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Original Article

Reproducibility of DXA Estimations of Body Fat in HIV Lipodystrophy

Implications for Clinical Research

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Abstract

Dual-energy X-ray absorptiometry (DXA) estimates of body fat are increasingly used for the evaluation of human immunodeficiency virus lipodystrophy (HIV LD); however, limited data are available on their reproducibility. This information is essential for using this tool as an end point in treatment trials or as a diagnostic tool. This study evaluates the reproducibility of DXA body fat estimation in HIV-positive subjects with and without lipodystrophy. Thirty subjects representing a spectrum of severity of fat redistribution underwent same-day repeat whole-body DXA scans (Hologic QDR 4500A scanner). Root mean square coefficients of variation (RMS-CV) were used to estimate minimum detectable differences (MDDs) for body fat content in different regions. Absolute MDD was calculated by multiplying the MDD by the mean fat-mass value for each anatomical area. The RMS-CV ranged from 4.0% for arm fat to 1.6% for total fat. Relative and absolute MDD values ranged from 11.0% or 160 g for arm fat to 4.3% or 628 g for total fat. DXA measurements of regional body fat mass in subjects with HIV show similar reproducibility to other populations. Minimal detectable differences were smaller than differences observed in published studies for all measurements. DXA is a sensitive tool for detecting changes in peripheral fat among patients with HIV lipodystrophy.

Key Words: HIV; lipodystrophy; dual-energy X-ray absorptiometry (DXA); reproducibility; coefficient of variation; body fat content.

Introduction

Human immunodeficiency virus lipodystrophy (HIV LD) is a term used to describe an increasingly common fat-redistribution syndrome affecting individuals with HIV, especially those treated with highly active antiretroviral therapy (HAART) *(1–3)*. It is characterized by loss of facial, buttock, and limb subcutaneous fat and/or accumulation of visceral and dorso-cervical adipose tissue, as well as lipoma formation *(4)*. Fat redistribution in HIV LD can also be accompanied by metabolic abnormalities in lipid and glucose metabolism *(5)*.

There is widespread recognition of the syndrome, and, recently, an objective definition of HIV LD has been reported *(4)*. Multiple tools have been used in assessing body-shape changes *(6)*, including questionnaires for self-report and physician assessment, anthropometric measurements, and radiographic techniques such as dual-energy X-ray absorptiometry (DXA) and single-slice computerized tomography. Objective measures add important information about quantitative changes and are likely more sensitive for detecting subtle changes in fat composition and objectively measuring response to therapy. Accordingly, several studies in HIV LD have used DXA estimates of body fat content as a means of

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quantifying the fat distribution changes in HIV LD *(1,7–9)*. The recent Case Definition study *(4)* included DXA body fat estimate variables in its model for the diagnosis of HIV LD.

Despite widespread use of DXA, there have been limited studies evaluating the reliability of DXA body fat content estimates in this population *(9)*. Moreover, no studies have specifically addressed test–retest reliability.

Reproducibility of DXA measurements is influenced by equipment and technical factors *(10)*, as well as by population and disease-specific characteristics *(11)*. Knowledge of reproducibility is needed to establish whether differences between measurements are significant. In HIV LD, this is essential both for the purposes of using DXA as a diagnostic tool and for longitudinal evaluations of affected individuals and responses to therapy such as switching or discontinuing certain components of HAART therapy. This study was conducted to determine the reproducibility of DXA measurements of body fat in HIV patients representing a spectrum of severity of fat redistribution.

Methods

Subjects

Consecutive volunteers were enrolled from among HIV-positive subjects participating in two studies of HIV lipodystrophy at the Immunodeficiency Clinic at the Toronto General Hospital in Toronto, Canada. One was a prospective study of previously antiretroviral-naive patients initiated on HAART containing a protease inhibitor. The other was an ongoing double-blinded intervention trial in patients with established lipodystrophy as identified by self-reported questionnaire and assessment by an experienced physician. This substudy was approved by the Ethics Review Board of the University Health Network and all subjects provided written informed consent to participate. As suggested in the literature, a sample size of 30 was required to be able to estimate the coefficients of variation within ±15%, with 95% confidence *(12)*.

