Severity of Lipodystrophy Is Associated with Decreased Health-Related Quality of Life

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Abstract

The impact of lipodystrophy (LD) on quality of life is high, but it has not been demonstrated in literature. The objective of the study was to assess the impact of LD on the health-related quality of life (HRQOL) in HIV-infected people on highly active antiretroviral therapy (HAART). Patients with LD phenotype defined by the Multicenter AIDS Cohort Study (MACS) were included. Three different methods were used to define LD severity: both patient and physician evaluation using the HIV Outpatient Study (HOPS) severity scales and the Lipodystrophy Case Definition (LDCD). The HRQOL was evaluated by MOS-HIV Health Survey. Four hundred one patients on HAART for a mean of 108 ± 52 months were evaluated for LD at the Metabolic Clinic of Modena and Reggio Emilia University were enrolled from January 2003 to July 2006. According to self-perceived or physician-based HOPS, 106 (26.5%) and 122 (30.4%) patients had severe LD. Females had significantly more severe LD. Few HRQOL scores correlated to LD severity using the physician-based score (both HOPSph and LDCD), while all the HRQOL scores correlated with LD severity when a patient-based score was used (HOPSpt). In multiple linear regression analysis, Mental Health HRQOL score, gender, body mass index, age, body image satisfaction were independent predictors of patient-based (HOPSpt) LD, while none of the HRQOL scores, but female gender, age, waist-to-hip ratio, limb fat, and body image satisfaction were correlated with physician-estimated HOPSph LD severity. HRQOL was strongly correlated with LD severity when a patient-based score was used. For an overall assessment of the impact of LD on HIV-infected people, both patient-based and physician-based measures are required.

Introduction

DESPITE THE DEMONSTRATED BENEFITS of highly active antiretroviral therapy (HAART), adverse events related to treatment can be a great burden to patients. Body habitus changes, named lipodystrophy (LD), are one of the most frequent clinical disorders associated with antiretroviral therapy. LD phenotype include fat atrophy affecting limbs, buttocks, and face, fat accumulation both intravisceral or subcutaneous and mixed forms as the result of a combination of the two. While lipodystrophy is clearly an HIV- and/or HIV-drug-related phenomenon, fat accumulation seems not specific for either.^{1,2} Unfortunately, there is neither consensus on the definition of LD, nor agreement on the best

method for measuring it. LD is a multidimensional construct and patient versus physician-detected incidence of LD may have variable level of concordance.³ Moreover, it is not known which is the best instrument to measure the subjective impact of LD on people with HIV.

Clinical experience suggests that LD can have a profound impact on quality of life. Changes in body image may stigmatize patients, producing erosion of self-esteem, decreasing social functioning including sexual relations, and leading to anxiety and depression.^{4,5} LD may result in an involuntary disclosure of HIV status and also appears to be correlated to suboptimal adherence to therapy.^{6,7}

Few studies have addressed quality-of-life issues in HIV-infected patients with LD, and its impact has not been es-

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established definitively. Some studies demonstrating effects have used instruments not widely validated in people with HIV infection,^{8,9} while others have failed to find correlations with health-related quality of life.^{10,11}

The main objective of this study was to identify the impact of LD on the health-related quality of life in HIV-infected people taking HAART. The identification of the best instrument for the assessment of the impact of LD on the health-related quality of life could provide useful tools in clinical practice, both for monitoring the psychosocial effects of LD and evaluating outcomes of interventions to improve or preserve quality of life.

Methods

Prospective observational study of consecutive HIV-infected adult outpatients attending the Metabolic Clinic (MC) of Modena and Reggio Emilia University, Italy¹² from January 2003 to July 2006. This is a referral centre where a multidisciplinary consultant service consisting of infectious disease physicians, cardiologists, endocrinologists, nutritionists, personal trainers for physical activities, psychologists and plastic surgeons offer patients a free-of-charge strategy for aesthetic correction of LD as well as cardiovascular risk reduction. Patients with self-perceived body habitus changes may have direct access or may be referred by their physicians for LD evaluation. Both subjective parameters (health-related quality of life, body image evaluation) and objective parameters (fasting lipids and glucose evaluation, anthropometric measures (body mass index [BMI], waist to hip ratio [WHR]), dermal and subcutaneous thickness of both cheeks measured with a high frequency ultrasound transducer (7.5 MHz), dual-energy x-ray absorptiometry (DEXA) evaluation of total body, trunk, and leg fat and lean mass, abdominal computed tomography (CT) scan for visceral (VAT) and subcutaneous adipose tissue (SAT) were routinely collected at the time of first encounter of the patients, before providing any medical or surgical treatment. To be

included in the present study, patients were required to be clinically stable, to have received more than 1 year of HAART (an antiretroviral regimen containing at least a protease inhibitor [PI] or a non-nucleoside reverse transcriptase inhibitor [NNRTI] or three nucleoside reverse transcriptase inhibitors [NRTIs]), to be able to complete the questionnaires in Italian, and to be willing to participate to the study. All participants provided written informed consent; the research protocol was approved by the Ethics Committee of the hospital.

