Dynamical Non-Linear Analysis of Heart Rate Variability in Patients with Aortic Stenosis

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Abstract

In this study the 24-h Heart Variability Signals (HRV) of 206 patients with Aortic Stenosis (AS) and 68 healthy subjects (NRM) were analyzed, using dynamical non-linear analysis to compare the complexity of the signals between these two groups during morning (7-12h), afternoon (15-20h) and night (0-5h).

The dynamical analysis defines an initial window of 10,000 beats and calculates the Correlation Dimension (CD) as a non-linear index. Then the window is moved 2,500 beats on the time series and the CD of the new window is calculated. This process is repeated until the whole signal is analyzed.

It was found that: 1) The CD of HRV has significant lower values in the morning than in the night for both groups. 2) The CD of males is lower than the CD values of females during morning for both groups. 3) The CD of NRM is lower than the CD of AS during the morning, while in the night the CD of NRM males is higher.

1. Introduction

During recent years, non-linear analysis of Heart Rate Variability (HRV) has been used to characterize healthy people and a variety of heart diseases and different levels of risk [1-5].

Different non-linear measures are used for this purpose, like Hurst and Lyapunov exponents, entropies, complexity and information indexes, symbolic logic and dimensional analysis. This latter one, estimates the dimension of the attractor formed by the set of points in the phase space, which is a statistical measure of the self similarity of the geometry of points and is related to the number of independent variables (degrees of freedom) needed to generate a corresponding process. A method to measure the dimension of the attractor is the correlation dimension (CD) [6].

CD has been determined for HRV in several circumstances and cardiac disorders. It has been observed that the CD of HRV has lower values in illness subjects compared with healthy ones [7-9].

The HRV of healthy people has a circadian rhythm. The RR values during night are higher than during the day. Modifications in this rhythm in some pathologies and special situations has been reported [10-12]. In healthy subjects non-linear indexes, such as CD and approximate entropy, also show a circadian rhythm, characterized by low values in the morning and high values at night [13]. Healthy females have higher CD values compared with healthy males [14].

In this study we analyze the complexity of the HRV, by means of CD, in healthy subjects (NRM) and in patients with aortic stenosis (AS). This pathology is a narrowing or obstruction of the aortic heart valve, causing it to not open properly and to obstruct the flow of blood from the left ventricle to the aorta. Surgical repair or replacement of the valve is the preferred treatment for symptomatic AS. Using the dynamical analysis proposed by our group [6,15], we calculate the CD of HRV for NRM and AS, comparing the results by gender and age.

2. Materials and methods

2.1. Analyzed data

HRV signals were obtained from 24-h ECG Holter recordings sampled at 256 Hz, from the database of the National Institute of Cardiology at Warsaw, Poland. HRV signals were selected from 206 AS patients and 68 signals from NRM group. All ECG had QRS<120 ms, no conduction abnormalities. All RR intervals were analyzed without any filtration and the number of ectopic beats was below 100 in all cases.

2.2. Correlation dimension

To calculate CD from the RR time series, Takens theorem is used [16]:

The RR values are a data vector $(y_i,\ i=1,\ldots,N)$, where N is the number of beats. A m-dimensional phase-space is constructed, m is the *embedding dimension*, obtaining:

$$\vec{x}_i \equiv \left(y_i, y_{i+\tau}, y_{i+2\tau}, \ldots, y_{i+(m-1)\tau}\right), \quad i = 1,\ldots N-(m-1)\,\tau \tag{1}$$

where τ is the time-delay or *lag*, expressed as a number of beats. Grassberger and Procaccia [17] showed that the dimension d could be obtained from:

$$d = \lim_{r\to 0}\left[\frac{\log_2(C_m(r))}{\log_2(r)}\right] \tag{2}$$

where $C_m(r)$ is the Correlation Integral, which measures the number of points x_j that are correlated with each other in a sphere of radius r around the points x_i. This algorithm is also known as *sphere counting method*. Thus, in the phase-space, the Correlation Integral $C_m(r)$ is defined as:

$$C_m(r) = \lim_{N\to\infty}\frac{1}{N^2}\sum_{i=1}^{N}\sum_{j=1}^{N}\Theta\left(r - \left|\vec{x}_i - \vec{x}_j\right|\right) \tag{3}$$

where N is the number of points, $\Theta(z)$ is the Heaviside function:

$$\Theta(z) = 0 \;\; if \;\; z \le 0$$
$$\Theta(z) = 1 \;\; if \;\; z > 0$$

and $\| x_i - x_j \|$ is the Euclidean distance between a pair of points within the attractor:

$$\left\|\vec{x}_i - \vec{x}_j\right\| = \sqrt{\sum_{k=1}^{m}\left(x_{i,k} - x_{j,k}\right)^2} \tag{4}$$

where m is the dimensionality of the phase-space, corresponding to the embedding dimension.

