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Cardiovascular Risk in HIV/AIDS and Lipodystrophy Syndrome Patients

ORIGINAL

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Abstract

Background: The treatment of people living with AIDS, known a highly active antiretroviral therapy (HAART), has increased considerably, and the disease has therefore acquired chronic features. Several changes have been observed, especially in cardiovascular disease risk.

Objective: To assess cardiovascular risk in HIV/AIDS patients treated with HAART and compare this with Lipodystrophy Syndrome (LS) carriers.

Methods: This is a descriptive cross-sectional study. 192 patients were recruited from a lipodystrophy outpatient centre, using Framingham risk scores.

Results: After criteria inclusion/exclusion, the final sample consisted of 81 patients divided into two groups (HIV/AIDS -without lipodystrophy and HIV/LS- with lipodystrophy). The mean age of HIV/AIDS was 46.5 years, and of the HIV/LS patients was 52 years. In accordance with Framingham scores the cardiovascular risk in HIV/AIDS was 46.59% and 14.29% in HIV/LS.

Conclusion: The risk of cardiovascular disease over 10 years is significantly higher in patients with lipodystrophy syndrome.

Keywords
HIV; AIDS, Cardiovascular Disease, Highly Active; Antiretroviral Therapy.

Introduction

Highly active antiretroviral therapy -HAART- changed the course of HIV infection, improving quality of life and increasing the life expectancy of people infected by HIV [1]. An increase in metabolic disorders (dyLSipidaemia, insulin resistance) and phenotypic changes (lipodystrophy syndrome) was, however, noted in patients treated with HAART, in addition to an increased risk of cardiovascular disease (coronary artery disease and stroke) [2-10]. There is a lack of studies that assess the cardiovascular risk for patients with HIV/AIDS compared to HIV/AIDS with LS, which requires changes to HIV treatment.

In 1998 Carr and co-workers [11] described the association between HIV and lipodystrophy syndrome, marked by dorsocervical adipose tissue hypertrophy (also known as buffalo hump), increased abdominal circumference, increased breast size and facial lipoatrophy, buttocks and limbs, and a prominence of the superficial veins of extremities. The overall prevalence of at least one physical abnormality in patients with HIV/AIDS treated with HAART seems to be around 50%, although the reported rates are between 18-83% [10]. The differences in prevalence rates can be attributed to age or the type/duration of antiretroviral therapy [10].

The prevalence of hyperlipidaemia may vary from 28% to 80% in patients receiving HAART, including hypertriglyceridemia (40-80%) and elevated total cholesterol (10% -50%) [4-7, 12-14]. Data from the literature seems conflicting in respect to HAART as is the incidence of coronary heart disease (angina or myocardial infarction) in HIV/AIDS patients [12-17]. Although differences in study design, patient selection and statistical analyses might explain this disparity, it is consistent that longer exposure to HAART, especially the regimens currently used, can increase the risk of coronary syndromes. The *Data Collection on Adverse Events of Anti-HIV Drugs* study showed that the relative increase in myocardial infarction risk was 26% per year of exposure to HAART [14].

Many studies have shown that there is a high cardiovascular risk in patients with HIV/AIDS treated with HAART and lipodystrophy syndrome [18-21], however without considering the groups separately. This study thus aims to assess the cardiovascular risk in HIV/AIDS patients receiving HAART compared to HIV/AIDS associated with lipodystrophy syndrome people.

Methods

This is a descriptive cross-sectional study, conducted in the outpatient lipodystrophy department of a medical specialties centre at the Health Department of Sao Bernardo do Campo, São Paulo, Brazil. The research was conducted with the approval of the Committee of Ethics in Research of the Federal University of São Paulo under protocol number 231.977.

The study was carried out between March 2013 and February 2014. Patients were included if at the time of data collection, they had been receiving HAART for at least two months, had not used any medication that could affect lipid profile (diuretics, statins, fibrates, hormones, etc.) were not affected by co-infections (hepatitis and tuberculosis, etc.) and did not present any history of heart disease. All participants signed an informed consent form.

