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Cardiovascular Bioengineering in characterizing the variability of heart rate based on an analysis spectral and temporal nonlinear patients with Chagas disease

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Abstract

The article summarizes the research results concerning the characterization of the variability of heart rate in patients with Chagas disease, located in the state of Meta in Colombia. Currently Chagas disease is present in one million people of the Colombian population and 7 million people in Latin America. For this reason it is a condition that deserves to be studied and researched in order to contribute to the health sector of modern society. The methodology used was experimental, where two patients groups were organized with residents and natives of the department of Meta. A group affected by Chagas disease and the other group consisting of people not affected by the disease. Therefore, the study population underwent an electrocardiogram (ECG) with measuring instruments calibrated and approved by the FDA.. The results once applied the techniques of spectral analysis and time using the Kubios software indicate values of heart rate (HR), standard heartbeat and heart rate, percentage deviation and number of beats, entropy, low and high frequency . Finally it concluded that in patients with Chagas disease so there is less entropy less variability in heart rate compared to patients in the control group unaffected by the disease.

Keywords: Bioengineering Cardiovascular, Heart Rate Variability, spectral and temporal analysis, Chagas Disease

I. INTRODUCTION

Understanding bioengineering cardiovascular as a practical assuming an interdisciplinary approach to an approach of the doctor-circulatory environment, converging various branches of science, directing their actions in different working areas of the applied and basic research, in which are present the medical sciences, physical, biological, in interaction with engineering (signal analysis, applied mathematics), offering the possibility to delve into various application fields of medical technology. One of the lines of research are biopotentials and surface electrocardiography, and the processing of these signals can be used mathematical modeling techniques and methods such as computer numerical-analysis of heart rate variability (HRV) as a state of heart conditions. This test consists in analyzing variations in the time interval between consecutive heartbeats (RR intervals) rather than the heart rate itself. And it serves to quantify the autonomic influence on the heart and therefore be a predictor of mortality in HRV-positive patients with Chagas disease or myocarditis Chagasic which affects the functioning of the heart [1]. but the heart rate itself. And it serves to quantify the autonomic influence on the heart and therefore be a predictor of mortality in HRV-positive patients with Chagas disease or myocarditis Chagasic which affects the functioning of the heart [1]. but the heart rate itself. And it serves to quantify the autonomic influence on the heart and therefore be a predictor of mortality in HRV-positive patients with Chagas disease or myocarditis Chagasic which affects the functioning of the heart [1].

II. APPROXIMATE ENTROPY

Approximate entropy (APEN) is a group of Measures statistical, Which Allows to measure the regularity of small series of Data with noise [2]. A time series Containing many repetitive patterns has a Relatively small Apen, and a less predictable process has a higher ApEn.

In a time series of length N, to calculate your ApEn it is Necessary to Set two parameters:

A value m (length of run of data Compared) and tolerance range r (filtering level). The ApEn Measures the similarity logarithmic That repetitive patterns or nearby, separated less than r, for m contiguous observations, REMAIN a distance less than r in the following comparisons by Increasing of m With repetitive patterns of length m + 1.

Let {x (n)} be a time series of length N, to calculate as a function of ApEn N, m and r, That Is, ApEn (N, m, r), as well:

1 Form a time series of data u (1) or (2), ..., u (N). These are N raw data values from measurement equally spaced in time.

2 Fix r, a positive actual number, and m an integer.

3 Form a sequence of vectors x (1), x (2), ..., x (N-m + 1) in Rm, defined by

x(I) = [u (i) u (i + 1), ..., u (i + m-1)]. Next, for each defined i, 1≤ i ≤ N-m + 1

C_i^m = (Number of x (j) Such that) $d[x(i), x(j)] \leq r/(N - m + 1$

$C_i^m = \frac{d[x(i),x(j)]}{(N-m+1)}$

C_i^m is the value of frequency of a similar length m patterns for a tolerance r is defined as in Which $d[x(i), x(j)]$

$$d[x(i), x(j)] = max_{k=1,2,3\ldots m}[|x(i + k) - x(j + k)|]$$

4 define

$$\Phi^m(r) = \frac{1}{N-m+1} \sum_{i=1}^{N-m+1} \ln(C_i^m(r))$$

5 Approximate defines Entropy (APEN) as

$$ApEn = \Phi^m(r) - \Phi^{m+1}(r),$$

for *r*, A positive actual number, and m, an integer as fixed in step 2.

III. SAMPLE ENTROPY

Sample Entropy (SampEn) is a measure of improved and normalized approximate entropy (APEN) and reduces the bias That Caused by self-matching. SampEn is the negative logarithm of the probability That if two sets of simultaneous data points of length m Have distance <r Then two sets of simultaneous data points of length m + 1 Also have distance <r. It is Represented by SampEn (N, m, r, t) with T as sampling time, as well:

one $SempEn = -\ln\left(\frac{C_{m+1}(r)}{C_m(r)}\right),$

two With,

$$C_m(r) = \frac{\text{Num. pro. pairs } i,j \text{ such that } d|x_i^m,\ x_j^m| < r,\ i \neq j}{N - m + 1}$$

3 Belong Where the space of dimension m, x_i^m *and* $x_j^m N$ is the length of the time series and rRepresent the tolerable standard deviation of the time series. Then:

$$SampEn = \frac{\text{Num. pro. pairs } i,j \text{ such that } d|x_i^{m+1},\ x_j^{m+1}|<r,\ i\neq j}{\text{Num. pro. pairs } i,j \text{ such that } d|x_i^m,\ x_j^m|<r,\ i\neq j}$$

From the foregoing and in accordance with the context of Chagas disease in the region, it is estimated that the number of people infected with Chagas disease in Latin America will reach about six and seven million people, of whom more than the 30% will develop symptoms of chronic disease, especially cardiomyopathy. As a result this will result in twelve thousand deaths a year. (PHAO / WHO, 2017). The estimated prevalence of people infected with Trypanosoma cruzi (etiologic agent of this disease) in Colombia is 436,000 individuals. The number of new cases of vector-borne transmission per year is 5250, and the population exposed in the endemic areas are 4,792,000. where the areas most affected are the departments of Santander, Norte de Santander, Boyaca, Cundinamarca, Casanare and Arauca. Two of the characteristics of Chagas disease during chronic phase parasitemia is reduced, and the presence of parasites induced lesions found in the heart and gastrointestinal tract. However, in the chronic phase of the disease, Chagas Cardiomyopathy is more frequent and severe [3].

