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Impact of lipoatrophy on quality of life in HIV patients receiving anti-retroviral therapy[1]

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Metabolic and morphological side-effects occur in HIV-infected individuals receiving anti-retroviral treatment (ART). Peripheral fat loss that occurs particularly in the face, limbs and/or buttocks is referred to as lipoatrophy and has been found to be highly stigmatizing and to adversely impact the health-related quality of life (HRQL). Consumer Health Sciences Survey data collected between November 2003 and January 2006 were utilized to evaluate the impact of lipoatrophy on the HRQL in HIV-infected individuals receiving ART. This was evaluated using analysis of variance with item scores and mental component summary (MCS) and physical component summary (PCS) scores from the Medical Outcomes Trust questionnaire, SF-8 as dependent variables and lipoatrophy as the independent variable controlling for baseline age, sex and ethnicity. Clinical meaningfulness (mean difference divided by population standard deviation, δ/σ) of differences between the groups with and without lipoatrophy was also evaluated. A cohort of 1124 subjects with at least six months of ART was selected based on the availability of data on whether or not lipoatrophy was present. Subjects were primarily male (80%), between the ages of 30 and 60 years (90%), Hispanic (37%) and about 25% each of African American and White. Overall, prevalence of lipoatrophy in this cohort of HIV patients was 18.9%. Statistically significant ($p < 0.001$) differences in quality of life (as measured by SF-8 individual item scores and MCS and PCS scores) were observed between the two groups. The differences between the groups in item and summary scores were clinically meaningful in the small to near medium range (0.28–0.43). HIV-infected patients already experience a considerable deficiency in HRQL compared to general population; this study demonstrates that lipoatrophy further enhances that negative impact on HRQL.

Keywords: HIV/AIDS; lipoatrophy; facial fat loss; health-related quality of life

Introduction

Metabolic and morphological side-effects occur in HIV-1 infected individuals receiving anti-retroviral treatment (ART) (Moyle, Brown, Lysakova, Barton, et al., 2006). Peripheral fat loss, particularly occurring in the face, limbs and/or buttocks, is also known as lipoatrophy. In a Swiss HIV cohort study, the prevalence of abnormal body fat distribution in HIV-treated individuals was assessed (Bernasconi et al., 2002) and fat loss in the face, leg(s), arm(s) and/or buttock(s) was reported by 28% of the study subjects. Santos, Felipe, Braga, Ramos, Lima, et al. (2005), from Brazil, interviewed a total of 457 patients in a university outpatient facility for the treatment of adults and adolescents with HIV/AIDS in the city of Sao Paulo, Brazil, between September and December 2001. They reported about 37% of self-perceived peripheral fat loss. In ACTG study 5142 (ACTG, 2007), where a protease inhibitor (PI)-sparing group, a non-nucleoside reverse transcriptase inhibitor (NNRTI)-sparing group and a nucleoside/nucleotide reverse transcriptase inhibitor (NRTI)-sparing group were compared, lipoatrophy was diagnosed by Dual-X-Ray Absorptiometry (DEXA) and greater than 20% loss of extremity fat was considered lipoatrophy. Incidence of lipoatrophy was 32% in the PI-sparing group, 17% in the NNRTI-sparing group and 9% in the NRTI-sparing group.

HIV-infected individuals with no report of lipoatrophy experience HRQL reductions commensurate with disease severity (Table 1) (Revicki, Sorenson, Wu, et al., 1998; Ware et al., 2001). Lipoatrophy results in noticeable weight loss in the extremities and reductions in physical and mental strength and vitality and can be highly stigmatizing (Bernasconi, Boubaker, Junghans, Flepp, Furrer, et al., 2002; Tien & Grunfeld, 2004). Patients with lipoatrophy face the potential of worsening fat redistribution with continued therapy or the possibility of worsening virologic control and disease progression with a change in therapy (Lenert & Feddersen, 2002). The combination of negative effects on physical and mental function and self-esteem may have a further adverse impact on HRQL, attitude towards treatments and

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Table 1. Comparison of SF-8 Norms for the general US population with those for HIV-infected individuals.

