Comparison of Wavelet Transform Modulus Maxima and Multifractal Detrended Fluctuation Analysis of Heart Rate in Patients with Systolic Dysfunction of Left Ventricle

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Background: In recent years the WTMM (wavelet transform modulus maxima) and MDFA (multifractal detrended fluctuation analysis) methods have become widely used techniques for the determination of nonlinear, multifractal heart rate (HR) dynamics. The purpose of our study was to compare multifractal parameters of heart rate calculated using both methods in a group of 90 patients with reduced left ventricular systolic function (rlvs group) and in a group of 39 healthy persons (nsr group).

Methods: For each subject from the rlvs group (LVEF $\leq$40%) and the nsr group, a 24-hour ECG Holter monitoring was performed. The width of the multifractal spectrum and global Hurst exponent were calculated by means of WTMM and MDFA methods for 5-hour daytime and nighttime subsets.

Results: The width of the multifractal spectrum was significantly lower and the Hurst exponent was significantly higher in rlvs group in comparison to nsr group both during diurnal activity and nocturnal rest according to MDFA and only during diurnal activity according to WTMM method. In both groups we observed significant differences of the multifractal spectrum width and the global Hurst exponent between the nighttime and daytime recordings.

Conclusions: MDFA seems to be more sensitive as compared with WTMM method in differentiation between multifractal properties of the heart rate in healthy subjects and patients with left ventricular systolic dysfunction. **Ann Noninvasive Electrocardiol 2008;13(2):155–164**

multifractal analysis, heart rate variability, heart failure

Variations in the heart rate (HR) may be evaluated by a number of methods. The clinical importance of heart rate variability (HRV) became apparent in the late 1980s after it had proved to be a strong and independent predictor of mortality following an acute myocardial infarction. With the availability of new, digital, high-frequency, 24-hour electrocardiographic recorders, HRV has gained potential to provide additional valuable insight into physiological and pathological conditions and to enhance the risk stratification. A number of new methods have been developed to quantify complex HR dynamics and to complement the conventional measures of HRV.[1,2,3] Those conventional techniques include analysis of means, standard deviations, and other features of histograms (time-domain methods) as well as classic power-spectrum analysis (frequency-domain methods). The time-domain and frequency-domain methods share limitations of HRV estimation imposed by the irregularity of the RR interval series.[4] Complex RR interval data sets may contain "hidden information," which cannot be extracted with traditional methods of analysis because nonlinear phenomena also contribute to the genesis of HRV.[5,6,7] Moreover, the problem of HR "stationarity" is frequently discussed with regard to long-term HRV recordings. These nonstationary and nonlinear fluctuations of

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the RR intervals are related mainly to nonlinear interaction between competing neuroautonomic inputs. Therefore, more complex statistical measures can be calculated on the basis of a series of RR intervals preferably recorded over longer periods of time. These new parameters differ from the traditional measures of the HR variability in that they are not designed to assess the magnitude of variability. Rather, they estimate the correlation properties of the HR variability.

Many physiological time series—such as RR intervals are in fact inhomogeneous, suggesting that different parts of the signal have various scaling properties. In recent years, the detrended fluctuation analysis (DFA) method has become a widely used technique for the determination of long-range correlations of noisy, nonstationary time series and their relation to a fractal-like $1/f^{\beta}$ decay of spectral density for f <0.04 Hz in a classic power-spectrum picture. It has successfully been applied to measure HR dynamics.[8,9,10] However, many RR interval series do not exhibit a simple monofractal scaling behavior, which can be accounted for by a single-scaling exponent. Very often the scaling behavior is more complicated, and various scaling exponents are required for different parts of the series. In this case a multifractal analysis must be applied. In the early 1990s an improved multifractal formalism was developed. The wavelet transform modulus maxima (WTMM) method was introduced,[11] which is based on wavelet analysis and involves tracing the maxima lines in the continuous wavelet transform over all scales.[12,13] Kantelhardt et al.[14] proposed an alternative approach based on a generalization of the DFA method—multifractal detrended fluctuation analysis (MDFA). They have shown that the MDFA method can reliably determine the multifractal scaling behavior of the time series, similar to the WTMM method that seems to be more complicated procedure for this purpose.

It has been speculated that the analysis of HRV based on the methods of nonlinear dynamics and fractal dynamics might elicit valuable information for the physiological interpretation of HRV and also for the assessment of the risk of sudden death. At present, the nonlinear methods represent potentially promising tools for HRV assessment, but standards are lacking and the full scope of these methods cannot be properly evaluated.

This research was designed to study HR multifractal dynamics by means of WTMM and MDFA methods in healthy subjects and patients with reduced left ventricular systolic function.

