ORIGINAL ARTICLE

Diagnostic Relevance of Recurrence Plots for the Characterization of Health, Disease or Death in Humans

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Abstract

Introduction: Recurrence plots have been increasingly used to evaluate complex dynamic systems of which the human body is an excellent model. The different quantitative and qualitative elements of recurrence plots in health, disease, and death were analysed. A time series of normal heartbeats were collected in healthy newborns, healthy children, healthy young adults, healthy middle-aged adults, elderly individuals living in nursing homes, individuals with advanced chronic kidney disease, and individuals with declared brain death or in a state of imminent death. Healthy young adults showed the best homeostasis (lower recurrence). Healthy newborns and individuals with declared brain death or in a state of imminent death had higher recurrence values. At the qualitative visual level, healthy young adults showed a more diffuse and uniform distribution, indicative of better homeostasis; for individuals with declared brain death or in a state of imminent death this was totally linear – the worst condition. A parabolic pattern was clearly evidenced. In conclusion, it was possible, using the correlation of only two variables (SDNN and TT), to easily differentiate states of health, disease, and death using recurrence plots.

Keywords: autonomic nervous system, heart rate variability, health, disease, death, recurrence plots.

What is the purpose of this study?
This study was conducted to determine a simple method of detecting homeostasis impairment based on heart rate variability and recurrence plots.

What researchers did and found?
The quantitative and qualitative evaluation of recurrence plots allowed the selection of two variables (standard deviation of the RR normal intervals (SDNN) and the average length of the vertical lines (trapping time)), that when correlated in a phase space, discriminate individuals with adequate autonomic control (healthy children and adults), from those with autonomic systems compromised by immaturity or progressive loss of function.

What do these findings mean?
These findings indicate the possibility of using a simple, low-cost, and non-invasive method to estimate the degree of autonomic impairment in humans and to define functional profiles.

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INTRODUCTION

The human body is a clear example of a "Complex System", characterized by the continuous interaction of its multiple organs, aiming at the maintenance of life.

Its complexity results in a mode of behavior that, in normal situations, is typically non-linear or, although deterministic in the very short term, it displays characteristics of low predictability in the long term, since the interaction of countless concomitant variables contributes to the occurrence of emergent behaviors, i.e., those that cannot be predicted by the isolated analysis of each component.

The human body, like any natural physical system, performs or is subject to processes involving mixing, exchanges and diffusion, among others. Therefore, it tends to move towards states of uniformity or equilibrium in the absence of counteracting actions. Thus, in order to stay alive, the human body must necessarily obtain energy to allow the respective chemical reactions that are part of the normal metabolism, therefore acting as a thermodynamic machine.

At the completion of a physical or mental work, the yield is never kept at 100%. A certain amount of energy with no capacity to produce work will remain in the system. It will be a muss less-ordered system as several processes were carried out with numerous interactions, considerably increasing the amount of system microstates, and consequently increasing Entropy and reducing homeostasis.

The harmonious control of homeostasis is mostly coordinated by the Autonomic Nervous System (ANS), which is divided into the Sympathetic and Parasympathetic branches. Presumably, there will be a positive correlation between the functioning of those components and the state of health since there is enough evidence that several morbid conditions reduce the functioning of the autonomic nervous system and, reciprocally, diseases are caused by alterations in that system[1-7].

The heart remains connected by network with basically all other organs through the autonomic nervous system. The variation of a normal heart rhythm, called Heart Rate Variability (HRV), has been considered an effective marker of the presence or not of adequate homeostasis[8-9].

Recurrence Plots (RP), idealized by Eckmann *et al*. (1987), propose to analyze the behavior of systems, represented by time series, in an abstract space called phase space[10]. Their construct is quite simple, based on a square in which both the x-axis and the y-axis contain the elements of the time series sequentially arranged from the first to the last, making correlations two by two. From then on, according to pre-established parameters (dimension, delay and ratio), the recurrence of values can be verified. Recurrence Plots have been shown to be a useful tool to evaluate the autonomic nervous system, especially because they allow quantification and qualification of Heart Rate Variability[11-12].

It is very useful to verify whether there are well-defined patterns in the Recurrence Plots in states with adequate homeostasis and in the different degrees of impairment because, from the physiological point of view, Heart Rate Variability tends to decrease with aging and with the onset of diseases[13-16].

Thus, the objective of the present study was to evaluate the quantitative and qualitative elements of Recurrence Plots and their potential relevance in the comparative analysis of time series for Heart Rate Variability in states of Health, Disease and Death.

