Fractal behaviour of pathological heart rate variability dynamics

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Abstract

Heart rate variability analysis (HRV) is a well recognized tool in the autonomic control assessment. It has been suggested that nonlinear analysis of HRV might provide more valuable information than traditional linear methods. Several non linear fractal techniques recently gained wide interest: that based on indirect fractal dimension (FD) estimation from the 1/f spectral power relationship, and that based on a direct FD estimation from HRV time sequences. Aim of the study was to assess whether FD discriminates pathological HRV dynamics, comparing results with normal subjects and traditional linear indexes. We studied 7 groups of 10 ECG 24h-Holter recordings in normal and different pathologies: obstructive pulmonary disease, stroke, hypertension, post myocardial infarction, heart failure, heart transplanted. HRV was assessed by spectral power in very low, low and high frequency bands and standard deviation between normal beats. FD was estimated directly from the HRV sequences by Higuchi method (HM) and from the 1/f slope of spectral power relationship (beta). Results showed differences in the autonomic control impairments better described by FD than by traditional linear methods. Although HM and beta tried to measure the same FD property, the latter seemed to be rather insensitive to changes in autonomic control. These preliminary results clearly suggest that FD, estimated by HM, contains relevant information related to different HRV pathological dynamics.

Keywords: HRV, fractal analysis, nonlinear dynamics.

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1 Introduction

Heart rate variability (HRV) is a well known noninvasive tool in the investigation of the heart autonomic control.

Although most studies on HRV have been performed using time- and frequency-domain linear methods, it has been suggested that HRV nonlinear analysis might provide more valuable information for physiological interpretation of heart rate fluctuations and for cardiac risk assessment [1].

Fractal analysis is an emerging nonlinear technique and, among several methods proposed so far to measure the fractal behaviour of the HRV signal, that based on spectral power-law relationship [2–7], and that based on iterative algorithms directly from RR time series, [8,9] have gained wide interest in the last years. The first way has traditionally been approached following the chaos-theory, with the aim of modelling the attractor extracted from HRV sequences [6], estimating the fractal dimension from the slope of the 1/f-like relationship [7].

Alternatively a fractal dimension value can be directly estimated from HRV sequences by means of Higuchi algorithm [9].

All two the approaches were followed in this study, estimating fractal features by beta exponent of the 1/f (beta) and by fractal dimension of the Higuchi algorithm (HM).

The latter method, whose good reproducibility has been already studied in congestive heart failure [10], allows a better fractal estimation, eliminating the errors due to the indirect estimation of FD from the spectral power.

HRV has been usually investigated in cardiac patients, where abnormalities of the autonomic control to the heart have a common diagnostic and prognostic use [11,12].

Evidences of clinically significant impairment of the autonomic nervous system are known in two others widely diffuse pathologies like stroke and chronic obstructive pulmonary disease, although only limited data are available on the use of HRV in the assessment in these not strictly cardiac patients.

Impaired cardiovascular autonomic regulation has been described in stroke patients with abnormalities hypothesized to be mediated by the central nervous system as a result of the cerebrovascular event, whereas the mechanism of this phenomenon is not fully understood [13,14].

Respiratory arrhythmia in chronic obstructive pulmonary disease, represents the most recognizable evidence of a functional link between neural cardiac and respiratory controls.

Changes in respiratory patterns and lung volumes in these patients influence the autonomic outflows by complex reflex adjustments, mediated by both vagal and sympathetic efferent activity [15,16].

Aim of the study was to assess whether FD discriminates pathological HRV dynamics, comparing results with normal subjects and traditional linear indexes.

2 Study population

All enrolled patients were admitted to S. Maugeri Foundation Rehabilitation Institute of Telese Terme, Italy.

We studied 7 groups of ECG 24h-Holter recordings in normal (NR) and different pathologies: hypertension (HY), post myocardial infarction (MI), heart failure (HF), heart transplanted (TR), obstructive pulmonary disease (COPD), stroke (SP).