In practice, it can be shown that it is sufficient to take randomly only 10% of points as *reference points* (N_{ref}) to calculate the correlation integral [6]. Thus equation (3) is modified:

$$C_m(r) = \frac{1}{N_{ref}\left[N-(m-1)\tau-1\right]}\sum_{i=1}^{N_{ref}}\sum_{j=i+1}^{N-(m-1)\tau}\Theta\left(r - \left|\vec{x}_i - \vec{x}_j\right|\right) \tag{5}$$

For each point the distance to all other points in the attractor is calculated and Theiler's correction is applied to avoid autocorrelation effects [18].

When $\log_2(C_m(r))$ is plotted versus $\log_2(r)$, a straight line is obtained at low values of r (*scaling region*) for each embedding dimension m. The slope of each line is the dimension for that m, named $d(m)$. Several $C_m(r)$ are computed for increasing values of the embedding dimension (1 to m), obtaining a sequence of $d(m)$. As m is increased, $d(m)$ tends to a constant value of saturation, which is the value of CD [19].

To obtain this saturation value, an exponential fit is applied (Figure 1) [6]:

$$d(m) = CD\left(1 - e^{-km}\right) \tag{5}$$

The values of CD and k are estimated using the Levenberg-Marquardt method [20].

As a result of this methodology, the *Dck* index is calculated as the product of CD by k. This new index has demonstrated interesting characteristics and it can discriminate high risk patients [6].

2.3. Dynamical analysis

In order to observe the changes in HRV complexity during the 24-h ECG recording, a dynamical analysis is applied [16]. For each signal, a first window of 10,000 beats is defined from samples 1 to 10,000 and the CD of this window is calculated. Then the window is moved 2,500 beats in the time series (points 2,501 to 12,500) and a new CD is calculated. This procedure continues until the whole signal is analyzed. In this study all CD calculations were done using up to m=20 and τ=5 [6].

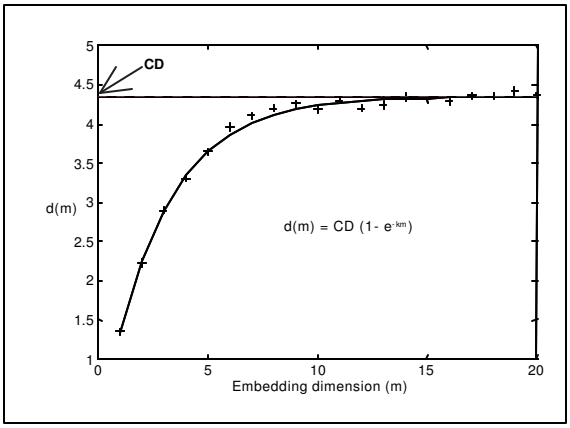

Figure 1. Exponential fit to estimate CD.

The resulting values of CD are classified respect to the time of the day in: Morning (7 to 12 am), Afternoon (3 to 8 pm) and Night (0 to 5 am). To belong to one of these groups the considered window of 10,000 beats must be inside the specified range of time, otherwise it is not classified. After the classification, statistical analysis is applied.

3. Results

The results obtained in this study are summarized in tables 1 to 3.

Table 1. Number of windows (10,000 beats) used for statistical analysis

	NRM		AS	
Time	**Males**	**Females**	**Males**	**Females**
Morning	121	106	103	90
Afternoon	308	165	481	382
Night	181	115	359	288

Table 2. Mean values of CD ± standard deviation.

	NRM		AS	
Time	**Males**	**Females**	**Males**	**Females**
Morning	6.3 ± 2.6	7.2 ± 2.6	8.2 ± 1.9	9.5 ± 2.9
Afternoon	9.3 ± 2.8	10.4 ± 3.0	9.7 ± 2.5	9.8 ± 2.4
Night	12.1 ± 2.5	11.8 ± 2.7	11.3 ± 3.1	11.5± 2.7

Table 3. Mean values of *Dck* index ± standard deviation. *Dck* values are showed in absolute value.

	NRM		AS	
Time	**Males**	**Females**	**Males**	**Females**
Morning	1.50±1.43	1.41±1.21	1.31±1.03	1.29±0.86
Afternoon	1.26±1.22	1.22±0.90	1.29±0.87	1.28±1.06
Night	1.21±1.09	1.19±0.83	1.24±0.94	1.22±0.97

Figures 2 and 3 show the behavior of the CD and *Dck* index, for NRM and AS in Morning, Afternoon and Night for males and females.

