

## Early Diagnosis of Coronary Heart Disease Risk by the Expert Automated System Based on the Results of Heart Rate Variability Analysis

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**Abstract:** The possibility of improving the accuracy of early (preclinical) diagnosis of Coronary Heart Disease (CHD) by Automated Expert System (AES) due to the inclusion of the vegetative regulation of the major established risk factors for coronary heart disease, currently used in the system is studied in this study. According to the results, obtained by clinical trial team a comparative analysis of the diagnostic value of the proposed approaches to identify autonomic dysfunction was conducted. The possibility of implementing the results of heart rate variability analysis to quantify the risk of coronary heart disease in the early stages of the automated diagnostic expert system was also investigated.

**Key words:** Heart rate variability analysis, autonomic dysfunction, coronary heart disease, the expert automated system, cardiology, the risk of coronary heart disease

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### INTRODUCTION

Coronary Heart Disease (CHD) is a leader in the structure of overall morbidity and mortality as one of the main causes of permanent or long-term disability (Gijsberts, 2015). To prevent the risk of CHD development it is very important to identify its formation at early stages (Efremova *et al.*, 2013; Lloyd-Jones, 2006).

We study the possibility of improving the accuracy of early (preclinical) diagnosis of CHD by the Automated Expert System (AES) due to the inclusion of the vegetative regulation of the major established risk factors for coronary heart disease, currently used in the system (Nikitin *et al.*, 2013). At the same time, improving the accuracy of early (preclinical) diagnosis of CHD risk may be carried out by taking into account the role of the Autonomic Nervous System (ANS) at the very early stages of CHD. This, in turn will allow realizing the possibility of controlling the parameters of the autonomic regulation.

The studies related to the identification of informative diagnostic signs of the risk of developing coronary heart disease early diagnosis were carried out taking into account the provisions on well-known scientific fact that almost none of the diseases does not pass without changing autonomic functions (Wayne, 2003). At the same time, it was emphasized that the autonomic system plays a significant role in the pathogenesis of coronary heart disease (Nasari Jr., 2015). The method of diagnosis

using VNS analysis of Heart Rate Variability (HRV) was used as the basic research method. This method is fairly simple to use, non-invasive, objective and sufficiently demanded (Bayevskii and Ivanov, 2000; Goldkorn, 2015). Indeed, HRV indicators are highly independent predictors of ventricular tachycardia, fibrillation and sudden death in patients with coronary artery disease (Arsenos, 2012; Oieru, 2015). In addition, the analysis of HRV helps in choosing drug therapy ( $\beta$ -blockers, nitro agents) and evaluation of its effectiveness (Mironova, 2015; Satoh and Cyclophilin, 2015). Also, the HRV data in conjunction with clinical and echocardiographic parameters, improve the accuracy of long-term prognosis of the disease.

The aim of this study was to investigate the possibility of applying the method of HRV analysis for preclinical diagnosis of CHD risk by automated expert system.

The objectives of the study included; to explore the possibility of using known methods for assessing the autonomic regulation in different categories of the population to approve methods of HRV analysis with the help of Hardware and Software Complex (HSC) "Omega" to range the examined cohort on the level of the autonomic functions to evaluate the diagnostic potential of the applied methods and their possible use in the automated expert system for risk assessment of coronary heart disease in the early stages.

## **MATERIALS AND METHODS**

In clinical trials, the team examined the several categories of people with different levels of suspected autonomic regulation. The first group consisted of 54 sportsmen arresters, candidates and masters of sports, middle-aged  $19.1 \pm 0.7$  years. The second group included 55 students of 1-6 courses with no diseases and is considered according to the health of the practically healthy, the average age in this group was  $18.5 \pm 0.5$  years. The third group consisted of patients with chronic diseases 34 patients with Chronic Viral Hepatitis (CVH), the average age  $55.0 \pm 2.2$  years and 39 patients with angina pectoris, the average age  $62.3 \pm 1.8$  years. Also, 31 people with early signs of acute respiratory viral infection were examined with no other diseases, the average age  $19.5 \pm 0.4$  years.

During the formation of the mentioned experimental groups who participated in clinical trials, it has been excluded the contingent with acute emotional stress, pregnant women, patients with cancer, renal, liver and heart failure. All experimental groups were formed at about the same gender composition.

To diagnose CHD the data of general clinical research was analyzed including instrumental and laboratory methods. All patients received basic therapy depending on the evidence.

The study was conducted in Regional State Budgetary Healthcare Institution (RSBHI) "Belgorod City hospital No. 2" in NSU of Physical Education, Sport and Health named after P.F. Lesgaft in Olympic Reserve School No. 2 of St. Petersburg on the clinical base of St. Petersburg State Medical Academy named after I.I. Mechnikov from 2009-2013.

