterol (TC) and triglycerides (TG), reduction of high-density lipoproteins (HDL), increase of low-density lipoproteins (LDL), insulin resistance, and type 2 diabetes mellitus. Combined, these disorders are called lipodystrophy syndrome and represent an atherogenic profile, increasing the risk for developing cardiovascular diseases [6].

The change in adipose tissue observed in lipodystrophy syndrome can be divided into two processes: lipoatrophy and lipohypertrophy. Lipoatrophy involves the loss of subcutaneous adipose tissue typically occurring in the upper and lower limbs, the buttocks, and the face. Lipohypertrophy is observed mainly in the visceral compartment of the abdomen, in the mammary

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tissue of women and less commonly in men and, even more rarely, in the dorsocervical area [7]. Adipose tissue is the major factor triggering metabolic changes and the development of chronic diseases, and its redistribution is the central point of lipodystrophy syndrome.

The determination of body composition is currently used in clinical practice and in the nutritional evaluation of large populations, mainly due to the association of body fat with the various metabolic changes, and has significant importance in HIV-infected individuals [8,9].

The techniques normally used are dual-energy X-ray absorptiometry (DXA) and bioelectrical impedance analysis (BIA), anthropometric measurements, magnetic resonance imaging, computed tomography, and hydrostatic weighing.

DXA and hydrostatic weighing are considered the gold standards used in studies to validate new strategies [10]. However, despite the accurate results they provide, they involve high costs and their availability is not a reality in most institutions.

Anthropometry and BIA, however, are considered simple, noninvasive techniques for the estimate of body composition with more accessible cost. For these reasons, their use has attracted considerable attention in the literature [11]. Anthropometric and BIA measurements are used in equations that predict the quantity of body fat; however, these equations must be used for the specific groups for which they were elaborated.

Anthropometric equations elaborated for persons with normal fat distribution have not been efficient for HIV-seropositive patients [12]. It is also important to point out that the monitoring of total body fat is not sufficient for the follow-up of HIV-seropositive patients on HAART because these individuals can gain and lose fat in certain segments while maintaining the same amount of total fat.

Based on the same principles of total BIA, a great innovation in the analysis of body composition is segmental BIA. This method permits an accurate prediction of body composition by means of measurements of length and resistance of some body segments such as the arm, leg, and trunk [13].

To our knowledge, no practical validated measurements are currently available in the literature for the monitoring of the amount of fat per body segment in these patients. Thus, simple, low-cost methods are necessary to precisely and reliably evaluate the quantity of body fat in relation to total body mass, as well as body distribution. The objective of the present study was to elaborate equations for the estimation of total body fat in each segment (arm, trunk, and leg) by anthropometric and BIA methods in HIV-infected patients on HAART.

Methods

The study was conducted at a university hospital. HIV-seropositive patients were selected at the Dyslipidemia Outpatient Clinic and the Immunodeficiency Syndrome Outpatient Clinic, both part of the Specialized Unit for the Treatment of Contagious-Infectious Diseases.

The study was approved by the institution's Research Ethics Committee and the volunteers provided written informed consent.

Inclusion criteria were stable HIV-seropositive patients using HAART for at least 6 mo; CD4 T-cell count >200 cells/mm^3; undetectable viral load; age 18 to 60 y; stable weight (<10% change in past year) and body mass index (BMI) between 18.5 and 30 kg/m^2.

Exclusion criteria were presence of edema; changes in thyroid function; severe organ dysfunction (renal, cardiac, pulmonary, and hepatic alterations); signs or symptoms of opportunistic infections, and presence of pacemaker or metal prosthesis.

Criteria for the definitions of lipodystrophy

For the classification of lipodystrophy, the patient was assumed to report peripheral lipoatrophy confirmed by clinical examination by the investigator, accompanied or not by lipohypertrophy [14].

Body composition: reference method

The Hologic model QDR 4500 W® apparatus was used for DXA, with the exam performed by a trained technician, with standard procedures used for the positioning of the individuals during execution of the exam. The participants were first instructed to remove all metal objects, shoes, and clothing and then asked to lie in dorsal decubitus on the apparatus. Transverse scanning was performed from the head to the feet and the images obtained were processed with the more recent program of the system, version 11.2:5 for Windows.

