

## Non linear analysis of heart rate variability in HIV/AIDS infections

Análise não linear da variabilidade da frequência cardíaca em infecções por HIV/AIDS

Análisis no lineal de la variabilidad de la frecuencia cardíaca en infecciones por VIH/SIDA

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### Abstract

The availability of Antiretroviral Therapy (ART) resulted in a drastic reduction of morbidity and mortality associated with the human immunodeficiency virus (HIV). However, the therapy has a series of adverse effects, including autonomic dysfunction. The analysis of HRV allows the evaluation of the sympathetic and parasympathetic involvement in the cardiac neuromodulation. Given the above, the objectives were: to verify whether HIV infections produce changes in cardiac autonomic modulation; to identify whether the cardiac autonomic modulation of the HIV-infected population is sensitive to respiratory sinus arrhythmia (RSA); and to investigate whether time to diagnosis of HIV infection influences HRV. A total of 49 individuals with HIV/AIDS and 21 healthy individuals were assessed. HRV measurements were taken for 20 minutes in the supine position, using the heart rate monitor Polar RS810CX, followed by the RSA maneuver. In both conditions, the RR intervals, typical of HRV, were analyzed by linear and nonlinear indices. Only two nonlinear indices, i.e., %REC and Shannon Entropy, showed statistically significant difference ( $p=0.004$ ), when comparing both HIV/AIDS and control groups, indicating reduced HRV in the HIV/AIDS group. It is suggested that the RSA maneuver, in turn, improved the autonomic modulation, because the reduction of %REC after the maneuver indicates increase in the parasympathetic modulation. In this way, it is concluded that the HIV/AIDS group showed decreased HRV in the nonlinear analysis; and increased vagal modulation was observed during the ART maneuver. The time to diagnosis has shown to have no influence on HRV.

**Keywords:** Autonomic nervous system; Heart rate; Immunodeficiency; Infectious diseases.

### Resumo

A disponibilidade da Terapia Antirretroviral (TARV) resultou em uma redução drástica da morbimortalidade associada ao vírus da imunodeficiência humana (HIV). No entanto, a terapia tem uma série de efeitos adversos, incluindo disfunção autonômica. A análise da VFC permite avaliar o envolvimento simpático e parassimpático na neuromodulação cardíaca. Diante do exposto, os objetivos foram: verificar se as infecções pelo HIV produzem alterações na modulação autonômica cardíaca; identificar se a modulação autonômica cardíaca da população infectada pelo HIV é sensível à arritmia sinusal respiratória (ASR); e investigar se o tempo de diagnóstico da infecção pelo HIV influencia a VFC. Foram avaliados 49 indivíduos com HIV/AIDS e 21 indivíduos saudáveis. As medidas da VFC foram realizadas por 20 minutos em decúbito dorsal, utilizando o monitor de frequência cardíaca Polar RS810CX, seguida da manobra RSA. Em ambas as condições, os intervalos RR, típicos da VFC, foram analisados por índices lineares e não lineares. Apenas dois índices não lineares, ou seja, %REC e Shannon Entropy, apresentaram diferença

estatisticamente significativa ( $p=0,004$ ), quando comparados os grupos HIV/AIDS e controle, indicando redução da VFC no grupo HIV/AIDS. Sugere-se que a manobra RSA, por sua vez, melhorou a modulação autonômica, pois a redução do %REC após a manobra indica aumento da modulação parassimpática. Desta forma, conclui-se que o grupo HIV/AIDS apresentou VFC diminuída na análise não linear; e aumento da modulação vagal foi observado durante a manobra de ART. O tempo até o diagnóstico mostrou não ter influência na VFC.

