Multifractal Property Assessment in the Very Low Frequency Range, in Subjects with Different Progression of Aortic Valve Stenosis Disease

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Abstract

Aortic valve stenosis is the third commonest heart disease in developed countries. When the opening of the aortic valve is narrowed, the ability of the heart to pump blood is severely limited. This inhibits the ability of the circulation system to adapt to changing external requirements. This can drastically change state of the nonlinear system and therefore should be clearly visible in signals coming from it.

Aortic valve replacement is connected with a high non-postoperative mortality. It would be interesting to predict the mortality risk based on pre-operative heart rate variability properties.

We analyzed 418 heart rate variability recordings from subjects before the operation, who had different stages of aortic valve stenosis (age 22-82, male and female, ejection fraction 10-95%, aortic gradient 28-218 mmHg, where 352 subjects had critical aortic valve stenosis >70 mmHg).

In our analysis, besides classical linear heart rate variability measures and echocardiography, we applied Multiscale Multifractal Analysis (MMA) [1] – a method yielding the dependence of the local Hurst exponent as a function of the parameter q and of the scale (the Hurst surface). It is designed to analyze correlation properties of the signal at very low frequencies.

We discuss characteristic patterns in the shape of the Hurst surface and abnormalities in heart rate variability of the patients and observe important changes in comparison with the Hurst surface obtained for a group of healthy subjects analyzed in our earlier studies. However, no well-defined correlation of the properties of the Hurst surface with the level of ejection fraction or aortic gradient was obtained.

1. Introduction

When the opening of the aortic valve is narrowed, the ability of the heart to pump blood is severely limited. This inhibits the ability of the circulation system to adapt to changing external requirements. This can drastically change state of the nonlinear system and therefore should be clearly visible in signals coming from it, we would like to check, if this thesis is true.

Aortic valve replacement is connected with a high non-postoperative mortality. It would be interesting to predict the mortality risk based on pre-operative heart rate variability properties.

1.1. Multiscale multifractal analysis

In our analysis, besides classical linear heart rate variability measures and echocardiography, we applied Multiscale Multifractal Analysis (MMA) [1] – a method yielding the dependence of the local Hurst exponent as a function of the parameter q and of the scale s (the Hurst surface). It is based on and derived from MF-DFA method. MMA is designed to analyze correlation properties of the signal at very low frequencies.

MF-DFA (Multifractal Detrended Fluctuation Analysis) developed by Kantelhardt et al. [2], is an effective numerical method to examine the scaling properties of fluctuations by calculating a set of multifractal fluctuation functions $F_q(s)$. Each $F_q(s)$ curve describes the level of fluctuations versus their magnitude (controlled by q) and the scale of observation (s, the size of the window in which $F_q(s)$ is computed).

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

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

where s - scale (window width), $Y(j)$ - data profile (the integrated series), v - current window number, y_v - polynomial fit within current window v. Fluctuations $F^2(v,s)$ are used to determine the fluctuation functions $F_q(s)$, N_s - the number of contiguous windows of length s, q - order of fluctuations.

The power law scaling function in the form:

$$F_q(s) \sim s^{h(q)}$$

lets us easily determine the generalized Hurst exponent *h(q)* as a function of the magnitude of the fluctuations.

In the generalization of MF-DFA method, i.e. MMA method, we use a moving fitting window, sweeping through all the range of the scales *s* along the $F_q(s)$ plot. This allows us to study quasi-continuous changes of the *h(q)* dependence versus the range of the scale *s* and as a result to obtain the generalized dependence *h(q,s)*.

1.2. Hurst surface interpretation

Similarly as for the standard *h(q)* for fixed scale ranges, the part of the *h(q,s)* plot for $q < 0$ correspond to low variance (small fluctuations) in the signal while $q > 0$ describe the fragments of the signal with a large variance (large fluctuations). Interpretation: $h \in < 0,0.5 >$ indicates antipersistency of the time series, $h = 0.5$ uncorrelated noise, $h \in < 0.5,1 >$ persistency of the time series, $h = 1.5$ Brownian motion (integrated noise), $h \geq 2$ black noise [3].

For the healthy subjects, it appears that there is a characteristic distribution of fluctuation scaling (i.e. distribution of properties of correlations) versus fluctuation magnitude and frequency band. We were able to define six characteristic criteria describing configuration of scaling properties. Two of these criteria were directly related to the properties and frequency of occurrence of arrhythmia in the recording studied [1]. We also converted the criteria into an algorithm. In our recent study analyzing the *h(q,s)* obtained for the full data set automatically using this algorithm, we obtained very promising statistical results. In particular, 3 of the 5 cardiac arrest cases without organic heart disease [4] were properly recognized.

2. Data

We analyzed 418 heart rate variability recordings from subjects before the operation, who had different stages of aortic valve stenosis (age 22-82, male and female, ejection fraction 10-95%, aortic gradient 28-218 mmHg, where 352 subjects had critical aortic valve stenosis >70 mmHg).