Measurements

Participants were evaluated with same-day repeat whole-body DXA scans. DXA measurements were performed while the patient was lying in a supine position, with standard positioning of the arms and feet. Subjects were then asked to get off the scanning table and were repositioned after standing for the second scan. They were asked to abstain from any fluid or food intake or elimination between the two examinations. Scans were acquired and analyzed with automated software (v 11.2) by the same technologist using a Hologic QDR 4500A (Hologic, Waltham, MA) fan-beam densitometer in the array mode and were reviewed later by a certified clinical densitometrist. Each scan was analyzed independently.

Analysis

Regional fat mass values were grouped and analyzed for the following anatomical regions: arms, legs, limbs (arms + legs), trunk, subtotal body (whole body excluding head), and whole body.

Table 1
Baseline Characteristics of the Study Population and DXA Values for Regional and Total-Body Fat Mass

	Mean	STD	Range
Age (yr)	45.9	7.4	32.5–62.0
Weight (kg)	77.3	15.1	52–135
Height (cm)	173.8	6.1	159–186
BMI (kg/m^2)	25.5	4	18.3–39.0
Arm fat mass (kg)	1.4	0.8	0.7–5.4
Leg fat mass (kg)	3.7	2.9	1.2–15.7
Limb fat mass (kg)	5.1	3.7	1.9–21.1
Trunk fat mass (kg)	8.5	3.8	3.3–22.9
Subtotal fat mass (kg)	13.6	7.0	5.4–43.5
Total-body fat mass (kg)	14.6	7.1	6.3–45.0
Total-body fat (%)	18.3	5.3	9.3–32.9

The standard deviation (SD) and coefficient of variation (CV = SD/mean) were calculated for the pair of measurements for each anatomical region for each participant. Average values for SD and CV were calculated for the study population using the root mean square (RMS) formulas:

$$\text{RMS}-\text{SD}=\sqrt{\sum_{i=1}^{n}\text{SD}i^2/n} \quad \text{and} \quad \text{RMS}-\text{CV}=\sqrt{\sum_{i=1}^{n}\text{CV}i^2/n}$$

Minimum detectable differences (MDDs) that would be significant at the 95% confidence level were calculated for each anatomical region using the following formula *(13)*:

$$\text{MDD}=1.96\sqrt{2(\text{RMS}-\text{CV})^2}$$

Absolute MDDs were calculated to provide a numerical estimate of detectable change for an individual with average body fat mass. This was done by multiplying MDDs by the mean fat-mass value for each body area.

Results

The baseline characteristics of the study population are shown in Table 1. All 30 subjects enrolled were male and the average age was 45.9 yr, which was representative of patients at the clinic where the study was conducted. Weight, height, and body mass index (BMI) ranges are representative of the diverse population the study set out to include.

Table 1 also lists the results of DXA body fat values for the study population. Because we included subjects without fat redistribution, individuals with peripheral lipoatrophy, and those with centripetal accumulation, values represent a wide spectrum of regional and total-body fat content.

Table 2 lists the RMS-CVs for each anatomical area, as well as percent MDDs and absolute MDDs. The RMS-CV was lower for overall limb fat mass measurement than for arm and leg fat mass measurements: RMS-CV of 2.6% for limb fat mass vs 3.1% and 4.0% for legs and arms, respectively. The relative MDDs calculated in our study are less than fat mass changes from published studies of HIV LD that reported DXA results *(1,4)*.

Table 2
CVs, and MDDs (in Percentage and Grams) by Field; Comparisons With Data in the Literature

Field	CV RMS-CV (%)	Relative MDD 2.77* RMS-CV (%)	Absolute MDD MDD × Mean (g)	Ref. 1 Mean Change 21 mo (%)	Ref. 4 Cases vs Controls (%)
Head fat mass	2.5	7.0	72.7	—	—
Arm fat mass	4.0	11.0	159.8	17.8	—
Left arm fat mass	5.4	14.9	97.2		
Right arm fat mass	6.2	17.2	121.4		
Leg fat mass	3.1	8.5	312.7	15.8	—
Left leg fat mass	5.7	15.9	181.5		
Right leg fat mass	4.1	11.4	142.2		
Limb fat mass	2.6	7.3	375.7	16.4	28.8
Trunk fat mass	2.1	5.9	499.2	8.3	—
Subtotal fat mass	1.7	4.6	624.1	—	—

Figure 1 shows scatterplots of DXA CVs for each anatomical region vs the mean regional fat mass for each pair of measurements. No systematic change in variability is seen with changes in mean values of fat mass.