In a study carried out by the Shaio clinic involving 120 patients diagnosed with Chagas disease (Mora et all, 1998), yot it was reported that the main electrocardiographic features of Chagas are right bundle branch block (BRD) 40% second and third degree atrioventricular block 29.2% of the sinus node dysfunction 28.3%, 23% ventricular tachycardia, atrial fibrillation 19%, left anterior hemi block 17.2%, 3.3% atrial flutter, and locking branch left (BRI) 3.3%. These characteristics are similar to those reported by [4][5].This disease dysfunction of the autonomic nervous system is also produced; More specifically, sympathetic activity and creates cardiovagal denervation is increased, which can be measured by quantifying the variability of the heart rate (HRV) [6]. The studies concluded that chronic Chagas old cardiomyopathy is the most common form of cardiomyopathy seen in Latin America, where it has become a real public health problem. Because of this, we have created a database of electrocardiograms (ECG) of patients with Chagas disease were reported by the Health Department of Meta. From these ECG findings in the analysis of HRV as well as the characteristic features in the ECG signals they are linked to Chagas disease early warning are now easier to recognize. From these ECG findings in the analysis of HRV as well as the characteristic features in the ECG signals they are linked to Chagas disease early warning are now easier to recognize.

HRV is a parameter defined as the variability within the time interval between beats of the heart [7]. This determination is based on the measurement of waves R consecutive and a calculation in milliseconds of the time between them [8] [9]. The study of HRV allows the vagus parasympathetic balance to be determined in an indirect way. [10] [11] [12].

HRV is assessed by parameters of time domain, frequency and nonlinear [9]. The time domain parameters are the result of the measurement of RR intervals. These are affected by the activity of the autonomic nervous system and include: standard deviation of RR (SDNN) intervals; square root of the

mean of the sum of the squares of the differences between adjacent RR intervals (RMSSD); and the number and the percentage of consecutive RR intervals which differ by more than 50 ms (NN50 and pNN50).

IV. METHOD

This study was performed taking into account Resolution 8430 of 1993 Article 11 and 15 of the Ministry of Health of Colombia and the Law 842 of 2003 of the Code of Professional Ethics in Biomedical Engineering practice. The study was conducted at the Laboratory of Physiology at the University of the Llanos (4 ° 4 '30 "N, 73 ° 35' 7" W), located 4 kilometers from the city of Villavicencio, in the rural area of Barcelona. Climatic characteristics common are: average annual temperature 25 ° C, average annual rainfall 4050 mm, average relative humidity of 75%, and the elevation above sea level 420m.

As an experimental population appeal a database of patients already diagnosed with Chagas, of the Health Department of Meta. From this database, contact chance 50 patients between women and men was established, only 19 were included in the study, five women and fourteen men (mean age 52 years). The other 31 patients were excluded because they were currently living in other parts of Colombia. Selected patients had no history of heart disease, smoking or diabetes, and were taking no medication. Control volunteers, four women and fifteen men (mean age 32 years) were young and healthy students in college. Table 1 shows the characteristics of seropositive patients.

Table 1. Individuals seropositive for Chagas

CODE	SEX	Year old)	Recording time (min)
H001C22	M	22	10
M002C49	F	49	10
M003C58	F	58	10
H004C53	M	53	10
H005C56	M	56	10
H006C41	M	41	10
M007C54	F	54	10
M008C55	F	55	10
H009C65	M	65	10
H010C62	M	62	10
H011C48	M	48	10
H012C54	M	54	3
H013C43	M	42	3
M014C50	F	50	3
H015C50	M	50	3
H016C55	M	55	3
H017C70	M	70	3
H018C40	M	40	3
M019C62	F	62	3
Middle Ages		**52**	

Table 2 presents the characterization of patients formed the control groups.

Table 2. Control of individuals

CODE	SEX	Age (years)	The recording time (min)
M001-43	F	43	10
H002-21	M	20	10
H003-21	M	20	10
H004-22	M	22	10
H005-24	M	24	10
H006-23	M	2. 3	10
H007-57	M	57	10
H008-22	M	22	10
H009-24	M	24	10
H010-53	M	53	10
H011-42	M	42	10
H012-43	M	43	10
H013-51	M	51	10
H014-44	M	44	10
H015-15	M	50	10
H016.42	M	42	10
M017-22	F	22	10
M018-23	F	2. 3	10
M019-21	F	21	10
Middle Ages		**32**	

Recording and processing of electrocardiograms

All participants included in this study were individually transferred to the Laboratory of Physiology of the Faculty of Animal Sciences at the University of the Llanos. They study objectives and steps for obtaining the ECG recording were explained. Once approval was obtained for participation signed a form giving their informed consent. The experiment was conducted in a cubicle, which was isolated from the rest of the lab environment. The temperature was kept constant during the test periods. The research team and a nursing assistant accompanied each participant during testing to comply with the recommendations made by the Ethics Committee

In order to obtain ECG recordings, 8 channels with a polygraph AD Instruments PowerLab reference mark 8/30 62.5 nvolts resolution, scale +/- 2 mV, 2,2uV noise, low pass filter 0 50Hz, and the rate of sampling 2000 samples / min was used. It was also equipped with a conditioner to electrocardiography, and assembled to a bio-amplifier with DIN port allowing for entry of three electrodes. The display of the recording was carried out through the polygraph connection for a laptop, which also has software for information processing. Recording high-resolution DII met with a sampling range from three to ten minutes duration per patient.