Anthropometric and BIA variables for the elaboration of the equations

Body weight (kg) was measured with a Filizola electronic scale with precision of 0.1 kg and height was measured with a stadiometer with 0.1 cm precision.

Arm, waist, hip, thigh, and calf circumferences were determined according to a previously described standardized method [15]. Tricipital, bicipital, subscapular, and suprailiac skinfolds were measured with a Lange Skinfold Caliper® (Beta Technology Incorporated, Cambridge, MD, USA) according to a previously described standardized method [16].

For the segmental BIA exam, the length of each segment was measured and the electrodes were properly positioned to obtain resistance and reactance values for each segment: arm, trunk, and leg [13,17].

Statistical analysis

After testing normality (Komogorov-Smirnov), all continuous variables were reported as means and SDs and the categorical variables were reported as frequencies and percentages.

For the elaboration of the equations, multiple linear regression analysis was applied to the models suggested (anthropometry and BIA) of whole body and each body segment, with DXA considered as reference.

Bland and Altman concordance graphs were constructed with the selected models of equations and DXA [18].

Results

The final sample consisted of 100 stable HIV-seropositive men taking HAART for at least 6 mo. Mean age was 43.6 ± 9 y; mean time of positive serology was 9.7 ± 6.4 y; and mean time of HAART use was 8.3 ± 5.4 y. The mean weight of the population studied was 71.1 ± 11.5 kg; mean height was 171 ± 6.8 cm, and mean calculated BMI was 24 ± 3.1 kg/m^2.

Regarding HAART regimen type, 45% were taking the combination of two nucleoside analog reverse transcriptase inhibitors (NRTI) with a non-nucleoside analog reverse transcriptase inhibitor (NNRTI); 48% were taking a combination of two NRTIs with a protease inhibitor (PI); and 7% were taking a combination of an NRTI, an NNRTI, and a PI. Among all patients, 10% were taking stavudine (d4T).

Thirty-three percent of the patients had hypercholesterolemia; 59% had hypertriacylglycerolemia; 66% had reduced HDL; and 38% had increased LDL. Sixteen percent were taking oral lipid-lowering medications such as statins and fibrates. Nineteen percent of the patients had a diagnosis of systemic arterial hypertension, 22% had altered fasting glycemia, and 8% had a diagnosis of diabetes mellitus, however, none of them was taking insulin, an agent that may determine redistribution of body fat. Clinical examination revealed that 58% of the patients had lipodystrophy, with 22% having the mixed form (with lipohypertrophy) and 36% having lipoatrophy alone.

The anthropometric and BIA measurements and the body composition measurements by DXA of the patients are presented in Table 1.

The equations selected were those showing higher coefficients of determination, practicalities of the models, and smaller numbers of independent variables. The models of the equations selected for the estimate of whole body fat-free mass (FFM), of arm, trunk, and leg fat and their respective coefficients

Table 1
Anthropometric and bioelectrical impedance analysis measurements and body composition obtained with DXA

Variables	Mean	SD
Arm circumference (cm)	29.51	3.50
Waist circumference (cm)	91.15	8.48
Hip circumference (cm)	92.5	7.21
Thigh circumference (cm)	50.75	5.02
Calf circumference (cm)	35.41	3.02
Bicipital skinfold (mm)	7.39	3.44
Tricipital skinfold (mm)	8.48	3.91
Subscapular skinfold (mm)	15.96	4.96
Suprailiac skinfold (mm)	16.83	7.73
Arm resistance (ohm)	227.38	33.63
Arm reactance (ohm	30.16	4.7
Trunk resistance (ohm)	74.39	13.82
Trunk reactance (ohm)	20.42	8.16
Leg resistance (ohm)	224.61	36.28
Leg reactance (ohm)	38.81	9.9
Whole-body resistance (ohm)	489.98	66.6
Whole-body reactance (ohm)	60.2	10.75
Arm fat measured by DXA (kg)	0.83	0.42
Trunk fat measured by DXA (kg)	9.08	3.78
Leg fat measured by DXA (kg)	2.33	1.24
Fat-free mass fat measured by DXA (kg)	52.81	7.27
Whole-body fat measured by DXA (kg)	16.52	6.39

DXA, dual-energy X-ray absorptiometry

of determination are listed in Table 2. Additionally, we observed a correlation coefficient (R) higher than 0.7 in all models of equations.