METHODS

The rlvs (reduced left ventricular systolic function) group consisted of 90 patients (9 women, 81 men, age on average 57 ± 10 years, NYHA class I–10%, II–55%, III–34%, IV–1%) with low left ventricular ejection fraction (LVEF ≤40%, mean LVEF = 30.2 ± 6.7%) that had been hospitalized at the First Department of Cardiology, Medical University of Gdansk, Poland. The additional exclusion criteria from the rlvs group were as follows: myocardial infarction within the last 6 months, persistent atrial fibrillation, sinus node disease, diagnosed diabetes mellitus, coronary revascularization within the last 6 months, or kidney failure with the creatinine level >2 mg/dL. The control group (nsr group) consisted of 39 healthy individuals (4 women, 35 men, age on average 52 ± 8 years) with no history of cardiovascular disease, and normal both echocardiogram (mean LVEF = 68.0 ± 4.7%) and electrocardiogram. Each subject from the two groups was monitored with ECG Holter for 24 hours. The ECG signal was digitized using Del Mar Avionics (Irvine, CA) recorder (Digicorder) and then analyzed and annotated using Del Mar Accuplus 363 system (fully interactive method) by an experienced cardiologist. The minimum percentage of qualified sinus beats required for the signal to enter the study was 85%.[15]

For the calculations the software accessible from PhysioNet[16] was used. We used specifically DFA.C program by J. Mietus, C.K. Peng, and G. Moody to find the statistics of signal departures from dominated polynomial trends (MDFA) and the multifractal.c written by Y. Ashkenazy for estimation of local maxima of the WTMM). Multifractal spectra were then obtained by the Legendre transformation.[17] Because of the numerical approach, each spectrum consisted of points, h, D(h), where h is the local Hurst exponent and D(h) is the probability that such a value occurs in a series after interpolation from a multifractal spectral curve. The Hurst exponent h is the one that describes scaling of the variance of a process. We call h a local Hurst exponent because we searched for power-law dependences for large scales, namely from 50 to 1000 heart beats. The method of calculations was tested with a series of known multifractal properties, that is, fractional Brownian motions (fBm)—the basic

monofractals, which are distinguished by the same Hurst exponent at every point, with white noise (Hurst = 0) random walk (Hurst = 0.5) as crucial examples, and binomial series where multifractal spectra are given by analytical formulae.[18] The results of our analyses for monofractal fBm series are shown in Figure 1. The corresponding spectra are not points as might be expected but do have some width. The width depends on the method, since a wider spectrum is obtained for WTMM estimates. However, the maximum of the spectrum curve is close to the theoretical value of the Hurst exponent for both methods and that maximum is densely occupied by spectra points.

In order to perform multifractal analysis of RR series, we extracted from 24-hour ECG recordings two 5-hour subsets: daytime (2.00 pm–7.00 pm) and nighttime (0.00 pm–5.00 am). Next multifractal spectra were found using Legendre transformation. The average structure functions $\tau(q)$ were found at $q = -4, -3.9, -3.8, \ldots -0.1, 0, 0.1, \ldots 3.9, 4.0$ for each group of data: day and night, nsr and rlvs, and each method: WTMM and MDFA. At each $\tau(q)$ point the Shapiro-Wilk normality test was performed and only the data sets characterized by P value lower than 0.05 were accepted for further transformations. Then multifractal spectra (h, D(h)) were found using Legendre transformation. We calculated the following parameters for each group's multifractal MDFA and WTMM spectra: the width: h_{max}–h_{min} and the global Hurst exponent: $H = 1/2(1+\tau(2))$. Error bars for the group's spectra were estimated by the jackknife method.

Simultaneously, we performed time analysis for both 5-hour subsets using widely accepted SDNN, SDNNi, SDANN, RMSSD, and PNN50 parameters[4] to asses HRV in both groups by means of traditional measurements. Data are expressed as mean ± standard deviation. Student's *t*-test was used to determine the difference of HRV parameters between daytime/nighttime periods as well as between nsr/rlvs groups. The Pearson correlation coefficient was used to estimate the correlations between different multifractal variables. A P value lower than 0.05 was considered statistically significant.

RESULTS

The clinical characteristics of the cardiac patient group and the control one are presented in

