DYNAMIC ANALYSIS OF THE CORRELATION INTEGRAL OF HEART RATE VARIABILITY IN HYPERTROPHIC CARDIOMYOPATHY PATIENTS

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Abstract - **A dynamic analysis of the Correlation Integral (C_m) of the Heart Rate Variability signal (HRV) was applied to 50 patients with Hypertrophic Cardiomyopathy (HCM). A group of 55 healthy subjects was considered as a control group. The Correlation Integral is calculated within a moving time window in order to characterize the nonlinear dynamical behavior of the HRV of HCM patients that cannot be described by classical correlation dimension.**

Keywords – **Complexity analysis, dynamic analysis, correlation integral.**

I. INTRODUCTION

The analysis of Heart Rate Variability (HRV) has been relevant in the study of several cardiovascular phenomena. In the present study Hypertrophic Cardiomyopathy (HCM) patients are described by the Heart Rate Variability (HRV) using complexity analysis. In HCM patients there is an increased risk of premature death, which can occur with little or no warning. Sudden cardiac death (SCD) can strike at any age.

Several studies have indicated the non-linear nature of heartbeat dynamics and cardiac function. The fluctuations in time between beats in a healthy heart may be due to an intrinsic variability of the autonomic nervous system control of non-linear nature, which accounts for this chaotic behavior, while illness is associated to an increasing regularity or complexity decrease [1,2]. In the case of hypertrophic cardiomyopathy patients, some attempts to characterize this cardiac illness using some non-linear tools like Poincaré plots and entropies have been made [3,4]. One of the measures of the time series complexity is the Correlation Dimension (D_c), which gives a statistical measure of the self-similarity of the geometry of a set of points (attractor) in a phase space [5].

Based on these concepts, this work presents a dynamic analysis of the Correlation Integral (C_m) applied to the Heart Rate Variability in order to characterize HCM patients. In this study, C_m was calculated on a moving window, which was moved along the RR file several beats successively for all calculations. This methodology permits to analyze complexity changes throughout time. The number of beats (N) considered was common to both groups (HCM and NRM), in order to obtain comparable results. The correlation dimension based on Grassberger and Procaccia [6] criteria was also applied to these signals without considering the moving window.

Furthermore, the dynamic analysis of the Correlation Integral (C_m) was applied to RR series of a patient with cardiac arrest and a patient with aortic stenosis.

II. ANALYZED DATA

HRV signals were obtained, using software developed by our group [7], from 24-hour ECG recordings sampled at 256 Hz of 50 patients with HCM of the NIC database (National Institute of Cardiology, Warsaw). All patients had QRS<120ms, no conduction abnormalities, less than 100/24h ectopic beats and did not receive medication during recording. A group of 55 normal subjects (NRM) was considered as a control group

In order to emphasize specific aspects of the methodology, signals from two subjects without HCM were also considered: CA, patient with cardiac arrest; AS, patient with aortic stenosis. These Holter recordings were sampled at 128 Hz and RR interval extracted using Del Mar 563 Strata Scan software.

Heart Rate Variability depends on many factors. One of them is patient activity during recording. To achieve the most comparable recording conditions and the best signal quality, we have selected RR data series segments of 4 night hours recorded approximately from 2 to 6 am, while patients were sleeping.

III. METHODOLOGY

From a defined data vector (y_i, i=1,…,N), a m dimensional phase space (embedding dimension) is constructed, according to Takens theorem [8], obtaining

$$Xt \equiv (y_t, y_{t+\tau}, y_{t+2\tau}, \ldots, y_{t+(m-1)\tau}),\ t = 1, \ldots, N-(m-1)\tau \qquad (1)$$

where τ is the lag, expressed as a number of beats.

In the phase space, 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 can be defined by

$$C_m(r) = \frac{1}{N_{ref}\left[N-(m-1)\tau+1\right]} \sum_{i=1}^{N_{ref}} \sum_{j=1}^{N-(m-1)\tau} \Theta\left(r - \left\| x_i - x_j \right\|\right) \qquad (2)$$

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

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Abstract

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$$\Theta(z) = 0 \text{ if } z \le 0$$
$$\Theta(z) = 1 \text{ if } z > 0$$

The distance $\| x_i - x_j \|$ between a pair of points in the attractor has been computed as the euclidean norm

$$\left\| \vec{x}_i - \vec{x}_j \right\| = \sqrt{\sum_{k=1}^{m} \left(x_{i,k} - x_{j,k} \right)^2} \qquad (3)$$

In practice, it has been shown that it is sufficient to take randomly only 10% of the points as reference points (N_{ref}) to calculate the Correlation Integral [9].