Of the total, 81 patients matched the inclusion criteria and were divided in two groups: HIV/AIDS (patients without lipodystrophy syndrome) and HIV/LS (patients with lipodystrophy syndrome). All patients then answered questionnaires about coronary heart disease, diabetes, smoking and medications that could affect the lipid profile. They were assessed via electrocardiogram, total cholesterol, low density lipoprotein (LDL-C), high density lipoprotein (HDL-C) and triglyceride levels, and CD4 + cell counts. Cardiovascular risk was calculated using the Framingham risk score [21].

Means and standard deviations were considered. All data was standardised and put into a database configured specifically for the present investigation.

The level of statistical significance was set at 0.05 (α = 5%), and the software *Estatístico para Ciências Sociais*, version 12.0 for Windows was used for all analyses.

Results

The study included 81 people with HIV/AIDS receiving HAART divided into two groups: 42 patients without lipodystrophy syndrome (HIV/AIDS) and 39 with LS (HIV/LS). The HIV/LS group had a higher median age of 52 years (25-75 percentile of 46-61 years), while the HIV/AIDS group had a median age of 46.5 years (25-75 percentile of 33-56 years). When the values between the two groups were compared, we found significance in the variables: age, weight, and dyastolic arterial pressure as shown in **Table 1**.

Table 2 shows the characterisation of the lipid profiles of patients; the HIV/LS group showed higher HDL levels with median 46.5 mg/dL (25-75 percentile of 41-53mg/dL) LDL median 111 mg/dl (percentile 25-75 for 96-138 mg / dl), total cholesterol median 212 mg/dL (25-75 percentile of 180-236 mg/dl) and low Body Mass Index with median 23.83 (25-75 percentile 22.37 to 25.03 kg/m^2).

The infection period as higher in the HIV/LS group with a median of 12 years (25-75 percentile of 6-16 years), and a median the time of using HAART of 15 years (25-75 percentile of 12-18 years). The viral load

Table 1. Characteristics of Infected Individuals by Group in a Lipodystrophy Outpatient Centre, 2014, by Group.

Variables	With Lipodystrophy Syndrome	Without Lipodystrophy Syndrome	p*
	Median (p.25-p.75)		
Age (year)	52 (46-61)	46.5 (33-56)	0.0008*
Weight (Kg)	66 (57-735)	68.5 (62-81)	0.0462*
Height (m)	1.7 (1.56-1.74)	1.655 (1.58-1.71)	0.9497
Heart Rate (bpm)	68 (64-76)	74.5 (68-79)	0.3160
Systolic Arterial Pressure (mmHg)	115 (110-125)	120 (110-130)	0.2908
Dyastolic Arterial Pressure (mmHg)	80 (75-80)	82.5 (80-90)	0.0145*

p.25-p.75, percentiles 25% and 75%, respectively; * Probabilistic value of Mann-Whitney test.

Table 2. Lipid Profile by Group of Infected Individuals Attending Lipodystrophy Outpatient Centre, 2014.

Variables	With Lipodystrophy Syndrome	Without Lipodystrophy Syndrome	p*
	Median (p.25-p.75)		
Body Mass Index	23.83 (22.37-25.03)	25.25 (22.76-28.47)	0.0398*
Abdominal Circumference (cm)	90 (86-94)	91 (86-101)	0.3415
Glucose (mg/dL)	91.5 (83-107)	86 (80-97)	0.1207
Total Cholesterol (mg/dL)	212 (180-236)	172 (149-204)	0.0004*
HDL (mg/dL)	46.5 (41-53)	43 (37-54)	0.3539
LDL (mg/dL)	111 (96-138)	90 (61-105)	0.0013*
Haemoglobin (g/dL)	14.6 (13.5-15.8)	13.9 (13.01-14.8)	0.1687
Triglycerides (mg/dL)	194 (130-268)	146.5 (108-213)	0.0402
Erythrocytes (min/mm^3)	4.1 (3.71-4.55)	4.15 (3.85-4.53)	0.6364

HDL – High-Density Lipoprotein; LDL – Low-Density Lipoprotein; p.25-p.75, percentiles 25% and 75%, respectively; * Probabilistic value of Mann-Whitney test.

in both groups was lower than 10 million copies as shown in **Table 3**.