METHODS

Based on a large institutional database, heart time series of interest for the purpose of this study were re-analyzed. All individuals included in the present study (or their legal guardians) agreed to participate and the approval by the Institutional Ethics Committee was obtained (CAAE: 44820515.5.0000.5415).

The electrocardiographic time series had been collected during 15 to 20 minutes, using a pulse frequency meter (Polar RS 800 CX ; Polar Eletro OY, Kempele, Finland) at rest and in supine position. This methodology has been validated in relation to Holter system and has demonstrated to produce accurate and reliable data[17-18]. Only time series with basal sinus rhythm and with a maximum of 5% artifacts prior to filtering were included. All series were submitted to filtering to avoid noise effects using the T-RR filter software[19].

Were studied four clinically distinct groups: healthy individuals (Group A), elderly individuals living in nursing homes (Group B), individuals with advanced chronic kidney disease (Group C), and individuals with declared brain death or in state of imminent death (Group D). In the imminent death group, were included the patients who died up to one week after collection of the time series.

Given the influence of age on measures of Heart Rate Variability, group A was divided into subgroups: healthy newborns (Group A1, N=30), healthy children (Group A2, N=30), healthy young adults (Group A3, N=29) and healthy middle-aged adults (Group A4, N=18). In groups B, C and D, 33, 33 and 37 individuals were included, respectively.

The temporal series were analyzed using Visual Recurrence Analysis software (VRA – Version 5.01, Eugene Kononov, http://visual-recurrence-analysis.software.informer.com. Recurrence plots were constructed with the following parameters, chosen accordingly to Iwanski & Bradley (1998)20: dimension=2, time delay=2, ratio=70, line=2 and the color scheme was Volcano.

The studied variables were: mean of RR Intervals (meanRR), standard deviation of the average of normal RR intervals (SDNN), the percentage of recurrence points in an RP (Recurrence Rate; RR%), the percentage of recurrence points forming diagonal lines (Determinism; DET%), the percentage of recurrence points forming vertical lines (Laminarity; LAM%), the average length of the vertical lines (Trapping Time; TT), the ratio between DET% and REC% (RATIO), Shannon Entropy, a measure indicating the complexity of the system (ShanEntr), the maximum length of the diagonal line (Lmax) and how the density of points changes as you move away from the line of identity (Trend)[21-22].

In the descriptive statistical analysis, mean values,

standard deviation, median and interquartile range were used. For the inferential statistical analysis, ANOVA was used with Tukey Post-test to detect differences between groups. The graphical characterization was done with Box-Plot graphs. An alpha error of 5% was set, and p-value of equal or less than 5% were considered as significant.

RESULTS

Table 1 summarizes all the values obtained with the studied variables. As age goes up and the state of health changes into state of disease and eventually death, there is a clear parabolic behavior with group A3, showing, for most of the studied variables, the most compatible autonomic behavior with optimal homeostasis. Thus, healthy young adults (A3) have greater standard deviation of intervals indicating higher Heart Rate Variability and, according, lower Recurrence Rate, lower Determinism, lower Laminarity and shorter Trapping Time. Maximum Length of the Diagonal Line (Lmax) is also clearly lower in group A3.

Table 1: Mean values, standard deviation, median and interquartile range of all quantitative variables studied using Recurrence Plot.