	Norm for US general population ($n = 7472$)*		Scores for HIV-infected individuals ($n = 871$)**
SF-8 item	Mean	SD***	Mean
Physical functioning (PF)	48.27	7.75	43.87
Role physical (RP)	48.59	7.83	43.48
Bodily pain (BP)	50.00	8.58	45.87
General health (GH)	49.44	7.45	46.75
Vitality (VT)	50.06	7.82	46.65
Social function (SF)	48.54	8.21	42.81
Role emotion (RE)	47.04	7.18	41.90
Mental health (MH)	48.97	8.77	41.40

Notes: *Data "Norm for US general population" are from the MOS scoring manual.
**Data for the HIV-infected individuals (with no lipoatrophy reported) are from CHS survey. *N* for the 8 items ranged from 859–871.
***Using this standard deviation (SD), the clinically meaningful difference between the groups (Cohen's effect size) for each item ranges from medium to large.

adherence and treatment effectiveness (Ammassari, Antinori, Cozzi-Lepri, Trotta, Nasti et al., 2002; Guaraldi, Murri, Orlando, Orlandi, Sterrantino et al., 2003; Power, Tate, McGill & Taylor, 2003; Reynolds, Neidig, Wu, Gifford & Holmes, 2006).

The objective of this data analysis was to evaluate the impact of lipoatrophy on the health-related quality of life in HIV-infected individuals receiving ART using the Consumer Health Sciences (CHS) Survey data collected between November 2003 and January 2006.

Methods

Survey database

Consumer Health Sciences survey data are marketed to any pharmaceutical company interested in purchasing the survey data. The pharmaceutical companies may or may not have a product in the market/development. Various pharmaceutical companies provide funding for this questionnaire, but by no means do CHS promote any products.

The questionnaire does not necessarily target any particular side-effect for the HIV cohort. The HIV-infected individuals are asked to check off whatever conditions they have, either as co-morbidities or as side-effects, from the exhaustive list on the survey. In addition, they are all administered the SF-8 Medical Outcomes Trust questionnaire to evaluate their health-related quality of life. Consumer Health Sciences recruited HIV patients from both community-based centers and clinics for uninsured persons and also using advertisement in newspapers and websites via Lightspeed Research panel of US customers. Recruiters contacted the centers and asked them to participate in the survey activities. They were then sent a pack of materials required for the project. The centers would be paid per completed questionnaire returned to CHS and respondents would also be paid an incentive for their participation. Multiple-source methodology removes the inherent bias of using too few sources and enhances the quality of the panel. The goal for CHS was to have a nationally representative view of the HIV/AIDS marketplace.

Given that the database for Wave 1 was not readily available in addition to the time limitations of the project, only Waves 2 and 3 were utilized.

The response data were managed by the CHS, Inc. and were licensed out for research purposes. Survey data were collected in two waves as follows:

- Wave 2: Survey packages were distributed to HIV-infected individuals in 257 community centers/clinics and interested HIV-infected individuals completed the surveys, which were returned to CHS: $n = 1024$; data collected from November 2003 through February 2005.
- Wave 3: In addition to the above method, in-person (self-administered) interviews and Internet interviews were used with HIV-infected individuals: $n = 1001$; data collected from October 2005 through January 2006 (Table 2).

The number of individuals to whom the survey was distributed in the community centers/clinics was not documented. However, it is apparent that the individuals' decision-making process to respond was highly unlikely to be influenced by the presence or absence of lipoatrophy. We are certain that this bias

Table 2. Data collected during the period from 11/03 to 01/06.

