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Lipodystrophy and the relationship with cardiovascular risk factors and metabolic syndrome in HIV-infected patients

Lipodistrofia e a relação com fatores de risco cardiovascular e síndrome metabólica em pacientes infectados pelo vírus HIV

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ABSTRACT

Introduction: HIV-positive patient lipodystrophy is the redistribution of body fat and may be accompanied by cardiovascular and metabolic disorders.

Objective: Was to investigate the prevalence of lipodystrophy in adults infected with HIV, as well as its relationship with cardiovascular risk factors and metabolic syndrome.

Methodology: Cross-sectional study with HIV-positive adult patients taking antiretroviral medication. Data were collected through a questionnaire and through medical records (viral RNA, CD4, blood glucose, LDL, HDL, triglycerides). In addition to anthropometry (waist circumference, body weight, height and BMI).

Results: 120 people studied among them (50.8%) had lipodystrophy, the highest prevalence of lipodystrophy (52.1%) occurred in males and the most widely used medication was the NRTI + PI (24,2%). The lipodystrophy was more frequent in patients with cardiovascular disease (68.4%), metabolic syndrome (59.3%) and those with increased waist circumference (55.1%). Significant differences ($p < 0.05$) among the analyzed subgroups (with or without lipodystrophy) occurred with triglycerides, LDL and glucose levels. Discussion: The use of HAART tends to improve the condition of immunity and is associated with the onset of lipodystrophy. This also associated with excess weight and fat accumulation predisposes to the development of metabolic syndrome.

Conclusion: the study contributed to direct the focus and attention profile of specialized services for HIV/AIDS.

KEY - WORDS

Cardiovascular disease; body fat, AIDS.

LIST OF ABBREVIATIONS

AIDS: Syndrome Acquired Immunodeficiency.

ART: Antiretroviral Therapy.

BMI: Body mass index.

HAART: Highly Active Antiretroviral Therapy.

HDL: High Density Lipoprotein.

HIV: Human immunodeficiency virus.

LDL: Low Density Lipoprotein.

MS: Metabolic Syndrome.

NCEP: National Cholesterol Education Program.

PI: Protease Inhibitors.

RNA: Ribonucleic acid.

SPSS: Statistical Package for Social Sciences.

WC: Waist circumference.

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INTRODUCTION

The Syndrome Acquired Immunodeficiency (AIDS) is characterized by a severe dysfunction of the immune system of the individual infected with the human immunodeficiency virus (HIV), which progression causes an appreciable destruction of CD4+ T lymphocytes and can be divided into three stages: acute infection, asymptomatic infection, symptomatic disease[1]. The breakthrough in chronic HIV infection may reflect the advancing prevalence of multiple metabolic and anthropometric abnormalities in the affected people, and thus, exposing HIV-positive patients to all risk factors for cardiovascular disease[2].

The latest HIV/AIDS Epidemiological Bulletin from 2014, from the Ministry of Health in Brazil, estimates that almost 734,000 people had HIV/AIDS in 2014, corresponding to a prevalence of 0.4%. The proportional distribution of cases of AIDS in Brazil by region shows a concentration of cases in the Southeast and South, corresponding to 54.4% and 20.0% of all identified cases from 1980 to June 2014; the Northeast account for 14.3% of cases, occupying the 3rd place. Over the past five years, Sergipe was the northeastern state with fewer cases of HIV reported in SINAN/SIM/SISCEL, with a total of 3,068 cases, and the capital Aracaju, follows the ranking in 24th place in AIDS case detection in 2013[3].

The natural history of the disease has been considerably modified by Antiretroviral Therapy (ART)[1], because the use of so-called Highly Active Antiretroviral Therapy (HAART) has resulted in an increased life expectancy of these patients. However, with the use of this medication some individuals began to show metabolic disorders such as dyslipidemia, insulin resistance, abnormal glucose, among others, and, the called, HIV lipodystrophy[4].

The lipodystrophy of the HIV positive patient or lipodystrophy syndrome is the redistribution of body fat and may be accompanied by metabolic and cardiovascular disorders[1,2]. The Ministry of Health reports that due to differences in diagnostic criteria, selection of the study population and duration of follow-up, there are several reports of lipodystrophy's prevalence, ranging from 8% to 84%, with an average of 42% in patients treated with diets containing PI (Protease Inhibitors). But there is no consensus in the literature, making it difficult to determine its actual prevalence, etiology and treatment. The diagnosis of HIV-associated lipodystrophy is based on the agreement between the complaints reported by the patient and the assessment made by the health team[5].