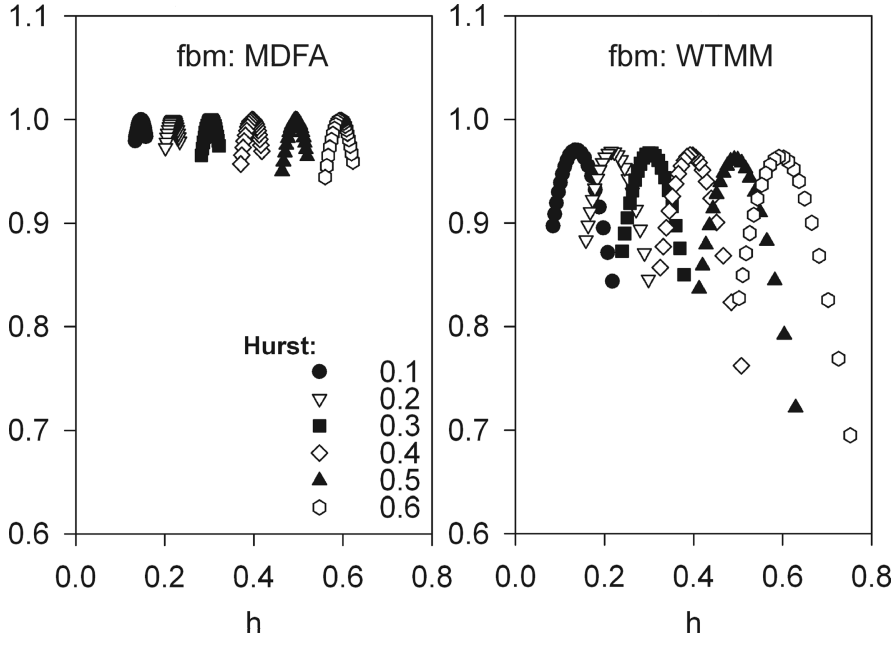

Figure 1. Multifractal spectra for monofractal signals (fBm) calculated by MDFA (left) and WTMM (right) method; labels of curves indicate the Hurst exponent. h = local Hurst exponent; MDFA = multifractal detrended fluctuation analysis; WTMM = wavelet transform modulus maxima.

Table 1. Clinical Characteristics of Patient with Left Ventricular Dysfunction (rlvs) and Control Group (nsr)

	Nsr Group	Rlvs Group	P
	(n = 39)	(n = 90)	
Age	54 ± 7	57 ± 10	ns
Gender	4 K. 36 M	9 K. 81 M	ns
LVEF (%)	68 ± 4.7	30.2 ± 6.7	<0.001
SBP (mmHg)	125 ± 10	116 ± 14	<0.001
DBP (mmHg)	80 ± 7	73 ± 12	<0.001

nsr = control group; rlvs = reduced left ventricular systolic function group; LVEF = left ventricular ejection fraction; SBP = systolic blood pressure; DBP = diastolic blood pressure.

Table 1. There were no significant age and gender differences between the study groups. As expected, we observed decreased ejection fraction (30.2 ± 6.7% vs 68 ± 4.7%, $P < 0.001$) and lower values of systolic (116 ± 14 mmHg vs 125 ± 10 mmHg, $P < 0.001$) and diastolic (73 ± 12 mmHg vs 80 ± 8 mmHg, $P < 0.001$) blood pressure in patients with systolic heart failure as compared to the control group.

The multifractal spectra obtained from the average structure functions in both groups are presented in Figures 2 and 3. The multifractal group parameters calculated using both methods are extracted from these plots and presented separately in Table 2 (MDFA) and Table 3 (WTMM).

The width of the multifractal spectrum was significantly lower in patients with left ventricular dysfunction (MDFA day: 0.121 ± 0.016 vs 0.153 ± 0.024, $P < 0.05$; MDFA night: 0.190 ± 0.017 vs. 0.248 ± 0.024, $P < 0.05$; WTMM day: 0.221 ± 0.039 vs 0.239 ± 0.038, $P < 0.05$) as compared to the control group except for nighttime data calculated by WTMM method. Moreover, the global Hurst exponent was significantly higher in patients with heart failure (MDFA day: 0.186 ± 0.013 vs 0.155 ± 0.014, $P < 0.05$; MDFA night: 0.103 ± 0.011 vs 0.082 ± 0.019, $P < 0.05$; WTMM day: 0.186 ± 0.018 vs 0.155 ± 0.027, $P < 0.05$) that indicates less anticorrelated behavior of RR intervals, also with the exception of nighttime data calculated by WTMM method.

In both groups we observed significant differences between nighttime and daytime recordings with regard to multifractal spectrum width and the global Hurst exponents. According to MDFA method the global Hurst exponent of the nighttime recordings was lower than that of the daytime (nsr group: 0.082 ± 0.019 vs 0.155 ± 0.014,

