Possibilities of high-resolution HRV analysis

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ABSTRACT

Objective: The purpose of the study was to present the results of 15-year application in practical cardiology of the method of high-resolution registration and analysis of heart rate variability (HRV) for diagnosis of the cardiovascular pathology.

Methods: Database consists of more than 46 thousand cases with different cardiovascular diseases. Here are shown some peculiarities of the HRV analysis and perspective possibilities of the method, named rhythmocardiography.

Results: Experience of rhythmocardiography use in cardiology supposes a wide perspective of this method application for the cardiovascular diagnosis. It allows to define various disregulations of the sinus node pacemaker activity, characterized for every form of the coronary artery disease, cardiac arrhythmias, stages of the hypertension disease, syndrome of autonomic cardioneuropathy, high risk of lethal outcome and etc. The rhythmocardiography may be used in treatment choice, in control of the therapy and studying of the autonomic efficacy of some drugs.

Conclusion: Thereby, rhythmocardiography is an informative method for diagnosis of the cardiovascular pathology. The high-resolution measurement of HRV and following such computer analysis in time-domain and frequency-domain can be considered highly informative, because of reliable correspondence and comparable RCG-results with data of other studies and clinical symptoms of the diseases.

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Key words: heart rate variability, high-resolution analysis

Introduction

The purpose of this article was to present the results of 15-year application in practical cardiology of the method of high-resolution registration and analysis of heart rate variability (HRV) for diagnosis of the cardiovascular pathology. The basis of HRV analysis is estimation of the wave structure variability of the temporary intervals length between systoles – RR intervals. The methodology of HRV analysis, as scientific base, as well as mathematical methods for HRV evaluation, were created on the basis of the results of numerous physiological studies (1- 7).

Methods

The method for practical medicine, named rhythmocardiography (RCG), with clinical interpretation of the HRV data was created in Chelyabinsk State Medical Academy and was approved with positive results in 65 hospitals. Rhythmocardiography is founded on diagnosis of different variants of the sinus node (SN) disregulation, characteristic for certain cardiovascular diseases. Rhythmocardiography intends for analysis of the sinus heart rhythm wave structure and doesn't extend on rhythms from other parts of the conduction heart system.

Heart rate variability waves are modulating by sympathetic, parasympathetic limbs of the autonomic nervous system and the humoral-metabolic factors. There are characteristic HRV-waves of the certain length and frequencies for each of these factors. One of the necessary conditions for correct clinical interpretation is the accuracy of measurement of electrocardiosignals (ECS) - with discretization in 1000 Hz. We used the apparatus-program computer complex CAP-RC-01-"Micor" (Russia) for short 300-interval records. The registration of ECS was performed with accuracy in 1 millisecond, that more is exact, than used in equipments for electrocardiogram (ECG) and Holter monitoring (HM) recordings. The extraction of RR-intervals from standard HM with smaller accuracy and absence of physician control during 24-hour recording is often mistaken.

The fluctuations of ECG isoline and obstacles were diverted by the system of technical and program filters in the CAP-RC-complex. The recording was made in strictly stationary controlled conditions at rest and 4 stimulation tests. The episodes of nonstationarities were deleted before analysis by graphic, window editors, or automatic special program. Those episodes carrying clinical importance were analyzed separately. The program of computer analysis of RCG contains the automatic analysis of 5 stationary poststimulation rhythmocardiograms (RCGm) consisted on 300 intervals in each test, more 1500 elements under 25-minute registration. The program consists of modules: "Record RCG" for registration and buildings RCG on screen at the current real time; "Enter data" for information about patient (pt), "Editing" by 4 means for correction or removing of nonstationarities before analysis; "Analysis" for automated statistics and spectral analysis of the HRV wave structure and stimulation periods in tests; "Archive" for conservation of database and work with it; "Conclusion" for the

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formalized diagnostic conclusion. The special file contains 280 formalized diagnoses and other user comforts. Besides, package of the applied programs contains the program of the computer statistical analysis of the data. The method, software, and complex are protected by Russian patents, as exclusive intellectual property.