Hypertension diagnosis was defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg. A prior diagnosis or ECG evidence of Q waves was used to define MY patients. The diagnosis of chronic systolic heart failure was based on a HF history of at least 6 months and previous echocardiographic and/or scintigraphic evidence of an ejection fraction of <40%.

COPD selected patients had a positive medical history for obstructive pulmonary disease, without coronary artery disease. Patients were considered to be affected by COPD if they fulfilled either of the following criteria: 1) they had an FEV1/FVC of <70% and no change or an FEV1 increase of >12%, but not FEV1 normalisation after 100 mg fenoterol; or 2) they nor reported history of wheeze in the last year, had an FEV1/FVC of <70%, an FEV1 of <80% and an FEV1 increase of <12% after 100 mg fenoterol.

SP selected patients had a positive past medical history for previous first-ever stroke (ischemic and/or hemorrhagic), without coronary artery disease, presence of neuromotor monolateral deficit at physical examination, a CT finding of medium cerebral artery multiple lesions, and FIM score between 40 and 60.

The control group (N) consisted of 10 healthy subjects. See Table 1 for details.

Table 1: Descriptive statistics of studied populations.

Population	Code	#	Age
Normal	N	10	42 ± 6
Hypertension	HY	10	41 ± 1
Post-myocardial infarction	MI	10	50 ± 10
Heart failure	HF	10	54 ± 11
Heart transplanted	TR	10	45 ± 15
Obstructive pulmonary disease	COPD	16	68 ± 07
Post-stroke	SP	17	63 ± 05

3 Holter analysis

Twenty-four-hours Holter ECG recordings were assessed by a portable three-channel tape recorder, processed by a Marquette 8000 T system with a sampling frequency of 128 Hz. In order to be considered eligible for the study, each recording had to have at least 12 hours of analyzable RR intervals in sinus rhythm. Moreover, this period had to include at least half of the nighttime (from 00:00 AM through to 5:00 AM) and half of the daytime (from 7:30 AM through to 11:30 AM) [17]. Before analysis, identified RR time series were preprocessed according to the following criteria: 1) RR intervals associated with single or multiple ectopic beats or artefacts were automatically replaced by means of an interpolating algorithm, 2) RR values differing from the preceding one more than a prefixed threshold were replaced in the same way as for artefacts (Table 2). The RR time series were finally interpolated by piecewise cubic spline and resampled at 2 Hz. The signal was divided in one hour tracts; for each tract the linear and non linear parameters were calculated.

Table 2: Beats correction summary.

Population	**# beats**	**# corrections**	**%**
NR	102115	433	0.4
HY	107755	568	0.5
MI	98664	446	0.5
HF	107145	557	0.5
TR	116043	60	0.1
COPD	97658	4645	4.8
SP	93202	8857	8.7

4 Fractal dimension analysis

Fractal dimension was calculated by using the Higuchi's algorithm [18]. From a given time series X(1), X(2), ... X(N), the algorithm constructs k new time series; each of them, Xm^k, is defined as

$$Xm^k{:}X(m),X(m+k),X(m+2*k),..., X(m+int((N-m)/k)*k) \qquad (1)$$

where m=1,2,...,k and k are integers indicating the initial time and the interval time, respectively. Then the length, Lm(k), of each curve Xm^k is calculated and the length of the original curve for the time interval k, L(k), is estimated as the mean of the k values Lm(k) for m=1, 2, ..., k. In our analysis a k value of 6 was used. If the L(k) value is proportional to k-D, the curve is fractal-like with the dimension D. Then, if L(k) is plotted against k, for k ranging from 1 to kmax, on a double logarithmic scale, the data should fall on a straight line with a slope equal to -D. Thus, by means of a least-square linear best-fitting procedure applied to the series of pairs (k, L(k)), obtained by increasing the k value, the angular coefficient of the linear regression of the graph ln(L(k)) vs. ln(1/k), which constitutes the D estimation, is calculated (Fig. 1).