Source: Wave and site		Distributed/ attempted	Completed *n* (%)
Wave 2	Community Center/clinic	NA	1024 (NA)
Wave 3	Community Center/clinic	NA	313 (NA)
Wave 3	In-person interviews	261	237 (91)
Wave 3	Internet interviews	550	451 (82)
	Total	NA	2025

was avoided because: (1) the survey instrument contained an exhaustive list of items pertaining to HIV/AIDS (lipoatrophy was only one among them); and (2) the prevalence of lipoatrophy (18.9%) in our cohort is consistent with the range we found in the literature.

Eligibility criteria

Patients must have used an HIV prescription product for at least six months and have non-missing data for each of the covariates of interest (SF-8, lipoatrophy [occurrence of both weight loss and facial atrophy as reported by patients], age, gender and ethnicity). The total number of patients included in the analysis = 1124. The remaining 901 individuals who did not meet the criteria were excluded from the analysis.

Statistical analysis

The impact of lipoatrophy was evaluated using linear regression with: (1) each item score; (2) MCS; and (3) PCS scores from the Medical Outcomes Trust questionnaire, SF-8 as dependent variables. Lipoatrophy (based on the participant response of either 'yes' or 'no' to the survey question) was the primary independent variable controlling for baseline age, sex and ethnicity as covariates. All tests are two-sided with a significance level below 0.05.

Clinically meaningful effect measured as mean difference between the groups with and without lipoatrophy divided by population standard deviation (δ/σ) was also evaluated. This effect size is graded as small (≥ 0.2 and < 0.5), medium (≥ 0.5 and < 0.8) and large (≥ 0.8) (Cohen, 1988).

Results

A cohort of 1124 subjects met the selection criteria. Demographic data are shown in Table 3.

Overall, the prevalence of lipoatrophy was 18.9%. Statistically significant ($p < 0.001$) differences in HRQL (as measured by SF-8 individual item scores and MCS and CS scores) were observed between the two groups (Table 4). The differences between the groups in item and summary scores were clinically meaningful with Cohen's effect size in the small to near medium range (0.26 to 0.43).

Prevalence of lipoatrophy regardless of weight loss was 30.2% in this same cohort. In this secondary analysis, also, statistically significant ($p < 0.001$) differences in health-related quality of life (as measured by SF-8 individual item scores, MCS and PCS scores) were observed between the two groups. The clinically meaningful differences (Cohen's effect size) between the groups in item and summary scores ranged from 0.16–0.33 (data not shown).

Discussion

In this study, lipoatrophy was associated with a negative impact on the HRQL in HIV-infected individuals. Data used for this analysis were extracted from the CHS survey responses, which were voluntarily provided by a cohort of self-selected HIV-infected individuals. Whether the subjects that responded to surveys of this sort reflect the general population of HIV-infected individuals is not certain. Therefore, caution is essential in generalization of these data across diverse demographical groups. However, with regard to lipoatrophy, the prevalence of 18.9% is consistent with the prevalence of lipoatrophy found in other published data (ACTG 2007; Bernasconi, Boubaker, Junghans, Flepp, Furrer et al., 2002; Santos, Felipe, Braga, Ramos, Lima et al., 2005). Again, it should be noted that individual's self-perception was the sole support for the data. Structured research studies use objective evaluations to diagnose lipoatrophy and they vary in the criteria they use (for example, the ACTG study considered a patient to have lipoatrophy only if at least 20% of atrophy was demonstrated by DEXA (ACTG, 2007). Researchers have demonstrated that NRTI therapy is associated with mitochondrial DNA depletion and cell death, explaining the high end of incidence rate in the PI-sparing group of the ACTG study (Mauss, Corzillius, Wolf, Schwenk, Adam et al., 2002; Nolan, Hammond, Martin,

Table 3. Demographic characteristics of the study cohort of HIV-infected individuals.