For each reference point, the distance to all other points in the attractor is calculated and Theiler's correction is applied to avoid autocorrelation effects, excluding the four nearest neighbor points in time [10].

When $\log_2(C_m(r))$ is plotted versus $\log_2(r)$ (Fig. 1), the slope of the resulting straight line, determined by a linear regression at low r, yields the correlation dimension Dc as was showed by Grassberger and Procaccia [6].

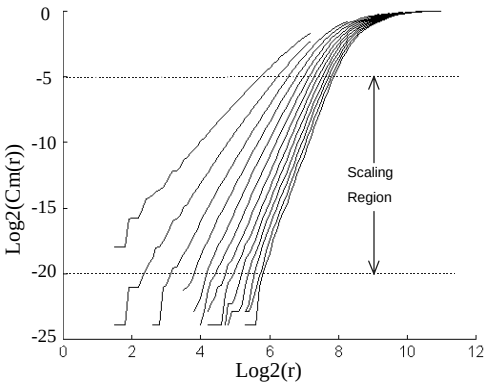

Fig. 1. Correlation Integral as a function of the sphere radius (*r*) for each embedding dimension.

There have been some proposals concerning the amount of data points N needed to estimate Dc [11,12]. This presents limitations when the Dc is calculated on a moving window of reduced RR samples. For this reason, we propose to estimate a correlation integral (C_m) in a moving time window instead of using the concept of Dc. In this way, several $C_m(r)$ are computed for increasing values of m, and the slopes (Sc) are determined from a scaling region of the log-log plot, obtaining a sequence of Sc(m).

To obtain the evolution of the slopes Sc for increasing m, a graph of the Sc(m) is plotted and an exponential model of the type

$$Sc=Sc^*(1-\exp(-km)) \qquad (4)$$

is fitted. The values of S_c^* and k are estimated using the Levenberg-Marquardt method.

The saturation value of the curve S_c^*, is the estimated value of the C_m slope at high m of the signal (Fig. 2).

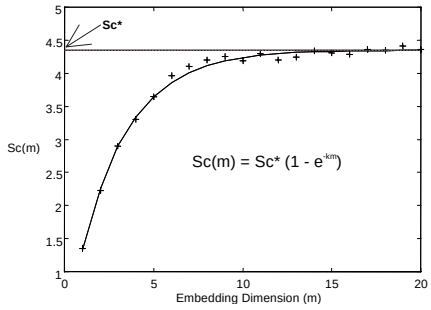

Fig. 2. Correlation integral as a function of the embedding dimension m with a fitted exponential curve.

This exponential model permits to calculate more accurately the correlation integral slope at high m values because all slopes of the correlation integrals, for all the different embedding dimensions m, are used at the same time. The exponential curve fit follows the asymptotic behavior of the calculated Sc(m). Thus, it is no longer necessary to define arbitrarily where the S_c curve becomes sufficiently constant to yield a saturation value for S_c. The error calculated as the mean square root of the S_c values and the fitted curve was less than 5%, with respect to the S_c* value.

Based on this proposed methodology we present a dynamic analysis of the Correlation Integral (C_m) using a moving window on the RR signal. In this approach, C_m is calculated for a moving window of 2,000 points, which is moved 100 samples along the signal successively for each new calculation of the Sc. In order to obtain an accurate measure of S_c we considered embedding dimensions m=1, 2,…,20, and the signal as belonging to a system with τ=5.

In order to emphasize specific aspects of the methodology, the dynamic analysis of the Correlation Integral (C_m) from signals of CA and AS patients was done on the total night period.

The number of beats (N) considered were common to both groups (HCM and NRM) of subjects considered, N=10,000, in order to obtain comparable results. The correlation dimension based on Grassberger and Procaccia [6] criteria was also applied to these signals without considering the moving window, on the N=10,000 beats and also during the total 4 night hours.

IV. Results

To show the usefulness of window correlation integral we present the results obtained from RR series of a patient who had had cardiac arrest (CA) (Fig. 3). As can be seen in the tachogram of Fig. 3.a, long periods of high-level arrhythmia are broken by short periods of extremely low variance behavior. Except for a slight shift in time, approximately the length of the time window, the dependence of the window correlation integral is strongly correlated with the behavior of the tachogram (Fig. 3.b). Contrarily to what one may expect from the shape of the tachogram for this case, the

window correlation integral slope decreases sharply during periods of arrhythmia. This is due to the fact that in 3-dimensional phase space, the trajectory for these periods is extremely simple (Fig. 3.c). On the other hand, the phase space trajectory becomes much more complex during the low variance HRV periods (Fig. 3.d).