Variable	A1 (30)	A2 (30)	A3 (29)	A4 (18)	B (33)	C (24)	D (37)
Age Group A1 : dias Group A2 - D: years	1.1±0.8 [1.0] {1.0 – 2.0}	11.3±2.0 [11.5] {10.0-13.0}	20.7±1.6 [21.0] {20.0– 22.0}	33.9±10.7 [33.5] {23.0-42.0}	73.3±8.7 [73.5] {66.0-78.7}	61.6±14.4 [64.5] {52.3-72.9}	59.4±19.9 [62.0] {47.5-73.0}
RR mean ms	498.5±66.9 [493.0] {445.4-543.5}	678.2±95.0 [653.1] {611.2-734.4}	853.6±115.8 [853.3] {758.8-960.9}	940.6±93.1 [938.7] {877.9-998.7}	806.1±89.4 [808.6] {760.6-840.0}	818.3±184.5 [807.7] {650.1-947.8}	705.9.2±185.2 [645.0] {577.8-770.5}
SDNN ms	33.2±18.5 [31.2] {22.2-35.9}	51.5±17.5 [51.3] {37.7-63.3}	55.3±21.3 [51.6] {38.4-69.4}	51.2±16.6 [48.0] {38.8-59.9}	32.4±19.1 [29.7] {17.3-42.8}	21.311.5 [19.3] {11.0-29.0}	15.3±12.4 [11.8] {5.6-22.6}
REC%	40.4±4.1 [40.8] {39.5-42.1}	35.9±2.5 [35.9] {34.4-37.2}	34.6±2.0 [34.7] {32.7-36.2}	37.0±3.4 [36.2] {33.8-38.8}	38.7±3.8 [38.4] {35.5-41.9}	39.4±3.1 [39.6] {37.3-42.2}	40.6±5.2 [40.2] {37.8-42.7}
DET%	91.5±5.6 [92.8] {88.7-96.4}	80.9±8.1 [83.0] {75.5-87.2}	71.1±10.6 [68.7] {63.7-83.2}	78.3±9.6 [92.8] {77.1-69.8}	82.9±10.3 [85.2] {76.9-92.0}	81.2±19.5 [85.7] {75.4-94.4}	84.1±11.8 [87.0] {72.8-94.5}
LAM%	93.9±5.2 [95.3] {91.5-97.5}	89.9±4.8 [91.5] {86.7-93.8}	83.6±9.1 [84.0] {78.0-92.8}	88.8±5.6 [89.4] {84.6-93.1}	90.8±5.9 [92.5] {88.3-94.9}	87.2±16.5 [91.6] {83.7-96.2}	90.9±7.4 [93.1] {85.5-96.9}
TT	12.0±5.1 [10.3] {8.3-14.3}	5.4±1.3 [5.3] {4.5-6.0}	4.2±1.3 [3.5] {3.3-4.5}	5.2±2.0 [4.5] {3.7-6.4}	8.0±3.6 [7.6] {4.9-10.4}	12.4±7.6 [10.8] {6.3-19.0}	14.1±14.9 [8.4] {5.7-21.2}
Ratio	2.2±0.4 [2.2] {2.1-2.3}	2.2±0.1 [2.2] {2.1-2.3}	2.0±0.2 [2.0] {1.7-2.2}	2.1±0.1 [2.0] {1.9-2.2}	2.1±0.1 [2.12] {2.0-2.2}	2.2±0.4 [2.2] {2.1-2.3}	2.0±0.2 [2.1] {1.9-2.2}
ShanEnt Bits	4.1±0.7 [4.1] {3.7-5.4}	3.2±0.3 [3.2] {2.9-3.4}	3.2±07 [3.0] {2.9-3.2}	3.3±0.4 [3.1] {2.9-3.6}	3.7±0.5 [3.7] {3.1-4.3}	4.1±0.7 [4.0] {3.5-4.8}	4.0±0.8 [3.7] {3.3-4.7
Lmax	398.8±302.9 [284] {163.5-554.7}	106.9±85.1 [78] {52.5-133.0}	77.9±52.8 [71] {50.0-84.5}	202.69±276.1 [77.5] {43.0-235.7}	239.8±236.2 [181] {77.5-308.0}	373.1±350.6 [168.5] {91.2-738.0}	456.4±460.6 [265.0] {107.5-709.5}
Trend	-17.8±25.5 [-13.4] {-24.5- -0.7}	-11.1±16.4 [-6.2] {-12.3-14.7}	-15.1±12.5 [-12.74] {-22.0 - -7.1}	-11.3±10.1 [-10.0] {-18.3- -3.7}	-23.1±21.5 [-14.8] {-38.2- -9.7}	-27.7±25.5 [-21.4] {-45.9- -9.5}	[-35.7±41.0] [-24.5] {-71.2-1.55}

Note: Mean RR (mean of RR Intervals); SDNN (standard deviation of the average of normal RR intervals); REC% (the percentage of recurrence points in an Recurrence Plot); DET% (the percentage of recurrence points forming diagonal lines); LAM% (the percentage of recurrence points forming vertical lines); TT (the average length of the vertical lines); Ratio (the ratio between DET% and RR%); ShanEntr (Shannon Entropy: a measure indicating the complexity of the system); Lmax (the maximum length of the diagonal line); Trend (how the density of points changes as you move away from the line of identity)

The group of healthy newborns (A1) and the group of individuals with declared brain death or in state of imminent death (D) represent the extreme positions of the parabola, both with higher values for Determinism, Recurrence Rate, Laminarity, Trapping Time, Shannon Entropy and Maximum Length of the Diagonal Line.