Physiological and mathematical background of the HRV analysis

The physiological base of RCG is an estimation of the peripheral autonomic sympathetic and parasympathetic regulation, as well as the humoral-metabolic-mediator influences on the SN. The sinus rhythm (SR) regulation appraises on visual and mathematical definition of three types of SR fluctuations of RCGm, determined in frequencies and periodicity. They are formed in accordance with difference of the impulse speed on the sympathetic and parasympathetic nerves, as well as influences of active substances concentrations in tissue environment on HRV fluctuations, acting directly upon chronotropic function of the SN pacemaker cells. Results of the experimental investigations (8, 9) proved physiological peculiarities of the high-frequency (HF) SR waves, connected with mainly parasympathetic negative influences upon pacemaker SN activity. This influence is formed by efferent impulses from cerebral level and, in greater measure, by reciprocal transmission on parasympathetic irritations of mechanical, irritant and juxtacapillar pulmonary parenchyma receptors during breathing (10). In accordance with results of previous investigations (1, 2) increase in rate of parasympathetic impulses causes prolongation of RR intervals that form high frequency (HF -0.15- 0.4 Hz) waves of the short period (2-10 sec). Their frequency and amplitude characterize mainly parasympathetic influences in SN, though within this spectrum there are known diapasons with mixed physiological nature.

The sympathetic fluctuations are connected with sympathetic activity and vessel tone. This is proved by the results of clinical observations and experiments (1-7). The period of these waves is longer and, correspondingly, frequency is low, because of slow speed of the nervous impulses on the sympathetic fibers. These SR waves have a period 10-30 sec and of low frequency 0.04-0.15 Hz, named LF, and characterize the sympathetic influences in SN. The third type of the HRV waves - VLF have period of 30-57 sec and frequency of 0.003-0.04 Hz. The VLF waves are connected with the humoral-metabolic influences upon SN pacemaker cell (1-7, 11). Thereby, three spectral ranges of HRV waves were obtained: 0.003-0.04; 0.04-0.15 and 0.15-0.4 Hz, namely very low frequency (VLF), low frequency (LF), high frequency (HF) fluctuations that share energy spectrum of SR (12).

For control of a recording, the RCGm was built at the real current time on the computer screen. Rhythmocardiogram is a graphic representation of the consequent temporary intervals between systoles, as a row of rectilinear fragments, which is equivalent of length to time pauses between heart contractions. Each interval begins on the abscissa axis with interval number, and lasts upwards parallel to ordinates with indexes of time in seconds. The mathematical analysis of RCGm was performed in Time-Domain and Frequency-Domain. There were the time statistic analysis of data, which were received by direct measurement of consequent RR (NN) intervals, and the spectral analysis with determination of spectral density powers by non-parametric periodogram method with using of spectral decomposition formula of Fast Fourier Transformation of consecutive NN values, as well as spectral windows - Hamming and Parsen. Interpretation of results included the building and evaluation of spectrogram and RCGm in real time, that provided control of artifacts and nonstationarities. Also, there were used the tests: Valsalva maneuver (Vm), Ashner test (pA), active orthostatic test (Aop) and dosed physical exercise on bicycle (PWC120). The RCG data during tests were compared with RCGm record at rest (Ph).

The next RCG indexes were defined as average value of RR (NN) intervals, σRR (SDNN) - an average value of quadratic dispersion of RR intervals. Three statistical average values of quadratic dispersions were defined, correspondingly to amplitudes humoral, sympathetic and parasympathetic waves - σl, σm, σs. This is the peculiarity of our analysis. These indexes are dependent on amplitude of the interval fluctuations. In frequency analysis the spectral densities of three ranges were used in total spectrum of HRV, accepted for 100% - VLF%, LF%, HF%. These RCG indexes characterized the correlation of three regulative factors, according to the "Law of the accentuated antagonism" in SN. The stimulant periods were valued on other indexes: tAB -absolute time of the achievement of maximal reaction to stimuli, ∇RR - maximal reaction to stimuli, and tr- absolute time (in sec and interval) of the reconstruction after action of the stimuli. Also normalization of the RCG indexes was used in test, as difference between the initial value index and its value at the stimulant period, divided by initial value index, according to the "Law of initial level"(13) - nuRR, nuσRR, nu σl, nuσm, nuσs, and nu σl%.

