The Loss of Multifractality as Evidence of Impaired Left Ventricular Ejection Fraction in Patients after Acute Myocardial Infarction

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Abstract

Multifractal analysis of heart rate variability (HRV) has been used to discriminate healthy subjects from patients with severe health conditions. We analyzed the fractal structures of the ECG recording of 11 patients who suffered acute myocardial infarction in order to identify those with impaired Left Ventricular Ejection Fraction (LVEF). Was estimated the multifractal spectrum in Matlab code from the series of RR intervals, in supine rest. The parables representing the multifractal spectrum will be closing in small arcs, as a monofractal structure to 4 these 11 patients. The change in shape of multifractal spectrum curve for this group can provide information on changes in cardiac dynamics of patients with greater impairment of the muscles of the heart. The degree of multifractality, defined as the width of multifractal spectrum, also was studied. Moreover, all patients had undergone Doppler echocardiography and a quantification of left ventricular function was done by the Simpson technique (for LVEF less than 50% the patient was classified as belonging to the group with depressed LVEF). The Mann-Whitney test (p-value <0.01) revealed that the degree of multifractality for the group with impaired LVEF is very significantly lower than for the group with preserved LVEF. We conclude that the loss of multifractality may indicate an impairment of left ventricular ejection fraction in patients after acute myocardial infarction, but we could not measure the extent of this loss as an indication of greater or lesser severity.

1. Introduction

There is evidence that the healthy human heartbeat has a multifractal temporal structure. Multifractal analysis of heart rate variability (HRV) has been used to discriminate healthy subjects from patients with severe health conditions. It has been found a loss of multifractality for a life-threatening condition, such as congestive heart failure [1-2].

The multifractal signals require lots of Hurst exponent to explain their behavior more complex and thus characterize the structures of scale entirely. In contrast, monofractais signals are homogeneous since they have the same properties of scales for the entire signal. Therefore, monofractais signals can be indexed by a single global Hurst exponent. This is another exploration of nonlinear dynamics parameters from our research group [3-7], always with a non-invasive goal in mind.

In this work we propose, through multifractal spectrum of power law exponents obtained by the robust Multifractal Detrended Fluctuation Analysis (MFDFA) method, to measure the degree of multifractality of HRV of subjects who suffered Acute Myocardial Infarction (AMI). Several studies have demonstrated the utility of HRV analysis as a prognostic index of survival and long and short-term after AMI [8]. Our goal was to discriminate patients with impaired Left Ventricular Ejection Fraction (LVEF) from those with preserved LVEF. We intended to quantify the loss of multifractality of HRV of the subjects with a more severe contraction of the heart muscle compared to the HRV of those with preserved LVE. We expected that the multifractal parameters provide us with new tools for diagnosis of patients with compromised LVEF from the analysis of HRV.

1.1. The MFDFA method

The method was developed by Kantelhard *et al.* [9]

and is an effective numerical method to analyze the scaling properties of fluctuations by calculating a set of multifractal fluctuations functions. MFDFA is a generalization of the DFA method which was also developed by Kantelhardt *et al.* that is an alternative to the classical method of Hurst (R/S). The MFDFA method enables a reliable multifractal characterization of no stationary time series.

Be a time series x(t) of length *p*. Applying the equation (1) to transform x (t) on a series of log-returns of length L = *p*-1.

$$r(t,1) \approx \ln\left(\frac{x(t+1)}{x(t)}\right) \quad (1)$$

Then, the profile data is calculated by (2):

$$Y(i) = \sum_{k=1}^{i}(x_k - \langle x\rangle), i = 1, \dots, L \quad (2)$$

Y(i) should be divided into N segments non-overlapping of size s, where N = int (L/s). Each segment is referred to as v. For each v, we calculate the fluctuation function:

$$F^2(s,v) = \frac{1}{s}\sum_{i=1}^{s}\{Y[(v-1)s+i] - y_v^m(i)\}^2 \quad (3)$$

where $y_v^m(i)$ represents a polynomial fit of order m.