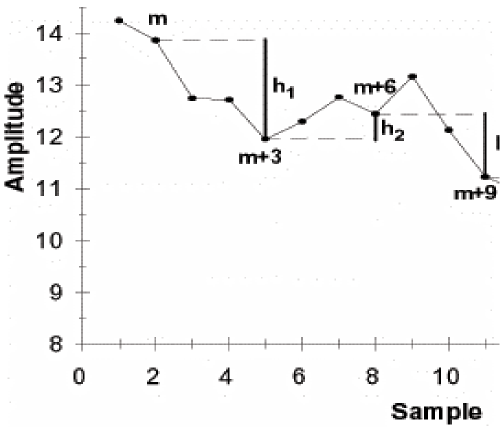

Figure 1: Example of an hi sequence determination on a curve for the length calculation. $h_i = |X(m+i*k) - X(m+(i-1)*k)|$ $k = 3$, $m= 2$.

5 1/f analysis

Power law beta exponent was calculated from the power spectral density function estimated by the Blackman-Tukey method after linear trend removal.

The beta index represents the slope of the linear regression analysis between log(power) and log(frequency) per-formed on the portion of the power spectrum between 10^{-4} and 10^{-2} Hz.

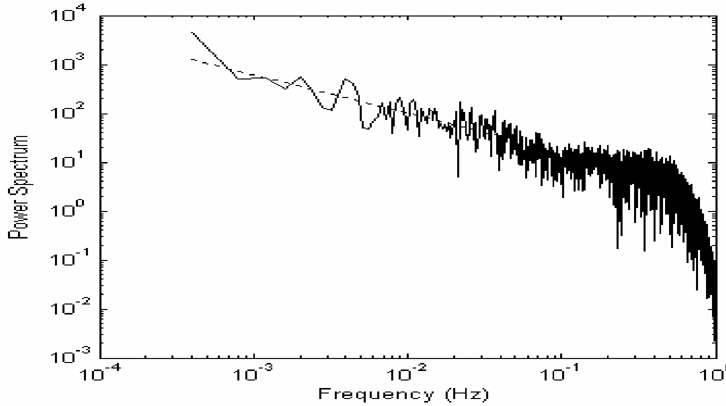

Figure 2: Example of the beta exponent evaluation by means of the slope of the linear best fitting (dashed line) of the power spectrum for frequencies < 0.05Hz.

6 Linear analysis

Spectral analysis was performed by homemade software [18] on 5-minute RR sequences extracted from 24-hours holter recordings.

Power spectral density was estimated by the Blackman-Tukey method in all accepted segments after linear trend removal. The total power and the power in the very low frequency band (VLF, 0.01-0.04 Hz), low frequency band (LF, 0.04-0.15 Hz) and high frequency bands (HF, 0.15-0.45 Hz) were then computed by numerical integration of the spectral density function.

Standard deviation between normal-to-normal RR values (SDNN) was also evaluated for all RR time series.

Table 3: Mean ± SD of HRV indexes in all the studied groups.

	N	COPD	SP	HY	MI	HF	TR
HM	1.35±0.06	1.68±0.11	1.86±0.10	1.58±0.06	1.67±0.08	1.76±0.13	1.96±0.12
Beta	-1.02±0.14	-1.10±0.13	-1.17±0.13	-1.26±0.06	-1.42±0.27	-1.50±0.30	-1.84±0.30
VLF	1048±362	260±139	1355±672	784±264	643±260	519±512	45±50
LF	1188±531	188±85	453±344	878±383	404±188	190±151	20±19
HF	366±254	266±187	169±116	433±314	205±147	112±108	28±24
SDNN	133±21	136±49	56±12	135±38	102±18	87±19	70±28