According to the Framingham risk scores showed in **Table 4**, the cardiovascular risk was intermediate to high in 43.6% (n17) of patients in the HIV/LS group and 14.3% (n6) in another group of patients. **Table 2** shows that there is a strong association between LS and Framingham risk score with statistically significant data between the two groups (p = 0.012).

Table 3. Immunity Profile by Group Infected Individuals Served in Lipodystrophy Clinic of Medical Specialties Centre of the Municipality of São Bernardo do Campo, 2014.

Variables	With Lipodystrophy Syndrome	Without Lipodystrophy Syndrome	p*
	Median (p.25-p.75)		
Infection Period (years)	12 (6-16)	8 (7-16)	0.7368
HAART Time§ (years)	15 (12-18)	5 (3-23)	<0.001
CD4 (Cell/mm^3)	682.5 (457-912.5)	655 (526-909)	0.837
Viral Load (copies)	<10,000	<10,000	<0.001

§HAART - highly active antiretroviral therapy; p.25-p.75, percentiles 25% and 75%, respectively;
* Probabilistic value of Mann-Whitney test.

Table 4. Framingham Score Ratings for Cardiovascular Risk by Group of Infected Individuals Seen in the Lipodystrophy Clinic of Medical Specialties Centre of the Municipality of São Bernardo do Campo, 2014.

10-year risk for cardiovascular disease	With Lipodystrophy Syndrome	Without Lipodystrophy Syndrome
	n (%)	n (%)
Low (0-10%)	22 (56.4)	36(85.7)
Intermediate (10-20%)	12(30.8)	5(11.9)
High (> 20%)	5 (12.8)	1(2.4)
p*	0.012	

*Probabilistic value of Chi-Square test.

Discussion

The risk equations for cardiovascular diseases (CVD) were applied in different groups with different configurations such as people with HIV [15]. New findings about HIV treatment, such as highly active antiretroviral therapy (HAART), have resulted in an increase of life expectancy and quality of life for these people. So heart affections became more prevalent just like in the entire world population. [8, 12, 19].

According to Pereira et al. the association between lipodystrophy syndrome and HIV/AIDS is an important risk marker for the development of CVD [22]. The study aimed to assess the cardiovascular risk of a sample of people with HIV/AIDS, comparing two distinct groups with and without lipodystrophy syndrome association, and including clinical and laboratory elements such as the Framingham score for cardiovascular disease risk in 10 years.

The sample consisted of people of both genders, showing stable clinical signs, all on antiretroviral treatment. The lipodystrophy syndrome group were older than the other group showing a significant difference between the values of the groups **(Table 1)**. Elevated cardiovascular risk was also noted in the same group when associated with older age, however this risk is present even in healthy older people, possibly due to a combination of multiple predisposing risk factors and it being more difficult to treat them [23].

On the other hand other studies show that increased cardiovascular risk is more significant in younger HIV/AIDS patients using HAART (men under 34 and women under 44 years), and that this starts to decrease in older age groups. Antiretroviral therapy was associated with an increased risk of coronary heart disease specifically among patients younger than 33 years (relative risk 2.06; p <0.001) [15, 24].

We found significant values of total cholesterol, LDL and BMI **(Table 2)**. According to the literature,

the use of antiretroviral treatment intensifies the tendency for increased triglyceride levels and decreased HDL-cholesterol, which already happens in HIV/AIDS patients. Hajjar et al. noted an increase of 28% of total cholesterol and 96% of triglycerides [24]. The redistribution of body fat (lipodystrophy syndrome) is a significant side effect of antiretroviral therapy use [9, 14].

Regarding the use of antiretroviral drugs **(Table 3)**, the lipodystrophy syndrome group presented a 15 year mean of use while another group presented just 5 years, so lipodystrophy syndrome was older than in the other group and this could reflect prolonged HAART exposure.

These findings agreed with the literature: according to Carr, et al. the mean time to lipodystrophy syndrome onset was 4 years [25]; according to Diehl's research (Diehl et al.) the mean age of lipodystrophy syndrome patients was more than 45 years and the mean duration of HAART use was more than 8 years [26].

In this paper the mean time of HIV infection was 12 years for patients with LS and 8 years for the other group **(Table 3)**. All these findings suggest that lipodystrophy syndrome mostly appears after longer periods of exposure to HAART, however, we can not affirm that lipodystrophy, in any degree of intensity of its manifestations, be delayed in onset, because this study did not look for changes in patients at different stages or phases of the disease and treatment.