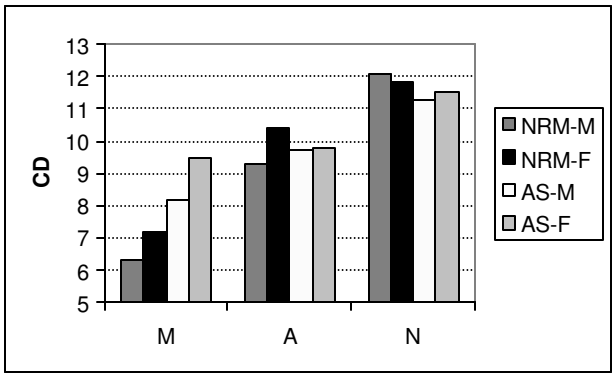

Figure 2. Mean CD values for Morning (M), Afternoon (A) and Night (N). -M and -F correspond to Males and Females.

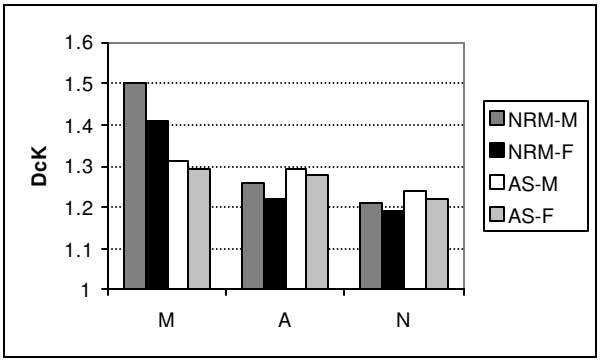

Figure 3. Mean *Dck* values for Morning (M), Afternoon (A) and Night (N). -M and -F correspond to Males and Females. *Dck* values are showed in absolute value.

As an example of the temporal changes in complexity, figure 4 shows the 24-h RR series for one healthy subject and the corresponding values of CD.

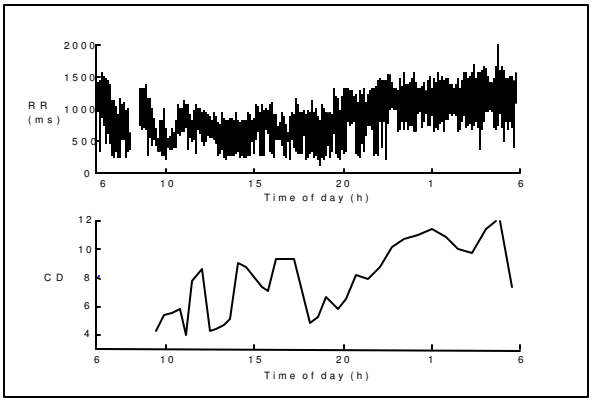

Figure 4. 24-h RR series for a healthy subject and its corresponding CD graph.

CD values were tested about its distribution. It was found that they have a normal distribution, thus parametric statistic was applied in order to determine significant differences between the groups. *Dck* index has no normal distribution, thus non-parametric statistic was applied for this index.

In the NRM group, there are significant differences for CD and *Dck* *($p<0.0005$)* between Morning and Afternoon, Morning and Night, and Afternoon and Night for both males and females. In the AS the behavior is similar, but there are not significant differences between Morning and Afternoon for females.

It is clear that CD values are lower in Morning. They increase in Afternoon and they have the highest values at Night, for both males and females.

Comparing males vs. females in the NRM group, it was found that there are significant differences *($p<0.01$)* in Morning and Afternoon, but not in Night. In the AS group there are significant differences *($p<0.001$)* in Morning but not in Afternoon and Night. When differences exist, CD values for females are greater than the corresponding value for males.

Comparing NRM vs. AS, it was found that there are significant differences *($p<0.0005$)* in Morning and Afternoon *($p<0.05$)* for both males and females. At night there are significant differences in males *($p<0.0005$)* but not in females.

It is important to note that when differences exist, the AS group has higher values in Morning, but in Night the behavior is inverse, i.e. the AS group has lower values than the NRM group.

In order to know if age has a role in the values of CD, correlation between CD and age was estimated. Pearson Coefficient was not significant.

4. Discussion and conclusions

In this study we have analyzed the complexity, by means of CD and *Dck* index, of the HRV signals in healthy subjects and patients with Aortic Stenosis. We have found that a circadian rhythm exists in the complexity of the signal, having the lowest values in Morning and the highest ones in Night for both groups NRM and AS. This conclusion agrees with similar studies for healthy people [13].

It has been found that females have higher values of CD during the day with respect to the values obtained for males, particularly in Morning, while in Night there are not statistical differences. This behavior have been observed in NRM and in AS groups. These results also agree with published data for healthy people [14].

Regarding the results obtained between NRM vs. AS, it is very interesting to observe that during the day, values of CD are lower in NRM group with respect to AS group but in the night there are no significant differences between the groups for females, but in males the CD values are higher in the NRM group.

In this study, *Dck* index demonstrates ability to discriminate between groups, as well as CD does. This fact suggest that this new index can be useful to characterize the complexity of HRV signals.

These results show that it is very important to consider the hour in which the ECG is recorded before any attempt to compare data.

From the results of the correlation between CD and age, it is concluded that age seems to be not relevant in the complexity of HRV.

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