The next step is to get the average generalized fluctuation function to the window v of size s to moments of order q by the expression:

$$F_q(s) = \left\{\frac{1}{N_s}\sum_{v=1}^{N_s}[F^2(s,v)]^{\frac{q}{2}}\right\}^{\frac{1}{q}} \quad (4)$$

where q can assume any real value, except zero. In the case of q = 0, a logarithmic averaging procedure has to be employed,

$$F_0(s) = exp\left\{\frac{1}{N_s}\sum_{v=1}^{N_s} ln[F^2(s,v)]\right\} \quad (5)$$

The goal is to determine how the function $F_q(s)$ depends on the time scale s for different values of q. The multifractal time series are not normal distributed and all q-order statistical moments should to be considered.

$F_q(s)$ follows a power law:

$$F_q(s) \sim s^{H_q} \quad (6)$$

H_q is obtained by linear regression for log $F_q(s)$. H_q is the slope of the line. It is called q-order Hurst exponent. For q = 2, H_q is the Hurst exponent (H).

H_q is only one several scaling exponents used to parameterize the multifractal structure of time series.

The usual procedure [9, 10] is first convert H_q to the q-order mass exponent t_q using the relation:

$$t_q = qH_q - 1 \quad (7)$$

The q-order singularity dimension D_q (8) as a function of the q-order singularity exponents h_q can quantify the statistical properties of multifractal signals.

$$D_q = qh_q - t_q, \text{ where } h_q = \frac{dt_q}{dq} \quad (8)$$

The plot of h_q versus D_q is referred to as the multifractal spectrum (see Figure 4). The width of the spectrum given by the difference between the maximum and minimum h_q (Δh_q) measures the degree of multifractality in the series.

2. Methods and tools

This study was approved by the Research Ethics Committee of Hospital of the Faculty of Medicine of Ribeirao Preto, University of Sao Paulo, Brazil. The subjects were patients in treatment of AMI that had presented in the acute phase of the event: 1) pre-cordial pain, ST-segment elevation in the ECG, the presence of myocardial necrosis marker CK-MB; 2) patients who fit in item 1 and who underwent reperfusion therapy prior, chemical or mechanical nature; 3) less than age 70 years; 4) male; 5) patients who belonged to clinical Killip classification I or II. Everyone should have received conventional treatment according to ACC/AHA, including B-blocker and were admitted within 12 hours after symptom onset. The protocol was applied in the morning and by the same examiner.

Exclusion criteria were: history of previous AMI, signs or symptoms of transient myocardial ischemia; angina or changes in the ST segment of the ECG greater than or equal to 3 mm; presence of refractory systemic blood pressure greater than 200/100 mmHg levels, atrial fibrillation, frequent ventricular premature beats and / or complex, sinus or supraventricular tachycardia greater than 120 bpm; atrioventricular block second or third degree, hypotension and low output signals or bankruptcy. The patients underwent Doppler echocardiography and cardiac catheterization. In order to quantify left ventricular function, we applied the Simpson technique, considering: group I with depressed LVEF (less than 50%) and group II, with preserved LVEF (equal to or greater than 50%). The experimental protocol was initiated 24 hours after the onset of AMI, patients with stable electrical and hemodynamic point of view and the data collected on the 5th day of hospitalization. For monitoring Heart Rate (HR) and to obtain instantaneous HR and successive RR intervals, the Polar® Heart Model S810i (Polar Electro Oy, Kempele, Finland) was used.

The system detects depolarization, corresponding to R wave of the ECG, with a range of 500Hz with a temporal resolution of 1ms. Once subscribed, the signals were transmitted to a computer for subsequent analysis. The patients had systemic blood pressure (BP) checked by auscultation. Medications and their dosages were also recorded daily and did not change during the application of the protocol to prevent possible influences on these variables.

The multifractal structures of the ECG recording of 11 patients were analyzed in the supine position with the head of the bed elevated to 40°, where the subjects were instructed to breathe spontaneously for 15 minutes.