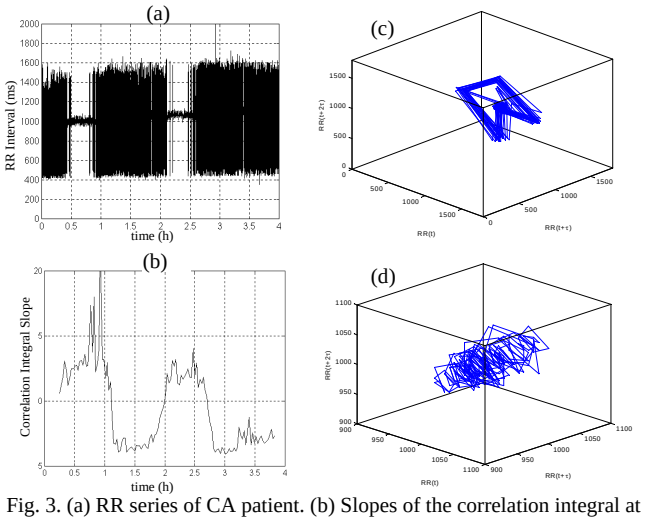

Fig. 3. (a) RR series of CA patient. (b) Slopes of the correlation integral at high m values, obtained with windows of 2,000 beats moving each window 100 beats. (c) Three-dimensional phase space trajectory of 200 beats during the high variance of HRV. (d) Three-dimensional phase space trajectory of 200 beats during the low variance of HRV.

Fig. 4 presents the results of a patient with aortic stenosis (AS), in which characteristic spiking in the HRV occurs. This spiking is unusually regular (Fig. 4.a). As a result, the windowed correlation integral slope is low and shows very little variance (Fig. 4.b). The 3-dimensional phase space trajectory is shown in Fig. 4.c.

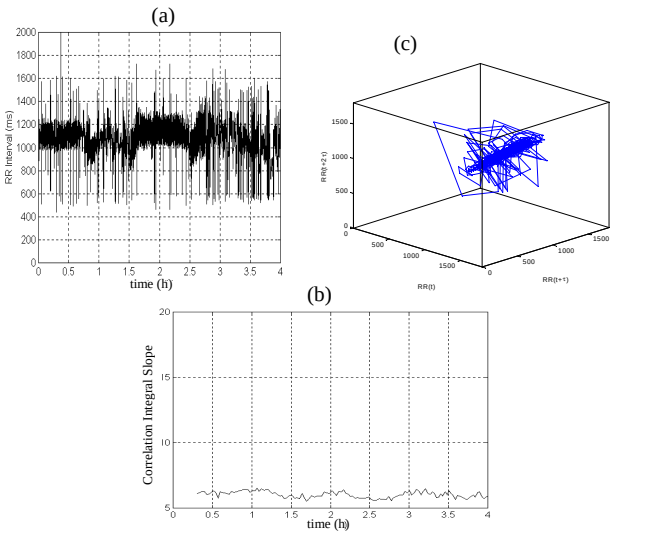

Fig. 4. (a) RR series of AS patient. (b) Slopes of the correlation integral at high m values, obtained with windows of 2,000 beats moving each window 100 beats. (c) Three-dimensional phase space trajectory of 2,000 beats.

Fig. 5 shows the evolution through the time of the slopes (Sc) at high embedding dimension m of the correlation integral (C_m) of a RR signal behavior, of a HCM patient.

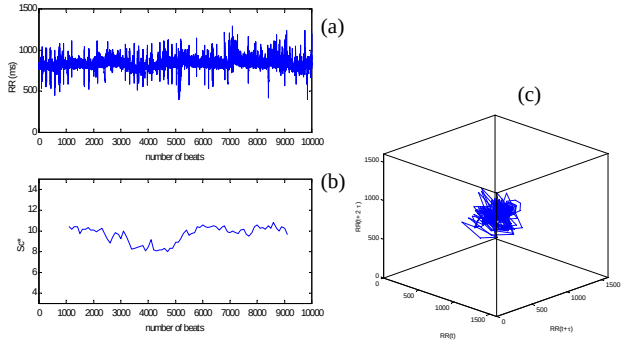

Fig. 5. (a) RR series of a HCM patient. (b) Evolution of the slopes (Sc) of the windowed correlation integral at high embedding dimensions. (c) Three-dimensional phase space trajectory of 2,000 beats.