**Palavras-chave:** Sistema nervoso autônomo; Frequência cardíaca; Imunodeficiência; Doenças infecciosas.

### Resumen

La disponibilidad de la Terapia Antirretroviral (TAR) ha resultado en una reducción drástica de la morbilidad y mortalidad asociadas con el virus de la inmunodeficiencia humana (VIH). Sin embargo, la terapia tiene una serie de efectos adversos, incluida la disfunción autonómica. El análisis HRV permite la evaluación de la participación simpática y parasimpática en la neuromodulación cardíaca. Dado lo anterior, los objetivos fueron: verificar si las infecciones por VIH producen cambios en la modulación autonómica cardíaca; identificar si la modulación autonómica cardíaca de la población infectada por el VIH es sensible a la arritmia sinusal respiratoria (RSA); e investigar si el momento del diagnóstico de la infección por el VIH influye en la VFC. Se evaluaron 49 personas con VIH/SIDA y 21 personas sanas. Las mediciones de HRV se realizaron durante 20 minutos en posición supina, utilizando el monitor de frecuencia cardíaca Polar RS810CX, seguido de la maniobra RSA. En ambas condiciones, los intervalos RR, típicos de HRV, fueron analizados por índices lineales y no lineales. Solo dos índices no lineales, es decir, %REC y Entropía de Shannon, mostraron una diferencia estadísticamente significativa ( $p=0,004$ ) al comparar los grupos de control y VIH/SIDA, lo que indica una reducción en la VFC en el grupo de VIH/SIDA. Se sugiere que la maniobra RSA, a su vez, mejoró la modulación autonómica, ya que la reducción en %REC después de la maniobra indica un aumento en la modulación parasimpática. Por lo tanto, se puede concluir que el grupo de VIH/SIDA tuvo una VFC disminuida en el análisis no lineal; y se observó un aumento de la modulación vagal durante la maniobra ART. Se demostró que el tiempo hasta el diagnóstico no tiene influencia en la VFC.

**Palabras clave:** Sistema nervioso autônomo; Frecuencia cardíaca; Imunodeficiencia; Enfermedades infecciosas.

## 1. Introduction

Human Immunodeficiency Virus (HIV) infection is a major health problem worldwide. Despite the increasing effectiveness of Antiretroviral Therapy (ART), HIV infection has shifted from a disease with high death rates to a chronic disease with substantial increase in longevity (Valdez et al., 2016). According to the World Health Organization, 73 % of the population living with HIV used ART in 2020 (World Health Organization, 2021).

HIV is a retrovirus (family *Retroviridae*, genus *Lentivirus*). Evolution of HIV infection is characterized by intense and continuous viral replication that results in the destruction and/or dysfunction of cells of the immune system, especially CD4 T lymphocytes (Greene, 2007). As a consequence, there is a progressive decline in cell population leading to immunodeficiency, which has several stages including a state of latent infection to eventually reach a stage of Acquired Immunodeficiency Syndrome (AIDS) (Brasil, 2021).

It is estimated that 37.9 million people are currently living with HIV in the world (Unaid, 2019). In 2018, 43,941 new cases of HIV and 37,161 cases of AIDS were reported in Brazil, with a detection rate of 17.8/100,000 inhabitants (2018), for a total of 966,058 AIDS detected cases in the country between 1980 and June 2019 (Brasil, 2021).

After 1996, with the introduction of combination ART, solid progress was made in the fight against the infection, resulting in increased survival and improved quality of life for HIV-infected individuals (Castelo Filho & Abrão, 2007; Hajjar et al., 2005). Although associated with improved quality of life, ART brought changes in the cardiovascular system (Hajjar et al., 2005), including the control of the Autonomic Nervous System (ANS) over the heart (Askgaard et al., 2011). This population has a two-fold higher risk of developing cardiovascular diseases (Shah et al., 2018).

The association of adverse effects of HIV and ART causes a decrease in heart rate variability (HRV), demonstrating malfunction of the sympathetic and parasympathetic nervous system, increasing the risk of CVD (Godijk et al., 2020).

HRV analysis is considered a predictive and quantitative indicator of autonomic activity, which can be analyzed by linear (time and frequency domain) and non-linear methods (Task Force, 1996).

The Chaos Theory approach can be highlighted among the non-linear methods. The chaotic behavior is typical of

systems that seem random but actually have some hidden order, namely dynamic, deterministic, governed by non-linear equations and highly sensitive to the initial conditions. It can be inferred that chaotic behavior, when related to biological systems, indicates adequate functioning, and is therefore related to health (Ferreira et al., 2010).

Changes in the normality of HRV indices indicate early poor behavior and impaired health status. They are usually classified according to increased or reduced variability. Therefore, increased HRV indicates good adaptability of the body and mainly of the ANS, showing good autonomic control in individuals without functional changes (Ferreira et al., 2010). Conversely, decreased HRV shows low adaptability to adverse situations and indicates an abnormality of the ANS, i.e., autonomic malfunction, representing risks to the individuals (Ferreira et al., 2010).