Patients with body changes LD phenotype defined by the Multicenter AIDS Cohort Study (MACS) were included.^{13,14} Three different methods were used to define LD severity: both the patient self-assessment and the physician evaluation using the HIV Outpatient Study (HOPS) severity scales,¹⁵ and the Lipodystrophy Case Definition (LDCD).^{16,17} LD definition criteria are summarized in Table 1.

Instruments for the assessment of health-related quality of life and body image included:

1. The Medical Outcomes Study HIV Health Survey (MOS-HIV)¹⁸ was used for measuring health-related quality of life. It includes 10 dimensions including pain, physical function, role function, social function, mental health, energy/vitality, health distress, cognitive function, general health perceptions, and quality of life. Two summary scores were calculated: a Physical Health Summary score (PHS) and a Mental Health Summary score (MHS).¹⁹ The PHS and MHS scores are standardized so that the mean is 50 and the standard deviation is 10. An Italian version has demonstrated good validity as a measure of health status in people with HIV.²⁰ An average of 15 minutes is needed to complete the questionnaire.
2. Body image was evaluated using an Italian version of the Adult AIDS Clinical Trials Group (ACTG) Assessment of Body Change and Distress (ALDD) questionnaire.²¹ The ALDD includes 22 items: the first question (ALDD7) asks about body image satisfaction (the lower the score the

TABLE 1. DEFINITION OF LIPODYSTROPHY USED IN THE PRESENT STUDY

Definition	Description	Rating scale	Notes
MACS ^a	Fat loss in the upper arms, legs, buttocks, and face, as well as fat accumulation in the abdomen, breast, and back of neck, and the presence of moon faces	Body alterations are scored as "none," "mild," "moderate," or "severe." Moderate or severe forms only account for lipodystrophy diagnosis.	Physician-based
HOPS ^b	8 items corresponding to 4 body fat alteration of face, arms, legs, and buttocks lipodystrophy and 4 features for breast, abdomen, back of the neck, and under the chin lipohypertrophy	A 4-point scale of severity for each item: 0 = none; 1 = mild; 2 = moderate; 3 = severe.	Both physician and patients
LDCD ^c	It includes demographic, clinical metabolic, as well as body composition variables	The degree of lipodystrophy, diffuse fat accumulation, or lipomatosis at every site on the body was rated on a 4-point scale of severity	Physician-based

^aMulticenter AIDS Cohort Study definition.

^bHIV Output Study Severity Scales.

^cLipodystrophy Case Definition.

TABLE 2. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE STUDY SAMPLE

Age, years, mean (SD)	45 (6.8)
Female (%)	149 (37.2)
Injecting drug user (%)	103 (25.7)
CDC group C (%)	110 (27.4)
HCV antibody + (%)	115/330 (28.7)
CD4/ μ L, mean (SD)	
current	535 (265)
nadir	170 (132)
HIV RNA load, log copies/mL, mean (SD)	2.39 (1.12)
Waist to hip ratio (W/H), mean (SD)	0.94 (0.06)
Body mass index (BMI), kg/m ² , mean (SD)	23.05 (3.5)
Visceral and subcutaneous adipose tissue ratio (VAT/SAT), mean (SD)	1.62 (2.14)
Leg fat, kg, mean (SD)	2.12 (1.55)
Cheek ultrasound thickness, mm, mean (SD)	6.81 (2.44)

SD, standard deviation; CDC, Centers for Disease Control and Prevention.

higher is body aesthetic satisfaction), the remaining 21 items allow to calculate a global value (ALDD8) that describes body changes interference with habits, social life and attitudinal aspects of body image (the higher the score the lower is interference of body changes with habits and social life).

3. Facial and body aesthetic satisfaction were measured by two separate visual analogue scales (VAS) with possible values from 0 to 10.
4. HIV-1-related data such as mode of HIV transmission, current CD4 cell count and HIV-1 RNA (copies per milliliter), prior opportunistic diseases, and both current and past antiretroviral therapy (ART) were obtained from medical files.

All patients underwent a physical examination including anthropometric variables: weight, height by stadiometer, and circumferential measurements of waist, hip, and thigh as the average of three measures.

Body composition was assessed using whole-body DEXA, and single-slice abdominal (L4) CT with standard protocols. DEXA data comprised legs, trunk, and total fat mass, CT data included VAT, SAT, and total adipose tissue volume (TAT) of the abdomen.