Once each recording, which were processed using software Laboratory Chart Pro, which has all the information on sampling and reports electrocardiographic parameters were obtained. In this study, which included the following: heart rate, RR interval, QRS interval, QT interval and QTc use for

proper analysis. These reports are stored in portable hard and then exported to Microsoft Excel. For the HRV parameters, the information stored in Excel was exported in the KUBIOS software version 2.1 of the University of Eastern Finland, Kuopio (Finland). This software processes the data and reports of subsequent HRV parameters: the time domain: HR (bpm), SDNN (ms) SDHR, RMSSD (ms), NN50 (I), pNN50 (%); frequency domain: LF (Hz), HF (Hz), and LF / HF ratio; and the nonlinear domain: Apen, and SampEn. Electrocardiographic parameters reported by the laboratory Chart Pro and HRV parameters reported by KUBIOS were organized in an Excel file that will be presented later for statistical analysis.

The statistical processing by SPSS, where statistics were obtained descriptive initials electrocardiographic findings and HRV parameters in both groups was performed. Subsequently, an analysis was made of the variance of one of the two parameters to establish significant differences between them, and to determine statistical significance between groups, t-test was performed for independent samples. They included in the results tables are mean ± SD value and $p < 0.05$ was considered significant.

IV. RESULTS

They were obtained thirty-eight ECG records, 19 of them HIV-positive patients for Chagas disease and another 19 controls. Tables 3 and 4 show the average of measured variables in each group.

Table 3. Electrocardiographic parameters of seropositive for Chagas Patients

CODE	HR (BPM)	RR (S)	PR (S)	QRS (S)	QT (S)	QTc (S)
H001C22	87.93	0.684	0.143	0.073	0.32	0.387
M002C49	78.73	0.765	0,131	0,067	0,336	0.384
M003C58	63.89	0.939	0.142	0,058	0.393	0,405
H004C53	84.05	0.714	0.188	0,087	0,333	0.394
H005C56	75	0.802	0.32	0.073	0,366	0.409
H006C41	84.08	0.717	0.13	0,068	0.316	0.373
M007C54	68.21	0.88	0,123	0,071	0,333	0.354
M008C55	61.52	0.977	0.168	0.077	0.394	0.399
H009C65	74.46	0.808	0.158	0,067	0.364	0.405
H010C62	67.26	0.894	0.18	0.108	0.365	0.387
H011C48	67.06	0.931	0.187	0,046	0.298	0.312
H012C54	81.53	0.737	0.144	0,049	0.342	0.4
H013C43	81.02	0.741	0.13	0.07	0.371	0.431
M014C50	71.3	0.842	0.12	0.081	0.367	0.4
H015C50	69.48	0.869	0.143	0.06	0.282	0.302
H016C55	67.3	0.909	0,145	0,057	0.341	0.357
H017C70	80.8	0.743	0.187	0.078	0.356	0.416
H018C40	80.41	0.747	0.184	0,065	0.308	0.356
M019C62	58.03	1,035	0,165	0.089	0.406	0.4
Mean	73.79 ± 8.58	0,83 ± 0.17	0.16 ± 0.04	0.07 ± 0.01	0.346 ± 0,033	0.382 ± 0,033

As shown in Tables 3 and 4, the average heart rate between groups showed no significant difference, however, it is notable that the SD is greater in the control population (11,95) in the group seropositive (8.58), which infers a higher variability of this parameter in the control population.

Table 4. Electrocardiographic parameters in the Control group.

CODE	HR (BPM)	RR (S)	PR (S)	QRS (S)	QT (S)	QTc (S)
H001C22	87.93	0.684	0.143	0.073	0.32	0.387
M002C49	78.73	0.765	0,131	0,067	0,336	0.384
M003C58	63.89	0.939	0.142	0,058	0.393	0,405
H004C53	84.05	0.714	0.188	0,087	0,333	0.394
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M008C55	61.52	0.977	0.168	0.077	0.394	0.399
H009C65	74.46	0.808	0.158	0,067	0.364	0.405
H010C62	67.26	0.894	0.18	0.108	0.365	0.387
H011C48	67.06	0.931	0.187	0,046	0.298	0.312
H012C54	81.53	0.737	0.144	0,049	0.342	0.4
H013C43	81.02	0.741	0.13	0.07	0.371	0.431
M014C50	71.3	0.842	0.12	0.081	0.367	0.4
H015C50	69.48	0.869	0.143	0.06	0.282	0.302
H016C55	67.3	0.909	0,145	0,057	0.341	0.357
H017C70	80.8	0.743	0.187	0.078	0.356	0.416
H018C40	80.41	0.747	0.184	0,065	0.308	0.356
M019C62	58.03	1,035	0,165	0.089	0.406	0.4
Mean	73.79 ± 8.58	0,83 ± 0.17	0.16 ± 0.04	0.07 ± 0.01	0.346 ± 0,033	0.382 ± 0,033

RR interval, determining the duration of a cardiac cycle was shorter in the control group; however, it had no statistical significance compared with the seropositive group. PR interval, determines the driving time of the electrical impulse from the atrioventricular, sinoatrial node to node also known as PQ, in contrast to the previous parameter was lower in the seropositive group, but without showing significant differences. With regard to the QRS complex, which indicates the time of an electric impulse has to go through the ventricular conduction system and muscle mass, they showed no significant differences between groups.