Discussion

This study is the first to report reproducibility for DXA estimates of body fat in HIV-positive individuals. Our results show similar reproducibility to that reported for other non-HIV-infected populations using a similar type of scanner and software *(11)*. Regional fat mass measurements are of interest in HIV LD because they capture the fat redistribution that is characteristic of the syndrome. We found that DXA estimations of fat mass for the arms, legs, limbs, and trunk had CVs in the 2 to 4% range, resulting in MMDs between 5 and 11%. Given the improved reproducibility of the combined limb fat values compared to individual arm or leg fat mass values, we propose limb fat as a better measurement for evaluation of peripheral lipoatrophy.

It is also necessary to evaluate reproducibility of DXA measurements according to the absolute values obtained. In analyzing the relationship between intermeasurement variability and mean fat mass values for different body areas, no trends were detected. This indicates that DXA remains reliable over the range of fat mass values in this population of HIV-infected individuals.

Furthermore, it is important to stress that the MDD is the magnitude of change that a pair of measurements must exceed in order to be considered statistically significant. Although this is different than the difference between two group means, MDD results do indicate the order of magnitude of a significant change in body fat mass for an individual, as measured by DXA.

With this in mind, we compared our MDDs to fat-mass changes observed in published studies of HIV LD that reported DXA results (Table 2). The first study *(1)* compared DXA fat-content measurements in 39 HIV LD subjects receiving HAART over a mean 21-follow-up. The second study *(4)* was a multicenter case–control study comparing subjects with and without lipodystrophy as defined by concordance between patient and physician reports of HIV LD. Although these studies used different DXA scanners than the one we evaluated, in both studies longitudinal *(1)* or case-vs-control *(4)* differences in DXA fat values were greater than our estimated MDD for all body areas reported. Assuming that the scanners used in these studies had similar reproducibility values to the one we studied, this would indicate that DXA is able to capture significant differences in body fat composition both longitudinally and between individuals with and without HIV LD. This further supports the use of DXA as a sensitive tool for detecting regional changes in body fat among patients with HIV LD.

Some studies of fat redistribution after changes in HAART therapy have also used DXA. Changes in limb fat in the Abacavir Substitution Study were on the order of 11% in the intervention arm and 2% in the control arm *(14)*. The Tarheel study followed patients over 24 wk after switching from D4T to ZDV or ABC and found median changes in DXA body fat for the arm, trunk, and leg on the order of 25, 9, and 6%, respectively *(15)*. DXA body fat changes in these studies are above our calculated MDDs for these body areas. The wide variability found in DXA body fat values underscores the importance of performing paired analyses when analyzing longitudinal studies.

It is important to note that MDDs reported in this study refer to a 95% statistical likelihood that a change has occurred. The extent of change that would be clinically significant remains to be determined. Moreover, a clinically significant difference for a treatment study might be different from a clinically significant difference for an individual followed over time. Variability values reported in this study refer to the specific equipment and software utilized and did not address variability between technologists or between different scanners. As such, they might not be generalizable to other equipment or studies in which multiple scanners are used *(16)*. Furthermore, DXA is not an adequate tool for evaluating facial fat changes because of the high fat content in the brain, which obscures small decreases in facial fat. Neither is it adequate for differentiating between subcutaneous and visceral fat accumulation in the truncal area. In both of these areas, a computerized