The LDCD definition was applied only to the 182 patients for whom all the needed variables for its calculation (age, gender, duration of HIV infection, HIV disease stage, waist to hip ratio, anion gap, serum HDL cholesterol concentration, trunk to peripheral fat ratio, percentage leg fat, and intra-abdominal to extra-abdominal fat ratio) were available.

Statistical analysis

The primary outcome of the study were the two summary scores PHS and MHS of MOS HIV questionnaire. Effect size for both PHS and MHS among people at different LD degree of severity were calculated. According to the Cohen's definition,²² an effect size from 0 to 0.2 was considered of a small significance, from 0.21 to 0.50 of a medium significance and more than 0.50 of a large significance.

Analysis of variance (ANOVA) and χ^2 test were done to identify variables correlated to physician-based or patient-reported LD severity. Spearman rank correlation coefficients were also calculated to confirm results of ANOVA.

As counterproof a backward stepwise logistic regression analysis was done to assess the independent effects of the significant ($p < 0.1$) explanatory variables on the HOPS scales. In particular, purpose of multivariable analysis was to evaluate the correlation among LD severity and health-related quality of life measures adjusting for several potential confounders. Statistical significance was determined at $p <$

TABLE 3. DISTRIBUTION OF ENROLLED PEOPLE ACCORDING TO THE DIFFERENT LIPODYSTROPHY DEFINITIONS

Definition	Features	n (%)
MACS	Not having LD ^a	47 (11.7)
	Lipoatrophy	164 (40.9)
	Fat accumulation	31 (7.7)
	Both lipoatrophy and fat accumulation	159 (39.7)
Patient-based HOPS	Not having LD	97 (24.2)
	Mild LD	90 (22.5)
	Moderate LD	107 (26.8)
	Severe LD	106 (26.5)
Physician-based HOPS	Not having LD	92 (22.9)
	Mild LD	68 (16.9)
	Moderate LD	119 (29.7)
	Severe LD	122 (30.4)
LDCD ^b	Not having LD	48 (26.4)
	Grade 1 LD, mild	55 (30.2)
	Grade 2 LD, moderate	29 (15.9)
	Grade 3 LD, severe	50 (29.8)

^aBody habitus changes.

^bLipodystrophy case definition (LDCD) was available for 182 patients.

MACS, Multicenter AIDS Cohort Study; HOPS, HIV Outpatient Study; LD, lipodystrophy.

0.05. SPSS software package version 13.0 (SPSS; Chicago, IL) was used for statistical analyses.

Results

Demographic and clinical characteristics of the study population are presented in Table 2. Eleven percent of people were receiving their first antiretroviral regimen. A PI-containing regimen was taken by 40.6%, an NNRTI-containing regimen by 30.5% (in 5 people PI and NNRTI were in the same regimen) and a fusion inhibitor-containing regimen by 2.5% of the study subjects; 49 patients (12.1%) were taking three NRTIs and 68 (16.8%) were not taking HAART at the moment of the survey. Table 3 shows the distribution of enrolled people according to the four LD definitions.

According to MACS classification, females had mixed phenotype (both lipoatrophy and fat accumulation) more frequently than men (50.7% versus 33.3%, respectively, $p < 0.0001$), while men had lipoatrophy more frequently than women (29.7% versus 47.6%, respectively, $p < 0.0001$).

Patient-based and physician-assessed HOPS scores were highly correlated ($R = 0.31$; $p < 0.0001$). However, the definitions sometime categorized patients differently from each

other. In particular, in 16% of cases physicians reported no LD, while patients referred a mild to moderate degree of LD, and in approximately 18% of cases physicians estimated a mild to severe LD when patients reported no LD.

Examining health-related quality of life, PHS and MHS mean scores were 50.6 (SD 8.7) and 43.6 (SD 7.3), respectively. Facial VAS score was 4.7 (SD 2.5), body VAS score was 4.4 (SD 2.4). Satisfaction with body image (ALDD7) mean was 3.5 (SD 1.0), while that of body change interference (ALDD8) was 70.3 (SD 17.5).

Tables 4A, 4B, and 4C show correlations among clinical parameters, subjective measures, and health-related quality of life with both patient and physician-assessed HOPS and LDCD. In all the definitions, females had significantly more severe LD than men. When the physician-based score was used, several clinical parameters, but not all the HRQOL scores were correlated with severity of LD. None of the HRQOL were correlated with LDCD. Using the patient-based score, both subjective and quality of life measures were correlated with the severity of LD.

