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Research Article

Using of Spectral Analysis of Heart Rate Variability for Increasing Reliability of Bicycle Ergometry Results

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ABSTRACT

The aim was to study the suitability of heart rate variability (HRV) spectral parameters for evaluations of bicycle ergometry results in coronary heart disease (CHD) patients. Our study included 243 male CHD patients aged 49±8 years. The coronary atherosclerosis was assessed by coronary angiography. The results of bicycle ergometry, Doppler echocardiography and HRV spectral analysis were analyzed also. The duration of each stage of bicycle ergometry was 3 min, the initial load value was 25 W. Dynamic load continued till the patient reached 75% of heart rate from his maximal age level. The maximal level of load achieved (i.e. load tolerance) was taken into consideration. We calculated sensitivity (Se), specificity (Sp), likelihood ratios of positive (LR+) and negative (LR-) bicycle ergometry results. All patients had similar clinical characteristics. LR+ becomes maximal under the moderate load tolerance. LR- is maximal in the CHD patients with high load tolerance. Thus, the excessiveness of false-negative results of bicycle ergometry is in CHD patients with high load tolerance. Reliability of results of bicycle ergometry increased under using assessments of low-frequency (LF) range power of HRV spectrum.Thus, using of LF range power of HRV spectrum increases a reliability of bicycle ergometry (or other load tests) results in CHD patients.

Keywords: Heart Rate Variability, Bicycle Ergometry, Coronary Heart Disease

1. INTRODUCTION

Submaximal exercise tests are used most frequently in diagnosis of coronary heart disease (CHD). But the sensitivity (Se) and specificity (Sp) of these tests are limited [1]. Defining the conditions, under which exercise tests may produce both true and false result, is an important task of applied cardiology.

It was shown, that the heart rate variability (HRV) parameters turned out to be a sensitive indicator of a myocardial and coronary status in CHD patients [2-3]. Model of heart control based on a baroreflex feedback loop [4-8] has great importance for researches of autonomic heart control. This model explains an origin of low-frequency (LF) component of HRV [9-15]. Thus, LF range of HRV spectrum is of the interest for evaluation of autonomic heart control in CHD patients during load tests.

The aim was to study the suitability of HRV spectral parameters for evaluations of bicycle ergometry results in CHD patients.

2. METHODS

2.1 Subjects

The study was approved by the Ethics Committee of the Saratov Research Institute of Cardiology in Saratov, Russia, and informed consent was obtained from all participants. Our study included 243 male CHD patients aged 49±8 years. 132 CHD patients had acute myocardial infarction six months prior to the start of the study. Pathological Q-wave on electrocardiogram (ECG) was observed in 67 CHD patients. Angina pectoris of I-II functional classes was observed in 86 CHD patients and 120 CHD patients had angina pectoris of III-IV functional classes. 59 CHD patients had arterial hypertension.

We excluded from this study CHD patients with renal pathology, valves heart disease, rhythm and conduction disorders hindering the HRV analysis.

2.2 Measurements and protocol

The coronary atherosclerosis was assessed by selective coronary angiography in all CHD patients. The severity of coronary atherosclerosis was assessed in according with the degree of maximal stenosis of coronary arteries (no less 75%). Bicycle ergometry results, Doppler echocardiography results and HRV spectral analysis were estimated also.

Systolic and diastolic sizes of heart left ventricle, ejection fraction of the left ventricle (EF), velocity of circumferential fiber shortening (V_{cf}), isovolumetric relaxation time (IRT) and condition of the left ventricle local contractility were determined by Doppler echocardiography.

Bicycle ergometry were performed by stepwise increasing load under electrocardiography (ECG) monitoring. The initial load was 25 W. Bicycle ergometry continued till each CHD patient reached 75% of maximal heart rate level [16]. In case of ST segment depression no less 2 mm in one ECG lead during bicycle ergometry, this load test results was considered to be positive. Bicycle ergometry result was considered negative if CHD patient either reached 50% of maximal heart rate level at the highest point of load or performed load of no less 150 W during 3 minutes without any criteria of test cessation. CHD patients with other causes of test cessation were not included in this study. The maximal level of load achieved (i.e. load tolerance) was assessed. All CHD patients have stopped the treatment by nitrates (24 hours prior) and beta-blockers (3-7 days prior) before bicycle ergometry.

