Article/Artigo

Lipodystrophy in HIV/AIDS patients with different levels of physical activity while on antiretroviral therapy

Lipodistrofia em pacientes com HIV/AIDS com diferentes hábitos de atividade física, em uso de terapia antirretroviral

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ABSTRACT

Introduction: Lipodystrophy is related to the use of highly active antiretroviral therapy (HAART) and can cause aesthetic stigma and increase the risk of developing cardiovascular diseases. Physical activity may be a valid alternative for the treatment and prevention of lipodystrophy. However, few studies address this issue. The objective of this study was to assess lipodystrophy related to highly active antiretroviral therapy in HIV/AIDS patients with different physical activity habits. **Methods:** The sample was composed of 42 HIV/AIDS patients taking HAART medication who were visiting the Counseling and Testing Center (CTC) in Presidente Prudente. The level of physical activity was obtained using the International Physical Activity Questionnaire (IPAQ); lipodystrophy was diagnosed using a self-report questionnaire that was administered to the patient and then followed up by medical confirmation. The percentage of trunk fat was estimated by dual X-Ray absorptiometry (DEXA). Information about sex, age, length of HAART treatment, CD4+ T lymphocyte count (CD4) and viral load was also collected. **Results:** A higher prevalence of lipodystrophy was observed in the sedentary group when compared to the physically active group, which indicates that physical activity may be a protective factor in relation to the occurrence of lipodystrophy. The group that had a higher CD4 had a higher proportion of lipodystrophy and a higher proportion of younger and physically active individuals. The patients with lipodystrophy had a higher percentage of trunk fat and were more sedentary than active individuals. **Conclusions:** A physically active lifestyle has a protective effect against the occurrence of lipodystrophy related to HAART.

Keywords: Body composition. Lipodystrophy. HIV/AIDS. Physical activity.

RESUMO

Introdução: A lipodistrofia relacionada ao uso de terapia antirretroviral (TARV) pode causar estigma estético e elevar o risco de doenças cardiovasculares. A atividade física pode ser uma alternativa válida para o tratamento e prevenção da lipodistrofia. Entretanto, poucos estudos tratam dessa temática. O objetivo deste estudo foi verificar a ocorrência de lipodistrofia relacionada ao uso de TARV em portadores de HIV/AIDS, com diferentes hábitos de atividades físicas. **Métodos:** A casuística foi formada por 42 portadores de HIV em uso de TARV, do Centro de Testagem e Aconselhamento de Presidente Prudente. Para obtenção do nível de atividade física aplicou-se o Questionário Internacional de Atividade Física (IPAQ); a lipodistrofia foi diagnosticada pelo autorrelato do paciente e a confirmação médica. O percentual de gordura de tronco foi estimado pela absortometria por raio-X de dupla energia (DEXA). Foram coletados também dados referentes a sexo, idade, tempo de uso de TARV, valores de CD4 e carga viral. **Resultados:** Verificou-se maior ocorrência de lipodistrofia no grupo sedentário quando comparado ao ativo, além de fator protetor da prática da atividade física em relação à ocorrência da lipodistrofia. O grupo com valores mais elevados de CD4 também apresentou maior proporção de sujeitos com lipodistrofia, além de maior proporção de ativos e de indivíduos com menor faixa etária. Os acometidos pela lipodistrofia apresentaram maiores valores de percentual de gordura de tronco, bem como, os sedentários em relação aos ativos. **Conclusões:** O estilo de vida fisicamente ativa resultou em efeito protetor para ocorrência da lipodistrofia relacionada ao uso da TARV.

Palavras-chaves: Composição corporal. Lipodistrofia. HIV/AIDS. Atividade física.

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INTRODUCTION

After 1996, with the introduction of highly active antiretroviral therapy (HAART), there was a significant increase in survival and improvement in the quality of life for HIV/AIDS patients[1-3]. With increased survival, the long-term effects of infection have become a focus of the scientific community. Therefore, we started to pay attention to the side effects of HAART. The focus of our research is lipodystrophy, which is characterized by the redistribution of body fat from the limbs, face, and buttocks (lipoatrophy) to the central region of the body (lipohypertrophy)[4].