Pain functioning, physical functioning, mental health, energy/vitality, cognitive functioning, current health perception, overall quality of life were the domains significantly correlated with the severity of patient-assessed LD. Both of

TABLE 4A. CORRELATIONS AMONG CLINICAL PARAMETERS, AND SUBJECTIVE MEASURES TO PATIENT-ASSESSED HOPS

	<i>Patient-based HOPS, mean (SD)</i>				<i>p</i>
	<i>0 = none (n = 97)</i>	<i>1 = mild (n = 90)</i>	<i>2 = moderate (n = 107)</i>	<i>3 = severe (n = 106)</i>	
Females (%)	30 (30.9)	15 (16.7)	38 (35.5)	65 (61.3)	<0.0001
Age, years	45.3 (7.4)	45.2 (6.0)	44.0 (6.2)	45.3 (7.5)	0.41
Injection drug use (%)	26 (26.8)	19 (21.1)	36 (33.6)	21 (19.8)	0.09
CDC Group C (%)	25 (26.6)	28 (32.6)	29 (28.2)	28 (27.5)	0.82
HCV-Ab+ (%)	26 (35.1)	24 (29.6)	43 (48.9)	22 (25.6)	0.008
CD4, μ L	555 (255)	504 (261)	523 (244)	559 (296)	0.46
HIV-RNA, log/mL	2.4 (1.1)	2.3 (1.1)	2.4 (1.2)	2.4 (1.1)	0.84
Waist-to-hip ratio	0.93 (0.06)	0.94 (0.07)	0.94 (0.006)	0.95 (0.006)	0.24
Body mass index, kg/m ²	22.8 (3.3)	23.3 (3.0)	22.5 (3.9)	23.6 (3.4)	0.09
VAT/SAT	2.1 (3.0)	1.8 (1.9)	1.7 (2.4)	1.1 (1.1)	0.03
Limb fat, kg	1.95 (1.25)	2.19 (2.05)	1.98 (1.29)	2.31 (1.45)	0.32
Ultrasound cheek, mm	6.4 (2.3)	7.3 (2.4)	6.7 (2.2)	6.8 (2.7)	0.07
VAS face	4.3 (2.7)	5.5 (2.2)	5.0 (2.5)	4.1 (2.4)	<0.0001
VAS body	4.2 (2.4)	5.3 (2.3)	4.5 (2.4)	3.4 (2.0)	<0.0001
ALDD7	3.3 (1.1)	3.0 (0.9)	3.6 (0.9)	4.1 (0.8)	<0.0001
ALDD8	72.4 (18.0)	80.7 (13.2)	68.7 (15.5)	61.6 (17.2)	<0.0001
Pain functioning	81.6 (23.3)	81.8 (24.1)	74.0 (26.1)	72.5 (25.1)	0.009
Physical functioning	80.8 (22.2)	88.7 (16.7)	78.2 (23.4)	75.9 (22.4)	<0.0001
Role functioning	79.4 (30.0)	80.8 (27.3)	76.4 (30.7)	73.8 (30.4)	0.35
Social functioning	83.9 (26.9)	88.9 (20.8)	81.9 (25.1)	82.1 (25.7)	0.18
Mental health	62.0 (21.5)	65.4 (18.7)	58.5 (18.3)	56.4 (21.8)	0.01
Energy/vitality	60.5 (19.3)	63.8 (17.4)	57.9 (17.4)	52.3 (22.0)	<0.0001
Health distress	77.7 (26.5)	83.6 (20.1)	75.3 (24.0)	72.9 (23.0)	0.01
Cognitive functioning	76.3 (23.2)	81.2 (18.1)	73.1 (23.6)	71.1 (24.8)	0.01
Current health perception	41.7 (20.3)	44.5 (20.5)	35.5 (19.1)	35.8 (20.9)	0.003
Quality of life	35.3 (21.9)	35.0 (20.1)	40.9 (17.0)	41.5 (20.1)	0.03
PHS	51.4 (8.7)	53.2 (7.7)	49.7 (8.8)	48.7 (8.9)	0.002
MHS	43.8 (8.0)	45.8 (6.1)	43.1 (7.2)	42.0 (7.3)	0.004

SD, standard deviation; HOPS, HIV Outpatient Study; CDC, Centers for Disease Control and Prevention; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; VAS, visual analogue scale; ALDD, Assessment of Body Change and Distress; PHS, Physical Health Summary score; MHS, Mental Health Summary score.