The selection and objectivation of the approach to the procedure for the identification of autonomic disorders has been carried out on the basis of a comparative analysis of the three well-known diagnostic methods: the questionnaire Method-Neuro-Psychological Adaptation test; Survey Data Questionnaire Method the scheme for identifying the vegetative violations and hardware and software analysis method of HRV. This provided sufficient reliability of the results of research in general.

The diagnosis of autonomic dysfunction was carried out on the results of clinical studies under the special scheme of Autonomic Disorders Identification (ADI) by A.M. Wayne. The scheme includes a set of questions aimed at identifying signs of autonomic disorders and contains 13 points. The total amount of points obtained in the study of signs of the scheme in healthy contingent should not be  $>25$  in the case of excess you can talk about the presence of Autonomic Dysfunction Syndrome (ADS) (Bayevskii and Ivanov, 2000).

To evaluate the level of patients' psycho-vegetative state the test of Neuro-Psychological Adaptation (NPA) by Gurvich (1992) was used. This test makes it possible to determine the place of the individual in the continuum of the NPA. The poles of the continuum are psycho vegetative health, on the one hand and manifested in the nosological forms psycho-vegetative pathology on the other. The central part of the continuum is occupied by prepathological (transition) state. Test results allow us to classify surveyed contingent on the group with the quantitative assessment of the level of their psycho-vegetative state.

To evaluate the state of the autonomic regulation the known method of analysis of heart rate variability was used and also the method of diagnosis using the Hardware and Software Complex (HSC) "Omega". Along with the classic indicators of heart rate variability (mode, mode amplitude, variation range, the index of stress and others) the Indicator of Vegetative Homeostasis (IVH) was used. This figure was calculated basing on  $>50$  basic parameters of heart rate: the results of variations, autocorrelation, spectral analysis and quantification of chaos-grams. In further, studies we believed that in the experimentally determined values (IVH) can serve as a quantitative assessment of the degree of autonomic regulation imbalance. To make the use of IVH easier in further studies it was calculated as a percentage. It was believed that the lower the calculated value of IVH, the higher the level of autonomic disorders (Bibikova and Yarilov, 2000).

The evaluation of the differences between the statistical distributions was performed using t-criterion. The correlation between the studied traits was detected by Pearson linear correlation coefficient. For qualitative characteristics Spearman rank correlation coefficient was used. To identify the similarity of the phenomena under study two-factor analysis of variance was used. The findings of the study were processed on a PC using Microsoft Excel spreadsheet and the statistical program SPSS 12.0.

## **RESULTS AND DISCUSSION**

Clinical examination of the above-mentioned groups under the scheme ADI revealed ADS in 15.1% of healthy people and in 82.2% of patients. In the group of athletes ADS was diagnosed in 16.7% of patients. Average rate in autonomic disorders survey scheme in the group of patients was higher ( $32.9 \pm 1.9$ ), than in the healthy group ( $14.9 \pm 1.3$ ;  $p < 0.05$ ) and a group of athletes ( $14.4 \pm 1.2$ ;  $p < 0.05$ ).

Figure 1 shows diagrams describing the frequency of detection of pathological and prepathological psycho-vegetative state in the groups of surveyed contingent. Thus, in the group of patients the signs of

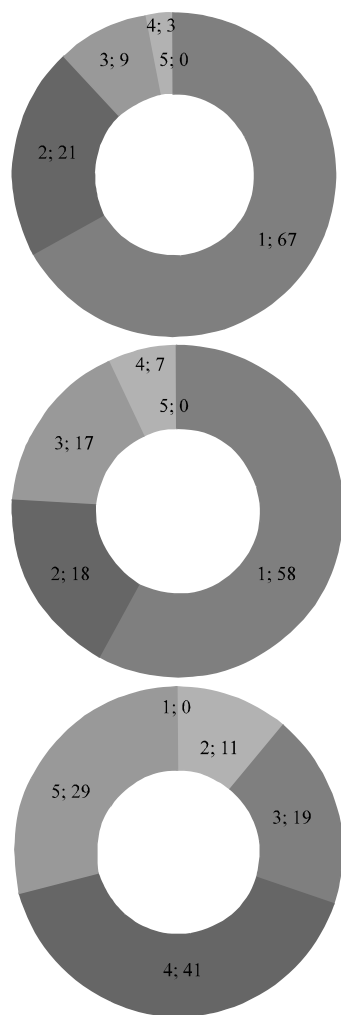


Fig. 1: The chart of the frequency detection options psycho vegetative state groups surveyed contingent (%); the most favorable psycho-vegetative state (0-10 points); the normal state with favorable prognostic features (11-20 points); normal state with unfavorable prognostic signs (21-30 points); the state of pre-pathology (31-40 points); signs of disease (40 points)

disease were found in 29% of patients in healthy people and athletes the surveyed pathological symptoms have not been identified. Prepathological condition was detected in 41% of patients, 7% of healthy subjects and 3% of the athletes.

