Indices of Symbolic Dynamic Distribution in Cardiac Patients

G D'Addio[1], M Romano[2], R Maestri[1], P Bifulco[2], M Cesarelli[2]

[1]S. Maugeri Foundation, Rehabilitation Institute of Telese, Telese Terme, Italy
[2]D.I.E.T.I, University of Naples "Federico II", Naples, Italy

Abstract

Although symbolic dynamics analysis (SDA) has been proposed for encoding words of different length and symbols, the resulting rapidly growing number of patterns has limited its clinical use. Aim of this study is to propose new SDA indices tested on a clinical data-set. We studied 40 ECG Holter of normal (NR), post-MI (MI), heart failure (HF) and transplanted (TR) subjects. RR differences were encoded into 5 symbols, deriving 3, 5 and 7 length words classified by a dominance's criterion in pattern words with a predominant vagal content (V), decelerating content (D), accelerating content (A), sympathetic content (S) and without variability content (0). Their distributions were then quantified by Kurtosis an Chi-square indexes. Results showed an optimum word-length of 3, where both Kurtosis (2.2±0.6; 2.2±0.9; 3.1±0.9; 4.0±0.4) and Chi-square (7±5; 8±5; 26±17; 106±42, respectively for N, MI, HF and TR) showed very significant p<0,0001 values at the ANOVA test among groups, mainly discriminating HF and TR subject by Tukey's post-test. SDA is an helpful technique in interpreting the encoded HRV information. The pattern words distributions clearly tend to lose their tails to the worsening of the autonomic impairment as immediately described by Kurtosy or chi-square index, especially for risk stratification of HF patients.

1. Introduction

Although linear HRV analysis has been known for decades as an important noninvasive tool for assessment of cardiac diseases, it has however been shown that such techniques are not able to gives complete information in case of rapid and non-repetitive changes [1].

Nonlinear methodologies have been hence proposed to detect and investigate these other features [2-7]. Symbolic dynamic analysis (SDA) of HRV is an emerging and very promising nonlinear technique providing parameters independent of those derived from time and frequency-domains which facilitates the analysis of dynamic aspects of the HRV [8]. Some authors demonstrated that the use of indexes originated from SDA, in addition to more traditional techniques, improves the discrimination between healthy persons and high risk patients founding that parameters from SDA discriminates significantly chronic heart failure patients with high risk to develop life-threatening arrhythmias from those with marginal risk, while time and frequency domain parameters are not able to separate the two populations [9]. Besides, Guzzetti et al. [1] showed that SDA in healthy subjects is sensible to the activation of sympathetic and parasympathetic autonomic nervous systems, whereas in their study standard HRV analysis did not show significant results. Different words of L-length of K-symbols have been proposed for the encoding phase, nevertheless the resulting rapidly growing number of patterns, contrasting the need of concise evaluation's indices, have until now limited clinical use of SDA. In this study is shown an application of SDA with the proposal of a patterns' redundancy reduction procedure, defining new indices tested over a clinical data-set of normal and cardiac patients.

2. Methods

2.1. Clinical data-set

The study population was extracted from the Noltisalis database, already employed for other studies [10], collected by the cooperation of several university departments and rehabilitation clinics in Italy. The acronym Noltisalis (NonLinear Time Series Analysis) was chosen to highlight the will to study the nonlinear nature of the HRV signal.

For this study we considered 40 RR series, extracted from the database, corresponding to different physio-pathological conditions: 10 series from normal subjects (NR age 42±6), 10 of post-myocardial infarction patients (post-MI 50±10), 10 of heart failure (HF 54±11) and 10 heart transplanted patients (TR 45±15). Series of inter-beat times (RR) were derived from standard 24-hours Holter recordings, using different devices. Before starting the SDA, ventricular premature beats as well as other arrhythmia and artifacts were removed from the RR series obtaining series of only normal beats.

2.2. Symbolic dynamic analysis

The core of the technique is adopted from a previously published method [11, 12]. First, we computed the time series ΔRR calculating the difference between consecutive RR values. Then, the ΔRR series was transformed into a symbols sequence from a given alphabet (for each RR value, one symbol is assigned) consisting of five symbols: V (vagal activation), D (deceleration of the heart rate), O (absence of significant variability), A (acceleration of the heart rate), S (sympathetic activation).

The symbol of our alphabet that had to be associated with a RR sample was chosen comparing the RR value with two set thresholds (a primary threshold – PT=10 ms - and a secondary threshold – ST=50 ms). If the ΔRR absolute value exceed ST, the symbol S or V was assigned according to its sign; if absolute value was between ST and PT, A or D was assigned; if it was lower than PT, O was chosen (please, see [12] for details).

Established the encoding rules, a sliding window of length L was shifted along the codified ΔRR series with an overlap of L-1points, transforming it in a sequence of words of L samples. The choice of the length L of the words is crucial in SDA, so we tested lengths equal to 3, 5 and 7 symbols. The number of different words which can be obtained with the encoding described is very high, so that could be quiet difficult to manage and interpret results. To reduce the amount of data to handle, regardless to their length, we grouped the words in different classes, by a dominance's criterion depending on the symbols' prevalence, corresponding to pattern words (PW) with a predominant vagal content (V), decelerating content (D), accelerating content (A), sympathetic content (S) and without variability content (0) (see rules reported in table 1).