TABLE 4B. CORRELATIONS AMONG CLINICAL PARAMETERS, AND SUBJECTIVE MEASURES TO PHYSICIAN-BASED HOPS

	<i>Physician-based HOPS, mean (SD)</i>				<i>p</i>
	<i>0 = none (n = 92)</i>	<i>1 = mild (n = 68)</i>	<i>2 = moderate (n = 119)</i>	<i>3 = severe (n = 122)</i>	
Females (%)	17 (37.0)	44 (26.8)	12 (38.7)	75 (47.2)	0.002
Age, years	43.1 (6.2)	45.9 (7.2)	44.4 (6.0)	46.2 (7.4)	0.004
Injection drug use (%)	17 (18.5)	21 (30.9)	33 (27.7)	32 (26.2)	0.29
CDC Group C (%)	15 (34.1)	46 (28.9)	6 (20.7)	43 (28.1)	0.67
HCV + serology (%)	9 (24.3)	55 (40.1)	5 (19.2)	46 (35.7)	0.10
CD4, μ L	511 (212)	569 (263)	558 (264)	514 (298)	0.37
HIV-RNA, log/mL	2.17 (0.95)	2.48 (1.24)	2.44 (1.16)	2.47 (1.11)	0.24
Waist-to-hip ratio	0.92 (0.06)	0.94 (0.06)	0.94 (0.006)	0.96 (0.006)	0.007
Body mass index, kg/m ²	23.6 (3.7)	23.3 (2.7)	22.7 (3.7)	22.9 (3.3)	0.24
VAT/SAT	1.62 (2.53)	1.55 (1.41)	1.73 (2.03)	1.56 (2.33)	0.95
Limb fat, kg	2.65 (2.03)	1.96 (1.52)	2.01 (1.37)	1.94 (1.22)	0.007
Ultrasound cheek, mm	7.9 (2.2)	7.5 (2.8)	6.7 (2.2)	5.7 (2.2)	<0.0001
VAS face	5.51 (2.45)	5.64 (2.45)	4.57 (2.29)	3.76 (2.45)	<0.0001
VAS body	5.44 (2.33)	5.32 (2.39)	4.16 (1.86)	3.47 (2.39)	<0.0001
ALDD7	3.2 (1.0)	3.0 (1.1)	3.7 (0.9)	3.9 (0.9)	<0.0001
ALDD8	76.2 (16.3)	74.3 (16.1)	69.6 (17.6)	64.4 (17.4)	<0.0001
Pain functioning	78.7 (24.4)	81.4 (24.0)	76.4 (25.2)	74.2 (25.7)	0.26
Physical functioning	85.5 (21.5)	82.1 (21.6)	78.6 (21.3)	77.9 (22.5)	0.05
Role functioning	76.9 (29.9)	80.1 (28.8)	75.4 (30.3)	78.1 (29.7)	0.76
Social functioning	87.8 (22.8)	83.8 (24.0)	83.4 (24.0)	82.0 (27.5)	0.38
Mental health	60.0 (18.6)	67.2 (20.1)	61.8 (20.6)	55.0 (20.4)	0.001
Energy/Vitality	59.6 (20.5)	62.6 (18.8)	57.0 (18.6)	56.1 (20.1)	0.13
Health distress	82.0 (20.1)	79.4 (23.5)	79.5 (21.4)	69.8 (27.1)	0.001
Cognitive functioning	80.6 (18.8)	73.8 (21.4)	72.9 (24.3)	73.9 (24.8)	0.07
Current health perception	39.6 (22.0)	44.3 (18.7)	38.4 (20.7)	36.4 (19.7)	0.08
Quality of life	39.1 (20.4)	34.6 (20.3)	37.2 (18.9)	41.2 (20.0)	0.14
PHS	52.2 (8.6)	51.5 (7.8)	49.6 (9.2)	49.9 (8.7)	0.11
MHS	44.7 (6.3)	44.8 (7.1)	43.8 (7.5)	41.8 (7.7)	0.01

SD, standard deviation; HOPS, HIV Outpatient Study; CDC, Centers for Disease Control; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; ALDD, Assessment of Body Change and Distress; VAS, visual analogue scale; PHS, Physical Health Summary score; MHS, Mental Health Summary score.

the two HRQOL summary scores were significantly correlated with the severity of patient-assessed LD.

The effect size of PHS for people with no LD compared to those with severe LD were 0.31 for the patient-based HOPS definition and 0.26 for the physician-based one, while the effect size of MHS for people with no LD compared to those with severe LD were 0.23 for the patient-based HOPS definition and 0.41 for the physician-based one.

In linear regression analysis HOPS was significantly correlated with both PHS ($B = -0.29$; 95% confidence interval [CI] $-0.47, -0.11$; $p = 0.002$) and MHS ($B = -0.28$; 95% CI $-0.43, -0.13$; $p < 0.0001$) in patient's estimation, but only with MHS ($B = -0.50$; 95% CI $-0.78, -0.21$; $p = 0.001$) in physician evaluation.

With regards to a qualitative assessment of LD, using a physician-based classification of LD according to MACS definition, no correlations were found among clinical parameters, subjective measures and health-related quality of life and LD score (data not shown). In Table 5 Spearman correlation coefficients are reported confirming the results of the study.