Cardiac autonomic function can also be assessed with the respiratory sinus arrhythmia (RSA) maneuver. The maneuver is determined by variability in heart rate (HR) associated with respiratory mechanics, i.e., there is an increase in HR during the inspiration process and a decrease in HR during exhalation. The relationship between HR and breathing refers to the functionality of vagal activity and inspiratory activity at the central level. Additionally, the RSA maneuver is influenced by receptors that recognize the changes coming from inspiratory and expiratory processes (Fenley et al., 2016).

Thus, the objectives of the present study were: to verify whether HIV infection produces changes in cardiac autonomic modulation; to identify whether the cardiac autonomic modulation in HIV-infected population is sensitive to the maneuver to accentuate respiratory sinus arrhythmia; and to verify whether the time to HIV diagnosis has an influence on HRV.

## 2. Methodology

### 2.1 Type of study and sample

This is a descriptive cross-sectional study, which used a quantitative methodology of convenience non-probability sampling.

Following the selection of participants, two groups were formed, namely:

- HIV/AIDS Group (HIV/AIDS-G): composed of 49 seropositive individuals (HIV) and with Acquired Immunodeficiency Syndrome (AIDS), with an average age of  $45 \pm 11$  years, and 28 of whom were male. All participants were treated in a Parasitology and Infectious Diseases Clinic in the municipality of Uberaba (MG), Brazil. There were no statistically significant differences between HIV-infected participants with and without AIDS and HRV indices; therefore, these individuals were allocated to a single group HIV/AIDS-G).

- Control Group (CG): composed of 21 participants not infected with HIV and not suffering from cardiovascular, respiratory, osteoarticular and/or metabolic diseases; non-drug users; non-smokers; individuals not regularly physically active; with average age  $42.2 \pm 11.6$  years; 12 of whom were male.

The following individuals were excluded from the study: individuals diagnosed with acute myocardial infarction, heart valve disease, congenital heart disease; individuals with a pacemaker; individuals with psychiatric and/or cognitive disorders; smokers; alcohol consumers; illicit drugs users; and regularly physically active individuals.

### 2.2 Experimental Procedure

The study procedures followed all the rules of CNS Resolution No. 466/12. It was approved by the Ethics and Research Committee of the Federal University of Triângulo Mineiro according to Protocol number 2716.

The data was collected from medical records to provide further details on each participant of HIV/AIDS-G. The variables collected were sex, age, marital status, educational level, time to diagnosis of viral infection, use or not of antiretroviral therapy, opportunistic diseases, CD4 T lymphocyte and CD8 T lymphocytes counts, CD4/CD8 ratio, Viral Load,

Total Cholesterol (TC), High Density Lipoprotein cholesterol (HDLc), Low Density Lipoprotein cholesterol (LDLc), Very Low Density Lipoprotein cholesterol (VLDLc), Triglycerides (TG), Blood Glucose, Sodium and Potassium.

All participants were instructed not to use substances that stimulated the activity of the autonomic nervous system or cardiovascular system (caffeine, alcohol, energy drinks) for 12 hours before the HRV measurements. During data collection, they were placed in a supine position and instructed to remain at rest and awake, to breathe spontaneously, and to avoid excessive body movement and conversations during the test.

The RR intervals (RRi) and heart rate were captured beat by beat, using a Polar® heart rate monitor model RS800CX, validated for this purpose, during 20 minutes (Vanderlei, et al., 2009). The intervals were digitally filtered to eliminate premature ectopic beats and artifacts, and then analyzed manually to exclude residual artifacts. For the analysis, the 1000 most stable RRi points in the time series with more than 95% sinus beats were selected (Godoy et al., 2005). Signal processing was performed using Kubios HRV and Visual Recurrence Analysis (VRA) software.

HRV was measured using linear time domain indices – the square root of the mean of the squares of the successive differences between adjacent normal RR intervals, in a time interval, expressed in milliseconds (rMSSD) and percentage of adjacent RR intervals with a difference in duration greater than 50 milliseconds (pNN50); frequency domain indices – high frequency (HF) and low frequency (LF) spectral densities, and the HF/LF ratio; and non-linear indices – Percentage of Recurrence (%REC), Shannon Entropy (SE), quantitative analysis (SD1- instantaneous record index of beat-to-beat variability; SD2 - represents HRV in long-term records), qualitative analysis of Poincaré Plot, and qualitative analysis of Recurrence Plot (RP).

For the visual analysis of the Poincaré Plot, the image of one participant of each group was utilized.