Table I presents the results of applying the proposed methodology to the HCM and NRM groups. The mean value and the standard deviation (sd) of Sc^* obtained in all studied windows characterized HCM group (mean Sc^*: 10.0±0.955; sd Sc^*: 1.589±0.624) with a significant level p=0.041 and p<0.0005, respectively, when both groups were compared. The minimum value of Sc^* could differentiate the groups (HCM: 6.603±1.755; NRM: 7.472±1.594) with a p=0.006. No statistical significant differences were found considering the maximum values of Sc^*, however the differences between the maximum and minimum value (HCM: 4.876±1.409; NRM: 5.949±1.807) presented a significant level p=0.001. The sum of the consecutive absolutes differences of the Sc^* values were also statistically significant with p=0.026.

TABLE I
SLOPES (Sc) AT HIGH EMBEDDING DIMENSION OF THE WINDOWED CORRELATION INTEGRAL C_m

	mean±sd		
groups	NRM	HCM	p-value
mean Sc^*	10.4±0.786	10.0±0.955	0.041
sd Sc^*	1.186±0.456	1.589±0.624	<0.0005
min Sc^*	7.472±1.594	6.603±1.755	0.006
max Sc^*	12.3±0.725	12.6±0.716	n.s.
$maxSc^*-minSc^*$	4.876±1.409	5.949±1.807	0.001
$\sum\lvert Sc^*(i)-Sc^*(i+1)\rvert$	0.389±0.067	0.426±0.089	0.026

n.s. no significant statistical level

It can be seen in Table II that Correlation Dimension (D_c) calculated from a non-windowed correlation integral and considering the complete night period of the RR series could not characterize the system complexity of HCM patients. Similarly, when using Dc to analyze 10,000 samples of the RR series (Table III), HCM and NRM subjects were not differentiated. However, both groups could be characterized, in the time domain, by the mean value of the RR series and the standard deviation (Tables II and III). Moreover, no statistical differences were found comparing Dc from the complete night period and 10,000 samples of the RR series.

TABLE II
CORRELATION DIMENSION D_c OF THE RR SERIES DURING 4 HOUR NIGHT PERIOD

	mean±sd		
groups	NRM	HCM	p-value
Dc	9.721±1.346	9.249±1.896	n.s.
mean RR	960.2±132.3	1028.9±154.3	0.028
sd RR	100.9±53.4	114.8±41.8	0.023

n.s. no significant statistical level

TABLE III
CORRELATION DIMENSION D_C OF THE RR SERIES 10,000 SAMPLES

	mean±sd		
groups	NRM	HCM	p-value
Dc	9.503±1.196	9.013±1.781	n.s.
mean RR	958.3±131.1	1027±155.7	0.016
sd RR	101.0±45.9	116.1±40.6	0.026

n.s. no significant statistical level

V. DISCUSSION AND CONCLUSIONS

A methodology to obtain dynamic Correlation Integral of the HRV signal has been presented. Using this methodology, 50 patients with Hypertrophic Cardiomyopathy and 55 subjects considered as a control group were analyzed.

With respect to the methodology, it is important to emphasize that the exponential fit to obtain the final value of the Correlation Integral slope, named here S_c*, seems to be a better approach to obtain the correct value, since it uses all the points of the $S_c(m)$ curve and defines the correlation integral slope as an asymptotic value attained with increasing embedding. The curve may be fit with a relative low error – less than 5% of the group of HCM patients studied here. With regard to the number of beats to analyze, it seems that 10,000 beats give sufficient information to calculate the evolution of S_c* consistently, if the night hours are chosen correctly.

As many biological phenomena are complex the approach of moving window correlation integral C_m could be an interesting way to analyze such systems. The value of S_c* for each window usually fluctuates around an average value but, as may be clearly seen for the arrhythmia case CA, may give valuable information about the changes in the dynamics of the system. In particular, window correlation integral may be used to detect relatively short episodes embedded in the time series. In the case of HCM patients, changes in complexity evaluated by the windowed correlation integral seems to be able to characterize this group of patients.

Contrarily, the results obtained from HCM patients applying correlation dimension D_c without considering a moving window, shows that D_c does not characterize heart rate variability in HCM patients.

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