In backward stepwise multiple linear regression analysis, female gender, BMI, age, ALDD8 and MHS were significantly and independently related to patient-based HOPS LD

scale while female gender, age, WHR, limb fat, and ALDD8 were significantly and independently correlated with physician-estimated HOPS LD scale (Table 6).

Discussion

Although it seems intuitively obvious that LD can decrease quality of life in people with HIV infection, to date, this association is not well corroborated in the published literature. This study demonstrates the significant impact of LD on patient-reported health status. The patient-assessed definition better describes the impact of severity of LD on health status compared to the physician-based one.

There are several ways changes in body image may affect patients' psychosocial function and quality of life. A recent paper found that 85% of patients with LD reported the changes have been noticed by family, friends, or work colleagues.²³ Disfigurement may cause stigma, erosion of self-esteem, decrease of desirability, attractiveness; it may influence social relations, and lead to anxiety and depression.¹ People experiencing LD report a drastic decrease of sexual activity.²⁴ LD may lead to forced disclosure of the diagnosis or increase the fear of adverse events related to antiretrovi-

TABLE 4C. CORRELATIONS AMONG CLINICAL PARAMETERS, AND SUBJECTIVE MEASURES AND LIPODYSTROPHY CASE DEFINITION (LD CD)

	<i>LD CD definition, mean (SD)</i>					<i>p</i>
	<i>0 = absent n = 48</i>	<i>Grade 1 n = 55</i>	<i>Grade 2 n = 29</i>	<i>Grade 3 n = 40</i>	<i>Grade 4 n = 10</i>	
Females (%)	11 (22.9)	34 (61.8)	8 (27.6)	11 (27.5)	6 (60.0)	<0.001
Age, years	42.9 (6.8)	45.0 (7.3)	44.3 (4.2)	48.2 (7.1)	45.3 (5.6)	0.009
IDU (%)	11 (22.9)	10 (18.2)	9 (31)	10 (25)	4 (40)	0.52
CDC Group C (%)	4 (8.7)	15 (27.8)	5 (17.2)	16 (44.4)	2 (22.8)	0.004
HCV+ serology (%)	12 (30.8)	12 (25.0)	12 (46.2)	14 (42.4)	4 (50.0)	0.25
CD4, μ L	530 (264)	576 (275)	601 (204)	461 (289)	545 (213)	0.21
HIV-RNA, log/mL	2.35 (1.20)	2.54 (1.13)	2.46 (1.16)	2.36 (1.17)	1.86 (0.32)	0.59
Waist-to-hip ratio	0.94 (0.07)	0.95 (0.07)	0.93 (0.05)	0.94 (0.06)	0.95 (0.09)	0.75
Body mass index, kg/m ²	23.9 (3.5)	24.4 (3.4)	22.7 (2.3)	21.8 (2.5)	22.2 (4.3)	0.001
VAT/SAT	0.82 (0.62)	0.83 (0.66)	3.3 (3.8)	2.8 (2.2)	4.4 (5.3)	<0.001
Limb fat, kg	2.85 (1.82)	2.76 (1.68)	1.43 (0.73)	1.25 (0.49)	1.15 (0.62)	<0.001
Ultrasound cheek, mm	7.0 (2.4)	7.3 (2.7)	6.7 (3.0)	6.6 (2.5)	5.1 (1.6)	0.24
VAS face	5.4 (2.7)	4.8 (2.4)	4.8 (2.8)	5.4 (2.3)	4.1 (3.0)	0.45
VAS body	4.9 (2.9)	4.4 (2.5)	4.7 (2.5)	4.8 (2.1)	5.2 (1.9)	0.94
ALDD7	3.5 (1.0)	3.7 (0.9)	3.4 (0.9)	3.3 (1.2)	3.8 (1.1)	0.45
ALDD8	71.9 (16.0)	66.1 (18.3)	71.1 (19.9)	72.8 (19.6)	61.2 (19.0)	0.18
Pain	77.8 (23.4)	70.7 (27.4)	78.2 (25.6)	78.0 (25.1)	74.4 (26.2)	0.55
Physical functioning	79.2 (23.4)	74.8 (27.0)	81.9 (21.4)	81.9 (22.1)	80.8 (19.3)	0.60
Role functioning	78.6 (29.6)	77.7 (27.5)	75.0 (36.6)	80.6 (26.2)	75.0 (23.6)	0.94
Social functioning	82.9 (26.1)	84.0 (26.8)	83.4 (23.9)	91.0 (18.1)	80.0 (21.1)	0.49
Mental health	60.1 (22.8)	58.8 (19.4)	66.7 (20.0)	61.6 (19.9)	56.4 (19.4)	0.48
Energy/Vitality	61.0 (21.8)	56.2 (20.5)	58.8 (23.2)	59.2 (19.0)	57.5 (24.7)	0.84
Health distress	81.4 (24.2)	75.7 (26.9)	79.3 (20.1)	79.0 (24.9)	71.0 (25.0)	0.68
Cognitive functioning	76.3 (23.1)	75.6 (22.6)	79.8 (21.9)	74.0 (24.0)	67.0 (24.5)	0.63
Current health perceptions	43.2 (23.8)	36.3 (20.9)	35.5 (20.4)	36.5 (19.3)	37.5 (24.6)	0.44
Quality of life	39.6 (19.2)	40.0 (20.7)	37.9 (23.7)	35.0 (16.8)	40.0 (12.9)	0.77
PHS	51.5 (9.5)	48.7 (9.4)	50.0 (9.3)	51.5 (7.8)	49.9 (8.7)	0.53
MHS	44.6 (8.3)	43.5 (6.8)	45.5 (5.8)	43.6 (7.9)	41.4 (8.6)	0.55