The QT interval defines the time an electrical impulse takes from the start of cardiac depolarization to the end of repolarization. This variable was higher in the seropositive group. Contrary to that, the QTc interval depends on the value heart rate in the seropositive group was significantly higher ($p \leqslant 0.005$).

Parameters Heart Rate Variability

HRV parameters were obtained from the software version 2.1 KUBIOS as previously reported. Table 5 presents the time and frequency domain nonlinear. The group HRV-positive for Chagas disease.

Table 6 presents the time and frequency domain nonlinear control group for Chagas disease.

As for the time domain parameters, SDNN variable in the control population had a mean of 56.23 ± 29.6ms, while in the

seropositive group was 40.62 ± 30.1ms. Clearly you can see further slippage in the first group, although the ANOVA test and T test did not establish a statistical significance between groups. However, a smaller SD card this variable in seropositive individuals would indicate a greater regularity of the RR interval in these patients. RMSSD values for both groups were 34.31 ± 31.94 ± 21.01ms and 37.33ms for the controls and the group of Chagas disease, respectively. In comparing the groups with SDNN values, this parameter was higher for the controls, but without establishing significant differences between them.

The NN50 parameter, defined as the number of consecutive RR intervals which differ by more than 50 ms, the results were as follows: in the control group 76.47 ± 78.3 beats, while in the group of seropositive 13.47 ± 36.8 beats, highly statistically significant (p=0.003). This indicates a narrower regularity of RR intervals in patients with Chagas disease. These results were correlated with the results of pNN50 which were 12.3 ± 13.3% and 2.64 ± 6.0% for control the experimental group, respectively, with highly significant P value ($p \leqslant 0.007$). HR ratio with NN50 and pNN50 greater number and proportion implies greater variability of the first. This is consistent with the functionality of a healthy heart, reflecting a better balance between the sympathetic and parasympathetic control of heart activity.

The median values of low frequency (LF) in the population was 0.109 ± 0.164 Hz control and at 0062 ± 0.03Hz HRV-positive group. The latter showed a lower frequency, without establishing statistical significance, however, this indicates a greater mastery of sympathetic activity at this frequency for the experimental group. The data regards the higher frequencies (HF) they were: 0.222 ± 0.07 0.271 ± 0.08 Hz and Hz for controls and chagasic respectively. These results were not statistically significant, and compared to reports LF, HF were higher in the group of Chagas disease. Therefore, this can be related to a parasympathetic activity superior to the frequency range obtained.

With respect to the LF / HF relationship we found: 3.923 ± 3.37 Hz patients in the control group and 2902 ± 3.0 Hz in Chagas patients. The results were not statistically significant. But significantly lower in the seropositive group. This indicates that HF are higher in the group of Chagas, and in terms of sinoatrial node activity, there is a predominance of parasympathetic over sympathetic activity.

Nonlinear variables, analyzing the structure and complexity of series of RR intervals through entropy results approximate entropy were 1.249 ± 0.134 in controls and 0.959 ± 0.325 in seropositive with signification statistic ($p \leqslant 0.001$) between them. And for sample entropy results they were 1.358 ± 0.264 and 1.102 ± 0.385 respectively in the control group and experimental, also with statistical significance ($p \leqslant 0, 02$). Results entropy were lower in patients with Chagas disease, placing them in line with the above parameters in the time and frequency domains. In other words, there is a greater regularity of events that interfere with generating RR intervals in the group of Chagas disease.

Table 5.HRV parameters in patients seropositive for Chagas disease.

CODE	HR (BPM)	SDNN (ms)	SDFC	RMSSD (ms)	NN50 (L)	pNN50 (%)	APPROX ENTROPY	SAMPLE ENTROPY	LF (Hz)	HF (Hz)	LF / HF
H001C22	87.94	34.6	4.52	13.9	1	0.1	1,19	1,24	0047	0304	2,61
M002C49	78.53	39.1	4.79	24.9	8	one	1.2	1.3	0051	0355	1.42
M003C58	63.89	21.7	1,47	12.8	1	0.2	1,24	1,44	0043	0266	1214
H004C53	84.06	21.4	2,58	9.7	0	0	1.26	1,37	0043	0285	3051
H005C56	75.01	35.1	3,32	15.2	2	0.3	1,17	1.2	0066	0.16	3.43
H006C41	84.04	47.4	5.68	23.5	25	3	1.33	1,44	0055	0164	3.6
M007C54	68.11	26.5	2,08	10	0	0	1,11	1,14	0063	0207	6.5
M008C55	61.52	25.2	1,62	17.1	8	1.3	1.29	1,48	0058	0273	1.7
H009C65	74.46	39.9	4,85	59.8	22	2.6	0,76	0,66	0.14	0398	0233
H010C62	67.25	35.6	3,96	26.3	4	0.6	1,12	1,17	0047	0375	1013
H011C48	67.11	148.9	16.85	145.1	162	25.1	0,82	.67	0074	0254	0,52
H012C54	81.53	23.6	2,59	4.3	0	0	-	-	0047	0152	68.14
H013C43	81.02	25.7	2,85	9.3	0	0	1,03	1,19	0047	0348	4081
M014C50	83.34	28.3	3,32	10.8	0	0	0,94	1222	0051	0152	10033
H015C50	69.34	64	5,75	111.1	17	9.9	0,56	0.5	0043	0,34	0161
H016C55	67.3	75.7	16.62	57.5	5	5.2	0.75	0,96	0043	0273	0441
H017C70	80.8	17.6	1,89	13.7	0	0	-	-	0148	0164	0614
H018C40	80.41	18,4	two	9.9	0	0	0,83	1.4	0.0703	0336	3597
M019C62	57.61	38.4	2,08	25.6	one	one	0,69	1327	0047	0348	0.9

Table 6.HRV parameters in the control group.

