Detrended Fluctuation Analysis of Heart Rate by Means of Symbolic Series

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Abstract

Detrended fluctuation analysis (DFA) has been shown to be a useful tool for diagnosis of patients with cardiac diseases. The scaling exponents obtained with DFA are an indicator of power-law correlations in signal fluctuation, independently of signal amplitude and external trends. In this work, an approach based on DFA was proposed for analyzing heart rate variability (HRV) by means of RR series. The proposal consisted on transforming consecutive RR increments to symbols, according to an adapted symbolic-quantization. Three scaling exponents were calculated, α_{HF}, α_{LF} and α_{VLF}, which correspond to the well known VLF, LF and HF frequency bands in the power spectral of the HRV. This DFA approach better characterized high and low risk of cardiac mortality in ischemic cardiomyiopathy patients than DFA applied to RR time series or RR increment series.

1. Introduction

Fluctuations of time intervals between consecutive heartbeats exhibit a complex dynamics, which is influenced by the activity of many regulatory systems interacting over a wide range of time or space scales [1,2]. Even though the seemingly erratic behavior of these fluctuations, the heart rate variability (HRV) can be approximately described by a power law over time scales of tens of minutes to days, indicating long-term correlations between heartbeats [3].

The study of heart rate time series using detrended fluctuation analysis (DFA) has been shown to be a useful tool for diagnostic in patients with cardiac diseases [1]. One advantage of DFA over conventional methods is that it permits the detection of long-range correlations embedded in a seemingly non-stationary time series. Indeed, DFA considers fluctuations only from local linear trend, which makes it insensitive to spurious correlations introduced by external nonstationary trends [4].

Previous studies [1,5] have indicated that correlation properties showed a crossover when several time scales were analyzed. Indeed, for healthy subjects and short-time scales, fluctuations were quite Brownian noise indicating random walk-like behavior, whereas fluctuations approached to $1/f$ behavior for long-time scales. In contrast, it was indicated that correlation properties of fluctuations can be altered by certain cardiac diseases, showing a quite random behavior for short-time scales, whereas fluctuations becomes smoother (like Brownian noise) as the time scales become larger.

Variability of heart rate fluctuations has been also studied by using RR increment series ($\triangle$RR series) and, particularly, by using series constructed with the magnitude and the sign of $\triangle$RR series [2]. This study has shown that DFA scaling exponents belonging to sign series allowed statistically differentiate between healthy subjects and patients with heart failure, obtaining similar or inclusive better results in comparison with those calculated over the original RR series.

In this work, an alternative methodology was introduced in order to improve the statistical differentiation between risk groups of suffering cardiac death, by applying DFA over $\triangle$RR series. The methodology considered a symbolic transformation of $\triangle$RR series by means of an alphabet with four symbols. Results were compared with those calculated over original RR series and, series corresponding with magnitude and sign of $\triangle$RR series.

2. Methods

2.1. Analyzed database

Patients from MUSIC (MUerte Subita en Insuficiencia Cardiaca, Sudden Death in Heart Failure) study were analyzed in the present work. A total of 222 patients (63.2±0.56 years, 86.9% male) with ischemic dilated cardiomyopathy (IDC) were enrolled in the present study. Patients were followed for three years. The inclusion criteria were: sinus rhythm, symptomatic chronic heart failure with New York Heart Association functional class (*NYHA*) II or III, and ischemic etiology of heart failure. Age-matched IDC patients were studied considering cardiac mortality as end-point. The analysis considers 30 patients that suffered cardiac mortality (CM) due to sudden cardiac death, progressive heart failure or myocardial infarction, as a high risk group and 192 survivor (SV) as a low risk group. The MUSIC study was approved by the Ethical Committee of the institution and all subjects gave their written informed consent before participation.

The RR series, intervals between consecutive heart beats, were obtained from 24h ECG-Holter recordings with a sampling frequency of 200 Hz (Spiderview recorders, ELA Medical, Sorin Group, Paris). An adaptive filter [6] was applied to the RR series in order to replace ectopic beats and artifacts by interpolated RR intervals. Indeed, the level of interpolated beats related to the total number of RR intervals was less than 1.5%. Therefore, a possible alteration of the results due to the filter procedure can be discarded. A common length of 60000 beats was selected for all the RR series.