Figure 1 illustrate, with Box-Plot graphs, this parabolic behavior in two of the studied variables. The graphic visual aspect (qualitative) of the recurrence plots were also evaluated, as observed in Figure 2. Twelve non-selected cases from each of the most representative groups, i.e., healthy newborns (A1), healthy young adults (A3), individuals with advanced chronic kidney disease (C), and individuals with declared brain death or in state of imminent death (D) were represented.

A more diffuse and uniform distribution can be differentiated in the group A3 (healthy young adults) indicating higher HRV, whereas, in the other groups, there are geometric patterns and higher recurrence, due to immaturity of the autonomic nervous system (group A1), advanced chronic kidney disease (Group C) or declared brain death or state of imminent death (Group D).

ANOVA and Tukey's Post-test demonstrate the statistic differences between the studied groups for each of the variables (Table 2). Gray highlights indicate statistically significant differences.

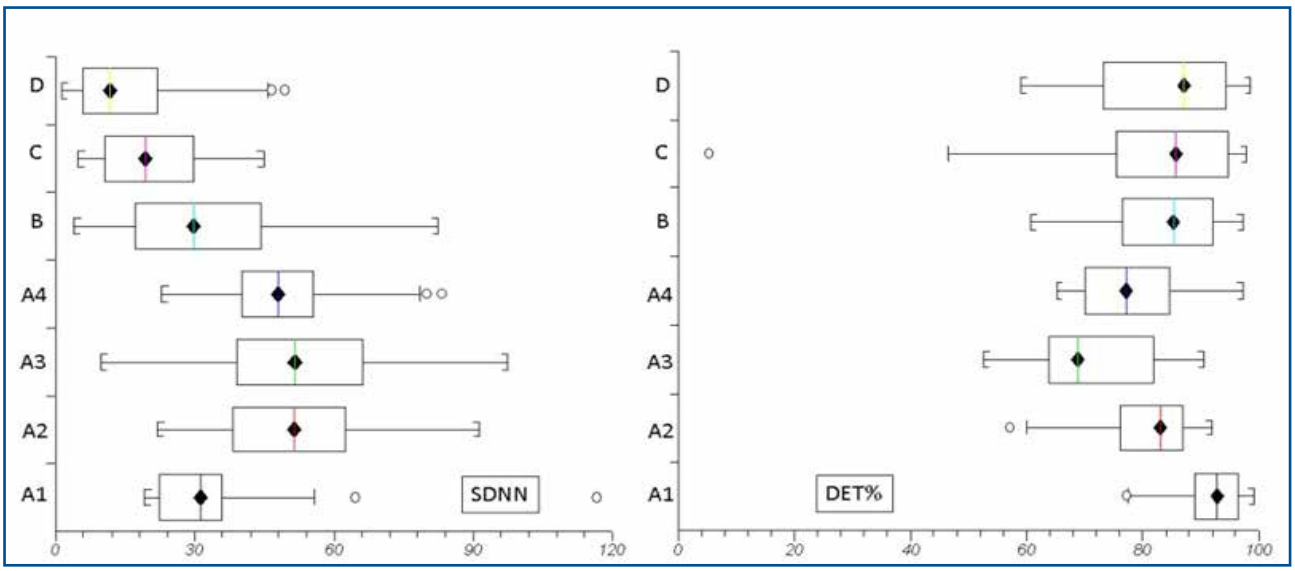

Figure 1: Box-Plot graphs of the variables SDNN and DET% in the different clinical groups studied. Note the clear parabolic behavior of the values obtained.