Metabolic Syndrome (MS) in HIV-infected individuals may be related to multifactorial disorder, as complex interactions between specific antiretroviral drugs, related factors to the virus and the host, sex, genetic predisposition and hormonal changes[6,7]. The knowledge of cardiovascular HIV manifestations points to the need to implement effective measures to reduce the occurrence of cardiovascular disease in this group, through a strict control of risk factors or the search for treatment with fewer side effects without compromising their efficiency[8].

There are few studies on the risk factors for cardiovascular disease and metabolic syndrome in the lipodystrophy syndrome in Brazil. Thus, the purpose of the study was to evaluate the prevalence of Lipodystrophy associated with HIV among infected Brazilian adults and its relationship to cardiovascular risk factors and Metabolic Syndrome (MS).

METHODOLOGY

Design and population

This is a cross-sectional study that evaluated patients, of both sexes, HIV/AIDS carriers, who receive care in a care home for people with AIDS located in Sergipe's capital. Inclusion criteria were age between 18 and 59 years, with positive serology for HIV and to use or not of antiretroviral therapy. Already exclusion criteria were adopted chronic use of glucocorticoids, be on pregnancy status and diagnosed mental illness.

The study followed the ethical principles established in the recommendations of the Declaration of Helsinki and the National Health Council set out in the Resolution nº 466/12, which regulates research involving human subjects, approved by the Research Ethics Committee in human beings of the Tiradentes University (Protocol n. 45299515.6.0000.5371).

Data collect

The anthropometry was realized with the measures of body weight, height and waist circumference (WC). Body mass was measured with subjects standing barefoot and in light clothing, by use of a portable electronic scale from the brand Filizola®, accuracy in 100g, capacity of 150kg, and the height was obtained by a portable stadiometer from the brand Avanutri®, accuracy of 1mm and capacity of 2.0m, barefoot and in orthostatic position. Body weight and height were used to calculate body mass index (BMI), which has been classified in accordance with the recommendations of the Ministry of Health[9] for adults. The WC was measured with inelastic tape at the midpoint between the last rib and the iliac crest and classified according with the WHO[10].

The second phase of data collection took place at the Medical Specialties Center of Aracaju which occurred collecting information from patient records. Clinical data (time of diagnosis, use of medication, the medication type and existing diseases) were collected by a questionnaire applied and checked in the medical records. The diagnosis of lipodystrophy was obtained by clinical evaluation (accumulation of abdominal fat, breast or cervical dorsal region and loss of sub-

cutaneous fat of the limbs, face and buttocks) and confirmation in the analyzed patient records.

We collected the following data: Viral RNA, CD4+ (flow cytometry), blood glucose, LDL, HDL, triglycerides, considering the tests on the same evaluation period. Only tests performed in the maximum interval of three months preceding the data collection were considered.

In biochemical evaluation, were considered as hyperglycemia, blood glucose levels >100[11]. Lipid levels were classified according to specific Brazilian guideline[12]. The viral load was classified according to the risk of progression or worsening of the disease: low (<10,000 RNA copies/ml), moderate (10.000 to 100.000 RNA copies/ml) and high (>100,000 copies of RNA/ml). The values of CD4+ T cell counts were classified according to the likelihood of the patient developing the opportunistic diseases in: low (>500 cell units/mm^3), moderate (200 to 500 units authorities cell/mm^3) and high (< 200 cell units/mm^3)[13].

The possible diagnosis of metabolic syndrome was held by the presence of three or more of this data changed: abdominal obesity by waist circumference (men > 90cm, women >80cm), triglycerides ≥150 mg/dL, HDL cholesterol (men <40 mg/dL and women <50 mg/dL), arterial blood pressure ≥130mmHg or ≥85mmHg, fasting glucose ≥100 mg/dL according to the National Cholesterol Education Program NCEP III consensus updated by the American Heart Association[14].