Counting the average score of the test NPA showed that psycho-vegetative disorders in patients ( $34.8 \pm 1.2$ ) were more manifested than in the healthy group ( $20.5 \pm 1.9$ ;  $p < 0.05$ ) and athletes ( $17.8 \pm 1.5$ ;  $p < 0.05$ ). This presumes the existence of the transition states of the norm to reduce psycho-vegetative functions or improve them.

The analysis of HRV using HSC "Omega" the highest level of autonomic regulation was detected among athletes and healthy people. Table 1 illustrates the computation of the results of clinical studies the average heart rate variability in healthy and sick.

The analysis of experimental data revealed that in patients with coronary artery disease the stabilizing effect of centralization of heart rhythm management (MA  $60.7 \pm 2.2\%$ ) was reduced. To a large extent the relationship between the activity of the sympathetic and parasympathetic divisions of the ANS was disrupted (IAB  $671.8 \pm 22.2$  cond. units). Vegetative balance shifted towards predominance of the sympathetic division of the ANS (VIR  $0.17 \pm 0.02$  cond. units). The influence of the sympathetic division of the ANS on the functioning of the sinus node increased (IARP  $81.7 \pm 4.2$  conv. units). The degree of centralization of heart rhythm increased (TI  $454.1 \pm 79.6$  cond. units). In general, the indicator of vegetative homeostasis is low (IVH  $20.4 \pm 2.1\%$ ).

Also, analysis of the results of clinical studies led to the conclusion that the IVH in patients with coronary artery disease ( $20.4 \pm 2.1$ ) was lower than in the group of patients with chronic viral hepatitis ( $28.3 \pm 4.2$ ;  $p < 0.05$ ) index voltage in these groups had no significant differences ( $532.4 \pm 112.6$  and  $454.1 \pm 79.6$ , respectively with  $p > 0.05$ ). IVH was different in groups of healthy people ( $63.0 \pm 3.2$ ) and athletes ( $73.3 \pm 2.6$ ;  $p < 0.05$ ). The method of HRV analysis revealed differences in the vegetative regulation in these groups whereas the survey scheme for the detection of autonomic disorders and test questionnaire NPA did not allow us to do so.

Table 1: Averages analysis of heart rate variability in healthy and sick

Groups surveyed	Indicator (measure unit)							
	IVH (%)	Mo (c)	MA (%)	VR (c)	IAB (Cond un.)	VIR (Cond un.)	IARP (Cond un.)	TI (Cond un.)
Norm	60-100	0.7-0.9	25-50	0.15-0.45	35-145	0.25-0.6	15-50	10-100
Athletes (M±M)	$73.3 \pm 2.6$	$0.75 \pm 0.01$	$26.0 \pm 1.0$	$0.33 \pm 0.01$	$86.8 \pm 5.2$	$0.43 \pm 0.01$	$36.2 \pm 1.9$	$61.2 \pm 4.4$
Healthy (M±M)	$63.0 \pm 3.2$	$0.72 \pm 0.02$	$29.7 \pm 1.6$	$0.29 \pm 0.01$	$140.6 \pm 21.8$	$0.39 \pm 0.01$	$43.9 \pm 3.1$	$110.1 \pm 21.0$
Sick (M±M)	$24.1 \pm 2.3$	$0.76 \pm 0.01$	$58.2 \pm 2.1$	$0.14 \pm 0.01$	$689.4 \pm 89.9$	$0.18 \pm 0.01$	$80.0 \pm 3.9$	$490.6 \pm 67.2$
SARS (M±M)	$33.9 \pm 2.7$	$0.63 \pm 0.01$	$43.3 \pm 2.3$	$0.15 \pm 0.01$	$258.9 \pm 28.6$	$0.31 \pm 0.01$	$69.9 \pm 4.4$	$212.1 \pm 26.1$
CVH (M±M)	$28.3 \pm 4.2$	$0.75 \pm 0.02$	$55.3 \pm 3.8$	$0.15 \pm 0.02$	$709.7 \pm 134.9$	$0.19 \pm 0.01$	$78.1 \pm 6.9$	$532.4 \pm 112.6$
CHD (M±M)	$20.4 \pm 2.1$	$0.77 \pm 0.02$	$60.7 \pm 2.2$	$0.13 \pm 0.01$	$671.8 \pm 22.2$	$0.17 \pm 0.02$	$81.7 \pm 4.2$	$454.1 \pm 79.6$

Mo: Mode; MA: Mode Amplitude; VR: Variation Range; IOM: an Index of Autonomic Balance; VIR: Vegetative Index Rhythm; IARP: an indicator of the adequacy of regulatory processes in: tension index; PVG: an indicator of vegetative homeostasis

Data analysis of HRV group of people with SARS, revealed changes in HRV in the early stages of the disease indicating the increased activity of the sympathetic system (IAB  $258.9 \pm 28.6$  cond. units, IARP  $69.9 \pm 4.4$  cond. units, TI  $212.1 \pm 26.1$  cond. units).