CODE	HR (BPM)	NN SD (ms)	SD FC	RMSS D (ms)	NN50 (L)	pNN50 (%)	APPROX ENTROPY	SAMPLE ENTROPY	LF (Hz)	HF (Hz)	LF / HF
M001-43	62.72	55.3	3.77	37.2	117	15.6	1,43	1,64	0066	0336	2.8
H002-21	69.25	63.4	5.21	36.4	96	13.9	1,24	1.33	0.07	0156	4.3
H003-21	74.8	69.2	6.46	40.1	139	18,6	1.1	1,18	0136	0156	2343

H004-22	71.72	61.3	4.96	25.2	35	4.8	1.08	1.1	0059	0152	15.08
H005-24	83.31	38.4	4,48	20.9	16	1.9	1.29	1.41	0043	0324	3.44
H006-23	52.47	159.5	10.18	102.6	246	48.2	1.26	1,37	0066	0184	2034
H007-57	69.99	53.4	4.37	26.4	38	5.5	1,21	1,32	0074	0215	3128
H008-22	68.06	75.1	5.85	61.3	43	20.58	1.41	1,72	0105	0348	1,43
H009-24	85.39	31.2	3.66	15.3	3	0.4	1,23	1,28	0,78	0164	6162
H010-53	64.61	25.6	1,82	12.1	1	0.2	1,19	1,32	0078	0277	5079
H011-42	72.5	37.1	3,23	28.4	60	8.1	1,43	1,74	0.07	0.25	2268
H012-43	63.17	77.6	5.3	32.2	67	10.5	1,28	1.15	0059	0.16	8201
H013-51	62.15	44	4.61	28.9	5	0.7	1065	1033	0066	0152	2096
H014-44	74.24	44.6	4,14	34.8	121	16.2	1,38	1,61	0082	0273	0762
H015-15	85.93	46.9	5.51	23.3	27	3.1	1,12	1,13	0074	0152	6423
H016.42	89.97	35.3	4.76	16,1	8	0.9	1.1	1,06	0082	0152	4287
M017-22	103.54	29.5	5.04	14	8	0.8	1.08	0.99	0074	0.27	2284
M018-23	72.53	70	6,28	47.6	191	26.4	1,39	1.53	0043	0191	1.81
M019-21	64.01	51	3.65	49.2	232	36.4	1,44	1,88	0047	0312	0676

V. DISCUSSION AND CONCLUSIONS

ECG was performed and developed from recordings of 19 patients with Chagas disease and nineteen controls. In each recording we measure the following variables: HR, RR interval, QRS, QT, QTc and PR segment. HR gave no statistical significance between the groups, but resulted in greater SD in the control group. This indicates a greater variability of this parameter in the last group. HR values were lower than reported in [30]. The results in patients Chagas were HR 79.5 ± 4.5 lpm; while in the control group were 75.0 ± 5.2 lpm; and statistical significance was observed between the two groups. It is important to note that in the above study, information was obtained for 24 hours Holter [13].

RR interval, determining the duration of a cardiac cycle was shorter in the control than in the seropositive group. And, despite the fact that no statistical significance was found in these results, it is interesting to note that, similarly to what we have seen with RA, the SD was higher in the control subjects (0.22) than individuals Chagas disease (0.17) for this variable. This implies a greater distribution of data and therefore greater variability in heart rate. A considerable explanation for the fact that statistical significance in human resources was not found could be due to the lack of variation in the length of the RR interval.

Measures the QRS complex showed no statistical significance between the groups, but was slightly lower in the control patients (0.068 ± 0.01 s) in the group of Chagas disease (0.07 ± 0.01 s). Furthermore, the length of this parameter is considered within the normal range (0.06 - 0.08s) in both groups.

Changes in the ECG most common in a patient with Chagas disease are: BRD, which can be associated with left anterior branch block, ST diffuse - changes in the T wave, premature ventricular complexes, and episodes of ventricular tachycardia not sustained. Other common features are abnormal Q waves atrioventricular, abnormal sinus bradycardia and varying degrees of blockage. In advanced stages of the disease, atrial fibrillation and low voltage QRS [13] may be present. Occasionally, some of the ECG changes that can be seen during the acute phase of the disease involves: ST - changes of the T wave, prolongation of the QT interval, low voltage, BRD, the first degree AV [14]. During the chronic phase, the characteristics of the ECG most frequently observed are: right bundle branch block with left anterior hemi, major and minor isolated ST - changes in the T wave, frequent premature beats and beats headphones, left anterior branch block, atrial fibrillation or flutter, first blocking AV grade, prolonging the QT interval and bradycardia [15].

In ECG recordings taken from patients with Chagas disease, it found that some of them had more episodes of ventricular premature complexes. The detection of these complexes, atrial fibrillation, BRD, major changes ST- T and left ventricular hypertrophy, are associated with a reduced life expectancy in patients with Chagas disease [15].

The analysis results showed QT intervals statistical significance between the groups, but it was observed that QT media was higher in the experimental group. This means there was a longer time for driving of the electrical impulse through the bundle of His, however, analyzing the QTc, means of communication it was significantly higher ($p \leqslant 0, 05$) in HRV-positive patients.