Statistical analysis

The data was analyzed descriptively through absolute frequencies and percentages for categorical variables and statistical measures: Average and standard deviation for numerical variables and analyzed inferentially through statistical tests: Chi-square test or Fisher's exact when condition to use the Chi-square test was not checked in the categorical variables and Student t-test with equal variances or Student t-test with unequal variances to compare the averages of numerical variables.

Verification of the data normality hypothesis was through the Shapiro-Wilk test and verification of variances equality hypothesis was through F Levene test. The margin of error used in the statistical tests was 5.0%. Data were entered in the Excel spreadsheet and the statistical program used to obtain the statistical calculations was SPSS (Statistical Package for Social Sciences) in version 21.

RESULTS

In Tables 1 to 4 are presented the results of the variables analyzed in the study for the total group and according to the presence or absence of lipodystrophy. The sample consisted of 120 patients, about half of patients (50.8%) had lipodystrophy and most (60.8%) were male. There was no significant difference (p>0.05) among those with lipodystrophy or not for any of the variables. Data presented in Table 1.

Table 1. Socio demographics assessment of individuals with HIV/AIDS research participants and their correlation with lipodystrophy.

Variable	Total group	Lipodystrophy		
		Yes	No	P value
Age: Average ± SD	43.11 ± 8.06	43.77 ± 7.52	42.42 ± 8.60	$p^1 = 0.363$
Age range: n (%)				
26 to 39 years	45 (37.5)	20 (44.4)	25 (55.6)	$p^2 = 0.553$
40 to 49 years	49 (40.8)	27 (55.1)	22 (44.9)	
50 to 59 years	26 (21.7)	14 (53.8)	12 (46.2)	
TOTAL	120 (100.0)	61 (50.8)	59 (49.2)	
Genre: n (%)				
Male	73 (60.8)	38 (52.1)	35 (47.9)	$p^2 = 0.739$
Female	47 (39.2)	23 (48.9)	24 (51.1)	
TOTAL	120 (100.0)	61 (50.8)	59 (49.2)	

1: Through the Student t-test with equal variances.
2: Through Pearson's chi-square test.
3: Through Fisher's exact test.

In relation to the clinical data contained in Table 2, it is emphasized that: in the whole group the highest percentage (40.0%) corresponded to patients who had more than 10 years of the discovery of the disease and the lowest (28.3%) to the ones who had 5 to 10 years; the most frequent types of ART were NRTI + PI (24.2%), NRTI + NNRTI (16.7%), 2INTR + NNRTI (15.8%), 2INTR + 2PI (15.0%). Just over half (52.5%) had 5 or more years in medication use; vascular diseases were identified in 19 (15.8%) people, which of these, 13 people (68.4%) had lipodystrophy and (26.7%) were diagnosed with metabolic syndromes. No significant differences were recorded ($p>0.05$) among those who had or not lipodystrophy in any of the variables analyzed in the table.

The results contained in Table 3 no significant differences were recorded between those with and those without lipodystrophy for any of the variables, but it is emphasized that the average body mass, BMI and WC were correspondingly higher in the group of those who had than in those who had not lipodystrophy. Regarding the ratings in the whole group (Table 3) that: 35.0% were overweight; the percentage of patients with risk of CVD by WC was 40.8%.

From the results of biochemical shown in Table 4, was noted that, in the total group, most (85.0%) was classified as low risk according to the quantification of viral RNA, more than half (56.6%) was classified as low risk by quantification of CD4+ T cells, when compared to triglycerides (TG). With significant differences ($p <0.05$) among the analyzed subgroups (with or without lipodystrophy) in numerical variables: triglycerides, LDL and glucose levels, and the three variables mentioned in particular the average that was proportionally higher in those who they had no lipodystrophy.

DISCUSSION

This study showed predominant age between 40-49 years (40.8%), not reflecting the current trend of HIV infection in Brazil, where there is a predominance of cases of this infection among persons aged 25-39 years in both sexes[3]. Furthermore, the increase in the number of individuals living with HIV over 50 years of age is justified both by the appearance of HAART, which is extending the life expectancy of those individuals as well as by the detection of new cases of infection with in the elderly population[15].