The qualitative analysis of the Poincaré Plot was conducted through the analysis of the figures formed by its attractor, as described by Tulppo. (Tulppo et al., 1998)

1. Figure showing an increase and dispersion of RR intervals, a known characteristic of a normal plot.

2. Figure with a small global beat-to-beat dispersion and no increase in long-term dispersion of RR intervals. The HRV analysis software - Version 2.0 was used to calculate these indices (Niskanen et al., 2004).

To construct the RP, a time series (from one participant representing each group) was used. The configuration of the Visual Recurrence Analysis Software included the following parameters: embedding dimension = 10, time delay = 1, radius = 70, line =  $2^{-24}$  and Volcano color scheme palette.

RP can be analyzed by small and large scale standards. The dots, diagonal and vertical lines are within the small scale patterns, which allow a qualitative analysis. For example, the RP of a healthy individual shows a diagonal line and less apparent squares, indicating a higher HRV; whereas in individuals with some impairment of autonomic modulation, the RP shows more squares defined in the plot, more geometric shapes, indicating the inherent periodicity, linear behavior and lower HRV (Ferreira et al., 2013) For the qualitative analysis, chaotic, randomized, periodic and linear systems constructed by mathematical formula were used as RP models (Takakura et al., 2017).

Next, HIV/AIDS-G participants performed the maneuver to accentuate respiratory sinus arrhythmia. They were instructed to perform a sequence of maximum inspirations and expirations, in a slow and calm manner, in order to change the lung volume from total lung capacity (maximal inspiration) to the residual volume (maximal expiration). Each respiratory cycle should be made in 10 seconds: 5 seconds of inspiration and 5 seconds of expiration, for a total of 5 to 6 breathing cycles per minute during 4 minutes (Fenley et al., 2016). The participants received verbal encouragement from the researcher to maintain control of the respiratory rate. Finally, the systolic and diastolic blood pressure of each participant was measured using a stethoscope and aneroid sphygmomanometer.

### 2.3 Statistical analysis

The data were subjected to the Kolmogorov-Smirnov normality test and Bartlett's test of Homogeneity of Variances. The comparison of the outcomes of interest between HIV/AIDS-G and CG was performed using the unpaired t-student test, and the paired t-student test was used in HIV/AIDS-G participants before and after the RSA maneuver. Pearson's correlation coefficient was used to verify the association between time to diagnosis of the virus and HRV indices. The level of significance for inferential procedures was set at 5%, and the data were presented as means and standard deviation.

### 3. Results

The time to diagnosis of HIV infection was  $4.3 \pm 3.5$  years for participants without AIDS and  $12.6 \pm 6.6$  years for participants with AIDS. No statistically significant correlations were found between the time to diagnosis of HIV and HRV indices.

High-density lipoprotein cholesterol (HDLc) and low-density lipoprotein cholesterol (LDLc) were slightly reduced and elevated in relation to the reference values, respectively (Table 1).

The results of the linear and non-linear HRV indices, regarding both HIV/AIDS-G and CG, showed worse autonomic modulation with significantly higher values of %REC and Shannon Entropy, which represents low variability, in the group with HIV-infected participants (Table 2).

**Table 1** - Characterization of the HIV/AIDS group (n = 49) according to vital and laboratory signs.

Variables	HIV/AIDS group Mean value (SD)	Reference Values
Heart Rate (bpm)	72.9 (12.5)	60 to 100
Systolic Blood Pressure (mmHg)	120.2 (11)	<120
Diastolic Blood Pressure (mmHg)	78.7 (14)	<80
CD4 (cells/mm <sup>3</sup> )	459.7 (282.8)	350 to 499
CD8 (cells/mm <sup>3</sup> )	380.2 (351.1)	160 to 880
CD4/CD8 (cells/mm <sup>3</sup> )	0.73 (0.67)	<1
Viral Load (copies/ml)	33 (67.3)	<50
Total Cholesterol (TC) (mg/dL)	178.4 (41.3)	≤200
High density lipoprotein (mg/dL)	49.6 (17.8)	≥60
Low density lipoprotein (mg/dL)	102.8 (39.5)	<100
Very Low density lipoprotein (mg/dL)	28.5 (12.5)	<30
Triglycerides (TG) (mg/dL)	143.0 (79.8)	<150
Blood Glucose (mg/dL)	95.3 (19.3)	<110
Sodium (mEq/L)	137.4 (4.41)	138 to 142
Potassium (mEq/L)	4.25 (0.95)	3.6 to 5.5

SD= standard deviation; CD4= Cluster of Differentiation 4; CD8= Cluster of Differentiation 8; CD4/CD8= CD4/CD8 ratio.