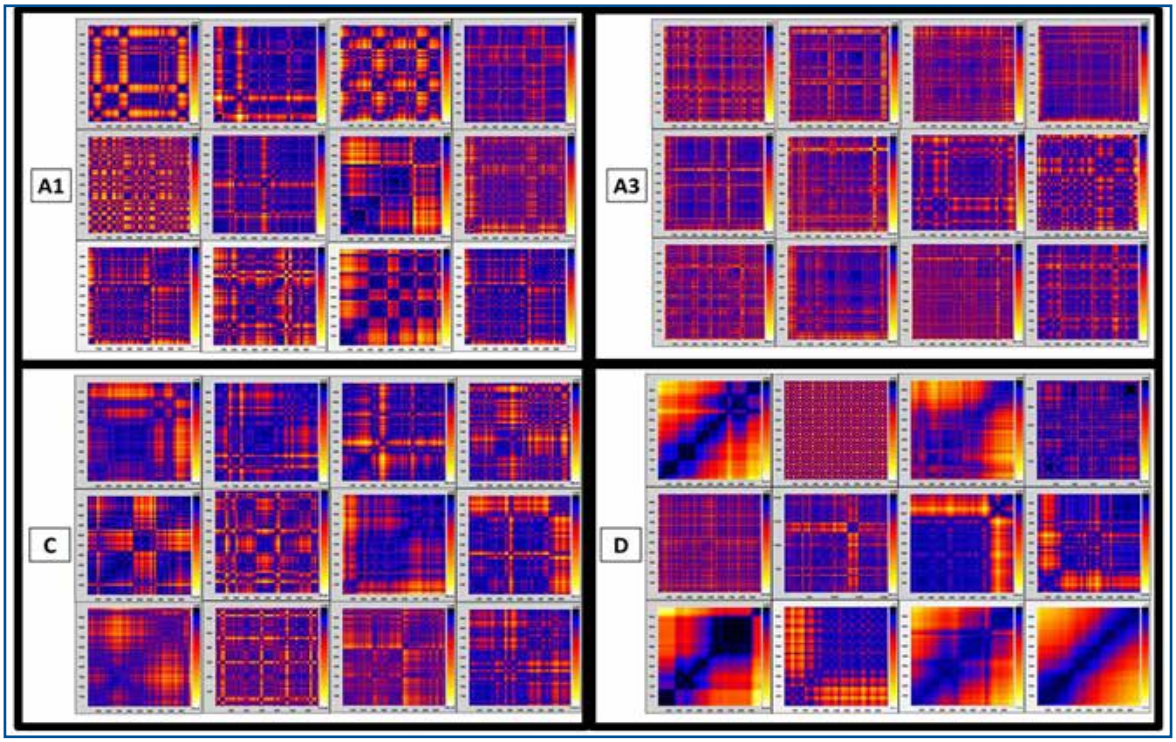

Figure 2: Visual Recurrence Analysis using Scheme Volcano of 12 non-selected individuals from each clinical group evaluated: A1 (healthy newborns); A3 (healthy young adults); C (individuals with advanced chronic kidney disease) and D (individuals with declared brain death or in state of imminent death). Note the clearly different geometric behavior of the groups.

Table 2: Recurrence Plot variables, with P-values, for the various intergroup comparisons (Tukey Post-test).

Grupos	RR médio [16/21]	SDNN [14/21]	REC% [9/21]	DET% [9/21]	LAM% [3/21]
A1XA2	< 0.0001	0.0010	0.0001	0.0073	0.5376
A1XA3	< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.0001
A1XA4	< 0.0001	0.0093	0.0489	0.0025	0.4128
A1XB	< 0.0001	> 0.9999	0.5587	0.0463	0.7650
A1XC	< 0.0001	0.1520	0.9739	0.0187	0.0676
A1XD	< 0.0001	0.0007	> 0.9999	0.1159	0.7843
A2XA3	< 0.0001	0.9779	0.8480	0.0178	0.0669
A2XA4	< 0.0001	> 0.9999	0.9381	0.9862	0.9995

Continuation - Table 2: Recurrence Plot variables, with P-values, for the various intergroup comparisons (Tukey Post-test).

Groups	Mean RR [16/21]	SDNN [14/21]	REC% [9/21]	DET% [9/21]	LAM% [3/21]
A2XB	0.0021	0.0003	0.0472	0.9938	0.9997
A2XC	0.0018	< 0.0001	0.0095	> 0.9999	0.9101
A2XD	0.9757	< 0.0001	< 0.0001	0.9189	0.9991
A3XA4	0.2681	0.9837	0.3057	0.3524	0.3799
A3XB	0.7700	< 0.0001	0.0005	0.0013	0.0176
A3XC	0.9541	< 0.0001	< 0.0001	0.0249	0.7048
A3XD	0.0001	< 0.0001	< 0.0001	0.0001	0.0105
A4XB	0.0078	0.0043	0.7437	0.8115	0.9865
A4XC	0.0399	< 0.0001	0.3712	0.9826	0.9968
A4XD	< 0.0001	< 0.0001	0.0187	0.5641	0.9779
BXC	0.9998	0.1984	0.9873	0.9979	0.7139
BXD	0.0218	0.0009	0.3345	0.9994	> 0.9999
CXD	0.0168	0.8387	0.9071	0.9591	0.6464

Note: Mean RR (mean of RR Intervals); SDNN (Standard Deviation of the average of normal RR intervals); REC% (the percentage of recurrence points in an Recurrence Plot); DET% (the percentage of recurrence points forming diagonal lines); LAM% (the percentage of recurrence points forming vertical lines).