Results

Our database consists of more than 46 000 RCG-studies of patients with different nosological forms of the cardiovascular and extracardiac pathology. At the creation of each scientific fragment RCG data of the assessments were compared with sex- and age-matched healthy control subjects, as well as with results of the clinical and other reference examinations - ECG with graded exercise, HM and blood pressure monitoring, echocardiography and other methods. The method proposed by Vlasov (14) was used for estimation of diagnostic value of chosen RCG-symptoms of the SN disregulation. The RCG sensitivity was within 70-85%, specificity 30-45%, positive and negative predictive values had ranged between 45% and 88.5%.

In healthy persons (68 cases) 3 types of waves (Fig.1) with predominance of the parasympathetic HRV-periodicity and adequate, sufficient reactions to tests were defined (7). The average values of RCG indexes were computed for healthy men and women. The results of statistical and correlation analysis of the RCG-material and comparison of HRV data with clinical symptoms of the diseases have allowed with high degree of validity ($p<0.01$- 0.001) to define RCG complexes, characterized by different forms of the cardiovascular pathology.

Overall, the RCG-data of 15720 patients with coronary artery disease (CAD) (11, 12) were analyzed. Among them 171 patients had a stable angina pectoris, 123 ischemic heart failure, 115 – acute coronary syndrome in the first day and acute myocardial infarction in the following; 4620 patients had an arrhythmia due to CAD, other patients had combined ischemic pathology. As a result of RCG-data analysis it was found that CAD was characterized with HRV symptoms of the SN disregulation, common for all CAD clinical forms and, in addition, these signs

determined CAD forms. To the common symptoms the following were referred: reduction of HRV, decrease in reactions to stimulation tests, decrease of the parasympathetic and sympathetic RCG-indexes, increase of the VLF% spectral share, in accordance with increase of the humoral influences in SN.

In angina pectoris during ischemic episodes, HRV stabilization was registered synchronous in 115 (67%) patients with ST depression, in 111 (65%) patients HRV stabilization complied with gripping pain behind sternum (Fig. 2). It was ascertained, that RCG allows to define fixed and variable ischemic thresholds, angiospastic angina pectoris and angina pectoris without pain. High resolution HRV analysis with RCGm allows computing the ischemic episodes length with high accuracy, dynamics of the disease during management and risk of the acute coronary syndrome and lethal outcome. The RCG-data allow to define the functional class of angina pectoris in Canadian classification.

Ischemic heart failure (123 patients) differed by progressing HRV stabilization, increase of the recovery time after physical exercise and after transitive period in Aop. There was a correlation between these symptoms with functional NYHA class of the heart failure.

The majority of the cardiac arrhythmias (CA) were registered on the RCG and the method also enables to interpret the background of the arrhythmogenic autonomic disregulation in the SN and hemodynamics value of every CA (Fig.3). At diagnosis of CA RCG-study allows to value the frequency of the CA, time of the appearance in diastole, quantify of the ectopic centers, differentiate the ventricular and supraventricular extrasystole, parasystole, bi- and trigeminy, sinus dysfunction and other arrhythmias. By means of RCG method, it is possible to diagnose more than 120 clinical and instrumental variants of the CA, their hemodynamic value and unlimited amount of the variants of the pathological arrhythmogenic background. There were evidences of the RCG possibilities: to define CA during the short RCG-monitoring, also the connection its changes with a primary pathomorphological substrates in the heart - additional conduction ways, active ectopic focuses, SN dysfunction or sick sinus syndrome (SSS). Ectopic rhythms usually appeared under the pathologically changed HRV- SR stabilization, reduction of reactions to stimuli, which indirectly was conditioned by dystrophic changes in the SN with an involvement of receptors and pacemaker cells. Besides, ectopic activity was dependent on the prevalence of either factors of SR regulation. During one of the stimulation tests CA became more frequent, infrequent or disappeared. Also RCG allows to define the prevalent connection of CA with the pathology of the coronary vessels, myocardium and SN dysfunction. If the leading pathology was connected with a coronary artery disease, CA appeared on the background of SR reduction or stabilization, during physical exercise and a reduced SR reaction in Aop. If the ectopic activity was linked with a myocardial failure, the RCG background consisted of the HRV stabilization, increase of transitive time in Aop, a non-attainment of dosed physical load and increase of the recovery time after it, as the myocardial rigidity. The ectopic centers activated mainly at a decrease of the SN activity. Sinus node dysfunction had its own image on the RCGm - there were supracompensative pauses after extrasystole, Wenckebach's or Mobitz's periodics. In these cases CA appeared on the bradycardia background and HRV stabilization, as an expressive oppression of the autonomic influences in SN. Rhythmocardiogram was useful in diagnosis of life-threatening CA with the changes in HRV wave structure. For example, electrical myocardial instability is accompanied by extrasystoles with a supracompensative pause on the sympathetic wave peak, after it HRV wave structure changed, often manifesting by decrease of all waves. The vasovagal syncope (12 patients) appeared on the background of inversely proportional interaction of changes of blood pressure and RR intervals, decrease of HRV and reduction of the rhythm reaction to stimuli.