ECG recorded during 3 min both for rest and load of 25 W during bicycle ergometry. ECG signal was sampled at 250 Hz and digitized at 14 bits. For further analysis only ECG and PPG records without artifacts, extrasystoles and considerable trends were left. ECG signal were recorded between 13 and 15 hours.

2.3. Statistical and data analysis

Spectral characteristics of HRV were calculated using parametric method of spectrum estimation based on 14 order autoregression model construction. High-frequency (HF) range, 0.15–0.4 Hz, and LF range, 0.04–0.15 Hz, of HRV were analysed [17].

Sensitivity (Se), specificity (Sp), likelihood ratios of positive (LR+) and negative (LR-) bicycle ergometry results were estimated.

For a statistical analysis the software package Statistica 6.1 was used. We apply the Shapiro–Wilk test to check whether the HRV spectral data are approximately normally distributed. Since these data occur to be non-normal, their further analysis was carried out using non-parametric statistical methods. To compare the variables we used the Mann–Whitney test. Continuous variables are reported as medians (Me) with inter-quartile ranges (25%, 75%). Categorical data are presented as frequencies and percentages. The obtained estimations were considered statistically significance if $P < 0.05$.

3. RESULTS AND DISCUSSION

CHD patients have been classified in two groups, according to bicycle ergometry results:

- First group included 125 CHD patients (aged 50±7 years) with positive bicycle ergometry results,
- Second group included 118 CHD patients (aged 47±8 years) with negative bicycle ergometry results.

It was shown that both CHD patient's groups had similar clinical characteristics (age, sex, frequency of myocardial infarction, arterial hypertension, EF, systolic and diastolic sizes of heart left ventricle, etc).

The group of CHD patients with positive bicycle ergometry results differed from the group with negative results in follows characteristics: 1) less load tolerance by 36% ($P<0.001$); 2) more clinically severe angina pectoris: 56% of CHD patients had III-IV functional class of angina and only 30% patients had angina of I-II functional class (versus 36% and 42% respectively in CHD patients with the negative bicycle ergometry results).

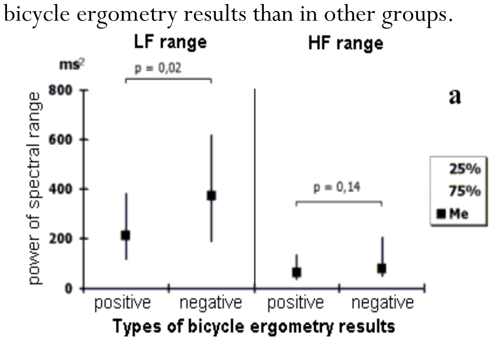
For the further analysis all CHD patients were divided in three groups according to load tolerance level: low level (<75 W), moderate level (75-125 W), high level (>125 W). It is supposed theoretically that load tolerance correlate with coronary atherosclerosis degree. These groups of patients had similar clinical characteristics. Frequency of positive bicycle ergometry results was greater in group of CHD patients with low load tolerance in comparison with other groups ($P=0.003$). Angina was principal cause of bicycle ergometry cessation in group of patients with low tolerance. Frequency of ECG ischemic changes was greater in group of CHD patients with high tolerance (77%) than in groups with moderate (64%) and low (41%) tolerance levels.

Frequency of significant coronary arteries stenosis decreased reliably under increase of the load tolerance in these patients groups (Table 1). In group of CHD patients with high load tolerance, frequency of significant coronary arteries stenosis decreased 1,7 times ($p<0.001$) in compare with group with low tolerance, and it decreased in 1,5 times ($p=0.02$) in group with high tolerance compared with group of patients with moderate tolerance ($p=0.03$). It is shown that *Se* of bicycle ergometry worsens under decrease of load tolerance in CHD patients (Table 1).

Table 1. Coronary atherosclerosis in CHD patients with different load tolerance. Dependence of bicycle ergometry sensitivity (Se) and specificity (Sp) from load tolerance in these patients.

Indices	Low tolerance level (< 75 W) n = 54	Moderate tolerance level (75-125 W) n = 113	High tolerance level (> 125 W) n = 59
Coronary artery stenosis, % of CHD patients	78	71	47
Se, %	93	69	29
Sp, %	25	79	81

Spectral analysis of HRV for rest and load of 25 W displayed reliable differences between groups of CHD patients with positive and negative bicycle ergometry results (Figure 1). CHD patients with negative test results had level of autonomic heart control differing from CHD patients with positive results in presence of similar clinical and instrumental status and coronary atherosclerosis. LF and HF ranges power of HRV spectrum was greater in CHD patients with the negative bicycle ergometry results than in other groups.