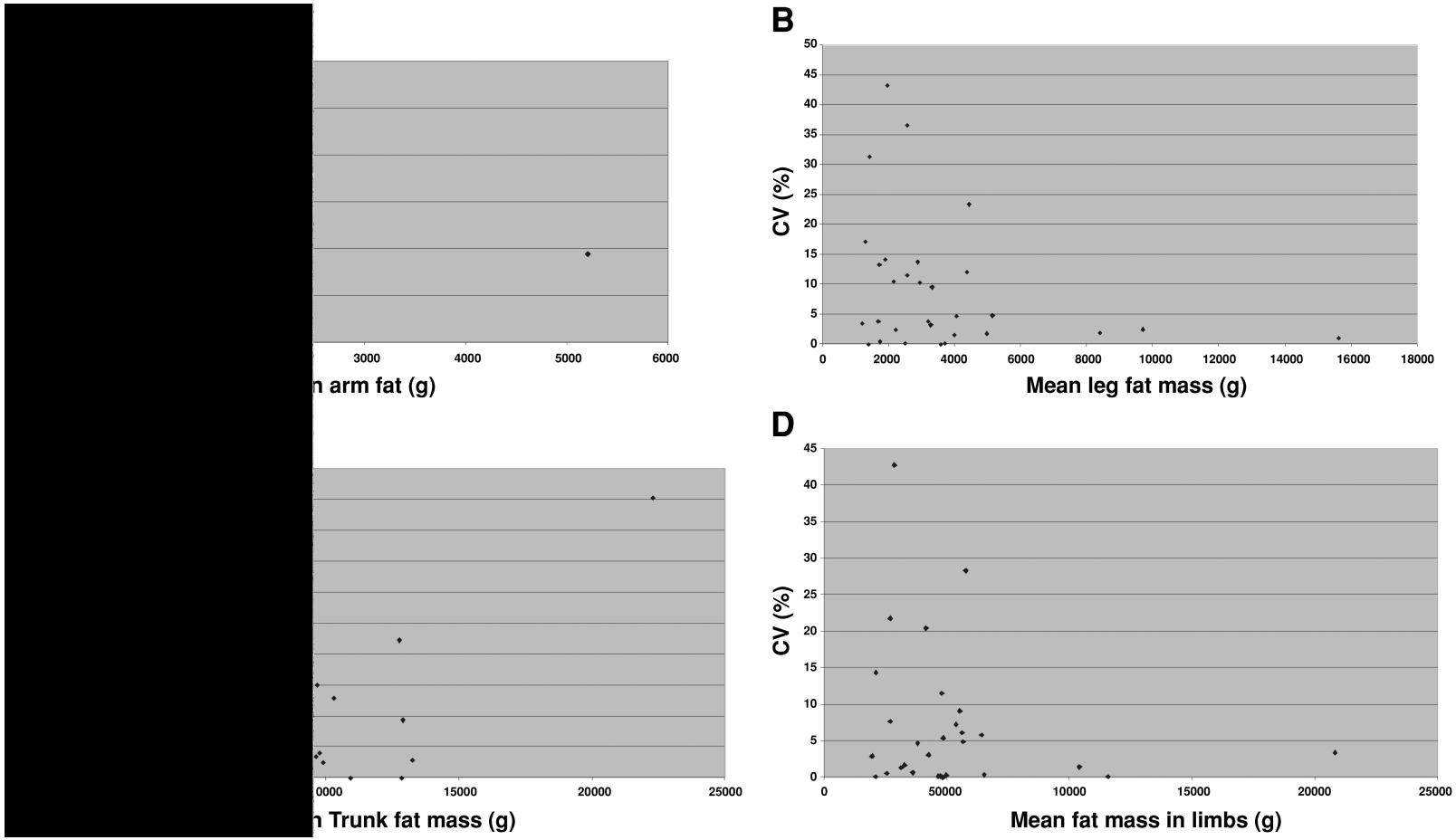

Fig. 1. Scatterplots of individual DXA coefficients of variation for each anatomical region vs mean regional fat mass for arm fat (**A**), leg fat (**B**), trunk fat (**C**), and limb fat (**D**).

tomography scan might provide better results. Finally, we did not include any females in this study. Gender is known to affect body composition, and females exhibit different patterns of fat redistribution. Therefore our values might not be generalizable to women being evaluated for HIV LD, an area requiring further research.

Further research is also needed to characterize patterns of fat distribution in subjects with HIV LD using DXA. This might allow single or combination fat-mass measurements to be selected for diagnostic purposes.

In summary, this is the first study to report the reproducibility of DXA measurements of regional body fat mass in HIV-positive subjects. Minimal detectable differences were smaller than differences observed in some published cohorts and cross-sectional studies. This supports the use of DXA as a tool for evaluating the presence and severity of HIV LD. The reported estimates of variability are useful in calculating sample size for studies using DXA as an end point and in determining whether longitudinal changes in DXA measurements are significant, in either observational or intervention trials. Finally, given the variability in DXA fat-mass values, longitudinal studies using DXA should endeavor to use paired analyses when reporting results.

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