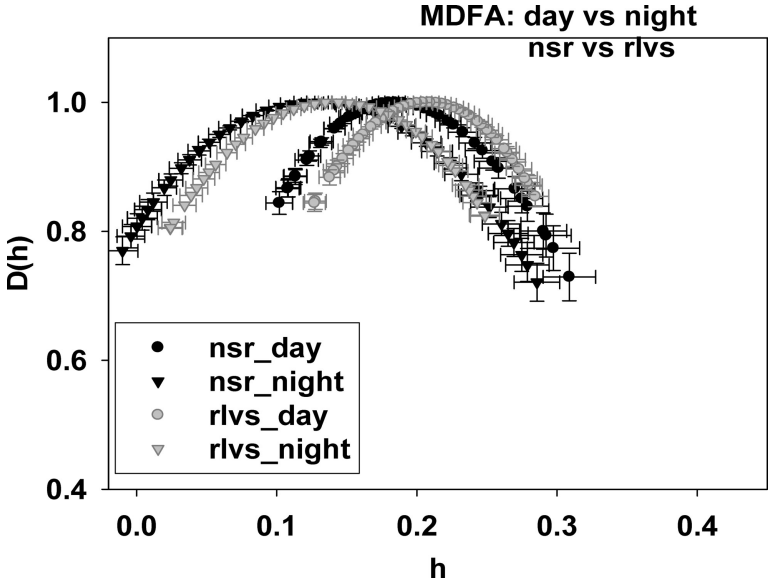

Figure 2. Multifractal spectra of RR intervals series in patients with left ventricular dysfunction (rlvs) and control group (nsr) calculated by means of MDFA method. h = local Hurst exponent; D(h) = probability that h value occurs in a series; nsr = control group; rlvs = reduced left ventricular systolic function group; MDFA = multifractal detrended fluctuation analysis. Error bars are determined by jackknife method.

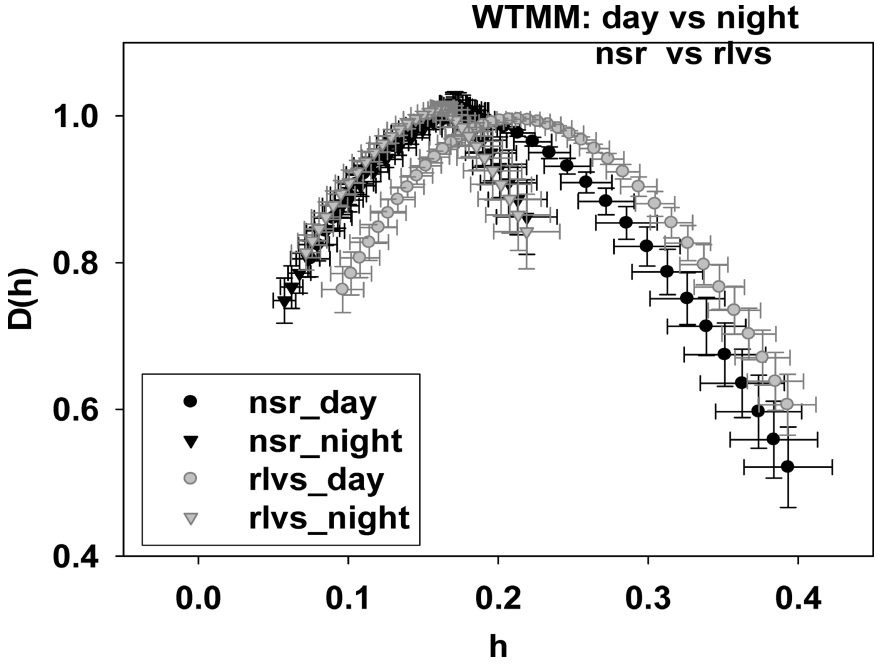

Figure 3. Multifractal spectra of RR intervals series in patients with left ventricular dysfunction (rlvs) and control group (nsr) calculated by means of WTMM method. h = local Hurst exponent; D(h) = probability that h value occurs in a series; nsr = control group; rlvs = reduced left ventricular systolic function group; WTMM = wavelet transform modulus maxima. Error bars are determined by jackknife method.

$P < 0.05$; rlvs group: 0.103 ± 0.011 vs 0.186 ± 0.013, $P < 0.05$). Moreover, the width of the multifractal spectrum was higher for the nighttime subset in both groups according to MDFA (nsr group: 0.248 ± 0.024 vs 0.153 ± 0.024; rlvs group: 0.190 ± 0.017 vs 0.121 ± 0.016, $P < 0.05$). The global Hurst exponent calculated by WTMM for the daytime recordings proved to be lower for nsr group (0.129 ± 0.021 vs 0.155 ± 0.027, $P < 0.05$) and higher for rlvs group (0.186 ± 0.018 vs 0.142 ± 0.017, $P < 0.05$) as compared to the nighttime recordings. The width of multifractal spectrum calculated by WTMM was higher for the daytime data set as compared to nighttime in both groups (nsr group: 0.239 ± 0.038 vs 0.104 ± 0.024; rlvs group: 0.221 ± 0.039 vs 0.096 ± 0.028, $P < 0.05$). A shift of the global Hurst exponent that we observed, indicates changes in the cardiac control mechanisms with regard to either day or night periods. It also supports the hypothesis that sleeping and awake periods lead to the systematic changes in the scaling properties of the heart beat dynamics. We also compared multifractal parameters obtained by means of both methods and calculated potential correlations between them (Table 4). All of them significantly correlated except for the width of the night multifractal spectrum in nsr group.