Besides creating a new aesthetic stigma[5] for this population, these changes in the distribution of adipose tissue may also increase the risk of developing cardiovascular diseases and diabetes[6-8] due to the excessive accumulation of abdominal fat. Thus, it is important to increase our understanding of the health consequences of central obesity, also called lipodystrophy, in HIV/AIDS patients.

Considering that currently there is no cure for HIV infection and that HAART is essential for maintaining the survival of infected people, it is necessary to adopt strategies to prevent and treat lipodystrophy and other possible side effects.

Therefore, physical activity may be used as an alternative intervention. Physical therapy has been recommended by Mutimura et al[9], Robinson et al[10] Lindegaard et al[11], Terry et al[12] and Thoni et al[13] who found that physical activity can help reduce central fat and the metabolic consequences that result from its accumulation. Physical therapy can induce favorable changes in both lipids and glucose levels and reduce the risk of developing cardiovascular disease. Despite evidence regarding the benefits of systematic physical exercise, physical activity also requires significant energy expenditure. Studies on the relationship of physical activity and central fat accumulation are scarce. Specifically, we were only able to find studies by Florindo et al.[14],

Ramirez-Marrero et al.[15] and Domingo et al.[16]. The results of these studies suggest that there is an inverse relationship between high levels of physical activity and lower rates of central body fat; however, only one[16] study addresses lipodystrophy.

The objective of the present study was to assess the prevalence of lipodystrophy associated with the use of highly active antiretroviral therapy in HIV/AIDS patients with different physical activity habits.

METHODS

During a three months period, all patients that attended the Counseling and Testing Center (CTC) were invited to participate in this study. This time frame was chosen because, according to the clinical staff of the institution, patients are recommended to return at least every three months for monitoring of immunological markers.

The CTC had the medical records of 638 patients, of which 635 were treated during the data collection period. The lead researcher was on location during the hours of the scheduled appointments for all three months. All patients were invited to participate; however, only 101 (15.9%) agreed to participate and go to the UNESP Campus at *Presidente Prudente*. They received a card with the local date and time of their appointment, at which they filled out the physical activity questionnaire, provided a self-report of lipodystrophy and had their body composition estimated by Dual X-Ray Absorptiometry (DEXA). Only 55 patients participated in the data collection. The interviews and evaluations were performed in the *Centro de Estudos e Laboratório de Avaliação e Prescrição de Atividades Motoras* (CELAPAM) at the *Universidade Estadual Paulista* (UNESP), *Campus de Presidente Prudente*, State of *São Paulo*, Brazil. The lead investigator of the project, aided by two trained collaborators, performed all of the procedures.

The sample included HIV/AIDS patients of both sexes who were over 18 years of age and were being treated with HAART. Additionally, the participants were not prisoners, did not have pacemakers and were not pregnant.

Of the 55 patients who were evaluated, only 42 met the requirements for the study. Patients were excluded for the following reasons: under 18 years of age (n = 1); reported recent applications of a synthetic substance to shape the body (n = 1); did not complete the assessment because of malaise (n = 1); reported a false name at the time of data collection (these patients were precluded for ethical reasons and to prevent them from derailing efforts to collect information from their clinical record) (n = 1); and were not taking HAART (n = 9).

Patients were informed about the objectives of the study and the exams that would be performed. It was clearly explained that the data collected during the survey would be used strictly for scientific purposes and that the anonymity of the participants would be ensured.

Diagnosis of lipodystrophy

Because there is no consensus on how best to diagnose lipodystrophy, we decided to use self-reporting with clinical confirmation by the physician responsible for monitoring the patients according to the procedures of Mutimura et al.[9] and Thoni et al.[13]

Self-reports were collected through interviews. The lead researcher explained to the patient that lipodystrophy is related to antiretroviral therapy, explained to the patient how it manifests in the body and then asked the patient if, after starting HAART, the patient had experienced a considerable accumulation of fat in the central region of the body.