The MFDFA method was applied in Matlab code in order to estimate the multifractal spectrum for the eleven RR series.

The input parameters to all RR series analyzed were: signal = RR series; scale = [6, 8, 10, …, 64]; q (q-order that weights the local variations) = [-5, -4, -3, -2, -1, 0, 1, 2, 3, 4, 5]; m (polynomial order for the detrending) = 1.

3. Results

The Δh_q and the quantification of LVEF for each RR series, with its respective size and adjusted R-Squared the polynomial model fit, are shown in Tables 1 and 2.

Table 1. Group I- Patients with impaired LVEF.

patient	Δh_q	n	LVEF	Adj.R^2
ACN	0.234	1181	< 50%	0.999
APS	0.351	1001	< 50%	0.995
JF	0.421	1059	< 50%	0.938
JMO	0.416	1041	< 50%	0.993

Table 2. Group II- Patients with preserved LVEF.

patient	Δh_q	n	LVEF	Adj.R^2
ACS	0.703	1145	≥ 50 %	0.990
AFN	0.739	957	≥ 50 %	0.891
APMN	0.825	749	≥ 50 %	0.993
FHG	0.607	1095	≥ 50 %	0.999
GK	0.577	756	≥ 50 %	0.998
JGS	0.742	954	≥ 50 %	0.987
LJB	0.704	864	≥ 50 %	0.990

It is observed in the Figure 1.a (a patient with impaired LVEF) a more linear range; so H_q is almost constant, which is a characteristic of monofractal series [10]. On the other hand, it is observed in Figure 1.b (a patient with preserved LVEF) a non-linear spectrum that is characteristic of multifractal series [10]. In this figure, as expected, all the F_q appears to converge as the scale increases.

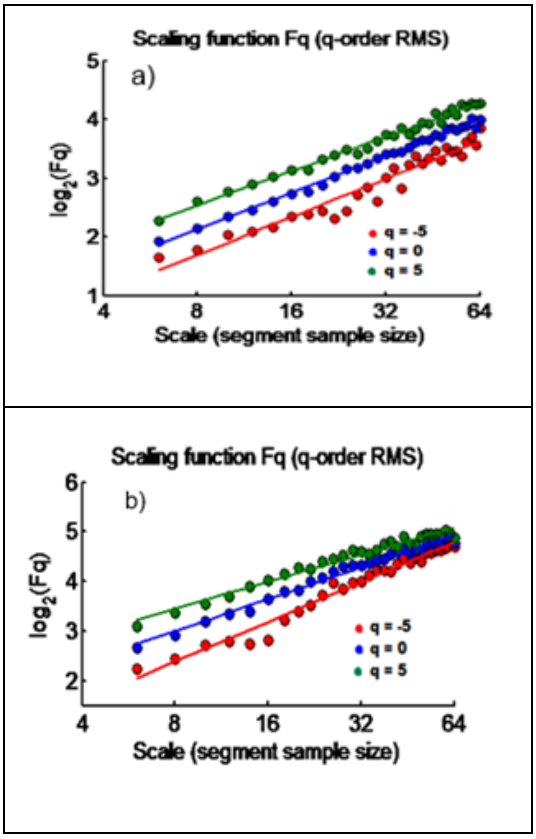

Figure 1. The scaling functions F_q (dots) and corresponding linear regression (traced lines).

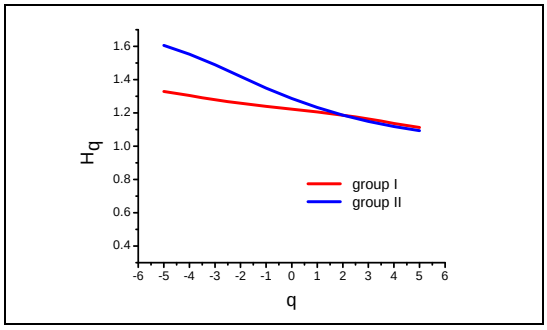

Figure 2. The q-order Hurst exponent H_q for the RR series of one patient from group I and group II. The intercept of the curves occurs near q = 2; so H_q is the Hurst exponent (H). Also note a monotonical decreasing H_q in group II as in the case of multifractal series [10].