Table 3: Recurrence Plot variables, with P-values, for the various intergroup comparisons (Tukey Post-test).

Groups	TT [10/21]	Ratio [3/21]	Shanent [9/21]	Lmax [6/21]	Trend [3/21]
A1XA2	0.0107	0.9780	< 0.0001	0.0027	0.9457
A1XA3	0.0014	0.0249	< 0.0001	0.0007	0.9996
A1XA4	0.0377	0.3267	0.0008	0.2706	0.9778
A1XB	0.3107	0.3317	0.1445	0.3215	0.9813
A1XC	> 0.9999	0.0317	>0.9999	> 0.9999	0.7793
A1XD	0.9260	0.0353	0.9339	0.9844	0.0627
A2XA3	0.9967	0.2180	>0.9999	0.9998	0.9965
A2XA4	> 0.9999	0.7970	0.9993	0.9273	> 0.9999
A2XB	0.8065	0.8675	0.0552	0.5451	0.4894
A2XC	0.0111	0.2360	<0.0001	0.0175	0.1983
A2XD	< 0.0001	0.3009	0.0002	< 0.0001	0.0018
A3XA4	0.9993	0.9947	0.9995	0.7880	0.9989
A3XB	0.4245	0.9045	0.0647	0.3109	0.8732
A3XC	0.0016	> 0.9999	<0.0001	0.0057	0.5352
A3XD	< 0.0001	> 0.9999	0.0002	< 0.0001	0.0191
A4XB	0.8710	0.9999	0.3739	0.9995	0.6874
A4XC	0.0345	0.9926	0.0040	0.4989	0.3641
A4XD	0.0010	0.9996	0.0125	0.0436	0.0156
BXC	0.2776	0.8979	0.3435	0.6139	0.9932
BXD	0.0128	0.9682	0.6885	0.0353	0.3600
CXD	0.9805	0.9998	0.9913	0.9307	0.8896

Note: TT (the average length of the vertical lines); Ratio (the ratio between DET% and RR%); ShanEntr (Shannon Entropy: a measure indicating the complexity of the system); Lmax (the maximum length of diagonal line); Trend (How the density of points changes as you move away from the line of identity); A1,A2,A3,A4,B,C,and D: the studied groups

A critical evaluation of Tables 2 and 3 reveals quite relevant clinical considerations as follows:

1.Of the 21 possibilities for intergroup comparison, the mean RR interval duration showed the greatest amount of significant differences (16/21, 76.2%) followed by RR standard deviation (14/21, 66.7%). Interestingly, in eight comparisons, there was no agreement between these two variables, i.e., one of them indicated a significant difference between the groups and the other did not. As an example, the comparison between healthy newborns and elderly individuals living in nursing homes (A1XB) showed mean RR interval significantly lower in group A1 when compared to group B (498.5 ± 66.9 ms x 806.1 ± 89.4 ms; P <0.0001). However, the standard deviation of this interval (SDNN) showed no difference between the groups (33.2 ± 18.5 ms x 32.4 ± 19.1 ms; P> 0.9999), indicating that the differences in HRV are not necessarily due to differences in heart rate. The same reasoning can be applied to the other 7 comparisons in which such discrepancy occurred.

2.Trapping Time (TT) with 10 occurrences of significant difference (10/21, 47.6%) and Recurrence Rate (REC%), Determinism (DET%) and Shannon Entropy each of them with 9 occurrences (9/21; 42.8%) proved to be useful variables for the differentiation between groups.

3.Laminarity (LAM), Ratio and Trend, in turn, showed very bad performance on clinical distinction between groups with only 3 significantly different comparisons (3/21; 14.3%); whereas the maximum length of the diagonal line (Lmax) showed weak performance (6/21, 28.6%)

4.The group of healthy young adults (A3) stood out with the highest Heart Rate Variability, with higher value of SDNN and lower values of indicators of recurrence, confirming that this group presents best functioning of the autonomic nervous system. Statistically, none of the variables managed to differentiate the group of healthy young adults from the healthy middle-aged adults (A3xA4). This could indicate that the normal functioning of the autonomic nervous system is not restricted to the young age and can reach middle adulthood.

5. It was clear that, in the group of elderly individuals living in nursing homes (B), the progressive deterioration of the autonomic function begins with the reduction of the variability and the increase of the recurrence indicators with the group A3, showing statistical differences in relation to group B in 8 of the 10 studied variables.

6.As expected, individuals with declared brain death or in state of imminent death (Group D) showed evidence of low variability and higher recurrence indicating progression towards the state of equilibrium.