Although the objective of this study did not include the identification of relevant ECG changes in patients with Chagas disease, as this is not part of the competence of the authors; it is important to mention that there are predictive factors for assessing the risk of sudden cardiac death in patients suffering from symptoms of Chagas disease. Among the features mentioned in the literature are: decreased ejection fraction left ventricular evident cardiomegaly on chest radiograph [17], QT interval, the ventricular tachycardia induced by electrophysiological studies age [18], left ventricular systolic diameter, intraventricular conduction disturbances.

During the course of the disease, severe arrhythmias can occur and lead to sudden cardiac death [19]. Mortality due to Chagas disease related to cardiac involvement [20] developed

a risk score for predicting sudden cardiac death in patients with chronic chagas, finding four major predictors: the dispersion of the interval QT, syncope, severe left ventricular dysfunction and ventricular tachycardia onset of ventricular premature. The not sustained during exercise is also considered a high risk factor for sudden cardiac death in Chagas disease [21]. Death from bradyarrhythmias or electromechanichal dissociation is less frequent [16] sympathetic and parasympathetic changes are observed during the course of the induced cardiomyopathy Chagas disease. These characteristics are influenced by an early increase in sympathetic activity associated with a progressive denervation cardiovagal along with non-specific immune changes. This could explain why sudden cardiac death is one of the first manifestations of the early stages of the disease [17] [22].

Electrocardiographic changes in patients with Chagas disease are a consequence of the effect of the infectious parasite in the structure of the heart. In the literature, it is said that there are different types of disorders including: engagement sinoatrial node and its cells infiltrate inflammatory chronic mononuclear cells replacing normal tissue fibrosis or tissue scarring, and sinoatrial dysfunction with mild to features severe clinical [23]. The participation of the bundle with blocks intraventricular right and beams left before affecting the bundle itself. the action of the factor tumor necrosis -. alpha (TNF-α) of negative inotropic effect, ventricular remodeling and dilated cardiomyopathy [24].

HRV parameters that were studied variables included time domain: SDNN, SDFC, RMSSD, NN50, and pNN50; variable frequency domain: LF, HF, and LF / HF ratio; and nonlinear parameters: ApEn and SampEn.

With regard to the specific variables for the time domain, it found a wide difference without statistical significance in SDNN between the mean values of the two groups, and this smaller number in the seropositive group. This finding correlates with the reported by [25]., with regard to the lack of significant association between HRV variables in control and patients with Chagas disease. However, the results provide evidence of changes in the HRV of seropositive individuals. However, it is important to note that in this study, 54.1% of patients with Chagas disease had significant changes in HRV compared to the control group. In the latter, these changes affected only 4% of the population. [25] [26] reported highly statistically significant ($p < 0.0001$) of values of the HRV in patients with Chagas disease and controls. In the first study, changes in SDNN were present in 34% of patients with Chagas disease, whereas these changes were only present in 1% of the control group. Both studies found a highly significant association between Chagas disease and HRV. De la Cruz established normal ranges of HRV parameters. SDNN less than 50 ms are considered high variability, from 50 to 100 ms of moderate variability, and numbers greater than 100 ms low variability. Regarding our study, according to these figures, our patients with Chagas disease were classified as high variability. SDNN values reported in healthy individuals with a high quality of life (69.78 ± 27.89 ms), and in healthy individuals, but with lower quality of life (46.0 ± 16.65 ms). The results are lower than those reported in our control group, however, higher than the results in the group of HIV-positive. [1] analyzed the HRV of 36 patients with Chagas disease compared to a control group. It was reported SDNN values of 149.75 ± 39.05 ms in the experimental group and 156.53 ± 41.84 ms in the control group. The study found no statistically significant differences between groups, according to data provided by De la Cruz these results could qualify as having low variability. This could be attributed to the age of the patients included in the study (mean age 36 years). At that young age, the parasite causing Chagas disease is unlikely to generate manifestations of heart damage, as reported by the [27].

RMSDD values in the two groups did not show statistical significance, however, the results were markedly higher in the control group than in seropositive. This was expected due to the fact that the numbers come from the SDNN. [1] reported 39.31 ± 15.56 ms in controls and 35.53 ± 13.4 ms in patients with Chagas disease. The results were higher in controls than in patients with the disease, agrees with the results of our study and the results therefore similar to ours. [29] RMSSD measured in healthy individuals with an average of 30.6 ms, results are quite similar to those obtained in the HIV-positive population of this study. It is likely that the result is due to the small number of participants analyzed [9] reported for the same parameter data with a median of 64. 0 ms in individuals considered healthy. Recordings of this study were five minutes long, which could have influenced the outcome. [29] assessed HRV in healthy athletes divided into two groups of high and low quality of life (health). The RMSSD in the first group was 64.37 ± 32.7 ms and 33.7 ± 26.18 the last ms. The result in the latter group was similar to the control group in this study who were not athletes. They concluded that individuals with a better quality of life have higher HRV, which is associated with increased vagal activity at rest. Furthermore, [25].found no statistical significance in the analysis of it also varies; Nevertheless, They said that there is a higher prevalence of disorders of HRV in patients with Chagas disease compared to people without the disease. Furthermore, .In contrast, [27].reported highly significant differences in HRV for mastering time between the experimental group and the control group. However, he did not explain the possible pathophysiological reasons like disease modifying variables, however, claimed that the HRV parameters are known and used to evaluate coronary cardiomyopathy. [30]conducted a study on circadian profiles of HRV in patients with chronic Chagas disease, reporting HRV control subjects during the day to be 34.0 ± 10.1 ms and 46.7 ± 26.3 at night. The figures reported during the day coincides with the results we obtained in our control group, whose recordings were also taken during the day. The results reported by the night for this variable was different from the group of Chagas disease which shows the following values: 42.1 ± 19. 0 ms in patients with mild changes in ECG and 59.0 ± 31.0 in patients with more severe changes in the ECG. Having said that, there were no statistically significant differences between controls and patients with Chagas disease with slight changes in the ECG and among the subgroup of patients with Chagas with ECG changes moderate compared with more severe electrocardiographic changes. HRV values were higher at night. These values above can be explained by the result of the disease, dysautonomia that alters the function