The traditional time-domain parameters calculated for both groups are presented in Table 5. In rlvs group we observed significantly lower day and night values of SDNN, SDNNI, SDANN as compared to the control group. We did not observe any significant difference between rlvs and nsr groups with regard to the nocturnal RMSSD and PNN50 parameters; however, their diurnal values were higher in the rlvs group than in the nsr one.

There was no significant difference between the mean RR interval in both groups during nighttime while diurnal RR mean interval was shorter in the nsr group (Table 5). We noticed significant correlations between day/night differences in most of the time-domain parameters and day/night differences in RR interval (Table 6), while changes in multifractal indices were independent of circadian differences in the mean RR interval (Table 7) except

Table 2. The Width of Multifractal Spectra and Global Hurst Exponent in Patients with Left Ventricular Dysfunction (rlvs) and in Control Group (nsr) Calculated by Means of the MDFA Method

Multifractal spectrum	nsr Group	rlvs Group	P
Hurst exponent			
Day	0.155 ± 0.014	0.186 ± 0.013	<0.05
Night	0.082 ± 0.019	0.103 ± 0.011	<0.05
P	<0.05	<0.05	
Width			
Day	0.153 ± 0.024	0.121 ± 0.016	<0.05
Night	0.248 ± 0.024	0.190 ± 0.017	<0.05
P	<0.05	<0.05	

nsr = control group; rlvs = reduced left ventricular systolic function group; MDFA = multifractal detrended fluctuation analysis.

Hurst exponent calculated using WTMM method (hWTMM) in rlvs group.

DISCUSSION

This is the first study that has determined multifractality of the heart rate by means of two separate methods in patients with left ventricular systolic dysfunction. It is well known that a decreased HRV is strongly associated with the high risk of sudden cardiac death especially in patients with history of myocardial infarction. The nonstationary and irregular fluctuations of the heart rate series are related to the nonlinear interaction between competing neuroautonomic inputs. Analytic methods deriving from nonlinear dynamics, based on the chaos theory and fractal mathematics have created new lines of approach to studying and understanding the characteristics of HR behavior. Although in principle these nonlinear methods proved to be powerful tools for characterization of various complex systems, no major breakthrough has yet been made with regard to their potential application in biomedical data analysis including HRV among others.[12,19,20]

Multifractal analysis of time series has a solid mathematical background. However, transferring mathematical ideas into real series of estimates is not so obvious. Basically, by multifractal study, one searches for singularities in a series. Then the multifractal spectrum measures the frequency of occurrence of a given singularity exponent. Since singularity values change along the series very vividly, the probability of occurrence is measured by the Hausdorff dimension of the subset of time where the same singularity exponent value is accounted. Both tasks, extracting singularity exponents and evaluating the Hausdorff dimension, are numerically difficult and calculations cannot be performed automatically. Fortunately, both properties can be estimated relying on the scaling (power-law dependence on a scale) properties of the partition function. For each scale, WTMM method provides the partition function as the sum of local maxima of modulus of wavelet transform while MDFA measures the signal oscillation by the sum

Table 3. The Width of Multifractal Spectra and Global Hurst Exponent in Patients with Left Ventricular Dysfunction (rlvs) and in Control Group (nsr) Calculated by Means of WTMM Method

Multifractal Spectrum	nsr Group	rlvs group	P
Hurst exponent			
Day	0.155 ± 0.027	0.186 ± 0.018	<0.05
Night	0.129 ± 0.021	0.142 ± 0.017	ns
P	<0.05	<0.05	
Width			
Day	0.239 ± 0.038	0.221 ± 0.039	<0.05
Night	0.104 ± 0.024	0.096 ± 0.028	ns
P	<0.05	<0.05	

nsr = control group; rlvs = reduced left ventricular systolic function group; WTMM = wavelet transform modulus maxima.

Table 4. The Correlation Coefficient between Multifractal Parameters Calculated by Means of MDFA and WTMM Methods in nsr and rlvs Groups

Multifractal Parameters	r	P
nsr		
Width day	0.60	<0.001
Width night	0.02	ns
Hurst exponent day	0.74	<0.001
Hurst exponent night	0.61	<0.001
rlvs		
Width day	0.42	<0.001
Width night	0.46	<0.001
Hurst exponent day	0.86	<0.0001
Hurst exponent night	0.57	<0.0001

nsr = control group; rlvs = reduced left ventricular systolic function group; MDFA = multifractal detrended fluctuation analysis; WTMM = wavelet transform modulus maxima.

of signal departures from polynomial trends dominated at a given scale. The scaling properties of the partition function are collected in the structure function $\tau(q)$.