Lipoatrophy and demographic variables	Overall	Lipoatrophy		*p*-value*
		Yes	No	
Self-report of lipoatrophy (*n*)	1124	212	912	
Age group		*n* = 212	*n* = 912	ns
20–29	4.9	7.6	4.3	
30–39	24.3	22.2	24.8	
40–49	43.6	43.9	43.5	
50–59	21.6	21.2	21.7	
60–69	4.3	3.3	4.5	
70 +	1.3	1.9	1.2	
Ethnicity		*n* = 204	*n* = 891	<0.0001
African American	28.1	16.7	30.8	
American Indian	2.9	8.8	1.6	
Asian	6.4	6.9	6.3	
Hispanic	37.6	36.3	37.9	
White	24.9	31.4	23.5	
Gender		*n* = 209	*n* = 900	ns
Female	21.3	19.6	21.7	
Male	78.7	80.4	78.3	
Employment status		*n* = 199	*n* = 839	ns
Full time	26.7	26.1	26.8	
Part time	9.8	8.5	10.1	
Homemaker	2.7	5.5	2	
Retired	4.9	3.5	5.2	
Unemployed	10.8	8.5	11.3	
Disabled	44.9	47.7	44.2	
No answer	0.2	0	0.2	

Notes: **p*-value based on Pearson Chi-square test for each demographic variable.

Taylor, Herrmann et al., 2003, Powderly, 2003; Sax & Gathe, 2005). In the ACTG-5142 study, subjects who received Efavirenz (EFV) in combination with NRTIs had significantly higher rates of lipoatrophy than subjects who received lopinavir/ritonavir in combination with NRTIs, not including the Tenofovir combinations (ACTG, 2007).

When patients report self-perceived fat loss in face, limbs and buttocks, they also report its negative impact on HRQL, particularly self-esteem, social

Table 4. Effect of lipoatrophy on SF-8. Summary scores and item scores.

SF-8 variables	Lipoatrophy				*p*-value	Diff	Total pop. SD	CMD*
	n	Yes	*n*	no				
Physical component summary (PCS)	190	40.58	832	45.17	<0.0001	4.585	10.626	0.431
Mental component summary (MCS)	190	37.83	832	41.54	0.0001	3.714	11.973	0.310
Daily activities (RE)	195	38.23	862	41.90	<0.0001	3.666	8.909	0.412
Emotional affect (MH)	198	38.56	866	41.40	0.0011	2.838	10.974	0.259
Energy (VT)	199	44.04	867	46.65	0.0004	2.612	9.205	0.284
General health (GH)	199	43.54	871	46.75	<0.0001	3.213	8.565	0.375
Pain (BP)	199	42.20	859	45.87	<0.0001	3.674	10.334	0.356
Physical problems (PF)	197	39.94	867	43.87	<0.0001	3.936	9.250	0.426
Social (SF)	198	38.63	861	42.81	<0.0001	4.172	9.948	0.419
Work (RP)	197	39.30	866	43.48	<0.0001	4.181	10.064	0.415

Notes: *CMD = Clinically meaningful differences. Patients with lipoatrophy had worse HRQL in both summary scores and in all eight individual questions, with the clinically meaningful differences ranging from 0.259–0.431 (small to medium)

contacts, sexuality and daily activities (Bernasconi, Boubaker, Junghans, Flepp, Furrer et al., 2002; Mauss, Corzillius, Wolf, Schwenk, Adam et al., 2002; Nolan, Hammond, Martin, Taylor, Herrmann et al., 2003; Powderly, 2003). The CHS data reflect similar findings that lipoatrophy contributes substantially to reductions in HRQL.

Conclusion

HIV-infected individuals experience a considerable reduction in health-related quality of life compared to the general population. The current analysis demonstrates that further significant reductions in HRQL occur in HIV-infected individuals who also report lipoatrophy.

Note

1. Presented at the 9th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV, Sydney, Australia, July 18–20, 2007

References

ACTG. (2007). *Metabolic outcomes of ACTG 5142: A prospective, randomized Phase III trial of NRTI-, PI- and NNRTI-sparing Regimens for initial treatment of HIV-1*. Presented at the 14th Conference on Retrivirus and Opportunistic Infections, February 25–28, Los Angeles, CA.