Q-wave myocardial infarction (QMI) in acute period (48 patients) corresponded to the absence of the HRV waves on the tachycardia background (12). The RCGm in anterior QMI was characterized by increased frequency and amplitude of the humoral waves (σl, VLF%) and increased average value of rhythm reactions to stimuli. In posterior QMI the rigid and unreactive rhythm on the bradycardia background in responses to stimuli was registered. The differences were conditioned by asymmetry and unevenness of intramural autonomic representation in the heart, because the epinephrine receptors dominate in the anterior wall of the left heart ventricle (12).

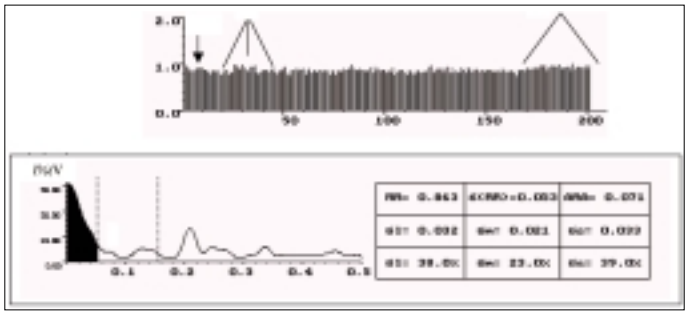

Figure 1. Rhythmocardiogram of the healthy man in rest. Here are three types HRV waves, connecting with parasympathetic(s), sympathetic(m), humoral-metabolic(l) influences on the pacemaker activity in the sinus node of the heart. The parasympathetic HRV waves are prevailing. On the spectrogram here are dark part (0.0033-0.04 Hz) applies to humoral-metabolic, middle part (0.04-0.015 Hz) applies to sympathetic, and part from 0.15 to 0.4 Hz – to parasympathetic influences on the SN. The spectral share of the high frequency range (0.15-0.4 Hz) is the most large in figures (σs%, corresponding to HF%) and in area of spectral density on the spectrogram

HRV- heart rate variability, HF- high frequency, SN- sinus node

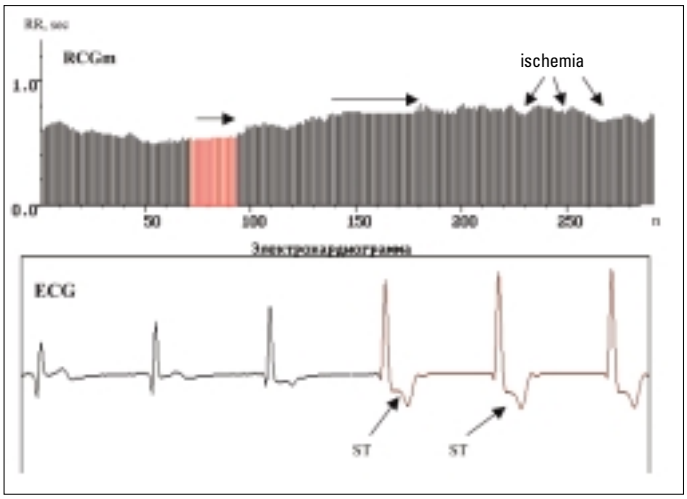

Figure 2. The example of rhythmocardiogram and electrocardiogram of the patient with the coronary artery disease and angina pectoris. The needles on RCGm show ischemic episodes accompanied by ST- depression on ECG