Ivanov et al.[12] described multifractal properties of healthy human heart beat and loss of these properties in patients with congestive heart failure. In our study we observed preservation of multifractal heart rate properties in patients with significantly decreased systolic function. However, multifractal properties represented by width of multifractal spectrum were significantly lower in patients with left ventricular dysfunction as compared to healthy controls. Increased multifractality in the control group indicates greater complexity of the healthy heart dynamics. Ivanov et al. presented monofractal behavior of the heart cycle series in patients

Table 6. The Correlation between Differences in Day/Night RR Interval and Differences in Day/Night Time-Domain HRV Parameters in nsr and rlvs Groups

Group	r (nsr)	P	r (rlvs)	P
ΔSDNN	0.43	<0.01	0.33	<0.01
ΔSDANN	0.48	<0.01	0.16	ns
ΔSDNNI	0.1	ns	0.39	<0.0001
ΔRMSSD	0.65	<0.0001	0.26	<0.01
ΔPNN50	0.51	<0.01	0.28	<0.01

nsr = control group; rlvs = reduced left ventricular systolic function group; Δ= difference between nocturnal and diurnal parameter.

Table 5. Time-Domain Parameters Calculated in Patients with Left Ventricular Dysfunction (rlvs) and in Control Group (nsr)

Time-Domain Parameters	nsr Group	rlvs Group	P
SDNN			
Day	85.5 ± 20.1	71.1 ± 25.8	<0.01
Night	87.9 ± 23.8	67.6 ± 27.2	<0.0001
P	ns	ns	
SDANN			
Day	71.8 ± 19.8	58.1 ± 21.9	0.001
Night	59.1 ± 20.2	45.9 ± 18.7	<0.001
P	<0.01	<0.0001	
SDNNi			
Day	50.3 ± 15.6	43.8 ± 18.8	0.06
Night	59.5 ± 20.3	48.1 ± 21.5	<0.01
P	<0.05	ns	
RMSSD			
Day	19.5 ± 10.5	30.9 ± 22.8	<0.01
Night	32.1 ± 18.3	32.8 ± 16.5	0.8
P	<0.001	ns	
PNN50 (%)			
Day	2.6 ± 3.1	6.7 ± 8.1	<0.01
Night	9.2 ± 9.6	8.45 ± 8.8	0.7
P	<0.0001	ns	
RR (ms)			
Day	724.1 ± 86.8	809 ± 138.4	<0.01
Night	921 ± 123.4	929.2 ± 145.2	ns
P	<0.0001	<0.0001	

nsr = control group; rlvs = reduced left ventricular systolic function group.

Table 7. The Correlation between Differences in Day/Night RR Interval and Differences in Day/Night Multifractal Parameters in nsr and rlvs Groups

Group	r (nsr)	P	r (rlvs)	P
ΔhMDFA	0.14	ns	0.2	ns
ΔhWTMM	0.19	ns	0.38	<0.05
ΔwMDFA	−0.1	ns	−0.2	ns
ΔwWTMM	0.2	ns	0.15	ns

nsr = control group; rlvs = reduced left ventricular systolic function group; Δ= difference between nocturnal and diurnal parameter; MDFA = multifractal detrended fluctuation analysis; WTMM = wavelet transform modulus maxima; H = Hurst exponent; W = width of the multifractal spectrum.

with congestive heart failure that was expressed by very narrow multifractal spectrum. They performed multifractal analysis in a rather small group of 12 patients with severe congestive heart failure and in 18 healthy subjects. Moreover, controls in the Ivanov et al. study were much younger. As we know linear parameters of HRV decrease with age.[21] Unfortunately, there are no data in the literature regarding the influence of age on multifractal properties of the heart rate. Costa et al.[22] observed decline of nonlinear HRV characteristics with age based on multiscale entropy analysis. It is very probable that multifractal HR characteristics could change significantly with age as well.

Using DFA method, Struzik et al.[23] observed decreased width of multifractal HR spectrum and an increase of the Hurst exponent toward random walk scaling in 12 patients with congestive heart failure (RR data downloaded from PhysioNet) as compared to control group of 115 healthy subjects. They suggested that observed changes in the multifractal spectrum were related to the parasympathetic activity suppression in patients with congestive heart failure.

Meyer et al.[24] performed multifractal analysis of the heart rate in patients with congestive heart failure as compared to healthy subjects based on a large deviation spectrum. In their opinion, Legendre transformation (used in our study and also by Ivanov's group) is more convenient and more robust than a large deviation spectrum though at the expense of severe loss of information. Meyer et al. observed broad-range spectrum indicating preserved multifractality in patients with congestive heart failure. In their study the Holder exponent was shifted to larger values similar to our results. These results suggest that in the rlvs group heart beat fluctuations are less anti-correlated (the heart rhythm is more regular). Moreover, they observed a markedly left-sided binomial shape of a multifractal spectrum in patients with heart failure.