In the Figure 3.a the series has a t_q with a linear q-dependency that leads to a constant h_q of these series because h_q is the tangent slope of t_q. This makes, in Figure 4.a the parables close at smaller arcs, as a monofractal structure [10].

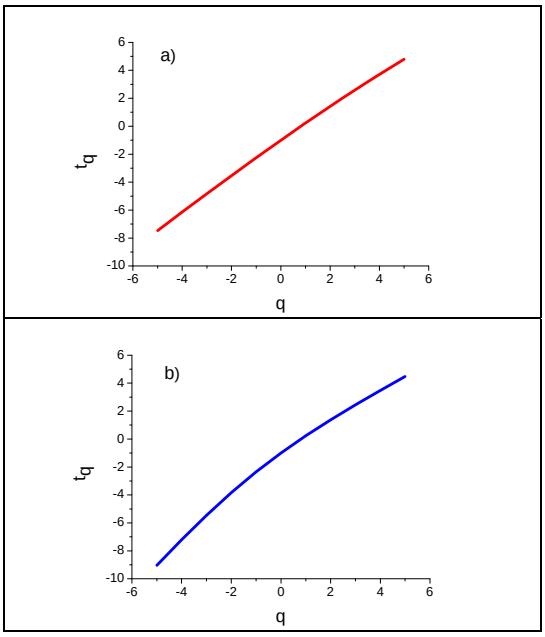

Figure 3. The q-order mass exponent t_q. 3.a (a patient from group I) and 3.b (a patient from group II).

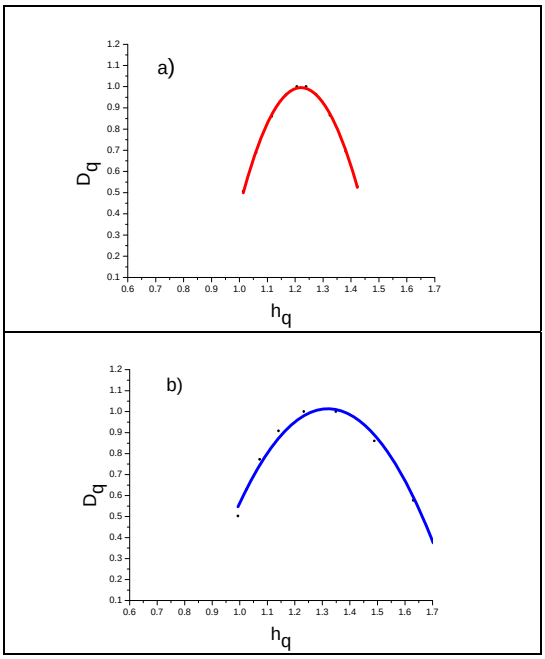

Figure 4. Multifractal spectrum. 4.a (a patient from group I) and 4.b (a patient from group II).

4. Conclusions

Although the series are very short, we can observe, first graphically, the obvious differences in the fractal structures of the two groups. The change in shape of multifractal spectrum curve for this group can provide information on changes in cardiac dynamics of patients with greater impairment of the muscles of the heart.

The Mann-Whitney test (p-value <0.01) revealed that the degree of multifractality for the group I is very significantly lower than for the group II.

Our future intention is to apply this methodology to a greater number of subjects and to larger RR series in order to find a threshold for Δh_q, which would separate the two groups. It would be an average between the maximum Δh_q of group I and minimum Δh_q of group II. The idea is to find a Threshold of Loss of Multifractality (TLM), i.e., a value below which we can say that there was a loss of multifractality as sign of illness. To the tables I and II, TLM would be 0.499 ($\cong$ 0.5).

If our analysis was more robust we could then say that, for $\Delta h_q < 0.50$, there is loss of multifractality.

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