2.2. Methodology

a) Detrended fluctuation analysis

In order to calculate the scaling exponents with DFA, a given series $x(i)$, with $1 \le i \le N$ being N the length of the series, is firstly integrated (1):

$$y(k) = \sum_{i=1}^{k} [x(i) - x_{ave}], \qquad k = 1, ..., N \tag{1}$$

where x_{ave} is the average of the series $x(i)$. Then, the integrate time series is divided into boxes of equal length, n, and in each box, a least square line is fit to the data. The y coordinate of the straight line segments is denoted by $y_n(k)$. Next, the integrated time series, $y(k)$, is detrended by subtracting the local trend, $y_n(k)$, in each box. After that, the root-mean-square fluctuation of the integrated and detrended time series is obtained (2):

$$F(n) = \sqrt{\frac{1}{N} \sum_{k=1}^{N} [y(k) - y_n(k)]^2} \tag{2}$$

where $F(n)$ represents the average fluctuation as a function of the box size, n. A linear relationship on a double log graph between $F(n)$ vs. n indicates the presence of scaling in the series. The fluctuation can be quantified by means of the slope of the line (the scaling exponent α), relating log $F(n)$ to log n. Values of $0<\alpha<0.5$ are associated with anti-correlation where large and small values of the time series are likely to alternate. The value $\alpha=0.5$ is related with Gaussian white noise indicating an uncorrelated behaviour. Values of $0.5<\alpha\le1$ indicate persistent long-range correlations. A special case is $\alpha=1$ and corresponds to $1/f$ noise. Values of $1<\alpha\le1.5$ are associated to stronger long-correlations, differing from power law [1,5].

In the present study, heart rate variability was analyzed by means of DFA applied to: a) RR series; b) RR increment series (△RR); c) magnitude of the △RR series; d) sign of the △RR series; e) symbolic series obtained from △RR series. The criterion used to transform △RR series into symbols is given in (3) [7]:

$$S_i = \begin{cases} 3 \text{ if } (\mu + sd) < \Delta RR_i < \infty \\ 2 \text{ if } \mu < \Delta RR_i \le (\mu + sd) \\ 1 \text{ if } (\mu - sd) < \Delta RR_i \le \mu \\ 0 \text{ if } -\infty < \Delta RR_i \le (\mu - sd) \end{cases} \quad i = 1, ..., M \tag{3}$$

where M, μ and sd are, respectively, the length, the mean value and the standard deviation of the series. Two alternative ways were considered in order to determine these parameters: a) $\triangle RR_{ST}$, symbolic transformation applied to the total 24-hour △RR series; b) $\triangle RR_{SW}$, △RR series were divided into windows of NW=1000 beats without overlapping and the symbolic transformation was applied to each one of the windows.

Several regions of scale invariance were considered, corresponding approximately to the well known VLF [0.003–0.04Hz], LF [0.04–0.15Hz] and HF [0.15–0.4Hz] frequency bands in the power spectral of HRV. In order to relate frequency values f_n in Hertz and the segment size n of DFA, the rough approximation $f_n \approx (\bar{s}n)^{-1}$ was used [5]. The scaling exponents of the DFA taken into account and related to these regions were: α_{HF} ($4 \le n < 8$), α_{LF} ($8 \le n < 30$) and α_{VLF} ($30 \le n \le 100$), where $\bar{s}$ has been approximated to 0.8s.

b) Time and frequency domain analysis

Time and frequency domain measures were taken into account. Mean (M_{RR}) and standard deviation (S_{RR}) of the RR series were calculated, as time domain measures. In order to obtain the frequency domain measures, the series of 60000 beats were analyzed according to frames of 300 beats with an overlap of 50%. Subsequences were interpolated and re-sampled at 5 Hz. Power spectrum was estimated over subsequences using an autoregressive approach (Burg method). The model order was a-priori assigned and equal to 12. The following measures were calculated: total power (P_{tot}); power in the high frequency

band (*HF*); power in the low frequency band (*LF*); power in the very low frequency band (*VLF*); *LF* and *HF* in normalized units (*LFn* and *HFn*); and the *LF/HF* ratio.

c) Statistical analysis

A statistical analysis based on ANOVA test was applied on each defined index α. Indeed, Levene's test for homogeneity of variance was used to confirm homoscedasticity. Indexes α that no fulfil homoscedasticity were statistically analyzed by applying U Mann-Whitney test. A significance level $p<0.05$ was considered for comparing statistically the risk groups.