In our study we observed significant daytime-nighttime differences in multifractal properties of the heart rate. Multifractal changes of parameters during nighttime were consistent with a hypothetical relative parasympathetic activation. The width of a multifractal spectrum increased while the global Hurst exponent decreased toward 0 value according to MDFA method. Shift of the global exponent toward the white-noise value indicates more anti-correlated behavior of RR fluctuations during sleep. It has already been shown that linear heart rate variability parameters vary depending on the time of day, particularly when comparing the day and night periods.[25] During the night, the heart rate variability parameters are most often increased. Ivanov et al.[26] compared fractal properties of 6-hour day and night recordings in various groups: healthy persons, patients with CHF, and astronauts. In all groups they observed decrease in α exponent during nighttime, which also indicates more anti-correlated behavior. They also analyzed changes of heart rate multifractal properties in healthy volunteers after atropine administration. Ivanov et al. noticed that atropine decreased width of multifractal spectrum and decreased the global Hurst exponent. In our both studied groups, we observed similar changes using MDFA method for daytime recordings that are biased by a relative sympathetic activation as compared to nighttime period. These results seem consistent with the previously observed fact that multifractality is not reduced with diminished physical activity as described by Struzik et al.[23] Using WTMM method we noticed different daytime-nighttime changes of the multifractal spectrum width as compared to MDFA method. A possible explanation for these results is that the WTMM method leads to nonconvex partition functions for nighttime data that result in numerical instability of spectra estimates, though the MDFA method provides regular shapes.

Kantelhardt et al. compared results of the multifractal analysis by WTMM method and MDFA method for the same time series and they obtained comparable results. The MDFA method was slightly better for short time series in comparison to WTMM. In our analysis MDFA method differentiated rlvs and nsr groups both during daytime and nighttime. On the other hand, according to

WTMM method, there were statistically significant differences between multifractal parameters only for daytime data. Nevertheless, most of nonlinear indices calculated by means of both methods were significantly correlated.

As expected, we noticed increase of diurnal and nocturnal HRV parameters in control group using traditional, linear parameter (SDNN, SDNNi, and SDANN). There were no differences between nocturnal RMSSD and PNN50 in nsr and rlvs groups, which was probably due to relatively low values of these parameters in the control group. Diurnal PNN50 and RMSSD were higher in the rlvs group as compared to the nsr group. These results could be at least partially explained by differences in physical activity of both groups and the use of beta-blockers by patients of the rlvs group, which significantly affected the heart rate (mean RR interval was significantly longer during the day in the rlvs group) and simultaneously HRV parameters. Another matter of concern is the presence of premature supraventricular and ventricular complexes that could change HRV measures. To minimize this effect, we excluded subjects with both premature beats or artifacts exceeding 15% of the total beats.

As might be expected, we noticed significant circadian differences in the nsr group except for SDNN where relatively small day/night differences did not reach statistical significance. These differences could be explained by day/night changes in the basal heart rate. We found significant correlations between differences in day/night time-domain parameters and day/night RR interval. Inverse correlations of the time-domain HRV parameters and the heart rate is a well-known fact reported previously.[27] In the rlvs group we observed significant day/night change only in SDANN parameter, though the mean RR interval was different during the day and night period. These results could be explained by an observation of Fleiss et al.[28] that a number of pathological conditions (including heart failure) are characterized by a decreased correlation of HRV and heart rate. On the other hand, we observed that significant day/night changes in the multifractal indices were generally independent of circadian changes in the heart rate (RR interval) (Table 7).

Multifractality of the heart rhythm indicates that many, coupled feedback mechanisms operating over a wide range of time scales are involved in the heart rate regulation. Unfortunately, the physiological mechanisms underlying multifractal variability of the heart rate have not been clearly identified. It is possible that these multifractal measures are not adequate for analysis of biological systems and thus, are too insensitive to detect the nonlinear perturbations of RR intervals that would be of physiological or practical importance. However, no systematic study has been conducted to investigate large groups of cardiac patients using these methods. Advances in technology and interpretation of the results of nonlinear methods are needed before they can be applied for physiological and clinical studies.

CONCLUSIONS

MDFA seems to be more sensitive as compared with WTMM method in differentiation of nonlinear heart rate variability between healthy subjects and cardiac patients with left ventricular dysfunction. The results obtained by MDFA method revealed statistically significant differences of the multifractal spectrum parameters observed between healthy subjects and patients with left ventricular dysfunction--both during the day and night. There were also statistically significant differences according to WTMM method but only with regard to diurnal data. The results of our analysis confirmed that the human sinus rhythm has multifractal properties. Markedly reduced systolic function leads to significant decrease of those properties. An increase of the global Hurst exponent in the group of patients indicates changes of the heart rate dynamics due to left ventricular dysfunction. The consecutive RR intervals of human sinus rhythm are less anti-correlated that is probably caused by disturbances of neuroautonomic heart rate control in patients with heart failure. Moreover, we noticed significant daytime-nighttime differences of heart rate multifractal properties presumably limited to respective changes of sympathovagal modulation during the day and night. In addition, we found that multifractal indices were generally independent of circadian changes of the heart rate. We believe that our findings are important for exploring the significance of multifractal analysis of autonomic heart rate regulation both in normal and pathological conditions.