As we need nighttime RR interval series only and our study group is very big, we prepared algorithm to extract automatically sleep stages from complete 24 h Holter ECG recordings. In a very simplified description, program is mainly based on assessing moving average of the signal, which increases significantly over the night (see Figure 1). After that, there are a few steps of the algorithm improving precision of finding borders of the sleep stage.

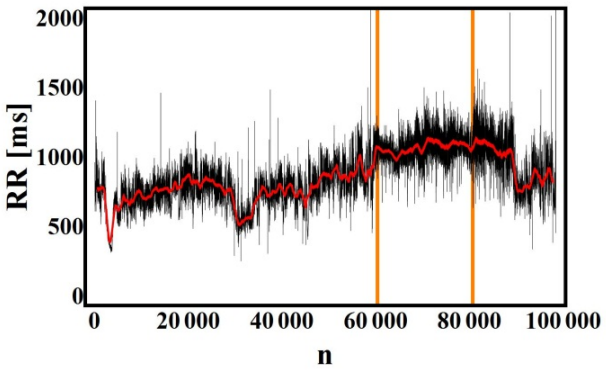

Figure 1. 24 h Holter ECG recording with moving average (window: 1200 data points) depicted by red (grey) line. Two vertical, orange (light grey) lines show six hours long stage of deepest sleep, automatically detected by our algorithm.

2.1. Correlation surface

In order to assess dependence of our results (i.e. Hurst surface) on ejection fraction and on aortic gradient, we introduced correlation surface. This surface shows Pearson's *r* correlation coefficients, calculated for whole group of analyzed datasets, for every single point on the *h(q,s)* surface. This means we take fixed *q* and *s*, then collect from all Hurst surfaces *h* values in this particular point, and then calculate correlation between *h* values and ejection fraction (or aortic gradient), obtaining *r(q,s)* surface (see Fig. 2 and Fig. 3).

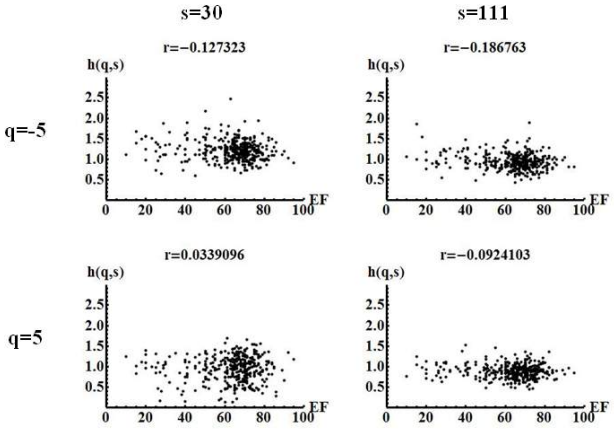

Figure 2. Group of graphs depicting process of calculation of the correlation surface *r(q,s)*. On vertical axis changes of *h* value for fixed *q* and fixed *s*, on horizontal axis pre-operative ejection fraction, for the group of subjects with aortic valve stenosis.

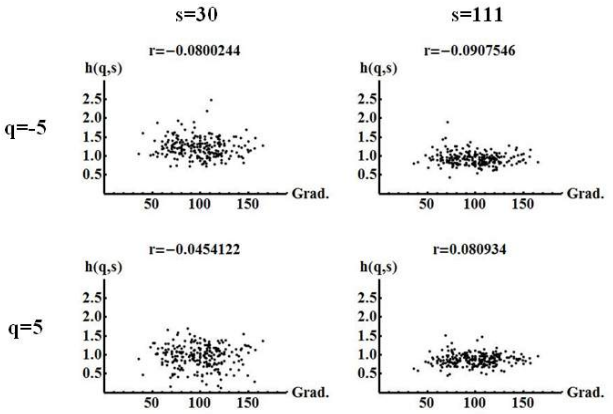

Figure 3. Similarly to Figure 2: on vertical axis changes of *h* value for fixed *q* and fixed *s*, on horizontal axis pre-operative aortic gradient, for the group of subjects with aortic valve stenosis.

3. Results

1. We observe clear changes in the results within the very low frequency band between the healthy and the subjects with stenosis (Fig. 4); MMA method is designed to analyze correlation properties of the signal at very low frequencies)

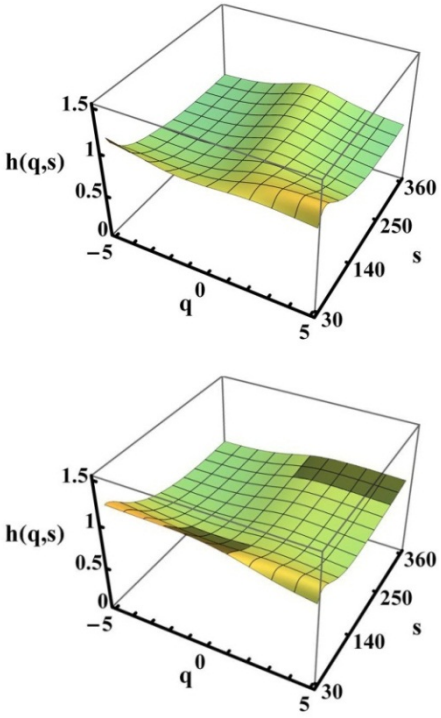

Figure 4. (upper) Mean Hurst surface *h(q,s)* calculated for a group of healthy (bottom) Mean Hurst surface calculated for a group with aortic valve stenosis. Clear differences in scaling exponents *h(q,s)* (i.e. in correlation properties) are visible especially for areas marked in dark grey.