The dispersal of the equations elaborated with DXA is presented in graphs (Fig. 1). The difference between methods (DXA-equations) for the equations elaborated for the estimate of FFM by anthropometry, of fat-free mass by BIA, and of arm, trunk, and leg fat and their limit of concordance (95% confidence interval) were 0.06 kg (−4.92 to 5.05), 0.23 kg (−5.43 to 5.91), 0.02 kg (−0.45 to 0.49), 0.03 kg (−3.61 to 3.67), and 0.08 kg (−1.74 to 1.90), respectively.

Discussion

In this study we elaborated equations to estimate total and segmental fat using anthropometric measurements and BIA. This is an original study and to our knowledge no previous report has suggested equations for body segments for HIV-seropositive patients.

The mean BMI values showed that the group tended to be in the upper limit of normal weight. We point out that the exclusion criteria adopted regarding the presence of opportunistic diseases (infections and tumors) may have led to a selection favoring excess weight and excluding low weight. However, with the intent to avoid a large discrepancy in the body mass within the investigated group for the elaboration of the equations, malnourished and obese patients were excluded, and only patients with BMI that characterizes normal or overweight were selected.

The group with lipohypertrophy was smaller (39%) than the group with lipoatrophy (58%). These results are similar to those of the FRAM (Fat Redistribution and Metabolic Change in HIV Infection) study, which revealed that men had a subcutaneous lipoatrophy syndrome, in which depletion of adipose tissue is more common than deposition. The FRAM study was a cross-sectional study that used clinical examination and magnetic resonance imaging for the evaluation of regional deposition of adipose tissue [19].

In our study, one third of the patients had high LDL levels and more than half had hypertriacylglycerolemia and low HDL, characterizing an atherogenic lipid profile, that agrees with the high risk for cardiovascular diseases represented by the pattern of body fat distribution, with central accumulation and peripheral loss in this population. The fact that only 17% of the group was receiving oral medication such as statins is concerning and demonstrates that improvement in the medical care of these individuals is warranted.

Because both abdominal adiposity and peripheral lipoatrophy (regardless of abdominal lipohypertrophy) are important predictors of insulin resistance in HIV-positive patients [20], it is necessary to monitor the fat of the body segments.

Equation models have been suggested for men. Previous authors have shown the importance of the patient sex for the development of BIA equations for HIV-infected patients. There are several reasons for the potential differences in the comparability of the various techniques used to evaluate the body composition of men and women, including the degree of absolute and relative fat and obvious differences related to the concentrations of endogenous hormones. Additionally, HIV may have sex-specific effects on fat mass and FFM as the disease progresses [21,22].

When estimating the fat mass of a group of HIV-seropositive men with lipodystrophy using the Durnin and Womersley equation (which uses the sum of skinfolds), one study reported a low concordance and correlation with DXA (0.46 and 0.35) [12,23]. This was probably due to the fact that the Durnin and Womersley equation (1974) had been developed for healthy individuals and so, could not be used for individuals with any kind of disease [24]. Moreover, a previous study compared six equations for the estimate of body fat using the sum of skinfolds in patients with AIDS and found that none of the patients showed good concordance with DXA [25].