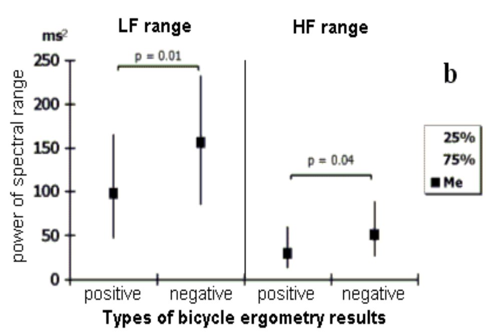


Figure 1: HRV indices in CHD patients with positive and negative bicycle ergometry results in rest (a) and load of 25 W (b).

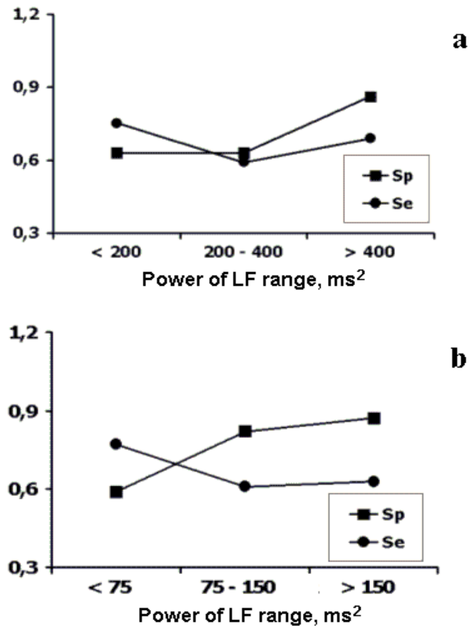


Figure 2. Assessments of Se and Sp of bicycle ergometry in CHD patients based LF range power in rest (a) and load of 25 W (b).

Load tolerance and HRV spectral parameters correlated with negative bicycle ergometry results under rest in CHD patients; multiple correlation coefficient was 0,41 ($p=0{,}004$). In group of CHD patients with positive test results there was no correlation between the HRV spectral parameters and load tolerance ($P=0.26$).

These distinctions of LF range became a basis for improvements of diagnostic effectiveness of bicycle ergometry. Using load of 25 W allows supposing autonomic heart control to be in some functional activity. This fact is a way of conditions standardization for using of HRV spectral analysis. Three ranges of LF power were chosen in all CHD patients. They were the following for the rest: <200 ms^2, 200-400 ms^2, >400 ms^2. And they were the following for 25 W load: <75 ms^2, 75-150 ms^2, >150 ms^2. The ranges intervals correspond to 33% and 66% percentiles of values in the sample of the examined patients, i.e. about one third of all CHD patients are presented in each group. It is shown that bicycle ergometry is of the most diagnostic value under LF_{rest} >400 ms^2 and $LF_{25\ W}$ >150 ms^2. In these cases, sum of *Se* and *Sp* is maximal (Figure 2).

Thus, for increase a reliability of bicycle ergometry in CHD patients It is possible to use LF range spectral power, it is applied for positive bicycle ergometry results especially (Figure 3). This concerns both for standard bicycle ergometry procedure and analysis of bicycle ergometry results taking into account load tolerance (Tables 2 and 3). Positive results of bicycle ergometry in CHD patients is more reliable under moderate load tolerance and $LF_{25\ W}$ >150 ms^2. Otherwise a diagnostic effectiveness of bicycle ergometry decreases. Reliability of negative bicycle ergometry results is maximal under high load tolerance, independently of LF range power of HRV spectrum.

***Table 2: Likelihood ratio (LR) the bicycle ergometry results in CHD patients for the LF range spectral power of HRV under the re**st*

LF range spectral power, ms^2	Load tolerance (W)		
	<75	75÷125	>125
	Positive result of bicycle ergometry		
<200 ms^2	3,1	8,6	3,9
200÷400 ms^2	2,5	6,9	3,2
>400 ms^2	5,3	14,5	6,6
	Negative result of bicycle ergometry		
<200 ms^2	0,2	0,2	0,4
200÷400 ms^2	0,2	0,2	0,5
>400 ms^2	0,2	0,2	0,4

Table 3. Likelihood ratio (LR) of bicycle ergometry results in CHD patients for the LF range spectral power of HRV under 25 W loading