The data analysis of immunological and virologic variables **(Table 3)** found a balanced control population in both groups with CD4 cell count ≥ 350 cells/mm 3 and viral load <10.000 copies.

For Framingham risk score **(Table 4)**, we found that cardiovascular risk was intermediate to high in 43.6% of LS patients and 14.3% of patients without LS. As shown in **Table 2**, there was a strong association between lipodystrophy syndrome and Framingham score at higher risk for LS patients, when compared to the other group ($p = 0.012$).

In convergence we see in the study byFreitas et al. of 345 patients infected with HIV/AIDS with risk of 58.7% between intermediate to high Framingham score [27] the results were similar to those of our study: the Framingham score in lipodystrophy syndrome patients was twice as high as another group. Lipodystrophy syndrome patients had a significantly higher risk of coronary heart disease in 10 years according to Framingham risk score [27, 28].

According to Dahlof et al., updated epidemiological predictions show that the world is heading for a "vascular tsunami" of pandemic proportions. The number of people at high risk of CVD is increasing: recent studies suggest only 2-7% of population do not have any cardiovascular risk factor, while more than 70% of individuals have multiple risk factors [29].

Kannel et al. found that risk factors rarely appear individually, it is more common that the integrated action of these factors culminates in a significant increase in overall risk. While the presence of one risk factor could increase the risk of vascular events by four times, the presence of five factors determines an increase of 60 times the same risk [30].

According to Wilson et al. most cardiovascular events occur in people with a LSight increase in multiple cardiovascular risk factors instead of a larger increase in a single factor, so for many patients death is the first demonstration of CVD [31].

Our study demonstrated the importance of increased cardiovascular risk in this population according to the literature [22], suggesting that lipodystrophy syndrome associated with HIV/AIDS in HAART treatment could cause sudden cardiac events, with a significant increase in cardiovascular morbidity and mortality of these patients.

Conclusion

The risk of cardiovascular disease over 10 years is significantly higher in HIV/AIDS patients with lipodystrophy syndrome.

Conflict of Interest

The authors declare no conflicts of interest.

Contributions of Authors

All authors determined the design, interpreted the data and drafted the manuscript. All authors read and gave approval for the final version.

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References

1. Palella FJ, Delaney KM, Moorman AC et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. N Engl J Med. 1998; 338: 853-60.
2. Suit, D, Chaves AM. Ser feminina: uma permissão para a soropositividade?. Rev. bras. crescimento desenvolv. hum. 2005; 15: 82-90.
3. Kawagoe J. et al. As dificuldades de adaptação do convívio social de pacientes portadores de HIV/AIDS. Rev. bras. crescimento desenvolv. hum. 2012; 22: 93-97.
4. Dube M, Sattler F. Metabolic complications of antiretroviral therapies. AIDS Clin Care. 1998; 10: 41-4.
5. Sweet DE. Metabolic complications of antiretroviral therapy. Top HIV Med. 2005; 13 (2): 70-74.
6. Currier JS, Havlir DV. Complications of HIV disease and antiretroviral therapy. Top HIV Med. 2005; 13 (1): 16-23.
7. Stein J. Dyslipidemia in the era of HIV protease inhibitors. Prog Cardiovasc Dis. 2003; 45: 293-304.
8. Barbaro G. Metabolic and cardiovascular complications of highly active antiretroviral therapy for HIV infection. Curr HIV Res. 2006; 4: 79-85.
9. Barbaro G. Highly active antiretroviral therapy-associated metabolic syndrome: pathogenesis and cardiovascular risk. Am J Therapeutics. 2006; 13: 248-60.
10. Grinspoon S, Carr A. Cardiovascular risk and body fat abnormalities in HIV-infected adults. N Engl J Med. 2005; 352: 48-62.
11. Carr A, Samaras K, Burton S et al. A syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance in patients receiving HIV protease inhibitors. AIDS. 1998; 12: 51-58.
12. Hajjar LA, Calderaro D, Yu PC, Giuliano I et al. Cardiovascular manifestations in patients with the human immunodeficiency virus. Arq Bras Cardiol. 2005; 85 (5): 365-77.
13. D'Arminio MA, Sabin CA, Phillips A, et al. The changing incidence of AIDS events in patients receiving highly active antiretroviral therapy. Arch Intern Med. 2005;165(4):416-23.
14. Friis-Moller N, Weber R, Reiss P et al. For the D.A.D Study Group. Cardiovascular disease risk factors in HIV patients - associations with antiretroviral therapy: results from the DAD Study. AIDS. 2003; 17: 1179-93.
15. Holmberg SD, Moorman AC, Williamson JM et. al. and the HIV Outpatient Study (HOPS) Investigators. Protease inhibitors and cardiovascular outcomes in patients with HIV-1. Lancet. 2002; 360: 1747-8.
16. Mary-Krause M, Cotte L, Simon A, Partisani M, Costagliola D and the Clinical Epidemiology Group from the French Hospital Database. Increased risk for myocardial infarction with duration of protease inhibitor therapy in HIV-infected men. AIDS. 2003; 17: 2479-86.