A discriminant linear function was built on each one of the indexes in order to classify the subjects. The sensitivity (Sen) and specificity (Spe) were taken into account in this statistical analysis. To test the association between the power spectral and DFA exponents, a two-tailed Pearson correlation coefficient (r) was calculated.

3. Results and discussion

3.1. Time and frequency domain analysis

Table 1 contains the mean and standard deviation of time and frequency domain measures, as well as the significance level of the statistical classification of subjects in their respective risk groups: survivor (low risk group) and cardiac death (high risk group). In time domain, the indexes M_{RR} and S_{RR} were not able to statistically differentiate between the two risk groups, however their mean values tended to be higher in SV than in CM. In frequency domain, *VLF*, *LFn* and *LF*/*HF* showed significant differences when risk groups were statistically compared (p=0.0181, p=0.0004, and p=0.0428, respectively). The mean values of *VLF*, *LFn* and *LF*/*HF* were lower in high risk group than in low risk group, suggesting a reduction in the sympathetic branch activity of the autonomic nervous system in CM group. The best diagnostic criteria (sensibility=53.4% and specificity=63.5%) were obtained with LFn component.

Chronic heart failure is characterized by a high sympathetic drive [8, 9]. Indeed, spectral analysis of the RR series would be reasonably expected to manifest predominantly *LF* component, but our results have revealed a decreased *LFn* component in high risk group compared with low risk group. However, the interpretation of a reduced *LFn* in chronic heart failure patients is still an open question including a depressed sinus node responsiveness, central abnormality in autonomic modulation, limitation in responsiveness to high levels of cardiac sympathetic activation, depressed baroreflex, and increased chemoreceptor sensitivity [9].

Concerning to the interpretation of *VLF* power spectral component, different physiological mechanisms have been proposed: physical activity, thermoregulation, rennin-angiotensin-aldosterone system, slow respiratory patterns, and parasympathetic mechanism. In this sense, the obtained *VLF* behaviour could have been influenced by a reduced physical activity in the patients who were more ill. Similar results were reported in [9].

Table 1. Time and frequency domain measures

Measures	SV (n=192)	CM (n=30)	p
M_{RR} [ms]	844.3±142.6	793±123.8	n.s.
S_{RR} [ms]	92.29±37.75	77.7±38.85	n.s.
Ptot [ms^2]	1269±1471	728±818	n.s.
VLF [ms^2]	563±568	307±393	0.0181
LF [ms^2]	289.4±340	165.6±229	n.s.
HF [ms^2]	167.8±288.5	96.8±127.9	n.s.
LFn	57.78±13.3	48.05±16	0.0004
HFn	27.96±8.9	30.09±8.789	n.s.
LF/HF	2.388±1.353	1.852±1.236	0.0428

SV, Survivor; CM, Cardiac mortality. Mean ± standard deviation. n.s.: non significant

3.2. Detrended fluctuation analysis

The values of the mean and standard deviation of DFA scaling exponents measured over RR series, △RR series, magnitude and sign of △RR series are shown in Table 2. A better significance level can be observed in α_{HF} and α_{LF} using △RR series than using RR series, whereas α_{VLF} scaling exponent showed a reverse behavior in RR series. Magnitude of △RR series has not presented scaling exponents able to differentiate both risk groups. Sign of △RR series exhibited scaling exponents with p value slightly better than those calculated over the original RR series or even the △RR series.