Source: Authors

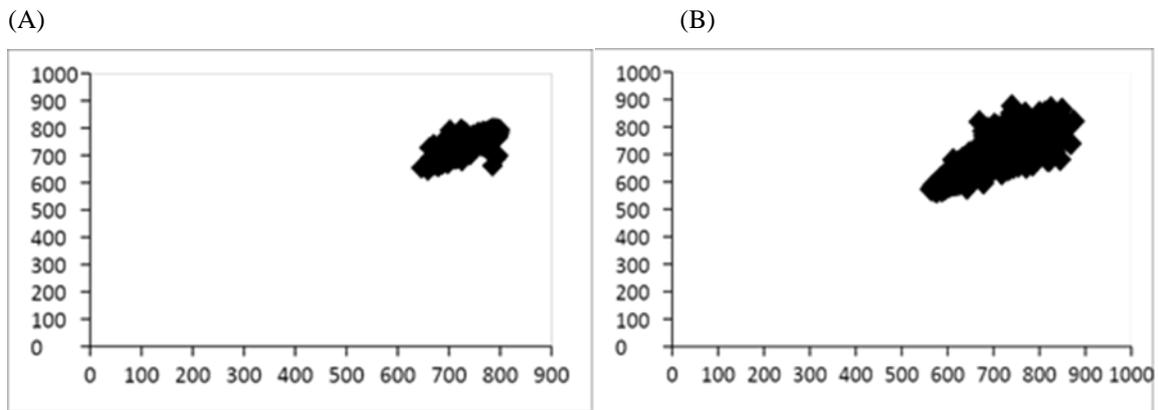
**Table 2** - Linear and non-linear HRV analysis rates for the HIV/AIDS (n = 49) and Control (n = 21) groups in the supine position at rest.

HRV Indices	HIV/AIDS group Mean value (SD)	Control group Mean value (SD)	p
rMSSD (ms)	22.2 (15.6)	26.53 (16.7)	0.314
pNN50 (%)	6.03 (9.14)	8.72 (13.14)	0.340
LF (un)	66.8 (17.3)	64.8 (16.1)	0.657
HF (un)	33.0 (17.2)	35.07 (16.1)	0.654
LF/HF	3.25 (3.2)	2.78 (2.4)	0.558
Percentage of recurrence (%REC)	34.4 (8.5)	27.7 (8.1)	0.004*
Shannon Entropy	5.02 (0.6)	4.30 (1.29)	0.004*
SD1 (ms)	15.7 (11.0)	18.7 (11.86)	0.314
SD2 (ms)	53.9 (35.7)	54.3 (21.0)	0.964

HRV= heart rate variability; SD= standard deviation; rMSSD= Square root of the mean of the square of the differences between adjacent normal RR intervals, in a time interval, expressed in ms; pNN50= Percentage of adjacent RR intervals with a difference in duration greater than 50 ms; LF= Low Frequency; HF= High Frequency; LF/HF= ratio of low frequency to high frequency. SD1= Instantaneous record index of beat-to-beat variability; SD2 = represents HRV in long-term records. \*p<0.05. Source: Authors

Figures 1A and 1B show common examples of the Poincaré Plot for participants with HIV/AIDS and controls, respectively.