Physical activity evaluation

The level of physical activity was determined by the *International Physical Activity Questionnaire* (IPAQ) - short version[17]. The information was obtained by interview. The classification proposed by Sjostrom et al.[18] was used, and the subjects were classified as active (high and moderate level of physical activity) or sedentary (low level of physical activity)

Body composition assessment

Dual-energy X-ray absorptiometry (DEXA) (GE-LUNAR DPX-NT) was used to estimate the percentage of trunk fat.

The evaluation was performed according to the manufacturer's recommendation. The subject was positioned in the supine position and stood still while the measurement was taken. The results were transmitted to a computer connected to the device and then stored in an Excel spreadsheet for further statistical analysis.

Biochemical markers related to the disease and duration of HAART

The following data on additional variables were collected from clinical records of the patients in the CTC: CD4, viral load and the duration of HAART use. The date these tests not exceeded the three months of the other evaluations. The results from these tests are as follows: CD4 (cells/mm3): I) < 282, II) > 282, 282 was the mean value; viral load (copies/ml): I) < 50 = undetectable, II) > 50 detectable.

Statistical analyses

The *Kolmogorov Smirnov* test was used to analyze all continuous variables, and all the data were normally distributed.

To characterize the variables, we used descriptive statistics including the mean, standard deviation and distribution of absolute and relative frequencies.

The chi-square test was used to determine whether there was an association between the diagnosis of lipodystrophy and sex, age, physical activity level and duration of HAART. The same test was also used to analyze the association of CD4 and viral load with gender, age, physical activity level and lipodystrophy. The odds ratio test (OR) was used to determine the association between physical activity level and lipodystrophy.

The Student's t-test for independent samples was used to determine whether there were differences in the percentage of trunk fat in relation to lipodystrophy and physical activity level.

SPSS software, version 13.0 was used for the analyses. The adopted significance level was set to 5%.

Ethical considerations

The study was approved by the Ethics committee in Research at the *Universidade Estadual Paulista Campus de Presidente Prudente* (protocol number 35/2010) and followed the recommendations of the Declaration of Helsinki for human research. All participants signed a consent form.

RESULTS

Distribution of absolute and relative frequencies of the variables sex, age, activity level and lipodystrophy. Of the 42 patients, 54.8% were male. The age of the participants ranged from 31 to 59 years. A total of 45.2% of the individuals were in the sedentary group. Lipodystrophy was diagnosed in 42.9% of the studied cases (**Table 1**).

The distribution of absolute and relative frequencies (%) of the studied variables according to the presence or absence of lipodystrophy and related statistical tests. There were no statistically significant differences in lipodystrophy when compared to sex (p = 0.140) and age (p = 0.964). However, the sedentary patients had a higher occurrence of the analyzed outcome when compared to the active patients (p = 0.035) or patients that had been taking HAART longer (p = 0.029) compared to patients who had been using the drugs for a smaller time period **(Table 2)**.

The CD4 and viral loads and their relationship to the other variables that were measured. The CD4 and the viral load are significantly associated with age (p = 0.031), physical activity level (p = 0.013) and lipodystrophy (p = 0.029) **(Table 3)**.

The binary logistic regression results indicate that there is an association between higher levels of physical activity and a lower incidence of lipodystrophy. In the multivariate model, active individuals had a 79% (OR = 0.21) less chance of developing lipodystrophy when compared with sedentary individuals **(Table 4)**.

TABLE 1 - Distribution of absolute and relative frequencies of the variables sex, age, activity level and lipodystrophy.

	Frequency	
Variables	absolute	relative (%)
Sex		
male	23	54.8
female	19	45.2
Age (years)		
31-42	22	52.4
43-59	20	47.6
Physical activity level		
active	23	54.8
sedentary	19	45.2
Lipodystrophy		
yes	18	42.9
no	24	57.1

TABLE 2 - Distribution of absolute and relative frequencies according to the presence or absence of lipodystrophy.

	Lipodystrophy					
	yes AF (RF)		no AF (RF)			
Variables	n	%	n	%	χ^2	p
Sex						
male	7	30.4	16	69.6	2.180	0.140
female	11	57.9	8	42.1		
Age (years)						
31-42	10	45.5	12	54.5	0.002	0.964
43-59	8	40.0	12	60.0		
Physical activity						
active	6	26.1	17	73.9	4.423	0.035
sedentary	12	63.2	7	36.8		
HAART use (years)						
≤ 8	5	23.8	16	76.2	4.764	0.029
> 8	13	61.9	8	38.1		

Chi-square statistical test (p < 0.05), **AF:** absolute frequency, **RF:** relative frequency (%), **HAART:** highly active antiretroviral therapy.