In agreement with data found in several studies, there was a predominance of males (60.8%). In 1989, the sex ratio was six cases of AIDS in men for each case among women, while in 2009 this ratio reached 1,6 cases in males for each female. From 2009, it is observed a reduction in AIDS cases in women and increase in cases in men, reflecting on the grounds of sex, which passed to be 18 cases of AIDS in men for every 10 cases in women in 2013[3]. This greater exposure of the male population to HIV due, probably, to sociocultural factors and the expected performance of the male role[16].

According to the disease discovery time the highest percentage, of 48 persons (40%), consisted of patients who had more than 10 years diagnosed with HIV infection, similar to data found on the study of Ponte[17], where it was observed that 43.3% also showed more than 10 years of diagnosis being the most prevalent results.

Among the components of HAART, protease inhibitors and reverse transcriptase inhibitors have been implicated as the cause of HIV-associated lipodystrophy[16], which can be explained by the fact that they are part of the first line of this class of drugs to ARV treatment[17]. In this study we were diagnosed with lipodystrophy 61 people, where 29 of them were using the combination NRTI + PI reinforcing the statements contained in comparative studies[2,4], where the presence of PI is related to the greater number of lipodystrophic patients.

The frequency of lipodystrophy in this study was (50.8%), being compatible with many studies, where the prevalence ranges from 18 to 83%[1,4,18]. In a systematic review of Brazilian studies of the prevalence of lipodystrophy in individuals living with HIV wheigted average resulted in 53.5%. The great variability between the observed prevalence can be attributed to the use of different diagnostic methods and the lack of consensus on the characterization of cases of lipodystrophy, as well as the heterogeneity of the populations studied[16]. There are reports in the literature that women have 2.5 times higher risk of developing HIV-associated lipodystrophy[2], yet in some studies, the male has great predominance[19,20], strengthening what was found in this study.

It was observed that the vast majority of participants showed $CD4^+$ lymphocyte values above 500 cells/mm^3 (56.6%) and the viral load with undetectable levels (85%), these findings demonstrated infection control, highlighting the benefits of ART in the immune profile of this population[18]. In the study of Justina[15] and Diehl et al.[18] it was not statistically different between the levels of CD4+ T lymphocytes and viral load with the presence of lipodystrophy in patients with HIV, controversial data were reported in the state of Alencastro et al.[21] which found an association between these factors. The use of HAART tends to improve the immunity condition and is associated with the onset of lipodystrophy. While individuals who do not use ART lipodystrophy may result from the deleterious impacts of HIV infection itself[16].

According to a study of Ladeira & Silva[22], formerly the implementation of antiretroviral therapy subjects were affected by undernourishment, but lately this situation has changed. In this research the majority of patients were eutrophic by BMI, the prevalence of lipodystrophy occurred in greater quantities in normal-weight patients. Comparing car-

Table 2. Description of the time of discovery of the disease, treatment and comorbidity of people with HIV/AIDS participants of the survey and its correlation with lipodystrophy.