17. Currier J, Taylor A, Boyd F et al. Coronary heart disease in HIV-infected individuals. J Acquir Immune Defic Syndr. 2003; 33: 506-12.
18. Wilson PW, Meigs JB, Sullivan L, et. al. Prediction of incident diabetes mellitus in middle-aged adults: the Framingham Offspring Study. Arch Intern Med. 2007;167:1068-74
19. Bruno R, Gazzaruso C, Sacchi P, et al. High prevalence of metabolic syndrome among HIV-infected patients: link with the cardiovascular risk. J Acquir Immune Defic Syndr. 2002; 31: 363-5.
20. Estrada V, Martinez-Larrad T, Gonzalez-Sanchez JL et al. Lipodystrophy and metabolic syndrome in HIV-infected patients treated with antiretroviral therapy. Metabolism. 2006; 55 (7): 940-5.
21. Dawber TR, Meadors GF, Moore FE Jr. Epidemiolofical approaches to heart disease: the Framingham Study. Am J Public Health. 1951; 41 (3): 279-81.
22. Pereira VX, Abreu LC, Valente VE et al. "The Lipodystrophy Syndrome as a Risk Marker for Cardiovascular Disease in Patients with HIV/AIDS Treated with HAART." International Archives of Medicine. 2015; 8: 1-12.
23. Mehta N, Reilly M. Atherosclerotic cardiovascular disease risk in the HAART-treated HIV-1 population. HIV Clin Trials, 2005; 6: 5-24.
24. Hajjar LA, Calderaro D, Yu PC, et al. Cardiovascular manifestations in patients infected with the human immunodeficiency virus. Arq Bras Cardiol, 2005; 85: 363-377
25. 25, Carr, A.; Cooper, D. A. Adverse effects of antiretroviral therapy. Lancet, 2000; 356: 1423-30.
26. Diehl LA, Dias JR, Paes AC, Thomazini MC, Garcia LR, Cinagawa E, Wiechmann SL, Carrilho AJ. Prevalence of HIV-associated lipodystrophy in Brazilian outpatients: relation with metabolic syndrome and cardiovascular risk factors. Arq Bras Endocrinol Metabol. 2008; 52: 658-67.
27. Freitas P. et. al. Impact of Lipodystrophy on the prevalence and components of metabolic syndrome in HIV-infected patients. BMC Infectious Diseases 2011; 11: 246-8.
28. Bergensen BM, Sandvik L, Brunn JN, Tonstad S. Elevated Framingham risk score in HIV-positive patients on highly active antiretroviral therapy: results from a Norwegian study of 721 subjects. Eur J Clin Microbiol Infect Dis. 2004; 23: 625-30.
29. Dahlöf, B. "Cardiovascular disease risk factors: epidemiology and risk assessment." Am J Cardiol. 2010; 105: 3-9.
30. Kannel, W. " Some lessons in cardiovascular epidemiology from Framingham." Am J Cardiol. 1976; 37: 269-282.
31. Wilson PW, K. W., Silbershatz H, D'Agostino RB. "Clustering of metabolic factors and coronary heart disease." Arch Intern Med. 1999; 159: 1104-1109.