2. The averaged Hurst surface for the stenosis group, breaks one of the six criteria (described in [1]) defining a healthy case (Fig. 4 (bottom) for large *s* and positive *q*, *h(q,s)* values are much higher, than they should be). This means that the large fluctuations observed, indicate a more persistent behavior.
3. There is no clear correlation between MMA results and pre-operative **ejection fraction** (Figure 5)

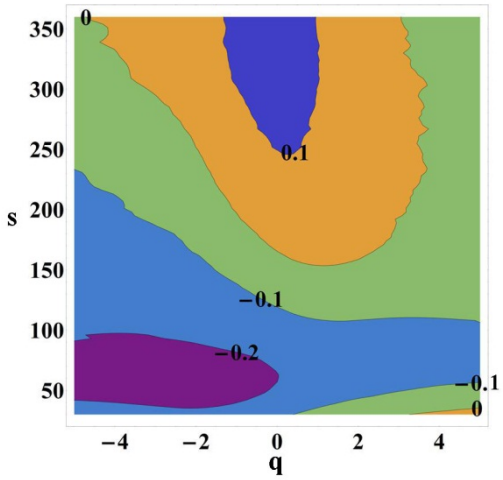

Figure 5. For every fixed pair *(q,s)* we calculated Pearson's correlation coefficients *r* between *h* values and ejection fraction, so in the next step we were able to plot correlation surface (i.e. correlation between scaling exponent *h* and ejection fraction for every possible combination of *q* and *s*). Resulting *r* values are very low.

4. There is no clear correlation between MMA results and pre-operative **aortic gradient** (Figure 6)

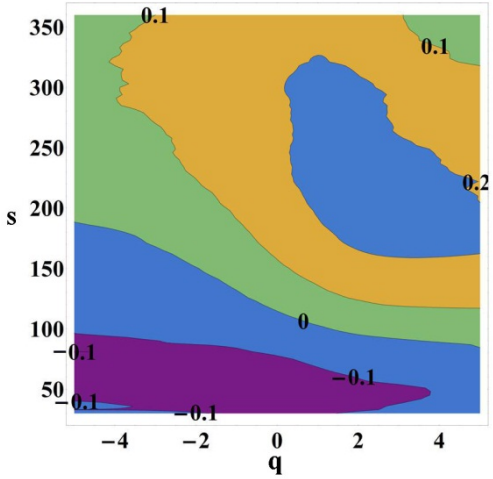

Figure 6. Pearson's *r* correlation coefficients surface, depicting correlation between local Hurst exponent *h* and aortic gradient. Resulting *r* values are very low.

5. For many stenosis cases, in the wavelet scalograms we observe a strong activity of unknown origin but with a very well defined frequency ~0.005 Hz (Figure 7).

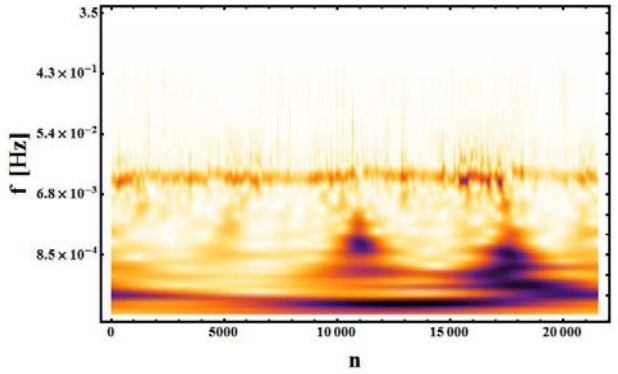

Figure 7. Example of a wavelet scalogram calculated for sleep stage recording, in subject with a severe aortic valve stenosis. Strong and stable spectral component of unknown origin is visible for frequency ~0.005 Hz. Similar results are obtained for tens of subjects from our group studied.

4. Conclusions

MMA method show abnormalities in correlation properties in VLF band in subjects with aortic valve stenosis. Main abnormalities are visible in range 0.005-0.0005 Hz, and these are:

a. spectral components of unknown origin

b. too high scaling exponents for large *s* and positive *q*.

Hurst surface properties, are not correlated neither with ejection fraction, nor with aortic gradient - it seems that abnormalities in HRV in subjects with aortic valve stenosis are clear, but independent of the stage of disease. In the case of aortic valve stenosis, MMA can be used at most as a screening method – it indicates abnormalities, but cannot tell anything about severity of disease.

Acknowledgements

The paper was supported by scholarship from: European Social Fund, Human Capital Programme, “Preparation and realization of Medical Physics Specialty”.

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