TABLE 3 - Distribution of absolute and relative frequencies by the CD4 and viral load.

	CD4 (cells/mm³)				Viral load (copies/ml)			
	≤282	>282			<50	≥50		
Variable	AF (RF)	AF (RF)	χ^2	p	AF (RF)	AF (RF)	χ^2	p
Sex								
male	15 (65.2)	8 (34.8)	3.460	0.063	9 (39.1)	14 (60.9)	3.717	0.054
female	6(31.6)	13 (68.4)			14 (73.7)	5 (26.3)		
Age (years)								
31-42	7 (31.8)	15 (68.2)	4.677	0.031	11 (50)	11 (50.0)	0.116	0.734
43-59	14 (70.0)	6 (30)			12 (60)	8 (40.0)		
PA level								
active	7 (30.4)	16 (69.6)	6.151	0.013	12 (52.2)	11 (47.8)	0.004	0.953
sedentary	14 (73.7)	5 (26.3)			11 (57.9)	8 (42.1)		
Lipodystrophy								
yes	5 (27.8)	13 (72.2)	4.764	0.029	11 (61.1)	7(38.9)	0.162	0.687
no	16 (66.7)	8 (33.3)			12 (50.0)	12 (50.0)		

PA: physical activity, **AF:** absolute frequency, **RF:** relative frequency (%).

TABLE 4 - Distribution of absolute and relative frequencies according to physical activity level and the respective logistic regression test.

	Lipodystrophy positive diagnosis	Binary logistic regression		
Physical activity	AF (RF%)	OR	CI95%	P
Active	6 (26.1)	0.21	(0.06-0.77)	0.019
Sedentary	12 (63.2)	1.00	-	-

CI: confidence interval of 95%: confidence interval of 95%; **OR:** odds ratio, **AF:** absolute frequency, **RF:** relative frequency (%).

The group with lipodystrophy had a statistically higher percentage of trunk fat than the group that did not have the syndrome as well as the sedentary group compared to the active group (**Table 5**).

TABLE 5 - Mean and standard deviation of the percentage of trunk fat of individuals with and without lipodystrophy according to physical activity levels.

	Percentage of trunk fat		
	mean	SD	p
Lipodystrophy			
yes	36.4	±8.2	0.005
no	26.6	±12.1	
Physical activity level			
active	26.8	± 12.9	0.013
sedentary	35.6	±7.4	

Note: statistical test: Student's t-test for independent samples. **SD:** standard deviation.

DISCUSSION

In this study, lipodystrophy was observed in 42.9% of the cases. The prevalence of lipodystrophy in any of the three forms of manifestation (lipoatrophy, lipodystrophy or mixed) is not well established in the literature. The fact that there is no consensus on the diagnostic method and the differences in the studied populations may account for variation between studies[19-22]. In a review by Tien and Grunfeld[23], several studies on lipodystrophy were analyzed, which reported that the rates of lipodystrophy range from 30% to 62%.

Despite the lack of a consensus on how to diagnose lipodystrophy, we believe that the method employed in this study was the most appropriate because the patient's self report and the medical confirmation criteria are regarded as indispensable for the diagnosis of a temporal relationship between perceived changes in redistribution of body fat in conjunction with the use of HAART. Although this is a subjective method, it is one of the most widely used and recommended methods for the diagnosis of lipodistrofia[6,10,19,23] and is inexpensive.

In the present study, the group that had been on HAART longer had higher rates of lipodystrophy, which strengthens the temporal relationship of HAART use with the development of the syndrome[19,22].

Studies by Martinez et al.[24] and Lichtenstein et al.[25] reported that lipodystrophy was associated with higher levels of CD4. These results coincide with the literature, as we also found a higher proportion of individuals with lipodystrophy who also had a CD4 greater than 282 cells/mm^3.