**Figure 1-** Visual pattern of the Poincaré Plot of a participant of HIV/AIDS-G (A) and CG (B).

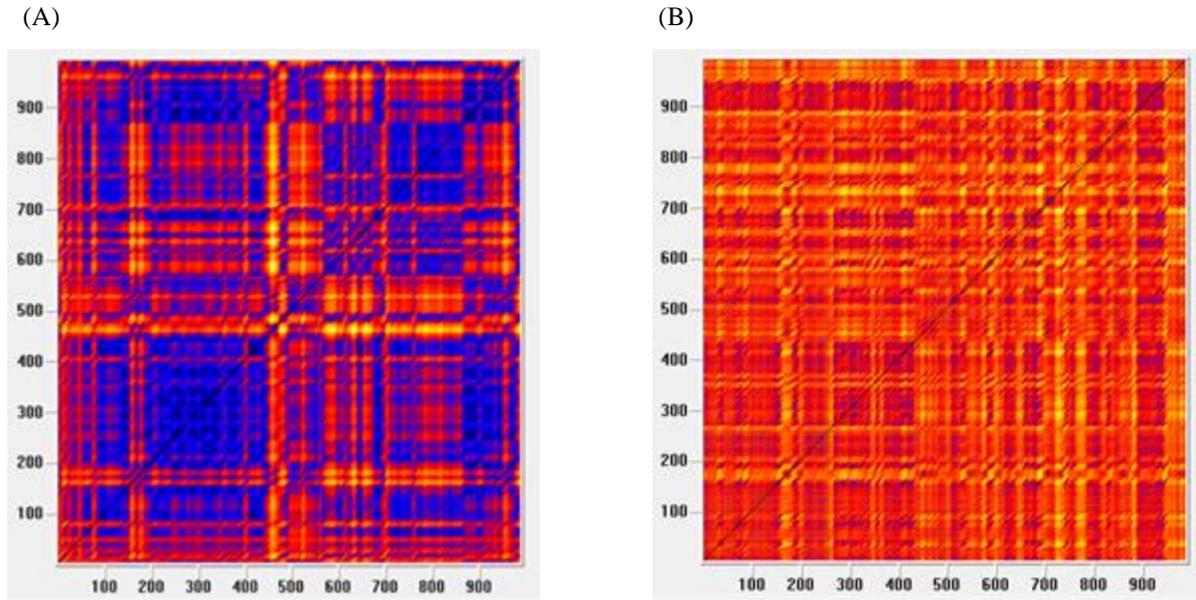


Source: Authors.

Figure 1A shows an image similar to a torpedo, a little far from the representative points of SD1 and long-term RR intervals; whereas Figure 1B shows CG and an image similar to a comet (Moraes et al., 2014).

The Recurrence Plot displayed a worsening in the pattern of HIV/AIDS-G, evidenced by the greater amount of dark squares, and more geometric shapes, indicating greater linearity, and therefore, less system homeostasis (Fig 2A), when compared to CG. In addition, when HIV/AIDS-G is compared to CG, a more chaotic pattern can be observed, with less apparent squares and more homogeneous in CG, indicating greater complexity and better homeostasis (Fig. 2B).

**Figure 2** - Recurrence plot of a participant of HIV/AIDS-G (A) and CG (B).



Source: Authors.

The maneuver to accentuate respiratory sinus arrhythmia promoted a significant increase in parasympathetic modulation in HIV/AIDS-G, except for Shannon Entropy (Table 3).

**Table 3** - Linear and non-linear HRV analysis rates comparing supine position at rest and during the maneuver to accentuate respiratory sinus arrhythmia (RSA) in the HIV/AIDS group (n = 35).

HRV Indices	HIV/AIDS		p
	Supine position at rest Mean value (SD)	During the RSA maneuver Mean value (SD)	
rMSSD (ms)	21.6 (16.2)	34.3 (29.5)	0.008*
pNN50 (%)	5.8 (9.1)	13.0 (15.1)	0.004*
Percentage of recurrence (%REC)	34.6 (9.4)	29.8 (8.3)	0.019*
Shannon entropy	5.04 (0.69)	4.85 (0.58)	0.206
SD1 (ms)	15.3 (11.4)	24.3 (20.9)	0.008*
SD2 (ms)	52.5 (38.0)	70.3 (41.0)	0.015*

HRV= heart rate variability; RSA= respiratory sinus arrhythmia; SD= standard deviation; rMSSD= Square root of the mean of the square of the differences between adjacent normal RR intervals, in a time interval, expressed in ms; pNN50= Percentage of adjacent RR intervals with a difference in duration greater than 50 ms; SD1= Instantaneous record index of beat-to-beat variability; SD2 = Represents HRV in long-term records. \*p<0.05. Source: Authors.

#### 4. Discussion

The present study investigated the cardiac autonomic behavior of HIV-infected individuals by comparing it to that of healthy individuals of the same age group.

The major findings in relation to HIV/AIDS-G were: 1) significant increase in %REC and Shannon Entropy, in the supine position and at rest; 2) greater linearity and less complexity evidenced in the qualitative analysis of RP; 3) little chaotic behavior demonstrated by a torpedo-like image in the Poincaré Plot; and 4) significant increase in rMSSD, pNN50, SD1 and significant decrease in %REC, during the RSA maneuver, compared to the supine position at rest.