Variable	Total group	Lipodystrophy		
		Yes	No	P value
TOTAL	120 (100.0)	61 (50.8)	59 (49.2)	
Discovery of the disease: N (%)				
Less than 5 years	38 (31.7)	18 (47.4)	20 (52.6)	p[1] = 0.817
5 to 10 years	34 (28.3)	17 (50.0)	17 (50.0)	
Over 10 years	48 (40.0)	26 (54.2)	22 (45.8)	
TARV1 Type: N (%)				
2INTR	8 (6.7)	5 (62.5)	3 (37.5)	p[2] = 0.816
2INTR + 2PI	18 (15.0)	9 (50.0)	9 (50.0)	
2INTR + 3PI	1 (0.8)	1 (100.0)	-	
2INTR + NNRTI	19 (15.8)	10 (52.6)	9 (47.4)	
2INTR + PI	13 (10.8)	8 (61.5)	5 (38.5)	
2INTR + PI + NNRTI	1 (0.8)	-	1 (100.0)	
2PI	1 (0.8)	-	1 (100.0)	
3INTR + NNRTI	1 (0.8)	-	1 (100.0)	
3INTR + PI	1 (0.8)	-	1 (100.0)	
NRTIs + 2PI	2 (1.7)	2 (100.0)	-	
NRTIs + NNRTI + 2PI	1 (0.8)	-	1 (100.0)	
NRTIs + 3PI	1 (0.8)	1 (100.0)	-	
NRTIs + NNRTI	20 (16.7)	9 (45.0)	11 (55.0)	
NRTIs + PI	29 (24.2)	15 (51.7)	14 (48.3)	
NRTIs + PI + NNRTI	4 (3.3)	1 (25.0)	3 (75.0)	
NRTIs	8 (6.7)	5 (62.5)	3 (37.5)	p[2] = 0.269
PI	1 (0.8)	-	1 (100.0)	
Comorbidities: n (%)[3]				
Hypercholesterolemia	23 (19.2)	15 (65.2)	8 (34.8)	p[1] = 0.125
HAS	19 (15.8)	8 (42.1)	11 (57.9)	p[1] = 0.407
Tuberculosis	19 (15.8)	11 (57.9)	8 (42.1)	p[1] = 0.502
Pneumonia	19 (19.2)	13 (68.4)	6 (31.6)	p[1] = 0.095
DM	7 (5.8)	3 (42.9)	4 (57.1)	p[2] = 0.715
Esophagitis	2 (1.7)	-	2 (100.0)	p[2] = 0.240
Another	33 (27.5)	18 (54.5)	15 (45.5)	p[1] = 0.616
None	41 (34.2)	19 (46.3)	22 (53.7)	p[1] = 0.478
Medication time: n (%)				
Less than 5 years	57 (47.5)	26 (45.6)	31 (54.4)	p[1] = 0.277
5+ years	63 (52.5)	35 (55.6)	28 (44.4)	
Metabolic syndrome: n (%)				
Yes	32 (26.7)	19 (59.3)	13 (40.7)	p[1] = 0, 259
No	88 (73.3)	42 (47.7)	46 (52.3)	

1: Through Pearson's chi-square test.
2: Through the Fisher's exact test.
3: Considering that a patient has more than one comorbidity, it is registered the basis for the calculation of percentages and not the total.

Table 3. Assessment of anthropometric data of individuals with HIV/AIDS and its association with lipodystrophy.

Variable	Total group	Lipodystrophy		
		Yes	No	P value
Weight:Average ± SD	67.27 ± 13.17	69.27 ± 13.18	65.19 ± 12.96	p^1 = 0, 090
Height: Average ± SD	1.64 ± 0, 09	1.65 ± 0.08	1.63 ± 0.09	p^1 = 0, 093
BMI: Average ± SD	24.90 ± 4.22	25.33 ± 4.49	24.46 ± 3.91	p^1 = 0, 260
BMI classified: n (%)				
Malnutrition	3 (2.5)	2 (66.7)	1 (33.3)	p^2 = 0, 487
Eutrophic	61 (50.8)	27 (44.3)	34 (55.7)	
Overweight	42 (35.0)	23 (54.8)	19 (45.2)	
Obesity	14 (11.7)	9 (64.3)	5 (35.7)	
TOTAL	120 (100.0)	61 (50.8)	59 (49.2)	
WC: Average ± SD	85.85 ± 11.94	86.58 ± 12.19	85.09 ± 11.74	p^1 = 0, 497
WC rating: n (%)				
Suitable	71 (59.2)	34 (47.9)	37 (52.1)	p^3 = 0, 437
CVD Risk	49 (40.8)	27 (55.1)	22 (44.9)	
TOTAL	120 (100.0)	61 (50.8)	59 (49.2)	

1: Through the Student t-test with equal variances.
2: Through the Fisher's exact test.
3: Through Pearson's chi-square test.

riers and noncarriers of lipodystrophy, there was a higher frequency increased waist in lipodystrophic[16], in this study the changes of the WC were 40.8%, of which 55.1% had lipodystrophy thus presenting a higher prevalence; the waist circumference measurements identifying people with androgenic obesity, a fact associated with a higher risk of chronic heart disease[21].

These results may also be related to the fact that 59.2% of respondents in this survey are sedentary, resembling other researchers where results ranging from 45.2% to 70%[15,19,22,23]. Besides this, other studies also have demonstrated the presence of excess weight in this population, worrying data, once that obesity itself has a number of social and psychological disorders complicating the health status of patients living with HIV. The use of HAART associated with excess weight and fat accumulation predisposes to the development of metabolic syndrome in these patients[24].