Table 1. Dominance criterion developed to group PW.

Description	Example	Meaning	Code
At least 2 symbols "S" anywhere in the word	SSX	high sympathetic activation	S
At least 2 symbols "A" anywhere in the word	AAX	sympathetic activation	A
At least 2 symbols "O" anywhere in the word	OOX	absence of variability	O
At least 2 symbols "D" anywhere in the word	DDX	vagal activation	D
At least 2 symbols "V" anywhere in the word	VVX	high vagal activation	V

Obtained all PW, for each group was computed the distribution of their mean percentages (here called p_V, p_D, p_A, p_S and p_O respectively). These distributions showed a shape Gaussian-like, so we chose as indexes for their characterization, the Kurtosis, measuring the distribution's peakedness, and the Chi-square, measuring deviation of the PW distributions from that observed in normal subjects.

3. Results

Table 2 shows p values of the ANOVA tests between the p values of each kind of words (p_S,p_A,p_O,p_V and p_D) for all studied groups (NR, post-MI, HF, TR) for each word length (L=3,5,7). Results showed that the lower p values have been obtained for word-length of 3 symbols, achieving the best discrimination among the four studied groups.

Distributions of the words' percentage for L=3 in the four studied populations are shown in figure 2 and 3.

Kurtosis and chi-square indexes computed for L=3 in the four studied populations are reported in table 3.

Table 2. ANOVA tests among the p values of each kind of words for all studied groups for each word-length. *** for p<0.001, ** for p< 0.01, * for p< 0.05 .

	S	A	O	D	V
L=3	**	***	***	***	***
L=4	**	Ns	Ns	**	**
L=5	*	Ns	Ns	Ns	**

Table 3. Values of kurtosis (K) and chi-square (Chi2) in the four studied populations (mean ± SD).

	NR	MI	HF	TR
K	2.2 ± 0.6	2.2 ± 0.9	3.1 ± 0.9	4.0 ± 0.4
Chi2	7 ± 5	8 ± 5	26 ± 17	106 ± 42

Table 4. ANOVA of kurtosis and Tukey's PostTest in the four studied populations.

One-way ANOVA	p < 0,0001***	
Tukey's PostTest	Mean Diff	Significance
NR vs MI	-0,04518	ns
NR vs HF	-0,9744	*
NR vs TR	-1,813	***
MI vs HF	-0,9292	*
MI vs TR	-1,768	***
HF vs TR	-0,8390	ns

Table 5. ANOVA of chi-square and Tukey's PostTest.

One-way ANOVA	p < 0,0001***	
Tukey's PostTest	Mean Diff	Significance
NR vs MI	-0,3574	ns
NR vs HF	-18,29	ns
NR vs TR	-98,51	***
MI vs HF	-17,94	ns
MI vs TR	-98,15	***
HF vs TR	-80,21	***

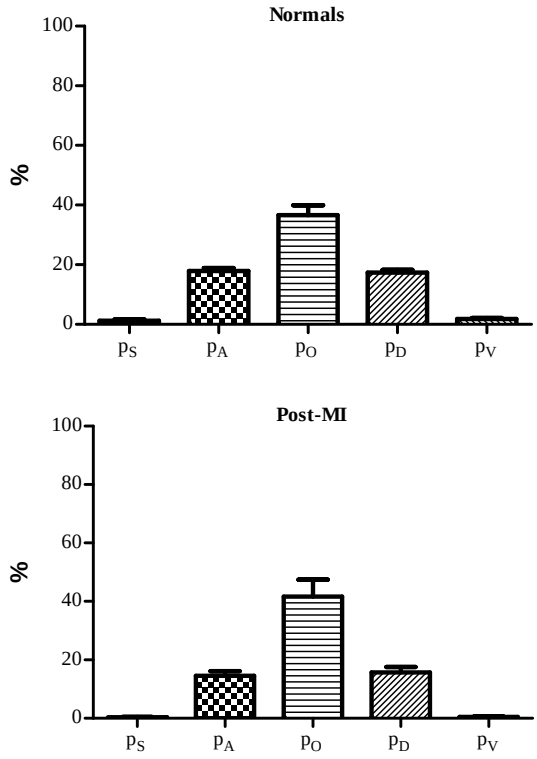

Figure 1. Distributions of the word percentages in Normals (upper panel) and post-MI (lower panel) subjects.

