# THE RAISING OF THE DIAGNOSTIC VALUE OF VELOERGOMETRIC TESTS ON BASIS OF THE HEART RATE VARIABILITY ANALYSIS

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**Abstract:** The aim is the studying of the significance of the heart rate variability (HRV) characteristics during the interpretation of the veloergometric (VEM) tests results in patients with ischemic heart disease. 243 patients with the stable angina of the II-III functional class (49 ± 8 years) were involved in the studying. The evidence of coronary pathology was assessed with the help of selective coronary angiography. Results of VEM testing, Doppler echocardiography and spectral analysis of HRV were analyzed. Registration of R-R chains was performed during 3 min in the relaxed condition and in 90 sec after the beginning of 25 Watt stage of the VEM test. Frequency assessments of HRV were obtained with the help of the parametric method of spectrum construction. The results showed, that using of the HRV spectrum indices allows to raise the diagnostic reliability of VEM tests. Negative result of a VEM trial is characterized by the low level of reliability and cannot be used as an index of absence of the coronary channel damage.

## ITRODUCTION:

In diagnosis of ischemic heart disease (IHD) submaximal tests with dynamic exercise are used most frequently. The sensitivity and specificity of these tests are severely limited that decreases their prognostic value.[1] Defining the conditions, under which submaximal exercise tests may produce both an adequate and inadequate result, is an important task of applied cardiology. The level of autonomic heart control turned out to be a sensitive indicator of a myocardial status.[2] One of non-invasive methods of study of autonomic influences on the heart is a spectral analysis of heart rate variability (HRV). The great importance was attached to creation of a model of heart rhythm control on the basis of baroreflex.[3] Later, the data has emerged that the stable component of HRV spectrum in the field of 0,1 Hz (low frequency, LF-range) characterizes the properties of the central link of the autonomic heart functioning control system.[4]

**The aim** of our investigation was to study the suitability of autonomic heart rhythm control parameters for the interpretation of stress tests results in patients with ischemic heart disease.

## METHOD:

243 patients with the stable angina of the II-III functional class, the male sex at the age from 27 to 67 years (average age is 49 ± 8 years) were involved in the studying. 132 of them had a history of acute myocardial infarction more then 3 months ago. Patients with the evidence of renal pathology, valvular heart disease, rhythm and conduction disorders hindering the analysis of HRV were excluded from the study.

The evidence of coronary pathology was assessed with the help of selective coronary angiography according to M. Jadkins's method. For this purpose "POLYDIAGNOST-C" angiographic complex produced by "PHILIPS" was used. In this method the severity of coronary atherosclerosis was assessed in according with the degree of maximal vessel lumen narrowing (no less then 50%). Summary percentage of coronary channel damage (SPCCD) was estimated. The results of veloergometric (VEM) test, Doppler echocardiography and spectral analysis of HRV were analyzed. VEM test was performed with the help of the method of stepwise increasing load. The duration of each stage of load was 3 minutes. The initial load value was 25 Wt. Veloergometric complex "ES-1200" produced by "HELLIGE" was used. Dynamic load continued till the patient reached 75% of heart rate (HR) from his maximal age predicted level [1]. During the test continuous ECG monitoring was performed to each probationer. In case of episode of ST segment depression no less then 2 millimeters of downsloping or horizontal type at least in one lead and (or) angina of no less then 2 points at peak exercise, this test was considered to be positive. The test result was considered negative if the patient either reached a submaximal (75%) age predicted HR at peak exercise or performed the test at the power of no less then 150 Wt during 3 minutes without any criteria of test cessation. Patients with other causes of test cessation were not included in the study. The maximal level of load achieved (tolerance) was taken into consideration in the analysis of submaximal exercise tests results. Preparing of patients for testing included antianginal drugs cessation: nitrates – with 24 hours advance before testing, β-adrenoblokers – with 3-7 days advance. Digital electrocardiographs "VSD-804" produced by "Volgotech" (Saratov, Russia) and "EK-53R" produced by "HELLIGE" were used. R-R chains registration was performed in a relaxed probationer's condition and in 90 seconds after the beginning of a load stage of VEM test. Analysis of HRV indices was performed in a relaxed condition and during low-intensive load (25 Wt). Analyzed R-R chains did not contain interferences, extrasystoles and definite linear trend. Frequency assessments of HRV were obtained with the help of the parametric method of spectrum construction. The program of spectrum analysis developed in Saratov Research Institute of Cardiology provided frequency resolution of 0,01 Hz in the range from 0,0002 to 0,5 Hz and the period of R-R intervals massive sampling of 0,5 seconds.

Likelihood ratios of positive (LR+) and negative (LR-) VEM test results were estimated together with the test sensitivity (Se) and specificity (Sp).

Statistical analysis of the results obtained was performed with the help of the program software Excel MS Office-97 Professional.