LF-range spectral power, ms^2	Load tolerance (W)		
	<75	75÷125	>125
	Positive result of bicycle ergometry		
<75 ms^2	2,3	6,3	2,9
75÷150 ms^2	4,1	11,2	5,1
>150 ms^2	5,8	15,8	7,2
	Negative result of bicycle ergometry		
<75 ms^2	0,2	0,2	0,4
75÷150 ms^2	0,2	0,2	0,5
>150 ms^2	0,2	0,2	0,4

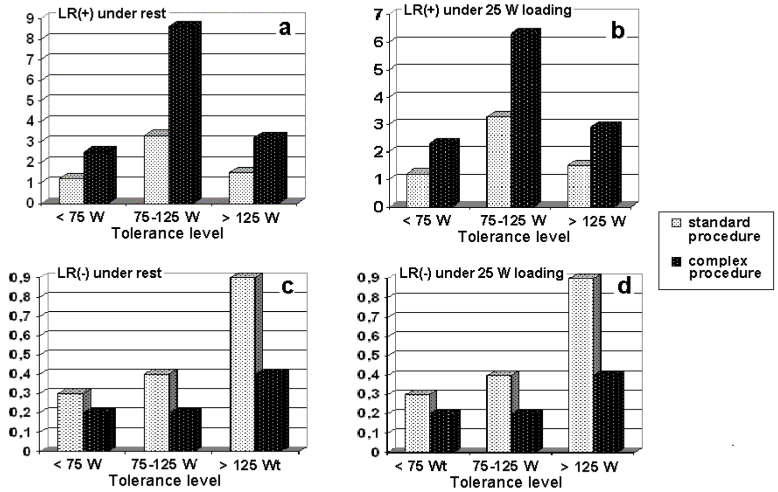


Figure 3. Likelihood ratio (LR) of standard procedure of bicycle ergometry results interpretation and likelihood ratio (LR) of complex assessment of bicycle ergometry results (tolerance level and the power of LF range of HRV spectrum) under the rest and 25 W loading. (a) LR(+) under rest; b) LR(+) under 25 W loading; c) LR(-) under rest; d) LR(-) under 25 W loading.

Probability of false-negative bicycle ergometry outcomes keeps on the level of standard procedure of testing results evaluation. It follows from this that any negative test result is characterized by low reliability and thus could not be used for the assessment of the severity of coronary pathology. It agrees with the European Association of Cardiology data showing that probability of CHD in a 65 years patient with true angina is more, then 75% even if the bicycle ergometry showed a negative result [18]. At the same time, the reliability of positive bicycle ergometry results could be assessed taking into consideration the load tolerance and the spectral power in LF range of HRV. As a criterion of the diagnostic value of the test results the likelihood ratio (LR) index could be used. This index gives direct knowledge of probability of CHD in the presence of a positive or negative physical load test outcome. In clinic of Saratov Institute of Cardiology LR+ values no less than 5 were used as a threshold for the positive result of exercise testing and LR- values less than 0.2 were used for the negative one. In the case of exceeding the likelihood ratio threshold values it is possible to consider that an exercise test results reliably conform to the clinical picture of illness. Otherwise, if LR values do not exceed the threshold ones, then a stress test result could be considered unreliable.

The approach offered allows to determine bicycle ergometry result reliability in cases of positive or negative results of the test individually in each patient and decreases possibility of diagnostic mistakes. Limitations of the method offered for CHD diagnostics are initial heart rate increase (heart rate more than 100 beats per minute) and impossibility to obtain suitable for the spectral analysis bicycle ergometry rhythmograms due to noise and artifacts presence.

4. CONCLUSION

Thus, the analysis of spectral power of LF range of HRV allows to advance diagnostic value of bicycle ergometry results in CHD patients. It is necessary to use a complex assessment of bicycle ergometry results taking into account load tolerance level and power of LF range of HRV spectrum. Combined use of load tolerance and LF range spectral power levels (in rest and during 25 W loading) 2-3 times raises the validity of an individual exercise (in particular, bicycle ergometry) test result compared with standard procedure of bicycle ergometry results analysis in CHD patients. Table 2 can be used for preliminary assessment of bicycle ergometry results especially in CHD patients with low levels of LF range spectral power (<400 ms^2). Further the obtained value of likelihood ratio can be specified with the help of Table 3. Tables data are constructed for CHD patients with hemodynamically significant atherosclerotic stenosis at least one coronary vessel (stenosis degree >50% according to data of coronarography).

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