A group of authors conducted a comparative analysis of the above methods of diagnosis of vegetative disorders which revealed the most informative approach assessment of autonomic dysfunction according to the heart rate. The methodology of the study of HRV analysis is quite simple and not time consuming, it takes no  $>7-10$  min. It was concluded that the main advantage of the analysis of HRV is a higher sensitivity to autonomic regulation changes in comparison with other methods used by us and allows us to observe these changes over time. That in turn, allows us to identify the changes of vegetative regulation at an earlier stage.

According to the analysis of clinical research data and conclusions the contingent classification of all surveyed into four classes was made depending on the level of the autonomic functions (indicator of vegetative homeostasis), calculated by the change in the parameters of heart rate variability: Class 1: elevated levels, characterized by high functionality (IVH 100-80%); Class 2: normal level (IVH 79-60%); Class 3: reduced level, manifesting autonomic dysfunction (IVH 59-40%); Class 4: a pathological level, manifesting autonomic failure (IVH 39-0%). The results of such gradations are illustrated in the graphs in Fig. 2.

The analysis of these diagrams concluded that all patients mainly presented in Groups III and IV with a lower level of vegetative regulation. Among patients with ischemic heart disease 92% of patients have the lowest level of regulation (IV Group). Athletes due to systematic physical exercise have higher levels of autonomic regulation, mainly represented in the Group I and II.

When screening the most attention was paid to the contingent with reduced vegetative indicators, when there are no nosological symptoms (Class 3). When working with the contingent who are in this class, the doctors must find out the causes of violations of the vegetative functions and to assess the risk factors for CHD. In addition, the physician must decide to conduct preventive actions aimed at reducing the impact of significant risk factors, the implementation of further over time observation of the state of the ANS.

In general, the analysis of data from clinical studies and the results of their statistical processing allows to make the assumption that it is possible to improve the accuracy of early (preclinical) diagnosis of CHD by automated expert system including indicators of autonomic regulation of the cardiovascular risk factors,

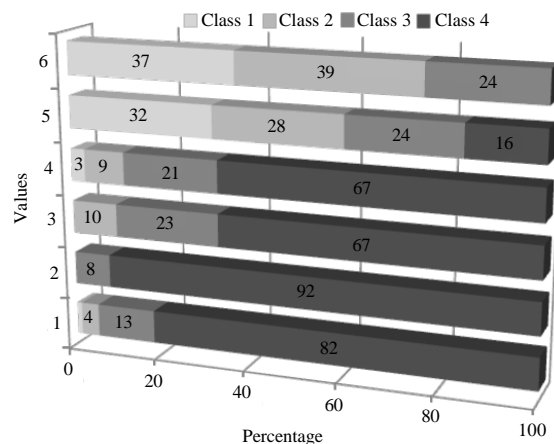


Fig. 2: Diagrams characterizing the distribution of surveyed contingent in groups depending on the level of autonomic regulation (index of vegetative homeostasis); group of patients ( $n = 73$ ); group of patients with coronary artery disease ( $n = 39$ ); group of patients with acute respiratory viral infection ( $n = 31$ ); group of patients with chronic viral hepatitis ( $n = 34$ ); healthy group ( $n = 55$ ); group of athletes ( $n = 54$ ); number 1: PVG 100-80%, number 2: PVG 79-60%, number 3: PVG 59-40%, number 4: PVG 39-0%

currently used. This in turn can help the doctor to develop the treatment strategies based on the resulting data set to identify risk factors for coronary heart disease, taking into account the state of the autonomic regulation.

The method of analysis of heart rate variability using HSC "Omega" allows us to classify patients into risk groups by the level of autonomic function, calculated in terms of vegetative homeostasis and the results of this analysis can be used for early diagnosis of vegetative disorders.

Diagnosis of autonomic dysfunction with the use of the method of analysis of HRV can be used in the automated expert system for more accurate assessment of the risk of coronary artery disease at an early stage.

Using an automated expert system as a training complex offers the opportunity for the user (student, doctor, expert, etc.) to assess the role of the ANS in the development of coronary heart disease to determine the status of autonomic regulation and objectively evaluate its changes on preclinical and any other point of reference patient.

## CONCLUSION

The results of the identification of autonomic dysfunction in the early stages with the help of heart rate

variability analysis will enhance the diagnostic capabilities of the automated expert system for risk assessment of coronary artery disease.

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