**RESULTS.**

According to VEM test results all of IHD patients were divided into two groups: the first group included 125 patients (aged of 50±7 years) who showed the positive result during VEM test; the second group included 118 patients (aged of 47±8 years) in whom the negative result during VEM testing was shown. The study conducted showed that patients differing in VEM test results had similar clinical and functional characteristics (age, sex, frequency of myocardial infarction with Q-wave in the groups, the frequency of concomitant arterial hypertension, indices of pumping and contractive functions of the left ventricle). The analysis of temporal HRV indices (SDNN, SDANN, SDNN-index, rMSSD, pNN50) based on the data of 24 hours ECG monitoring did not revealed statistically significant differences between the groups.

The diagnostic value of VEM test used in the present study was assessed in terms of sensitivity (Se) and specificity (Sp) taking into account SPCCD value. The method of coronary angiography was used as a referent diagnostic test. The significant dependence of VEM test sensitivity from SPCCD indices was not revealed (Figure 1). Thus, the data presented led to conclusion that VEM test results could not be reliable criteria for the assessment of the degree of coronary vessels damage.

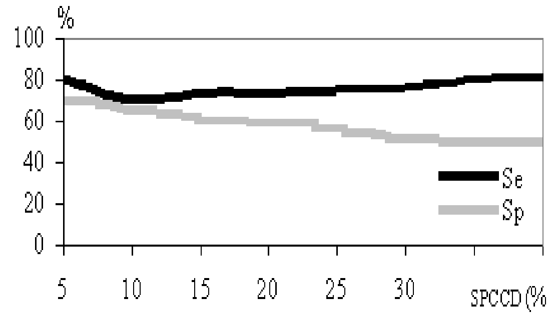


**Figure 1**

For the further analysis all of probationers were divided into three groups according to the exercise tolerance level: low level (<75Wt), moderate level (75-125Wt), high level (>125Wt). The patients had comparable history of old myocardial infarction and were of a similar age in all the groups. Echocardiography data about the heart chambers, contractive and pumping heart function did not differ from the same parameters among the groups either. Positive VEM tests results were more frequent in the group with low exercise tolerance in relation to the other groups (p<0,01). The principal cause of VEM test cessation in the group with low tolerance was angina. Among the probationers with the significant coronary artery stenosis higher SPCCD values were revealed in the group with low tolerance in relation to the groups with moderate (p<0,01) and high (p<0,01) tolerance under comparison with the help of F-criterion. Mean SPCCD values did not differ reliably. With an increase of the tolerance the frequency of significant coronary arteries stenosises decreased reliably in the groups. In the group with high tolerance this frequency decreased 1,7 times (p<0,001) in relation to the group with low tolerance and this index decreased in 1,5 times (p<0,01) in the group with high tolerance compared with the group with moderate tolerance (p<0,01). The data obtained emphasizes the conventional character of the tolerance to exercise use while VEM tests results interpreting as an index of the coronary damage severity.

It was revealed during the analysis of the data obtained from these groups that the ability of exercise test to the correct identification of IHD patients among all of examined raises together with the increase of tolerance. The ratio of true-positive result probability to false-positive one (LR+) becomes maximal under the moderate tolerance. The ratio of true-negative result probability to false-negative one (LR-) is maximal in the group with high tolerance. This fact point out the excessiveness of false-negative outcomes under the high tolerance to the standard VEM test procedure (Figure 2).

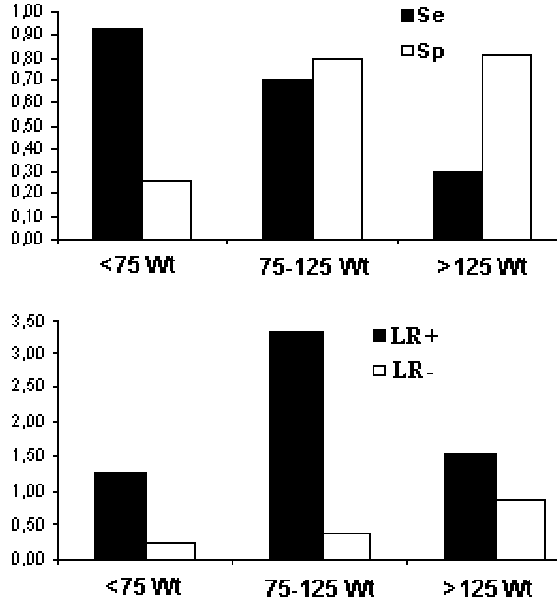


**Figure 2**

The analysis of spectral power indices of HRV spectrum displayed reliable differences between the groups of IHD patients having the positive and the negative VEM test results (Table 1).