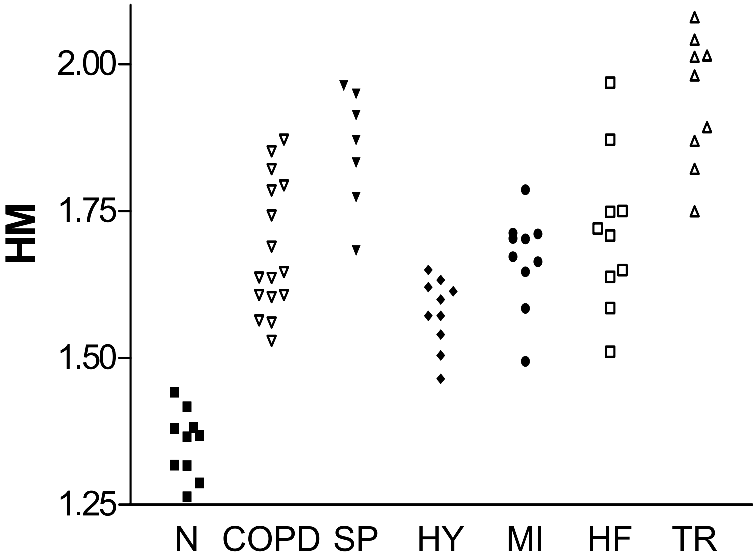

Figure 3: HM values in the seven studied populations.

7 Results

Descriptive statistics for HM, beta exponent, spectral and time-domain HRV indexes in all the studied groups are reported in Table 3.

Kolmogorov-Smirnov (KS) test was used to assess the normality of the distribution of all variables (P>0.1 for all variables).

According to the severity of the autonomic control impairment of the six patients' populations studied, the fractal dimension index, gradually increases from normals to heart transplanted subjects (Fig. 3).

A one-way ANOVA, with Tukey's multiple comparison test, was performed to assess statistical differences between each couple of studied populations (Tab.4).

Results showed that differences in the autonomic control impairments seem to be better described by HM and LF than by other HRV indexes.

Although several indexes were able to discriminate between some groups, only HM reached a significant p-value (p<0.001) in all the populations.

Table 4: Tukey's Multiple Comparison Test P values between N and pathological studied populations.

	HM	**Beta**	**VLF**	**LF**	**HF**	**SDNN**
N vs COPD	*P < 0.001*	P > 0.05	*P < 0.001*	*P < 0.001*	P > 0.05	P > 0.05
N vs SP	*P < 0.001*	P > 0.05	P > 0.05	*P < 0.001*	P > 0.05	*P < 0.001*
N vs HY	*P < 0.001*	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05
N vs MI	*P < 0.001*	*P < 0.01*	P > 0.05	*P < 0.001*	P > 0.05	P > 0.05
N vs HF	*P < 0.001*	*P < 0.001*	*P < 0.05*	*P < 0.001*	P > 0.05	*P < 0.05*
N vs TR	*P < 0.001*	*P < 0.001*	*P < 0.001*	*P < 0.001*	*P < 0.01*	*P < 0.001*

8 Discussion

These preliminary results allow to discuss the following three findings.

First of all, only FD by Higuchi method and LF parameters showed very significant differences between Normal and pathological studied groups, while beta and other linear indexes were not so able to detect significant differences.

The second novel finding is that the sensitivity of the HM and beta exponent parameters in regard to the severity of the central nervous system damage appears to be different. Indeed, the Higuchi's index strongly changes passing from normal to pathological subjects. The beta exponent, on the contrary, seems rather insensitive to changes in autonomic cardiovascular regulation. These considerations suggest that, although the two algorithms try to measure the same fractal property of HRV, they provide non superimposable results. This could be

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due to the fact that the beta exponent is usually calculated considering only the low band of the signal (<0.05 Hz). Probably the changes in autonomic cardiovascular regulation much more affect a band with higher frequency.

The third consideration is that the difference in the mean HM values between N and HF subjects, ranging about the 23% is very interesting because very much higher than the standard error of measurement of just about the 3.4% that we found in a reproducibility study of the same parameter in a HF population [10].

Although a major limitation of this study is the low sample size of the groups, nevertheless these preliminary results clearly suggest that HRV fractal dimension parameters, obtained from morphologic quantification of HRV directly in the time series sequence, contains relevant information related to different HRV dynamics and can be candidates for future risk assessment studies as relevant measures of the overall physiologic and functional status of these patients.

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