SD, standard deviation; IDU, injection drug use; CDC, Centers for Disease Control and Prevention; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; VAS, visual analogue scale; ALDD, Assessment of Body Change and Distress; PHS, Physical Health Summary score; MHS, Mental Health Summary score.

ral treatment²⁵⁻²⁷ and it can be a crucial determinant for cessation of treatment.^{6,7}

Results from the present study demonstrated that individuals with more severe LD had not only a worsen satisfaction with body image, but also a worse level of quality of life in almost all the investigated domains. Even the two HRQOL Summary Scores showed the same tendency, and effect size among patients at different LD degrees was considered "moderate"²³ revealing a significant difference among the strata of LD severity. These findings support a wider use in both routine care and research settings of both patient- and physician-based definition of LD to obtain a complete assessment of impact of LD on health status

Up to now, correlations between LD and quality of life have been obscured by the lack of specificity of the used instrument and by studies small sample size. No differences in quality of life were found between Spanish people with or without LD⁸ using a quality-of-life questionnaire not previously validated in patients with HIV infection. Even though the sample size was small, men scored lower on negative mood and homosexual men scored lower on psycho-

logical functioning. On a subsample of this study⁸ applying a different questionnaire, Blanch and coauthors⁹ found that changes in the breast, face, or legs were significantly associated with greater impairment of psychosocial functioning. In the multivariate analysis only changes in the breast remained significant. However, once again, authors did not use standardized questionnaires for measuring quality of life in HIV-infected people. Another recent paper¹¹ failed to demonstrate a correlation between a LD score, as assessed by a new specific instrument, and the domains of quality of life. Anyway, few items of quality of life were considered for the study. In a recently published paper,¹⁰ the total LD score was not found to be correlated with any domain of MOS-HIV Health Survey or HAT-QoL subscales except for physical function areas, while the LD score was strongly correlated with the patient-perceived body image score. Unfortunately the sample size of the study was too small (77 patients) to derive definitive conclusions. A recent analysis of factors correlated with lower quality of life in the HAART era in a large cohort²⁸ did not include LD as possible predictor of both physical and mental health. A dramatic association was

TABLE 5. SPEARMAN CORRELATION COEFFICIENTS OF THE PATIENT-BASED HOPS, PHYSICIAN-BASED HOPS, AND LDCD FOR THE DEFINITION OF SEVERITY OF LIPODYSTROPHY

	<i>Patient-based HOPS</i>	<i>Physician-based HOPS</i>	<i>LDCD</i>
Age	-0.02	0.132 ^a	0.266 ^a
CD4	0.0001	-0.020	0.010
HIV-RNA	0.072	0.063	0.001
WHR	0.102 ^b	0.172 ^a	-0.014
BMI	0.057	-0.081	-0.276 ^a
VAT/SAT	-0.200 ^a	-0.010	-0.514 ^a
Limb fat	0.113 ^b	0.145 ^a	-0.533 ^a
Ultrasound cheek	-0.007	-0.408 ^a	
VAS face	-0.073	-0.337 ^a	-0.007
VAS body	-0.188 ^a	-0.382 ^a	0.062
ALDD7	0.320 ^a	0.346 ^a	-0.50
ALDD8	-0.298 ^a	-0.276 ^a	0.015
Pain functioning	-0.161 ^a	-0.101 ^b	0.040
Physical functioning	-0.129 ^a	-0.158 ^a	0.073
Role functioning	-0.095	0.006	0.013
Social functioning	-0.097	-0.067	0.086
Mental health	-0.147 ^a	-0.142 ^a	0.038
Energy/vitality	-0.181 ^a	-0.095	-0.009
Health distress	-0.157 ^a	-0.197 ^a	-0.075
Cognitive functioning	-0.114 ^a	-0.086	-0.054
Current health perception	-0.143 ^a	-0.095	-0.072
Quality of life	-0.165 ^a	0.070	-0.090
Physical Health Summary	-0.163 ^a	-0.120 ^b	0.010
Mental Health Summary	-0.153 ^a	-0.163 ^a	-0.060
Patient-based HOPS	—	0.289 ^a	0.069
Physician-based HOPS	0.289 ^a	—	0.167 ^b
LDCD	0.069	0.167 ^b	—

^a $p < 0.01$.^b $p < 0.05$.