7.The low differentiation between group A1 and group D (3/10; 30.0% of the variables) has physiological reasons: on the one hand, newborns have low autonomic function as their autonomic nervous system is immature and still developing; on the other hand, the state of death has low autonomic functioning due to degeneration and exhaustion of the system. This differentiation was displayed as a parabolic pattern in the Box-Plot graphs (Figure 1).

Ultimately, since Trapping Time and the standard deviation of RR intervals were the most clinically relevant variables, the distribution of groups in a phase space was studied, correlating the two variables (Figure 4). A clear separation in the positioning of the groups can be observed, confirming the evolutionary parabolic behavior. These two pieces of information can serve as useful tools to suppose the clinical state of an individual (if healthy, sick or near death).

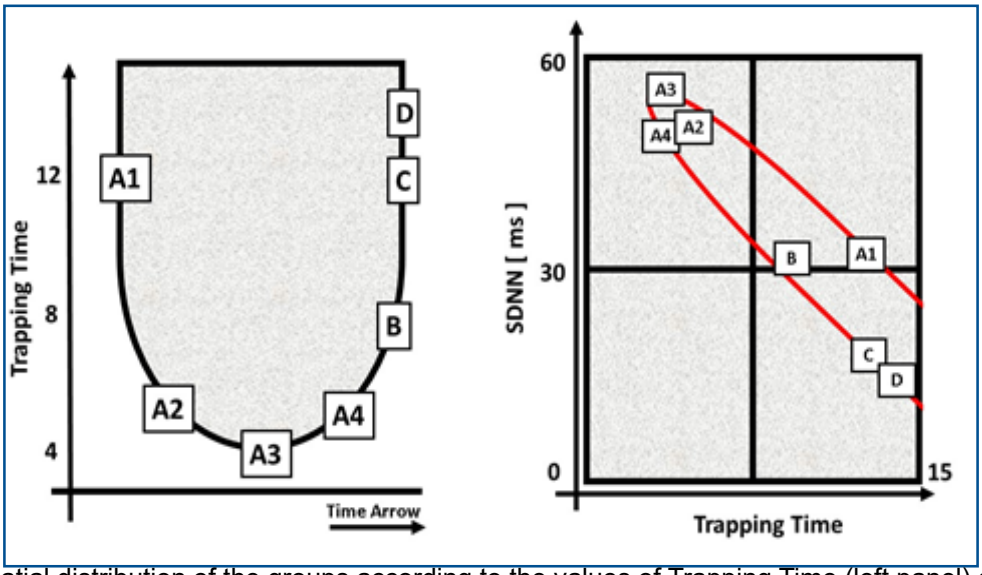

Figure 4: Spatial distribution of the groups according to the values of Trapping Time (left panel) and correlation between SDNN and Trapping Time (right panel)

DISCUSSION

The main purpose of the present study was to verify the ability of recurrence plots to allow differentiated recognition of three large clinical groups: healthy individuals, individuals with severe disease, and those in a state of death or imminent death.

Among the specific variables of the recurrence plot, trapping time (TT) with 10 occurrences of significant difference (10/21, 47.6%) and recurrence rate (REC%), determinism (DET%), and Shannon entropy, each with 9 occurrences of significant difference (9/21; 42.8%), proved to be useful variables for differentiation between groups. Notably, there is a differentiation between the groups from a statistical point of view; however, from a clinical point of view, the absolute values of REC%, DET%, and Shannon's entropy were relatively similar in each of the analysed groups. On the other hand, TT showed statistical difference as well as discrimination capacity at simple visual observation of the values (Table 3).

The intergroup differences for laminarity, trend, ratio, and Lmax were not clinically relevant and, according to our interpretation, should not be considered as appropriate for differentiation between the groups.

Therefore, we can say that the clinical relevance of the recurrence plots in the identification of the proposed groups is strongly based on the SDNN and TT variables.

The SDNN variable, one of the variables of the linear domain, has been extensively studied. It is related to the sympathetic and the parasympathetic components of the autonomic nervous system and usually presents

reduced values in cases of aging and diseases.

Hillebrand *et al.* (2013)[23] performed a meta-analysis to determine whether the variable SDNN, among others, is associated with the risk of occurrence of a first cardiovascular event in individuals without known cardiovascular diseases. In the eight selected studies, 21,988 participants were included. The relative risk of the group with the lowest SDNN values compared with those with the highest values was 1.35 with 95% confidence interval ranging from 1.10 to 1.67; i.e., lower SDNN values were significantly associated with the occurrence of a first cardiovascular event in individuals without previous cardiovascular disease, after a mean follow-up of 3.5 to 15 years.