Satisfactory immunological and biological levels have been detected, which indicates that CD4 T lymphocyte and

CD8 T lymphocyte, responsible for fighting HIV infection, are functioning in the right quantities to protect against opportunistic diseases. Furthermore, the viral load was reduced in most individuals, identifying a lower amount of virus. This can be associated with good adherence to antiretroviral treatment, having a positive effect on the control of the virus, in disagreement with other studies (Moraes et al., 2014; Remor et al., 2007).

An important piece of data related to the risk of cardiovascular diseases is the lipid profile presented by the sample. It can be seen that HDLc was below the reference values and LDLc was above them. Dyslipidemia is characterized by this alteration, and in seropositive individuals, it is associated with the use of ART (Askgaard et al., 2011). Kelesidis and Currier (2014) also found changes in lipid profile similar to the present study. Dyslipidemia accelerates the onset of atherosclerosis and the incidence of cardiovascular events, which is possibly related to the duration of drug therapy.

Studies on HRV in HIV-infected individuals report analyses in the domain of time and frequency, and there are a limited number of publications with non-linear analysis (%REC, Shannon Entropy and Recurrence Plot) of HRV in this population.

According to the non-linear indices, %REC and Shannon Entropy showed higher values with a statistically significant difference in HIV/AIDS-G ( $p=0.004$ ). Notably, in this study, both Shannon Entropy and the analysis of recurrence were conducted; Shannon Entropy showed high indices, demonstrating greater recurrence and stationarity of the signal and lower HRV.

Higher Shannon Entropy values indicate greater determinism, i.e., a more linear behavior, and therefore less stability, which, for a living and healthy cell, is dynamic and results from the balance between destruction and repair (Kelesidis & Currier, 2014).

Higher Shannon Entropy is also associated with a higher trend of disease and death (Godoy, 2016; Takahashi et al., 2012). In our study, Shannon Entropy was a sensitive marker of greater severity of HIV infection.

Percentage of Recurrence quantifies the percentage of recurring points falling within a specific radius (Takahashi et al., 2012). In this study, HIV/AIDS-G showed increased percentage values, which indicates repetition and periodicity of the same point. This can be interpreted as low HRV, abnormal and insufficient SNA adaptation, indicating an individual's physiological malfunction (Godoy et al., 2005).

These findings are confirmed when the qualitative aspect of RP is analyzed. Remarkably, the RP of a HIV/AIDS-G participant (Fig. 2A) has more apparent squares, greater homogeneous configuration, and higher recurring points, when compared to healthy individuals (CG). This indicates a more recurrent, less dynamic system and less complexity of autonomic modulation in this population (Vanzella et al., 2018).

The visual analysis of the Poincaré Plot in HIV/AIDS-G revealed an image similar to that of a torpedo, which indicates a minor chaotic behavior, showing lower HRV; whereas, an image similar to a comet was observed in CG, which is typical of chaotic behavior and a characteristic of a Poincaré plot within physiological conditions and higher HRV.

McIntosh (2016) conducted a meta-analysis including young adults with HIV undergoing antiretroviral therapy and demonstrated a general reduction in autonomic function with a shift to sympathetic dominance. This change may predispose HIV patients to an early and elevated risk of arrhythmias, cardiac events and accelerated progression of HIV disease.

It is worth mentioning that the duration of antiretroviral therapy did not show a significant correlation with HRV indices, indicating that HRV will be reduced regardless of the time that the individual is submitted to drug therapy.

Regarding the linear and non-linear HRV analysis indices, comparing the RSA maneuver in the supine position at rest in HIV/AIDS-G, there was an increase in the parasympathetic response during the maneuver, showing the influence of breathing in the heart rate oscillations. The HRV-related variables analyzed using linear time domain indices (pNN50, rMSSD, SD1 and SD2) brought evidence that patients with HIV/AIDS had greater parasympathetic modulation when influenced by the

respiratory system. This suggests good adaptability and physiological normality when inspiration and expiration are performed.

There is evidence of increased %REC in HIV/AIDS-G at rest, but this index was also influenced during the RSA maneuver, presenting values close to the reference values for healthy individuals.

Thus, it can be concluded that cardiac autonomic modulation indicates a sympathetic predominance with evidence of lower HRV in HIV-infected individuals. However, vagal modulation is marked during the RSA maneuver, suggesting that there is no complete impairment of cardiac autonomic control.

The time to diagnosis of HIV infection does not have an influence on HRV.

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