of the parasympathetic nervous system. It is noteworthy in this study than in the control group, the HRV was higher at night, when the vagal activity is more frequent. In a study of [37] variable RMSSD was evaluated before and after physical activity in patients with Chagas disease. It fluctuated between 30-83 -74 ms and 32 ms before and after exercise, respectively. These results no significance pre or post exercise statistics, or compared to the control group. However, an atypical result was expected as increased vagal activity during activity. This correlates with the results also presented by [30] who said that this effect is due to autonomic dysfunction, the presence of anti-muscarinic and damage to the sinus node; where the sinus node does not respond properly to the parasympathetic activity when regulating heart rate. This correlates with the results also presented by [30], who said that this effect is due to autonomic dysfunction, the presence of anti-muscarinic and damage to the sinus node; where the sinus node does not respond properly to the parasympathetic activity when regulating heart rate. This correlates with the results also presented by [30], who said that this effect is due to autonomic dysfunction, the presence of anti-muscarinic and damage to the sinus node;

The NN50 variable had highly significant results between the two study groups (P <0.003), being noticeably greater control group in the experimental group. In terms of pNN50, results in the control group were 12.3 ± 13.3% and seropositive group were 2.64 ± 6.0%. This sets high statistical significance between groups (P ⩽ 0.007), implying healthy hearts in terms of HRV in the control group. [1] reported in their studypNN50 values of 13.56 ± 10.18% in patients with Chagas disease and 15.37 ± 10.69% in the healthy counterpart, showing no statistical significance between groups. This study demonstrated greater homogeneity in our study population. The different results may be due to the average age of the patients (36 years old) in the study conducted by Gutierrez et to the. In another study published by [25]. pNN50 values above 15% was considered high variability, while numbers lower than 4% were classified as low variability. According to these criteria, patients with Chagas disease in this study showed very low variability. These findings, together with the results of the other variables in the time domain of the HRV they are considered a consequence of cardiac autonomic dysfunction in control. [27].also reported high statistical significance (p <0.0001) in the time domain variables of HRV in patients with Chagas disease, which was similar to our results. [30] reported 24 hours pNN50 values in controls (14.5 ± 10.8%) and in patients with Chagas disease (13.2 ± 9.9%). The results of the controls are similar to our findings, however, different in the case of HIV-positive patients; which can be explained by the level of cardiac involvement in patients participated in this study. Most of the participants in our study were in chronic phase of the disease (mean age 52 years). In the study published by [30]. It is noteworthy that the results obtained pNN50 overnight are higher in the control and in the experimental group (21.6 ± 21.2% and 19.5 ± 14.0%). As mentioned above, it is likely due to increased vagal activity overnight, allowing greater HRV. [9] reported values pNN50 in young healthy individuals (46%), which is greater than the pNN50 established in this study. One of the possible causes of this discrepancy is the recording time (5 minutes can be explained by the level of cardiac involvement in patients participated in this study. Most of the participants in our study were in chronic phase of the disease (mean age 52 years). In the study published by [30]. It is noteworthy that the results obtained pNN50 overnight are higher in the control and in the experimental group (21.6 ± 21.2% and 19.5 ± 14.0%). As mentioned above, it is likely due to increased vagal activity overnight, allowing greater HRV. 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With regard to the variables of frequency domain, which are part of the analysis of HRV. We found that related low frequencies (LF) were not statistically significant between the groups, although recordings the lowest frequency in the group of Chagas. This means that there is increased sympathetic activity in healthy individuals. Low frequencies vary from .04 to 0.014 Hz according to the [27]. These ranges are parallel to the results obtained in both groups of our study. In analyzing the variables of time domain HRV in patients with Chagas [37] found a significant increase in very low frequency (VLF) but not at low frequencies (LF) after exposure of individuals physical activity. [9] reports gathered in LF (means of 0. 0410

Hz) of healthy individuals, but their results were lower than ours in the control group. The authors explain that the LF obtained are a result of the interaction between the sympathetic and parasympathetic systems. However, they claim that long-term recordings give more information about sympathetic activity and baroreceptor, which is also in this frequency range. Baroreceptor report changes in blood pressure to the brain stem, controlling cardiovascular activity. The brainstem determines what to do next depending on the situation presented, through sympathetic or parasympathetic pathways, increasing or decreasing their activity. The authors explain that the LF obtained are a result of the interaction between the sympathetic and parasympathetic systems. However, they claim that long-term recordings give more information about sympathetic activity and baroreceptor, which is also in this frequency range. Baroreceptor report changes in blood pressure to the brain stem, which controls the cardiovascular activity. The brainstem determines what to do next depending on the situation presented, through sympathetic or parasympathetic pathways, increasing or decreasing their activity. The authors explain that the LF obtained are a result of the interaction between the sympathetic and parasympathetic systems. However, they claim that long-term recordings give more information about sympathetic activity and baroreceptor, which is also in this frequency range. Baroreceptor report changes in blood pressure to the brain stem, which controls the cardiovascular activity. The brainstem determines what to do next depending on the situation presented, through sympathetic or parasympathetic pathways, increasing or decreasing their activity. controlling cardiovascular activity. The brainstem determines what to do next depending on the situation presented, through sympathetic or parasympathetic pathways, increasing or decreasing their activity. controlling cardiovascular activity. The brainstem determines what to do next depending on the situation presented, through sympathetic or parasympathetic pathways, increasing or decreasing their activity.