Given the age group of the individuals assessed in this meta-analysis, it can be observed that they are in an intermediate position between our Groups A4 and B, therefore confirming the hypothesis of this study that individuals will progress towards the onset of the diseases as SDNN values decrease.

The TT variable has been less addressed and, therefore, some considerations should be made. This variable, along with laminarity, reflects the persistence of a state over a given time interval. More specifically, TT indicates the average length of vertical lines in the recurrence plot. Low TT values indicate high complexity in system dynamics ('a system without laminar states') because, in this situation, the system remains for a short period in a state similar to that of the previous moment. A system consisting predominantly of laminar or trapped states has high TT values[24-25].

The study conducted by Trunkvalterova *et al.* (2007)[26] assessed 34 young individuals, 17 with diabetes mellitus (DM) Type 1 (22.4 ± 1.0 yo), compared with 17 healthy controls (21.9 ± 0.9 yo). The authors found that TT was higher in the group with DM compared with control subjects. They reported that their results confirm the possibility of the occurrence of reduced complexity and increased predictability of heart rate dynamics even in young patients with DM.

These results also confirm our findings, because we could observe increased TT levels even in healthy newborns. Thus, aging is not the only factor that leads to the loss of complexity of the system, but also the presence of a disease in its varying stages or immaturity, as found in newborns. It is worth mentioning that, in our study, in relation to the TT variable, Group A1 was not significantly different from Groups B (P=0.3107), C (P>0.9999), and D (P=0.9260), which shows the sensitivity of the variable not only concerning age but also loss of complexity due to immaturity, disease, state of death, or imminent death.

The qualitative evaluation of recurrence plots also yielded interesting results. A presentation with more geometric patterns could be observed in healthy newborns, elderly individuals, and sick patients, which Marwan called 'large or big black rectangles'[12]. Thus, this characteristic indicates less variability in the heartbeats either due to immaturity of the autonomic nervous system or progressive loss of function. In healthy young adults, the more uniform and diffuse pattern confirms higher HRV and consequently lower recurrence, and therefore is without significant geometric patterns. A particular condition can be observed in patients with heart transplants. Here, although the patient shows good clinical condition and a better homeostatic condition has been reacquired, his/her heart is now totally denervated and shows morphological recurrence plot patterns equivalent to the state of death with exuberant geometric patterns[27].

Also, one of the important points to highlight is the possibility of verifying, with the help of recurrence plots, that changes in HRV are not always directly related to heart rate. Some authors maintain the need for value correction, normalizing the results according to the heart rate[28]. Although this correlation is true in some cases, the relative behaviour of several of the groups in the present study contradicts this fact (Table 2).

CONCLUSION

The quantitative and qualitative aspects of recurrence plots allow differentiation between states of health, advanced disease, and death or imminent death. Trapping time stands out among the most relevant variables and, together with SDNN, has proven to be an excellent tool for diagnosis and clinical decisions

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Resumo

Gráficos de recorrência (GR) têm sido utilizados para avaliar sistemas dinâmicos complexos, sendo o corpo humano um excelente modelo. Foram analisados os elementos quantitativos e qualitativos do GR na diferenciação de Saúde, Doença e Morte. Séries temporais de batimentos cardíacos normais foram coletadas em recém-nascidos saudáveis (Grupo A1), crianças saudáveis (Grupo A2), adultos jovens saudáveis (Grupo A3), adultos saudáveis de meia-idade (Grupo A4), idosos residentes em casas de repouso (Grupo B), indivíduos com doença renal crônica avançada (Grupo C) e indivíduos com morte encefálica declarada ou em estado de morte iminente (Grupo D). O grupo A3 apresentou a melhor homeostase (menor recorrência). Os grupos A1 e D apresentaram os maiores valores de recorrência. Em termos visuais qualitativos, o Grupo A3 apresentou distribuição mais difusa e uniforme, um indicativo de melhor homeostase e o Grupo D foi totalmente linear, a pior condição. Um padrão parabólico foi claramente evidenciado. Em conclusão, foi possível, utilizando a correlação de apenas duas variáveis (SDNN e TT), diferenciar tanto de modo quantitativo como qualitativo os estados de Saúde, Doença e Morte usando GR.

Palavras-chave: sistema nervoso autônomo, controle da frequência cardíaca, variabilidade da frequência cardíaca, saúde, doença, morte, recorrência, gráficos de recorrência.

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