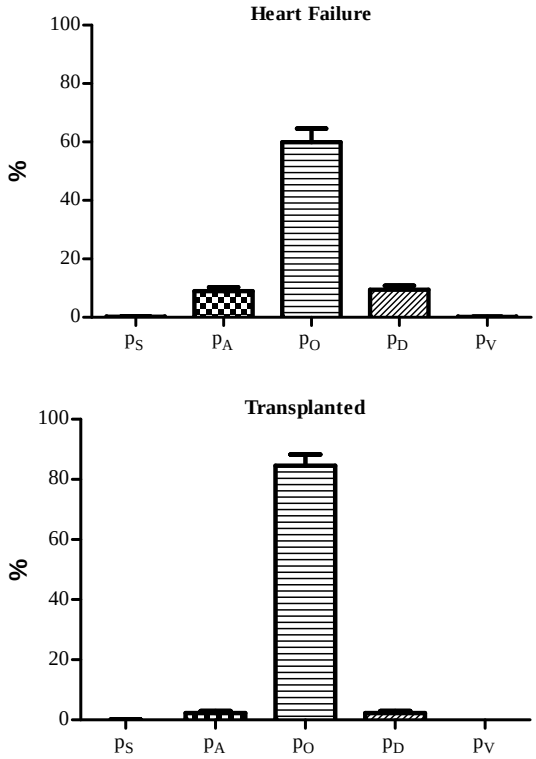

Figure 2. Distributions of the word percentages in Heart Failure (upper panel) and Transplanted (lower panel) subjects.

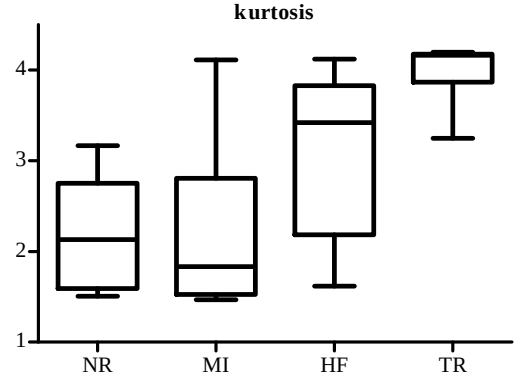

Figure 3. Box&Whiskers plot of kurtosis values in the four studied populations (lines from the bottom upwards respectively at 10th, 25th, median, 75th and 90th percentile of the distributions).

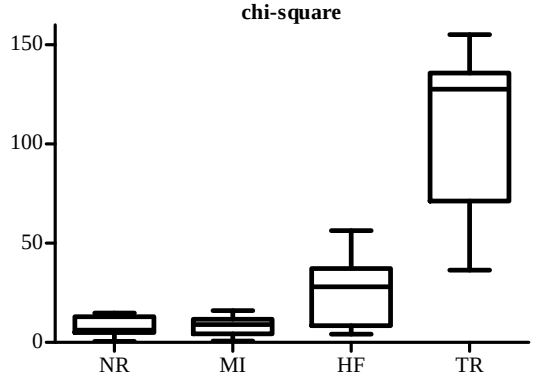

Figure 4. Box&Whiskers plot of chi-square values in the four studied populations (lines from the bottom upwards respectively at 10th, 25th, median, 75th and 90th percentile of the distributions).

Both indexes showed very significant $p<0.0001$ values at the ANOVA test among groups. Particularly while kurtosis mainly appears to discriminate NR from HF and TR subjects by Tukey's post-test (Table 4), chi-square index appears to discriminate just TR from other groups (Table 5).

4. Discussion

Analysis of HRV in time and frequency domains has proved very useful in adults and in human fetuses [13] but also showed some limitations. Therefore, nonlinear techniques have started to be used successfully in complex physiological signals, such as the RR series. It has been speculated, for example, that SDA might

provide more valuable information for the physiological interpretation of heart rate fluctuations and for the risk assessment in cardiac patients. SDA represents an attractive methodology also for its simplicity since, essentially, consists in the association of set symbols to the samples of the time series under analysis. In this study the authors proposed an application of SDA to HRV data derived from 24-hours Holter recordings both in healthy subjects and cardiac patients of different severity. Then, a dominance criterion to classify obtained PW and kurtosis and chi-square were employed to give a more simple and concise interpretation of the results. The study of mean percentages distributions of PW associated to the different subjects' groups and in particular the values of indexes used permit to separate series recorded from pathological subjects by those recorded from healthy subjects. These results indicate that the methodology here suggested is adequate to be employed in the study of cardiac pathologies and consistent with data and knowledge in the literature, according to which to a greater severity of disease is associated a lower variability of the heart rate. Further studies will aim to test other indexes to quantify the amount of variability into a signal, as already proposed for human foetuses [12], and other algorithms, for example intelligence [14] and/or genetic algorithms.

5. Conclusion

SDA has proved an helpful technique in interpreting the encoded HRV information, highlighting the following four novel findings. The first is that a word-length of three symbols appears as the optimal SDA time window, able to better discriminate the studied pathological conditions. The second is that the dominance criterion allows to reduce the initial number of possible words (equal to 125 for 5 symbols and L=3) to a minimum data set of 5 PW, able to discriminate the different dynamics in the studied pathological conditions. The third is that the bell shaped PW distribution in Normals clearly tends to lose both tails with increasing disease severity showing a very low number of PW at higher variability content. The forth is that particularly the kurtosis appears as an index immediately able to describe progressive deviation of PW distribution from normality toward pathological conditions.

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Address for correspondence.

Gianni D'Addio.
Fondazione S. Maugeri.
via Bagni Vecchi, 82037 Telese Terme (BN) Italy
gianni.daddio@fsm.it