Because of this limitation, in the present study we suggested a model to estimate of body composition using the four skinfolds (Tricipital, bicipital, subscapular, and suprailiac) and

Table 2
Models of Equations for Estimate of Total*, Arm, Trunk, and Leg Fat up obtained with DXA

Component	Equation	R^2
FFM (kg) 1	11.027 + (0.694 × W†) − (0.158 × sum of folds‡)	0.87
FFM (kg) 2	−4.834 + (0.305 × W) + (32.257 × H) + (−0.048 × R) − (0.063 × Xc)	0.84
Arm fat (kg)	−1.499 + (0.021 × W) + (0.018 × AC) + (0.023 × TSF) + (0.002 × A)	0.66
Trunk fat (kg)	−18.043 + (0.114 × W) + (0.169 × WC) + (0.117 × SISF) + (0.038 × A)	0.76
Leg fat (kg)	−7.346 + (0.022 × W) + (0.134 × TC) + (0.015 × leg L)	0.50

A, age; AC, arm circumference; FFM, fat-free mass; H, height; TC, thigh circumference; TSF, tricipital skinfold; SISF, suprailiac skinfold; W, weight; WC, waist circumference; Xc, reactance

* To calculate total fat (kg): W (kg) − fat-free mass (kg).

† Measurement determination for each value: W measured in kg; H in m; R and Xc in ohm AC, TC, and WC in cm; SISF and TSF in mm; A in y; and leg length in cm.

‡ Sum of folds (mm): bicipital skinfold + tricipital skinfold + subscapular skinfold + suprailiac skinfold.