The Metabolic Syndrome (MS) in this study was identified in 32 patients (26,7%), of which 19 were diagnosed with lipodystrophy. Faced with the facts, lipodystrophy appears to be a risk factor for HIV-positive patients in this unit with a diagnosis of MS. In Brazil, there are few published studies on the subject, Silva et al.[20] evaluated HIV-infected patients in São Paulo-SP, and found a prevalence of 13% of MS in patients using HAART and 12% among virgin of treatment patients. Diehl et al.[18] found a prevalence of 36% of MS in HIV-infected patients in Londrina, while Troian et al.[25] found 38.2% in HIV-infected patients seen at Santa Maria-RS.

Several evidences show that there is increase in metabolic disorders in HIV-infected patients, especially those using ART. But there are little information available in the literature on the contribution of modifiable cardiovascular risk factors among individuals infected with HIV treated in

Table 4. Evaluation of laboratory data of individuals with HIV/AIDS and its association with lipodystrophy.

Variable	Total group	Lipodystrophy		
		Yes	No	P value
Viral RNA: N (%)				
Low risk	102 (85.0)	49 (48.0)	53 (52.0)	$p^1 = 0.341$
Moderate risk	14 (11.7)	9 (64.3)	5 (35.7)	
High risk	4 (3.3)	3 (75.0)	1 (25.0)	
TOTAL	120 (100.0)	61 (50.8)	59 (49.2)	
CD4+ cells: n (%)				
Low risk	6 4 (6 5, 6)	32 (50.0)	32 (50.0)	$p^1 = 1.000$
Moderate risk	42 (37.2)	21 (50.0)	21 (50.0)	
High risk	7 (6: 2)	4 (57.1)	3 (42.9)	
TOTAL	113 (100.0)	57 (50.4)	56 (49.6)	
TG: Average ± SD	159.03 ± 115.91	133.40 ± 78.98	186.11 ± 140.90	$p^3 = 0, 017$*
TOTAL	109 (100.0)	56 (51.4)	53 (48.6)	
HDL: Average ± SD	46.39 ± 14.54	47.89 ± 16.10	44.89 ± 12.76	$p^2 = 0, 273$
Inappropriate n (%)	57 (50.0)	26 (45.6)	31 (54.4)	$p^4 = 0.349$
Suitable n (%)	57 (50.0)	31 (54.4)	26 (45.6)	
TOTAL	114 (100.0)	57 (50.0)	57 (50.0)	
LDL: Average ± SD	102.90 ± 32.63	96.35 ± 34.42	110.09 ± 29.20	$p^2 = 0,029$*
Great n (%)	52 (48.6)	32 (61.5)	20 (38.5)	$p^4 = 0.297$
Desirable n (%)	33 (30.8)	14 (42.4)	19 (57.6)	
Neighboring n (%)	17 (15.9)	8 (47.1)	9 (52.9)	
High / Very high n (%)	5 (4.7)	2 (40.0)	3 (60.0)	
TOTAL	107 (100.0)	56 (52.3)	51 (47.7)	
Glucose: Average ± SD	83.86 ± 20.88	72.76 ± 5.07	94.76 ± 24.55	$p^3 <0, 001$*
TOTAL	109 (100.0)	56 (51.4)	53 (48.6)	

*: Significant difference at the level of 5.0%.
1: Through the Fisher's exact test.
2: Through the Student t-test with equal variances.
3: Through the Student t-test with equal variances des.
4: Through Pearson's chi-square test.

Brazil. The important data is that the 19 patients diagnosed with cardiovascular disease, 13 of them had lipodystrophy (68.4%).

Hypertriglyceridemia is the most common lipid abnormality associated with HIV infection, and it may occur not aggregate or the hypercholesterolemia, especially in patients with evidence of lipodystrophy. This fact was observed in the study of Silva et al.[19], where 43.0% of patients had hypercholesterolemia, especially among women, however, the hypertriglyceridemia was most striking, being significantly associated with male gender ($p<0.001$), similar data to those found by Burgos et al.[26].

CONCLUSION

The scarcity of data in the literature limits us to make statements, but this study opens doors to new research and broadens the knowledge of the subject by clarifying and reinforcing some statements from previous studies. Being able to help direct the focus and attention profile of specialized services for HIV/AIDS. Further research is necessary to clarify the role they can perform metabolic complications.

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