ECG- electrocardiogram, RCGm- rhythmocardiogram

In vascular pathology RCG allows to define arterial hypertension, differentiate the stages of the hypertensive disease (HD), to analyse the background of the autonomic breaches in heart regulation. The HD 2nd stage differs from HD 1st stage by reduction of amplitudes of the HRV waves, decreased reactions in the stimulation tests and slow restoration after stimuli. High- resolution HRV allows to select drug therapy for patients with HD and control its management (15).

Recently, it has been shown that RCG with high-resolution HRV analysis is the sole method for diagnosis of the autonomic cardiac neuropathy (AN) in the setting of diabetes, ischemic cardiopathy, chronic nephropathy, because AN is secondary and polyetiological syndrome. Also we have the some experience of using HRV analysis in cardiac surgery (69 cases). High-resolution HRV analysis usefulness was proved for definition of cardiovascular risk, narcosis monitoring and management of patients after intervention.

Interesting and sometimes even unexpected were the RCG data, which were received in clinical pharmacology (830 cases). Control the pharmacological influence of drugs with registration RCG before and after administration of the drugs allows to value the direction of therapeutic correction, to reveal its forecast effect, and in some cases – by first dose, define the undesirable actions of the drug. The RCG control using the tests at the time of treatment by applying drugs, for example, propafenone, ß-blockers and others, has allowed to reveal its peripheral autonomic effects, as yet not described. Besides, some data on "independent" action drug -complexes under polypharmacy were received (12, 15). This allows to foresee the perspective for inclusion of RCG-studies in complex of the instrumental formalized methods under clinical investigations in the field of pharmacology.

Conclusion

Thereby, RCG is an informative method for diagnosis of the cardiovascular pathology. The high-resolution measurement of HRV and following such computer analysis in time-domain and frequency-domain can be considered highly informative, because of reliable correspondence and comparable RCG-results with data of other studies and clinical symptoms of the diseases. The method of RCG carries the possibility to analyse various peripheral autonomic disregulations of the pacemaker activity in the SN, as it is well known obligate and the most early manifestation of cardiovascular pathology under a number diseases, and always sinus node disregulations are the background of clinical symptoms. Heart rate variability analysis capable also to serve by control study for choice and evaluation of the drug efficiency, for management patients under complex pharmacotherapy of the cardiovascular pathology, for study autonomic effects of the some drugs.

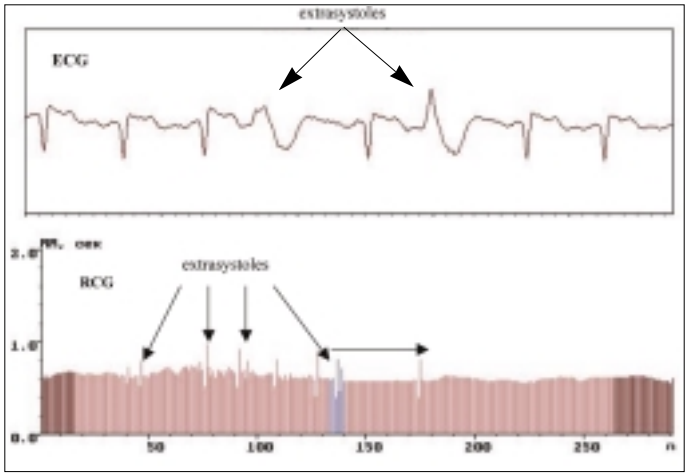

Figure 3. Electrocardiogram and rhythmocardiograms of the patient with coronary artery disease, angina pectoris and extrasystoles. The reduced HRV is seen. After paired extrasystoles the part of RCGm with stabilization (shown by horizontal needle) is observed during ischemic episode with typical gripping pain in the chest

HRV- heart rate variability, RCGm- rhythmocardiogram

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