Ammassari, A., Antinori, A., Cozzi-Lepri, A., Trotta, M.P., Nasti, G., Ridolfo, A.L., et al. (2002). Relationship between HAART adherence and adipose tissue alterations. *Journal of Acquired Immune Deficiency Sundrome*, *31*(Suppl. 3), S140–S144.

Bernasconi, E., Boubaker, K., Junghans, C., Flepp, M., Furrer, H.J., Haensel, A., et al. (2002). Abnormalities of body fat distribution in HIV-infected persons treated with antiretroviral drugs: The Swiss HIV cohort study. *Journal Acquired Immune Deficiency Syndrome*, *31*, 50–55.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed) (pp. 20–27). Hillsdale, NJ: Lawrence Eribaum.

Guaraldi, G., Murri, R., Orlando, G., Orlandi, E., Sterrantino, G., Borderi, M., et al. (2003). Morphologic alterations in HIV-infected people with lipodystrophy are associated with good adherence to HAART. *HIV Clinical Trials*, *4*, 99–106.

Lenert, L.A., & Feddersen, M. (2002). Adverse effects of medications and trade-offs between length of life and quality of life in human immunodeficiency virus infection. *American Journal of Medicine*, *113*, 229–232.

Mauss, S., Corzillius, M., Wolf, E., Schwenk, A., Adam, A., Jaeger, H., et al. (for the DAGNÄ Lipantiretroviral therapy study group). (2002). Risk factors for the HIV-associated lipodystrophy syndrome in a closed cohort of patients after three years of antiretroviral treatment. *HIV Medicine, 3*, 49–55.

Moyle, G.J., Brown, S., Lysakova, L., & Barton, S.E. (2006). A randomized comparative trial of tenofovir DF or abacavir as replacement for a thymidine analogue in persons with lipoatrophy. *AIDS*, *20*, 2043–2050.

Nolan, D., Hammond, E., Martin, A., Taylor, L., Herrmann, S., McKinnon, E., et al. (2003). Mitochondrial DNA depletion and morphologic changes in adipocytes associated with nucleoside reverse transcriptase inhibitor therapy. *AIDS*, *17*, 1329–1338.

Powderly, W.G. (2003). Limitations in HIV therapies: Opportunities for improvement. *Journal of AIDS*, *33*, S7–S16.

Power, R., Tate, H.L., McGill, S.M., & Taylor, C. (2003). A qualitative study of the psychosocial implications of lipodystrohy syndrome on HIV-positive individuals. *Sexually Transmitted Infections*, *79*, 137–141.

Revicki, D.A., Sorensen, S., & Wu, A.W. (1998). Reliability and validity of physical and mental health summary scores from the Medical Outcomes Study HIV Health Survey. *Medical Care*, *36*(2), 126–137.

Reynolds, N.R., Neidig, J.L., Wu, A.W., Gifford, A.L., Holmes, W.C., et al. (2006). Balancing disfigurement and fear of disease progression: Patient perceptions of HIV body fat redistribution. *AIDS Care, 18*(7), 663–673.

Santos, C.P., Felipe, Y.X., Braga, P.E., Ramos, D., Lima, R.O., & Segurado, A.C. (2005). Self-perception of body changes in persons living with HIV/AIDS: Prevalence and associated factors. *AIDS*, *19* (Suppl. 4), S14–21.

Sax, P.E., & Gathe, J.C., Jr. (2005). Beyond efficacy: Impact of combination antiretroviral therapy on quality of life. *AIDS Patient Care and STDs*, *19*(9), 563–576.

Tien, P.C., & Grunfeld, C. (2004). What is HIV-associated lipodystrophy? Defining fat distribution changes in HIV infection. *Current Opinion in Infectious Diseases*, *17*, 27–32.

Ware, J.E., Jr., & Kisinski, M., Dewey, J.E. & Gandek, B. (2001). *How to score and interpret Single-Item Health Status Measures. A manual for users of the SF-8™ Health Survey*. Lincoln, RI: QualityMetric.