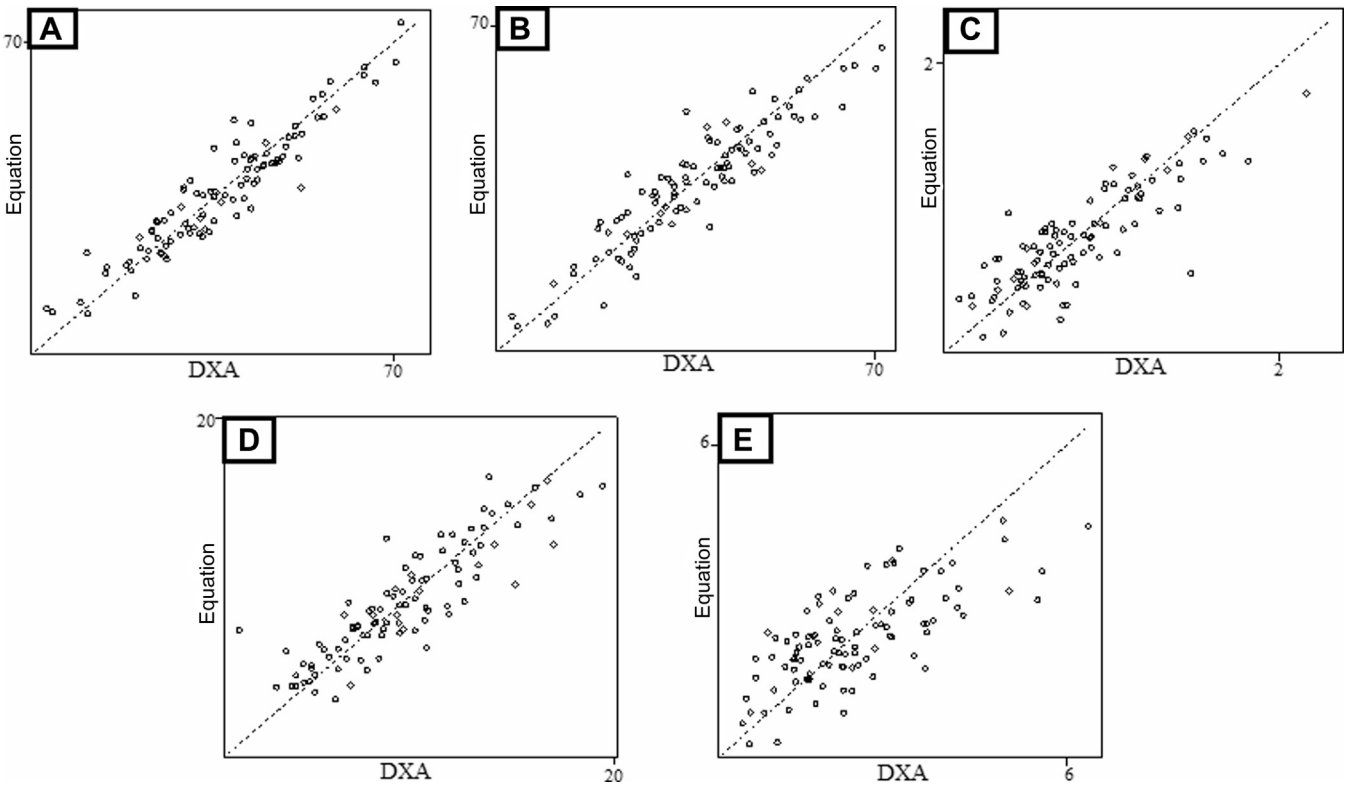

Fig. 1. Dispersal of the equations elaborated with DXA. (A) Equation to estimate FFM (kg) by anthropometry [FFM (kg) = 11.027 + (0.694 × W*) – (0.158 × sum of folds†)]. (B) Equation to estimate FFM (kg) by bioelectrical impedance analysis [FFM (kg) = −4.834 + (0.305 × W) + (32.257 × H) + (−0.048 × R) – (0.063 × Xc)]. (C) Equation to estimate arm fat [arm fat (kg) = −1.499 + (0.021 × W) + (0.018 × AC) + (0.023 × TSF) + (0.002 × A)]. (D) Equation to estimate trunk fat [trunk fat (kg) = −18.043 + (0.114 × W) + (0.169 × WC) + (0.117 × SISF) + (0.038 × A)]. (E) Equation to estimate leg fat [leg fat (kg) = −7.346 + (0.022 × W) + (0.134 × TC) + (0.015 × leg length)]. A, age; AC, arm circumference; DXA, dual-energy x-ray absorptiometry; FFM, fat-free mass; H, height; TC, thigh circumference; TSF, tricipital skinfold; SISF, suprailiac skinfold; W, weight; WC, waist circumference; Xc, reactance. *Measurement determination for each value: W measured in kg; H in m; R and Xc in ohm AC, TC, and WC in cm; SISF and TSF in mm; A in y; and leg length in cm. †Sum of folds (mm): bicipital skinfold + tricipital skinfold + subscapular skinfold + suprailiac skinfold.

observed a high coefficient of determination and excellent concordance with the reference method. To our knowledge, there is no previous description of an equation to estimate body composition in HIV-seropositive individuals using only anthropometric parameters.

One study evaluated eight BIA equations in American seropositive patients with criteria of definition of AIDS; these being opposite criteria compared with the group studied in the present investigation [26]. The authors showed that the BIA method was not as adequate as DXA to estimate body composition compared with the method of total body potassium, suggesting that the use of these BIA equations may generate even greater differences from reference methods in patients without AIDS with increased body fat and that therefore population-specific equations are necessary [26]. The BIA equation recommended by the European Society for Clinical Nutrition and Metabolism (ESPEN) for HIV-seropositive patients was validated in a study on white, black, and Hispanic HIV-infected individuals [21]. However, its use in the Brazilian population is still slightly ambiguous. In a Brazilian study, the use of the BIA equation was appropriate, with values showing high concordance with DXA (0.79 and 0.85 for patients with and without lipodystrophy, respectively) [12]. However, in another Brazilian study, the use of Kotler equation was inappropriate, showing 0.62 of concordance with the reference method for individuals with and without lipodystrophy [27]. On this basis, the study suggests a new model of BIA equation.

Regarding the equations for body segments, the best models selected for the estimate of arm, trunk, and leg fat presented independent anthropometric variables of weight, height, circumferences, and skinfolds that can be easily determined in ambulatory clinical practice. The graphs illustrate adequate concordance with the gold standard DXA method.

Importantly, although the equations developed were applied in the same group, which had been established, there is still need to assess its reproducibility in another group.

The measurement of minimal modifications of body fat in an objective manner can help health professionals to identify lipodystrophy early and thus prevent and minimize further future abnormalities.

Conclusions

The equations permitted the evaluation of total fat and of the fat of each body segment (arm, trunk, and leg) by means of accessible, precise, and reliable methods. The measurements used are not difficult to obtain and the health team can be trained to perform them routinely, thus contributing to the monitoring of lipodystrophy, permitting the appropriate clinical interventions and even preventing major changes in body composition.

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