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REFERENCES

1. Peng CK, Havlin S, Stanley HE, et al. Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series. Chaos 1995;5:82–87.
2. Pincus SM, Goldberger AL. Physiologic time-series analysis: What does regularity quantify? Am J Physiol 1994;226:H1643–H1656.
3. Saul JP, Albrecht P, Berger RD, et al. Analysis of long-term heart rate variability: Methods, 1/f scaling and implications. Comput Cardiol 1988;14:419–422.
4. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability standards of measurement, physiological interpretation, and clinical use. Circulation 1996;93:1043–1065.
5. Ivanov PCH, Rosenblum MG, Peng CK, et al. Scaling behaviour of heart beat intervals obtained by wavelet-based time-series analysis. Nature 1996;383:323–327.
6. Kurths J, Voss A, Saparin P, et al. Quantitative analysis of heart rate variability. Chaos 1995;5:88–94.
7. Denton TA, Diamond GA, Helfant RH, et al. Fascinating rhythm: A primer on chaos theory and its application to cardiology. Am Heart J 1990;120:1419–1424.
8. Ashkenazy Y, Ivanov PCH, Havlin S, et al. Magnitude and sign correlations in heartbeat fluctuations. Phys Rev Lett 2001;86:1900–1903.
9. Bunde A, Havlin S, Kantelhardt JW, et al. Correlated and uncorrelated regions in heart-rate fluctuations during sleep. Phys Rev Lett 2000;85:3736–3739.
10. Chen Z, Ivanov PCH, Hu K, et al. Effect of nonstationarities on detrended fluctuation analysis. Phys Rev E 2002;65:041107-1–041107-15.
11. Arneodo A, Grasseau G, Holschneider M. Wavelet transform of multifractals. Phys Rev Lett 1988;61:2281–2284.
12. Ivanov PCH, Amaral LAN, Goldberger AL, et al. Multifractality in human heartbeat dynamics. Nature 1999;399:461–465.
13. Amaral LAN, Ivanov PCH, Aoyagi N, et al. Behavioral-independent features of complex heartbeat dynamics. Phys Rev Lett 2001;86:6026–6029.
14. Kantelhardt JW, Zschiegner SA, Koscielny-Bunde E, et al. Multifractal detrended fluctuation analysis of nonstationary times series. Physica A 2002;316:87–114.
15. Huikuri HV, Jokinen V, Syvänne M, et al. For the Lopid Coronary Angioplasty Trial (LOCAT) study group, heart rate variability and progression of coronary atherosclerosis. Arterioscler Thromb Vasc Biol 1999;19:1979–1985.
16. www.physionet.org. [Accessed March 31, 2006].
17. Binney JJ, Dowrick NJ, Fisher AJ, et al. The Theory of Critical Phenomena. An Introduction to theRenormalization Group. Oxford, Clarendon Press, 1992.
18. Makowiec D, Galaska R, Dudkowska A, et al. Long range dependencies in heart rate signals – revisited. Physica A 2006;369:632–644.
19. Rak R, Drożdż S, Kwapień J, et al. Detecting subtle effects of persistence in the stock market dynamics. Acta Physica Polonica B 2005;36:2459–2468.
20. Szeto H, Chen PY, Decena JA, et al. Fractal properties of fetal breathing dynamics. Am J Physiol 1992;263:R141–R147.
21. Tsuji H, Venditti FJ, Manders ES, et al. Determinants of heart rate variability. J Am Coll Cardiol 1996;28:1539–1546.
22. Costa M, Goldberger AL, Peng CK. Multiscale entropy analysis of biological signals. Phys Rev E 2005;71:021906-1–021906-18.
23. Struzik Z, Hayano J, Sakata S, et al. 1/f scaling in heart rate requires antagonistic autonomic control. Phys Rev E 2004;70:050901.1–050901.4.
24. Meyer M, Siedl O. Self-affine fractal variability of human heartbeat interval dynamics in health and disease. Eur J Appl Physiol 2003;90:305–316.
25. Fauchier L, Babuty D, Autret ML, et al. Influence of duration and hour of recording on spectral measurements of heart rate variability. J Auton Nerv Syst 1998;73:1–6.
26. Ivanov PCH, Chen Z, Hu K, et al. Multiscale aspects of cardiac control. Physica A 2004;344:685–704.
27. Ramaekers D, Ector H, Aubert AE, Rubens A, et al. Heart rate variability in healthy volunteers. Is the female autonomic nervous system cardioprotective? Eur Heart J 1998;19:1334–1341.
28. Fleiss JL, Bigger JT, Rolnitzky LM. The correlation between heart rate period variability and mean period length. Stat Med 1992;11:125–129.