Table 2. DFA in RR series

Series	Index	SV (n=192)	CM (n=30)	p
RR	α_{HF}	1.0607±0.2262	0.9115±0.2342	0.0010
	α_{LF}	1.2148±0.1622	1.1206±0.2314	0.0243
	α_{VLF}	1.0939±0.117	1.155±0.1399	0.0103
△RR	α_{HF}	0.3796±0.1187	0.3154±0.0775	0.0027
	α_{LF}	0.313±0.1246	0.2346±0.1315	0.0017
	α_{VLF}	0.2345±0.0774	0.2185±0.1361	n.s.
|△RR|	α_{HF}	0.8313±0.1011	0.8563±0.1024	n.s.
	α_{LF}	0.7177±0.0964	0.7272±0.082	n.s.
	α_{VLF}	0.7156±0.0967	0.7381±0.0914	n.s.
Sign of △RR	α_{HF}	0.4671±0.0747	0.4309±0.0539	0.0114
	α_{LF}	0.4579±0.0655	0.4232±0.0668	0.0076
	α_{VLF}	0.4386±0.0530	0.4763±0.0845	0.0011

Mean ± standard deviation. n.s.: non significant

Table 3 contains the values of mean and standard deviation of DFA scaling exponents calculated over △RR series transformed to symbols by applying the two proposed algorithms: $\triangle RR_{ST}$ and $\triangle RR_{SW}$. Comparing △RR with $\triangle RR_{ST}$ and $\triangle RR_{SW}$ series, a better statistical difference was obtained with the symbolic transformation, especially for α_{VLF} that is statistically significant (p=0.0193 and p=0.0141 for $\triangle RR_{ST}$ and

$\triangle RR_{SW}$, respectively). The mean values of the scaling exponents of the symbolic transformed $\triangle$RR series (Table 3) have similar tendencies that those observed in the original RR and $\triangle$RR series (Table 2). Indeed α_{HF} and α_{LF} showed lower values in high risk group than in low risk group, whereas α_{VLF} showed a reverse behavior. It can be observed in Table 3 that $\triangle RR_{SW}$ obtains better statistical significances than $\triangle RR_{ST}$. The reason should be due that parameters μ and *sd* given in (3) are adaptively calculated in $\triangle RR_{SW}$ series and therefore the correlation properties are better characterized by this transformed series. Furthermore, $\triangle RR_{SW}$ series presented higher statistical differences than sign of $\triangle$RR series, when risk groups were compared. It should be due that sign of $\triangle$RR series is equivalent to a symbolic transformation using two symbols, whereas $\triangle RR_{SW}$ used a codification with four symbols. A linear combination of α_{HF}, α_{LF} and α_{VLF} in $\triangle RR_{SW}$ statistically classified with a sensibility=70.0% and specificity=68.2%, by using leaving-one-out cross-validation method.

Table 3. DFA measures in symbolic RR series

Series	Index	SV (n=192)	CM (n=30)	p
	α_{HF}	0.4171±0.105	0.3623±0.0696	0.0078
$\triangle RR_{ST}$	α_{LF}	0.4019±0.0977	0.3411±0.1055	0.0019
	α_{VLF}	0.3647±0.0532	0.3931±0.0989	0.0193
	α_{HF}	0.4113±0.1002	0.3548±0.0686	0.0027
$\triangle RR_{SW}$	α_{LF}	0.407±0.0991	0.3406±0.1091	0.0009
	α_{VLF}	0.3685±0.0607	0.4019±0.1076	0.0141

Mean ± standard deviation.

The scaling exponent α_{LF} of $\triangle RR_{SW}$ highly correlated with *LFn*, *LF*/*HF* and *HF* with r=0.894 ($p<0.0005$), r=0.834 ($p<0.0005$) and r=0.613 ($p<0.0005$), respectively. The last correlation suggests that a relationship seems to exist between respiration and α_{LF}, but the highest correlation is between α_{LF} and the sympathetic and vagal activity done in *LFn*. On the other hand, α_{HF} and *LFn* correlated with r=0.613 ($p<0.0005$), whereas non spectral power components correlated with α_{VLF}. Similar results were obtained in [10].

The mean values of DFA indicate anticorrelated behaviour in $\triangle$RR series with or without transformation to symbols. However, $\triangle RR_{ST}$ and $\triangle RR_{SW}$ series presented less anticorrelation compared with original $\triangle$RR series.

4. Conclusions

This study uses an approximation of DFA based on symbolic dynamics for analyzing heart rate variability by means of RR series which are characterized by long-range correlations. This approach was compared with other different proposals that involve RR increment series, magnitude and sign of those RR increment series. It seems that an adequate symbolic transformation of the RR series allowed DFA scaling exponents to better identify different correlation properties between the studied cardiac risk groups.

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