**Table 1:** HRV indices in IHD patients having the positive and the negative VEM test result in the initial condition and during 25 Wt loading

| HRV indices | Positive VEM test result Me (25%; 75%) | Negative VEM test result Me (25%; 75%) | p-level |
|---|---|---|---|
| Initial condition | | | |
| LF ($ms^2$) | 212 (118; 427) | 306 (157; 563) | 0.02 |
| HF ($ms^2$) | 64 (36; 136) | 77 (50; 207) | 0.14 |
| 25 Wt loading | | | |
| LF ($ms^2$) | 88 (48; 165) | 136 (75; 213) | 0,01 |
| HF ($ms^2$) | 29 (14; 60) | 51 (27; 89) | 0,04 |

The reliable prevalence of LF-range power of HRV spectrum and high frequency (HF) range power of HRV spectrum was observed in the group with the negative VEM test result. HRV parameters (HR, spectral powers in the spectrum ranges) measured in the initial condition did not depend on SPCCD value both in the positive and the negative VEM test outcomes. Tolerance to exercise and HRV parameters described correlated reliably in the initial condition only in the presence of negative VEM test results. In the group with positive VEM test result there was no reliable correlation between the HRV spectral parameters and the VEM test data (i.e. tolerance). Reliable distinctions revealed in LF-range frequency power and their independence the parameters evaluating during VEM test (HR, achieved exercise level etc.) in case of the positive and negative VEM test result became the basis of the analysis of the diagnostic effectiveness of this method taking into consideration LF-power value in patients both in the relaxed condition and during low level exercise. Using low-powered exercises (25 Wt) allows to suppose the heart rhythm control system to be in some functional tension in the moment of R-R chain registration. This fact could be interpreted as a way of standardization of the conditions when procedures of HRV spectral analysis may potentially be used. Three ranges of LF-power values were chosen in patients. They were the following for the relaxed condition: lower then 200 $ms^2$, from 200 to 400 $ms^2$, more then 400 $ms^2$. And they were the following for the 25 Wt load: lower then 75 $ms^2$, from 75 to 150 $ms^2$, more then 150 $ms^2$. The ranges intervals correspond to 33% and 66% percentiles of values in the sample of the examined persons, i.e. about one third of all the probationers are presented in each group.

The VEM test is of the most diagnostic value at LF-power values of HRV spectrum more then 400 $ms^2$ for the relaxed condition and more then 150 $ms^2$ for 25 Wt load. In these cases the sum of sensitivity and specificity values is maximal. Using assessments of LF-range spectral power in interpreting of VEM tests results will allow to increase the reliability of latter. This concerns both the standard VEM test procedure and the analysis of VEM test outcomes taking into account the maximal level of the achieved load (Table 2, 3). The VEM test gives more reliable positive results at moderate values of the achieved load and LF-range power more then 150 $ms^2$ during 25 Wt load. In other conditions the diagnostic effectiveness of the VEM test decreases. The reliability of negative VEM test outcomes is maximal under the high tolerance to the physical load independently of the spectral power in LF-range. Probability of false-negative VEM test outcomes keeps on the level of standard procedure of testing results evaluation. It follows from this that any negative test result is characterized by the low reliability and thus could not be used for the assessment of the severity of coronary pathology. At the same time, the reliability of positive VEM test results could be assessed taking into consideration the power of tolerable exercise 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 the probability of the disease in the presence of a positive or negative physical load test outcome. In clinic of Saratov Institute of Cardiology LR(+) values no less then 5 were used as a threshold for the positive result of exercise testing and LR(-) values less then 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 result 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 VEM test result reliability in cases of positive or negative results of the test individually in each patient and decrease possibility of diagnostic mistakes.

*Limitations* of the method offered for CHD diagnostics are initial heart rate increase (HR more then 100 beats per minute) and impossibility to obtain suitable for the spectral analysis VEM test rhythmograms due to noise and artifacts presence.

**CONCLUSIONS.**

The analysis of indices of LF-component of HRV spectrum allows to advance the diagnostic value of VEM test results in clinical practice. It was shown that any negative VEM test result could not be used as a marker of the severity of coronary vessels damage, because its validity level is low. Combined use of exercise tolerance and LF-range spectral power (in the initial condition and during 25 Wt load) levels 2-3 times raises the validity of an individual test result compared with the standard procedure of VEM test results analysis. Table 2 can be used for preliminary assessment of VEM test results especially in subjects with low levels of spectral power (lower then 400 $ms^2$). Further, the obtained value of likelihood ratio can be specified with the help of Table 3. Tables data are constructed for persons with hemodynamically significant stenosis of at least one coronary vessel. It is important that application of the method offered does not almost increase medical staff efforts during functional testing.

**Table 2:** Likelihood ratio (LR) of the exercise test results for the spectral power in the initial condition

| LF-range spectral power, | Maximal level of the achieved load (Wt) | | |
|---|---|---|---|
| | <75 | 75÷125 | >125 |
| Positive VEM test result | | | |
| <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 VEM test result | | | |
| <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 the exercise test results for the spectral power during 25 Wt loading

| LF-range spectral power, $ms^2$ | Maximal level of the achieved load (Wt) | | |
|---|---|---|---|
| | <75 | 75÷125 | >125 |
| Positive VEM test result | | | |
| <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 VEM test result | | | |
| <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 |

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