A statistically significant association between the level of physical activity (active and sedentary) and the CD4 levels was also observed, where more active patients had higher CD4 levels. Some studies have reported that increased CD4 is associated with the level of physical activity[26,27]. However, although the data seem to support these findings, this research presents a limitation. It is not clear whether the investigated subjects had higher CD4 because they were active or if they were more active because they had higher levels of CD4. Santos et al.[28] found that patients, assessed by Bouchard questionnaire, that presented low levels of CD4+ lymphocytes, also had low physical domain scores, which suggests that individuals with weakened immune systems are more prone to physical inactivity.

The patients in the older group had lower levels of CD4. Similarly, Eidam et al.[29] also performed research on the lifestyles of people living with HIV and dichotomized the variable CD4+ lymphocyte count and age according to the values of central tendency and variability.

The present study found an association of lipodystrophy with physical activity level. The active subjects had a lower incidence of lipodystrophy as compared to the sedentary subjects. Additionally, it is noteworthy that the magnitude of this difference was significant; the physically active patients were 79% less likely to have lipodystrophy than the sedentary patients.

Some studies, such as those by Mutimura et al.[9], Robinson et al.[10], Lindegaard et al.[11], Terry et al.[12] and Thoni et al.,[13] have suggested that regular exercise is beneficial for people living with HIV/AIDS. They also reported a decrease in the excessive accumulation of trunk body fat and improvement in the metabolic variables related to it, which suggests that there is a valid alternative for the treatment of lipodystrophy.

Few studies[14-16] were found in the literature that investigated the relationship of general physical activity and the body composition of HIV/AIDS patients, and only one of them[16] addressed lipodystrophy. The findings from these few papers are consistent with the findings of this research, which indicates that there is an inverse relationship between physical activity and the concentration of central adiposity.

Florindo et al.[14] investigated the relationship between habitual physical activity and body fat in HIV/AIDS patients using antiretroviral therapy. To do so, they assessed the physical activity of patients using the Baecke questionnaire and measured the concentration of central subcutaneous fat (by skinfolds) and the waist/hip ratio. The data were adjusted for sex, age, education, caloric intake, body mass index, smoking, time of HIV diagnosis, CD4 and the duration of protease inhibitor use. They observed a significant negative correlation between physical activity and central fat and a significant negative correlation between physical activity and waist/hip ratio.

Ramirez-Marrero et al.[15] studied HIV/AIDS patients on antiretroviral therapy and observed that the active subjects, when compared to the sedentary subjects, showed lower total and central fat, which was estimated from the sum of skinfolds. Domingo et al.[16] found that 42.9% of patients without and 21.2% of patients with lipodystrophy were physically active. In the bivariate analysis to assess factors that influence lipodystrophy, the level of physical activity was found to be associated with lipodystrophy.

The previous studies also found a strong correlation between physical activity and body fat; however, only one study[16] specifically addressed lipodystrophy. Therefore, additional studies are required In addition, the present study also collected more data, which further demonstrated the protective effect of physical activity in this context.

It is well established in the literature that the amount of body fat, especially fat concentrated in the central part of the body, is a risk factor for cardiovascular and metabolic diseases. Thus, the evidence from the trunk fat percentage is much higher in the group with lipodystrophy compared to the group without (**Table 5**), which reinforces the concern about harm that may arise from lipodystrophy[6-8].

The highest percentage of fat in the sedentary compared to the active subjects also corroborates with previous findings regarding the protective factor of physical activity for the presence of lipodystrophy.

Although it well known in the scientific community that lipodystrophy is a side effect of HAART and can increase the cardiovascular risk of people living with HIV/AIDS, few patients are educated about it[5,30,31]. Therefore, we suggest that health agencies make a more concerted effort to educate patients about the consequences of lipodystrophy and treatment and prevention options.

In summary, the present results suggest that a physically active lifestyle has a protective effect against lipodystrophy associated with the use of HAART. In particular, patients can avoid lipohypertrophy and prevent cardiovascular complications.

We suggest that initiatives to promote physical activity for HIV/AIDS patients to prevent and treat lipodystrophy be established.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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