HOPS, HIV Outpatient Study; WHR, waist to hip ratio; BMI, body mass index; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; VAS, visual analogue scale; LDCD, lipodystrophy case definition.

found only between LD severity and dissatisfaction with body image.^{10,24}

Previous studies demonstrated lack of concordance between physicians and patients in symptoms estimation.²⁹ Indeed, although patient experiences the lipodystrophy syndrome, only features that providers recognize and report affect treatment decision in most clinical settings. Actually we demonstrated that patients and physicians were not to-

tally concordant on the definition of LD. According to the present study in more than 13% of cases physician found moderate to severe LD, when patient did not perceive it and in more than 6% a moderate to severe patient-estimated LD was not captured by physician. It should be taken into account that the physicians involved in the present study had several years of experience with the MC model, and are likely to be more skilled on the assessment and management of LD

TABLE 6. MULTIVARIABLE LINEAR REGRESSION ANALYSIS: VARIABLES INDEPENDENTLY RELATED TO LIPODYSTROPHY SCORE

	<i>Patient-assessed HOPS</i>		<i>Physician-assessed HOPS</i>	
	<i>B (95% CI)</i>	<i>p</i>	<i>B (95% CI)</i>	<i>p</i>
Female	2.95 (1.69, 4.20)	<0.001	1.42 (0.58, 2.24)	0.001
Age	0.09 (0.01, 0.17)	0.027	0.05 (0.003, 0.09)	0.039
BMI	0.17 (0.01, 0.32)	0.036	0.09 (-0.06, 0.25)	0.22
WHR	—	—	15.75 (10.38, 21.11)	<0.001
Limb fat	—	—	-0.04 (-0.001, 0.0004)	0.002
ABCD8	-0.13 (-0.17, -0.08)	<0.001	-0.04 (-0.07, -0.02)	<0.001
PHS	0.02 (-0.49, 0.09)	0.52	0.02 (-0.02, 0.06)	0.27
MHS	0.09 (-0.007, 0.19)	0.067	-0.03 (-0.09, 0.03)	0.34

HOPS, HIV Outpatient Study; BMI, body mass index; ALDD8, Body changes interference scale; PHS, Physical Health Summary; MHS, Mental Health Summary.

manifestations. Then, even though data on comparison between patient- and physician-assessment of LD are scarce in the literature, the discordance between patient and physician could be even greater in other populations.

Results from the present study suggest that women have a more severe LD and a mixed phenotype (both lipoatrophy and fat accumulation) more frequently than men. We cannot rule out that including fat accumulation in the definition for LD we may have led to a gender bias. Women have more body fat than men and fat accumulation may not be more than the background of HIV-negative women. But it may also be possible that women perceived their syndrome as more severe than men. Since it is well demonstrated that body image is markedly influenced by gender,³⁰ we believe that gender-focused counseling for LD at the beginning or at an antiretroviral regimen switching is warranted.

A limitation of the published literature and of the present study is the lack of consensus on the definition of LD. Several classifications have been proposed for use in both the research setting and in clinical practice.^{13–17} Each focuses on different aspects of LD (phenotype, severity), but all show limitations. Using both patient- and physician-based definition of LD according to the classification proposed by Lichtenstein et al.¹⁵ seems to capture a wider description of the syndrome; moreover it is easy to assess. Since groups are disproportionately different in size, in our analysis we did not discriminate between lipoatrophy ($n = 164$) and lipoaccumulation ($n = 31$). It is possible that the impact on quality of life may differ for the two phenotypes. Finally, results of our study may not be generalized to other HIV-infected populations even though mean values of health-related quality of life were similar to that from other HIV cohorts.¹⁰

In conclusion, the importance of lipodystrophy lies not only in actual changes in body shape and in the association with lipid abnormalities, but also in the impact of changes on the patient's quality of life. Negative impact on quality of life may also decrease motivation and adherence to therapy and even lead to discontinuation of the treatment. The best overall assessment of the impact of LD may require both patient- and physician-based measures. Better measurement will help us be most effective in implementing strategies to reduce the burden of LD.³¹

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