After analyzing the high frequency (HF), the results were not statistically significant between the groups, but frequencies were higher in patients with Chagas disease. In other words, it increased parasympathetic activity was demonstrated in this frequency range (0.14 to 0.4 Hz) [25][27]. Gutierrez et him. (2009) reported the IC with respect to the spectral power in patients with Chagas disease, finding 15.72 ± 6.6 Hz in patients with Chagas disease and 17.23 ± 7.51 Hz in controls, with a smaller spectrum in the seropositive group. [reported no data specifically HF, but in the end statistical analysis of the different variables of HRV, Statistical significance (P <0.0001) .These data highly correlated with the detection of autoantibodies in patients antimuscarinic with Chagas disease was obtained. Muscarinic receptors are a subset of cholinergic receptors which are present in the postganglionic parasympathetic fibers. In the study published by [25] statistical significance (P <0.04) was found between patients with Chagas' disease and patients not sick in the frequency analysis VFC, and they also found that the presence of IgG anti-autonomous. The information described above was later confirmed by [27]. [37] evaluated the changes in the frequency domain in patients with Chagas before and after physical activity disease. The results showed 1. A significant increase in VLFP (very low frequency power) in patients exposed to physical activity versus controls (P = 0.047), 2. a nonsignificant increase in HFP (high frequency power) in individuals exerted and 3. a decrease in the same parameter in the control group. These results are consistent with autonomic dysfunction has been detected in patients with Chagas disease, despite the vagotonic effect of exercise. Moreover, the relationship between exercise and vagal index in healthy individuals HRV is remarkably strong. [9] reported HF 0.2227 Hz in a healthy population,

The LF / HF ratio was significantly higher in patients than in control patients seropositive, indicating increased activity of the sympathetic system in the long run and therefore a lower parasympathetic activity. This statement is in accordance with the above discussion. [25][27] felt that ranges normal for this ratio are 1.5 - 2.0, which are values that almost place the results of our patients Chagas disease in that proportion. This implies a low activity in the LF domains, which are related to sympathetic activity. [1] reported ratios of LF / HF 48.8 ± 13 in patients with Chagas disease and 49.9 ± 17.2 in controls. These values were reported as spectral power, without finding statistical significance. [28] studied healthy young individuals with a moderate level of physical activity, search ranges LF / HF to 2.18 (almost within normal ranges described above, but on the values of the results found in our control group). It [9] established a relationship of these frequencies expressed in percentage of the spectral power (0.493%), the definition of a low frequency power spectrum to be 23.1% and a high frequency power spectrum to be 46, 8%. According to the authors, the relationship between the two frequencies is the result of spectral analysis of HRV, and is used to estimate the related vagal tone with rest and HF and sympathetic activity, stress-related and LF. Thus, be able to estimate the sympathetic-parasympathetic balance. The authors concluded that a high HRV evaluated by this relationship, is present in healthy individuals, so it is a sign of good health. The ratio of these two frequencies in our study was higher in the control group (which do not suffer from heart disease, according to the self-declaration to the study entry).

The study of HRV in this academic work completed with the analysis of nonlinear variables which were measured through the approximate entropy and the entropy of the sample. Approximate entropy provides a rapid calculation of the regularity of the biological signals [2] and also quantifies the unpredictable fluctuations in the ranges of time series values previously know the same parameter. In this study, both entropies were significantly lower in the experimental group of patients. These variables analyzed chaotic behavior of HRV, as entropy is a concept that specifies the randomness and prediction of biological systems. These authors reported approximate entropy of 0.42 ± 0.1 in controls and 0.34 ± 0 15 in the experimental group (p = 0.002); ranges that do not coincide with ours, however, statistical significance is presented like. It is noteworthy that these results were obtained from patients during the acute phase of the disease, while ours were taken during the chronic phase. In both studies, the fact of having a higher approximate entropy in

controls, indicating a higher irregularity of the HRV therefore better health.

Through this discussion we mentioned that disturbances in HRV in patients with Chagas disease are a consequence of functional disorders of the sinoatrial node, more specifically in the ganglia of the autonomic nerves. [29] demonstrated that cardiovascular autonomic dysfunction was observed in 32-52% of patients with Chagas cardiomyopathy. Damage to the autonomic neurons is related to the destruction axons damage of axons and caused demyelination by neuropathic toxins and waste products of dead parasites [31]. These changes have been known to occur during the acute phase of the disease [32].

Studies have shown that autonomic dysfunction heart, especially parasympathetic affects patients with Chagas' disease [35] but has also been shown that there is the presence of circulating autoantibodies that bind to cholinergic and adrenergic receptors myocardial, triggering reactions that cause myocardial damage downregulation and desensitization of muscaricic and adrenergic receptors [33]. Parasympathetic abnormalities seen in Chagas cardiomyopathy is mainly characterized by the progressive and not reversible dysfunction cardiovagal reflections on the sinoatrial node [29][34]. During the chronic phase of the disease, the destruction of the cardiac conduction system, autonomic nerves heart, and myocardial cells have been described; processes that are related to the onset of cardiac arrhythmias and ventricular dysfunction [33] [35].

Several noninvasive techniques allow quantification of autonomic function in Chagas cardiomyopathy; identify gradual changes in the parasympathetic nervous system. It has been through the use of such techniques a progressive reduction of HRV described in the course of Chagas disease [35]. Furthermore, parasympathetic disturbance causes a reflection of the release of active biological molecules, such as noradrenaline, angiotensin II and endothelin, which contributes to the development of this cardiomyopathy driven disease [36]. Ultimately, there is a significant association between antimuscarinic autoantibodies (M2), the presence of HRV disturbances, changes in cardiovascular function and abnormal bradycardia in patients with Chagas cardiomyopathy.

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